Products of Peracid Oxidation of Organothiophosphorus Compounds

Eugene M. Bellet[1] and John E. Casida*

Organothiophosphorus compounds react with equimolar *m*-chloroperoxybenzoic acid in dichloromethane or chloroform, yielding simple to complex mixtures depending on the moieties bonded to the phosphorus and the type of phosphorus-sulfur bond. Phosphates are not degraded. Phosphoramidothiolates are probably attacked at the thiolate sulfur. Several phosphoro- and phosphonothionates and one phosphoramidothionate form variable amounts of the corresponding oxon, elemental sulfur, and cleavage products. One trialkylphosphine sulfide gives only the oxon and elemental sulfur. Phosphoro- and phosphonodithioates yield small amounts of the oxon and elemental sulfur, with larger amounts of nonphosphorus containing disulfides and the phosphorus acids resulting on cleavage. An additional product from the *O*-alkyl S-substituted phenyl phosphonodithioates is the corresponding substituted phenyl phosphinyl disulfide. The peracid oxidation products are often identical to those formed by microsomal oxidase metabolism and by photodecomposition. This procedure provides a chemical means of generating possible oxidative metabolites and photoproducts from thiophosphorus insecticide chemicals.

Thionophosphorus insecticide chemicals undergo metabolic and photochemical oxidation reactions to form the corresponding oxygen analogs (oxons) and one or more phosphorus acid cleavage products (Menzie, 1969). A simple chemical oxidation system that degrades thionophosphorus compounds to the same products formed by metabolism and photodecomposition would be useful in investigations on the biochemical toxicology and environmental fate of these pesticides.

Enzymatic and model oxidation systems in aqueous media are particularly useful in gaining an understanding of the metabolism of thionophosphorus compounds. However, these systems are usually not appropriate to obtain large amounts of the reaction products, in part because of the low water solubility of the substrates. Oxidation of thionophosphorus compounds by microsomal mixed function oxidases yields not only the oxons but also variable amounts of cleavage products. Atmospheric molecular oxygen is the source of oxygen incorporated into the oxons of fonfos and parathion but not in the thiophosphorus acid cleavage products, which ultimately arise by hydrolysis (McBain *et al.*, 1971a; Ptashne *et al.*, 1971). Peroxidase and the ethylenediaminetetraacetic acid–ferrous iron complex also catalyze both oxon formation and cleavage of parathion (Knaak *et al.*, 1962). These findings are interpreted to indicate that enzymatic desulfuration and cleavage reactions involve a common oxidized intermediate(s) formed by attack of oxygen on the thionophosphorus group (Knaak *et al.*, 1962; McBain *et al.*, 1971a,b; Ptashne *et al.*, 1971).

Peracids in organic solvents provide many of the desired features for a model chemical oxidation system. *m*-Chloroperoxybenzoic acid (MCPBA) in dichloromethane carries out the following conversions: (−)-menthyl methylphenylphosphinothioate to its oxon diastereomers and colloidal sulfur in almost quantitative yields (Herriott, 1971); fonfos to its oxon, *O*-ethyl ethylphosphonothioic and *O*-ethyl ethylphosphonic acids, thiophenol which is isolated as a disulfide, a small amount of elemental sulfur, and to a monooxygenated derivative (McBain *et al.*, 1971a,b) which is the corresponding phosphinyl disulfide (Wustner *et al.*, 1972); an *N*-(dimethoxyphosphinothioyl)carbamate ester to its oxon, sulfur, and the *N*-(dimethoxyphosphinylthio)carbamate ester formed by oxidation and rearrangement (Fahmy and Fukuto, 1972). Peroxytrifluoroacetic acid (PTFAA) in dichloromethane carries out the following conversions: parathion to its oxon, which is not further degraded, and to *O,O*-diethyl phosphorothioic acid and tepp; malathion to *O,O*-dimethyl phosphorothioic acid without oxon formation (Ptashne and Neal, 1972). Thus, on the attack of oxygen from a peracid at the thionophosphorus group, the ratio of desulfuration to cleavage varies with the thionophosphorus compound from essentially quantitative desulfuration and no cleavage to cleavage occurring in amounts equal to or much greater than desulfuration.

It appears likely that a better understanding of the MCPBA oxidations of a variety of organothiophosphorus compounds will provide further insight into the mechanisms by which they undergo metabolism and photodecomposition. It will also provide a means for preparation of possible metabolites and photoalteration products of thionophosphorus compounds not as readily accessible by other means.

MATERIALS AND METHODS

Chemicals. The abbreviations used for various substituents are as follows: Me = methyl, Et = ethyl, Pr = *n*-propyl, *i*-Pr = isopropyl, *t*-Bu = tertiary-butyl, Bz = benzyl, ϕ = phenyl, N = nitrogen, P = phosphorus, and S = sulfur. The common and chemical names of some of the insecticide chemicals investigated are given in Table I.

Commercial organophosphorus insecticides were obtained from the manufacturers and purified by chromatography when necessary. Other phosphorus compounds used as reactants or as standards for comparison with the oxidation products were prepared by modifications of published procedures. The general type syntheses are given by Kosolapoff (1950) and Schrader (1963). The structure of each compound was verified by appropriate analytical techniques. Three examples of these syntheses are given below.

S-Phenyl parathion, $(EtO)_2P(S)S\phi NO_2$-4, was obtained in 65% yield by dropwise addition of sodium methoxide (30 mmol) in methanol (50 ml) to a stirred solution of $(EtO)_2P(S)H$ (20 mmol) and $NCS\phi NO_2$-4 (20 mmol) in dry benzene (100 ml) at 25°, followed by stirring at 25° for 1 hr and at 50° for 30 min. The crystalline product was obtained by washing the benzene with water, drying, solvent evaporation, and purification by thin-layer chromatography (tlc) (solvent system A, described below).

O-Ethyl *S*-benzyl phosphoramidothioate, $EtO(NH_2)P(O)SBz$, was prepared according to Kayser *et al.* (1960) in 57% yield by saponifying $(EtO)_2P(S)NH_2$ (0.3 mmol) to its barium salt which was then reacted with BzCl (0.3

Division of Entomology and Parasitology, University of California, Berkeley, California 94720.

[1] Present address: Office of Pesticide Programs, Environmental Protection Agency, Washington, D. C. 20460.

Table I. Common and Chemical Names for Some of the Insecticides Studied

Common name	Chemical name
Diazinon	*O,O*-Diethyl *O*-(2-isopropyl-4-methyl-6-pyrimidinyl) phosphorothioate
EPN	*O*-Ethyl *O*-(*p*-nitrophenyl) phenylphosphonothioate
Fonfos	*O*-Ethyl *S*-phenyl ethylphosphonodithioate
Malathion	*O,O*-Dimethyl *S*-(1,2-dicarbethoxyethyl) phosphorodithioate
Monitor	*O,S*-Dimethyl phosphoramidothioate
Paraoxon	*O,O*-Diethyl *O*-(*p*-nitrophenyl) phosphate
Parathion	*O,O*-Diethyl *O*-(*p*-nitrophenyl) phosphorothioate
S-Phenyl parathion	*O,O*-Diethyl *S*-(*p*-nitrophenyl) phosphorodithioate
Phosmet	*O,O*-Dimethyl *S*-phthalimidomethyl phosphorodithioate
Phoxim	*O,O*-Diethyl phenylglyoxylonitrile oxime phosphorothioate
Tepp	*O,O,O,O*-Tetraethyl pyrophosphate

mmol) in acetone (50 ml) by holding at 25° for 2 hr and then refluxing for 2 hr. Filtration, removal of solvent, and preparative tlc (solvent system A) provided the desired crystalline material.

The sulfoxide analog of fonfos, $Et(EtO)P(S)S(O)\phi$, was prepared by coupling two known compounds, $Et(EtO)P(S)H$ (Michalski and Tulimowski, 1962) and $\phi S(O)Cl$ (Douglass *et al.*, 1961). A solution of 30 mmol of each of $Et(EtO)P(S)H$ and anhydrous pyridine in 30 ml of anhydrous ether at 0° was treated dropwise and under nitrogen with 30 mmol of $\phi S(O)Cl$. After stirring magnetically for 1 hr at 0°, the reaction mixture was filtered and the solvent removed under a gentle stream of dry nitrogen, giving an essentially quantitative yield of the pure sulfoxide (structure verified by pmr, ir, and ms). *Anal.* Calcd for $C_{10}H_{15}O_2PS_2$: C, 45.80; H, 5.76; P, 11.82; S, 24.40. Found: C, 45.82; H, 5.87; P, 11.66; S, 24.44. This sulfoxide undergoes decomposition on preparative tlc in solvent system A.

Chromatography and Analytical Procedures. Tlc was carried out for analytical purposes on 0.25 mm precoated silica gel 60 plates (EM Laboratories Inc., Elmsford, N. Y.) and for preparative isolations on 2-mm precoated silica gel GF plates (Analtech, Inc., Newark, Del.). The solvent systems used were: A = chloroform–dichloromethane–*n*-propanol–ethyl acetate (10:10:1:1) mixture; B = chloroform–hexane (2:1) mixture; C = carbon tetrachloride–ether (4:1) mixture; D = chloroform–dichloromethane–*n*-propanol–ethyl acetate (5:5:1:1) mixture. Chromogenic reagents used in detecting products and monitoring the reactions by tlc were: 2,6-dibromo-*N*-chloro-*p*-benzoquinone imine (1% w/v in methanol), which gives yellow to orange spots for elemental sulfur and most S-containing compounds (Menn *et al.*, 1957); ninhydrin (1% w/v in pyridine), which gives purple spots for all of the N-containing compounds studied after heating at 110° for 10 min (Dorough and Casida, 1964); 4-(*p*-nitrobenzyl)pyridine (1% w/v in acetone) then heating at 110° for 15 min, followed by a spray of tetraethylenepentamine (1% w/v in acetone) which gives blue spots on a white background for all P-containing compounds except for red with diazinon (Watts, 1965) and the oxon of diazinon but there are no visible spots appearing with $EtC(CH_2O)_3P(S)$, $EtC(CH_2O)_3P(O)$, $Et_3P(S)$, and $Et_3P(O)$. Florisil (80–100 mesh, Floridin Co., Tallahassee, Fla.) columns of 10–20 cm length and 4.5 cm i.d. were used for cleanup of reactants and reaction mixtures, monitoring the eluted fractions with tlc to locate the desired products.

Proton magnetic resonance (pmr) spectra were obtained on a Perkin-Elmer R12B instrument, infrared (ir) spectra on a Perkin-Elmer Model 457 grating ir spectrophotometer, and electron impact mass spectra (ms) on a CEC 21103-C mass spectrometer. Elemental analyses and high resolution ms studies were performed by the Department of Chemistry, University of California, Berkeley.

Generalized Oxidation Procedure. To a magnetically stirred solution of the organophosphorus compound (10–20 mmol) in either chloroform or dichloromethane (10–20 ml) at room temperature was added, slowly and in portions, a suspension of an equimolar amount of MCPBA in 10–20 ml of the same solvent. In most cases any reaction that occurs is immediate and exothermic, hence a reflux condenser is necessary. The reactants dissolve completely within a few minutes due to the exothermic nature of the reaction and the products are soluble materials with the exception of any elemental sulfur liberated; however, upon completion of the reaction and cooling to ambient conditions, a copious precipitate consisting mostly of *m*-chlorobenzoic acid is obtained. The same products are observed whether the reactions are run in chloroform or dichloromethane and with reaction times of 2 to 24 hr. The products were analyzed initially by direct tlc of a 10-μl aliquot of the reaction mixture. For ease of product isolation, the *m*-chlorobenzoic acid was removed by filtration with tlc analysis of the crystals to ascertain that no desired products were being discarded. The solvent was then evaporated using a stream of dry nitrogen and the soluble products were resolved by various types of chromatography, always involving tlc at some stage and detection of P-, S-, and N-containing materials with the appropriate chromogenic reagents. The emphasis was placed on identification of the neutral products rather than on quantitation of product yield; a portion of each product was lost during purification. Phosphorus acid cleavage products remaining at the origin on tlc are detected in many of the reaction mixtures. No attempt was made to identify the various phosphorus acids that form from the variety of compounds investigated.

The sulfur moiety liberated on oxidation of thionophosphorus compounds is elemental sulfur [mp 114–116°; ms identical to authentic sample; tlc R_f value (0.62) identical to the standard on development with hexane; the ether-insoluble material from the reaction mixture gives a positive sodium fusion test for sulfur (Schneider, 1964)]. This elemental sulfur is isolated, depending on the thionophosphorus compound, by filtering the reaction mixture shortly after MCPBA addition or as a high R_f product in the course of preparative tlc isolations. The fact that elemental sulfur is isolated by chromatography in certain cases where it does not immediately precipitate during the reaction suggests either that it is soluble in the mixture containing other reaction products or that it is liberated on decomposition of various oxidation products during workup.

RESULTS

The products obtained on MCPBA oxidation of various phosphorus compounds are considered on the basis of the number of sulfur atoms and their position in the molecule.

Compounds Lacking Sulfur. *Phosphates.* Paraoxon, $(EtO)_2P(O)O\phi NO_2$-4, and $(PrO)_2P(O)O\phi NO_2$-4 do not react with MCPBA under the conditions used in this study based on tlc analysis of the reaction mixtures.

Compounds Containing Only Thiolate Sulfur. *Phosphoramidothiolates* [$NH_2(RO)P(O)SR'$]. Monitor (R = R′

= Me) and two analogs prepared for this study (R = Et, R′ = Pr; R = Et, R′ = Bz) react immediately and exothermically with an equimolar amount of MCPBA. The following products from monitor listed in the order of increasing R_f values were isolated by preparative tlc (solvent system A): a trace amount of monitor; a minor unknown containing S but no P or N; $MeSS(O_2)Me$ (isolated by rechromatography on tlc first with solvent system A and then with solvent system B) (for independent synthesis of this compound, see Boldyrev *et al.*, 1966) identified by ir, pmr, ms, and high-resolution ms. *Anal.* Calcd for $C_2H_6O_2S_2$: C, 19.05; H, 4.79; S, 50.76. Found: C, 19.08; H, 4.64; S, 50.62; not any N or P. Up to three molar equivalents of MCPBA react with monitor under these conditions, so some of the initial oxidation and cleavage products must be further oxidized using more of the peracid; the yield of $MeSS(O_2)Me$ increases progressively on addition of MCPBA up to three molar equivalents. Each of the two monitor analogs yields a non-P-containing material at high tlc R_f value, suggesting that they form derivatives corresponding to $MeSS(O_2)Me$ as produced on oxidation of monitor. This product from the benzyl analog is a crystalline material (mp 118–119°) tentatively identified as $BzSS(O_2)Bz$; the ir spectrum (KBr) contained sharp bands at 1115 and 1310 cm^{-1} as expected for the SO_2 group (Boldyrev *et al.*, 1966); mass spectrum, 70 eV, major peaks at 214, 182, 123, and 91, with small peaks at 278 and 246; pmr consistent with the proposed structure. Minor products which chromatograph in solvent system A just below the starting material, increase in amount as the MCPBA level is increased from 0.5 to 3 molar equivalents and contain P, N, and S were detected as follows: none with $NH_2(MeO)P(O)SMe$; one or two with $NH_2(EtO)P(O)SBz$; and two with NHS(EtO)P(O)SPr. While these latter products, when present, may be the sulfoxides and sulfones of the parent molecules, they decompose on attempted isolation.

Compounds Containing Only Thionate Sulfur. *Phosphorothionates.* Diazinon, parathion $[(EtO)_2P(S)O\phi NO_2\text{-}4]$, and $EtC(CH_2O)_3P(S)$ are converted on reaction with equimolar amounts of MCPBA to the corresponding oxons, the yields of the oxons, and of elemental sulfur which precipitates immediately, increasing in the indicated order. A small amount of $HO\phi NO_2\text{-}4$ (tlc cochromatography with authentic material in solvent system A) is obtained from parathion and a relatively large amount of 2-isopropyl-4-methyl-6-pyrimidinol (appropriate ir, pmr, and ms) is produced from diazinon. The phosphorus acid cleavage products are minor with parathion and $EtC(CH_2O)_3P(S)$ but major with diazinon.

Phosphonothionates [*R*(*R′O*)*P*(*S*)*OR″*]. Eight phosphonothionates, including EPN (R = ϕ, R′ = Et, R″ = $\phi NO_2\text{-}4$), and seven others prepared for this study (R = ϕ, R′ = R″ = Pr; R = Me, R′ = Pr, R″ = ϕMe-4; R = Et, R′ = *i*-Pr, R″ = ϕMe-4; R = R′ = Et where R″ is any one of Et, ϕMe-4, ϕ-*t*-Bu-4 or $\phi Me_2\text{-}3,5$) react immediately and exothermically with equimolar amounts of MCPBA to give large quantities of elemental sulfur which precipitates immediately and of the corresponding oxons which were isolated by tlc (solvent system A) (tlc comparison with authentic compounds obtained by independent synthesis). The phenol cleavage product is detected (tlc cochromatography, solvent system A) in small amounts with each O-substituted-phenyl compound and there are also small amounts of the comparable phosphonothioic acids in each case.

Phosphoramidothionate. $NH_2(MeO)P(S)O\phi Cl_3\text{-}2,4,5$ reacts exothermically with MCPBA without precipitation of a significant amount of elemental sulfur. Tlc isolations in solvent system A followed by rechromatography in solvent system C and then A gave the following products: small amounts of elemental sulfur and the oxon (appropriate ir, pmr, and ms); a large amount of $HO\phi Cl_3\text{-}2,4,5$ [pmr identical to authentic standard; tlc cochromatography with authentic standard in solvent system A and in hexane–ether (4:1) mixture]; and large amounts of phosphorus acid cleavage products.

Phosphine Sulfide. $Et_3P(S)$ reacts immediately and exothermically with an equimolar amount of MCPBA to give essentially quantitative yields of elemental sulfur which precipitates and $Et_3P(O)$ isolated by tlc with solvent system A (ir, pmr, and tlc comparisons with authentic standard).

Compounds Containing both Thionate and Thiolate Sulfurs. *Phosphorodithioates* [$(RO)_2P(S)SR'$]. Treatment of each of malathion, phosmet, and *S*-phenyl parathion with equimolar amounts of MCPBA does not result in significant warming of the mixture nor the precipitation of sulfur with the last two compounds, but the reaction with malathion is immediate and exothermic although no sulfur is precipitated. A very small amount of elemental sulfur is isolated, however, in each case during the normal work-up procedures for the oxidation products. The oxidation products were isolated by chromatography on Florisil with ether (malathion) or by preparative tlc (solvent system A) (phosmet and *S*-phenyl parathion), yielding the following materials: small amounts of the corresponding oxons from malathion and phosmet (pmr, ir, and tlc comparisons with authentic standards) and from *S*-phenyl parathion (appropriate ir and ms); large amounts of the corresponding disulfide in each case (identity based on ir, pmr, ms, and high-resolution ms for the products from malathion and phosmet; identity based on ms, pmr, and tlc comparisons in solvent system A with authentic $4\text{-}NO_2\phi SS\phi NO_2\text{-}4$ for the product from *S*-phenyl parathion); and large amounts of various P-containing acids.

The disulfides can be misinterpreted as trisulfides when their identification is based on ms since the disulfides appear to be converted during ms analysis to a multitude of ion fragments, some of which recombine to form various linear arrays of sulfur, among them being the trisulfide. Thus, the disulfide from oxidation of phosmet and authentic $4\text{-}NO_2\phi SS\phi NO_2\text{-}4$ each gives high-resolution ms fragments appropriate for both the di- and trisulfides.

Phosphonodithioates [$R(R'O)P(S)S\phi X$]. The compounds examined were fonfos (R = R′ = Et, X = H) and 15 analogs (R = R′ = Et where X is any one of Cl-4, Me-3, Me-4, $Me_2\text{-}2,5$, OMe-4, *t*-Bu-4, $NO_2\text{-}4$; R = Me and R′ = Et where X is either Me-2 or Me-4; R = Et, R′ = Me where X is either Me-4 or *t*-Bu-4; R = Et, R′ = *i*-Pr where X is either Me-4 or *t*-Bu-4; R = Pr, R′ = Et, X = Me-4; R = Me, R′ = Pr, X = Me-4). These chemicals were provided by Stauffer Chemical Co., Richmond, Calif., with the exception of $Et(EtO)P(S)S\phi NO_2\text{-}4$, which was synthesized by a procedure similar to that described above for the corresponding phosphorodithioate, *S*-phenyl parathion.

Each of the 16 compounds reacts vigorously with an equimolar amount of MCPBA precipitating a large amount of elemental sulfur. The individual products from the reactions of $Et(EtO)P(S)S\phi$, $Et(EtO)P(S)S\phi Cl\text{-}4$, and $Me(PrO)P(S)S\phi Me\text{-}4$ were isolated by preparative tlc using solvent system A and then rechromatography of individual bands in solvent system D. The major product (20–30% yield) in each case is the corresponding phosphinyl disulfide identified by ir, pmr, and ms. The phosphinyl disulfides seem to undergo decomposition on silica gel and on storage of the neat compounds. *Anal.* Calcd for $Me(PrO)P(O)SS\phi Me\text{-}4$ or $C_{11}H_{17}O_2PS_2$: C, 47.82; H, 6.20; P, 11.22; S, 23.17. Found: C, 47.66; H, 5.96; P, 11.28; S, 23.14. The ^{31}P-nmr spectra in the $Me(PrO)P(S)S\phi Me\text{-}4$ series give positive shifts upfield (ppm) from phosphorus oxide of 47 for the phosphinyl disulfide, 15 for the phosphonodithioate, and 61 for the oxon, a similar relationship

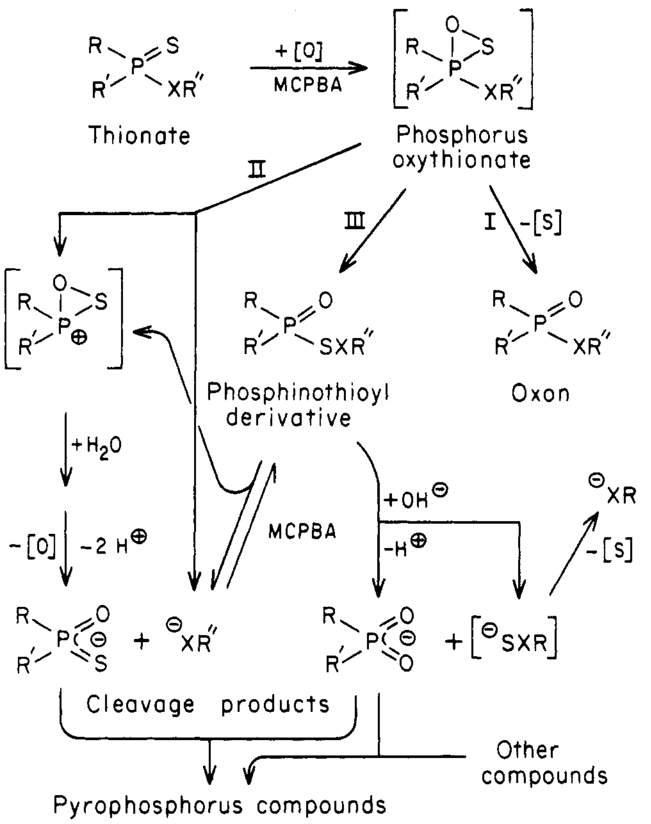


Figure 1. Proposed mechanisms leading to formation of various types of products on *m*-chloroperoxybenzoic acid (MCPBA) oxidation of thionophosphorus compounds. R, R′, and R″ in this investigation are the same or different alkyl, aryl, aralkyl, pyrimidinyl, alkoxy, or amino groups. X is N, O, S or is lacking. The phosphinothioyl derivatives are sufficiently stable for isolation only in some of the compounds where X is N or S.

to that observed in the fonfos series (McBain *et al.*, 1971b). Et(EtO)P(O)SSϕ is also formed (tlc cochromatography) on reacting equimolar amounts of Et(EtO)-P(O)SH and HSϕ in the presence of one molar equivalent of MCPBA. The oxons are poorly resolved from the phosphinyl disulfides in solvent system A but in solvent system D the phosphinyl disulfides chromatograph distinctly above the oxons. The oxons [Et(EtO)P(O)Sϕ, Et-(EtO)P(O)SϕCl-4, and Me(PrO)P(O)SϕMe-4] are present in about one-half the amounts of the corresponding phosphinyl disulfides; the oxons are identified in each case by ir, ms, pmr, and tlc comparisons (solvent systems A and D) with authentic compounds from independent synthesis. Other products are a small amount of 4-ClϕSSϕCl-4 (appropriate ms, nmr, and ir) from Et(EtO)P(S)SϕCl-4 and large amounts of phosphorus acids from each of the phosphonodithioates. The products from oxidation of the other phosphonodithioates appear to be analogous to those formed from the three compounds examined in more detail based on comparable tlc patterns in solvent systems A and D and chromogenic responses of the products.

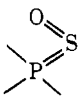
The sulfoxide analog of fonfos [Et(EtO)P(S)S(O)ϕ] was not found among the MCPBA oxidation products of fonfos; the authentic sulfoxide obtained by independent synthesis (described above) differs in its ir and mass spectra and in its chromatographic properties in tlc solvent system A and in chloroform-ethyl acetate (1:1) mixture (McBain *et al.*, 1971a) from those of any of the MCPBA oxidation products of fonfos.

The ratio of products formed on MCPBA oxidation of fonfos (and of EPN) was not altered when the oxidations were carried out in dichloromethane alone or in dichloromethane containing up to 3 parts by weight of trifluoroacetic acid relative to the amount of fonfos (or EPN).

DISCUSSION

Figure 1 summarizes the findings on MCPBA oxidation of thionophosphorus compounds by showing the proposed early intermediates and some of the terminal products. This scheme incorporates the findings and speculations of others (Fahmy and Fukuto, 1972; Herriott, 1971; McBain *et al.*, 1971a,b; Ptashne and Neal, 1972; Wustner *et al.*, 1972) along with our results.

The reactions are initiated by addition of oxygen to the sulfur or to the P=S moiety, giving one or more unstable intermediates referred to collectively for convenience as the "phosphorus oxythionate." Although this is shown as a cyclic P-S-O intermediate, it can also be other resonance and tautomeric forms (for example, **A** and **B**), a cyclic transition state, or five-membered cyclic adduct (March, 1968) such as **C** formed from the peracid and the thionophosphorus moiety, or a diradical such as **D.** None of the investigations to date adequately define the structure of the phosphorus oxythionate, whether one or more forms are involved, and whether the various reactions of this intermediate(s) occur as concerted or successive processes.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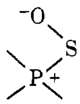
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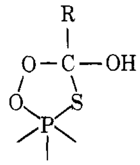
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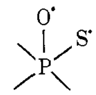
D

The unstable phosphorus oxythionate intermediate, shown in Figure 1 as a cyclic resonance form of **A**, **B**, and **D** for convenience, can rearrange and decompose by any one of three possible mechanisms, yielding products generated by pathways I, II, and III which are considered in sequence. Although the intermediates are shown as ionic materials in Figure 1, a comparable sequence of reactions with radical intermediates is appropriate if the oxidation is initiated by formation of a diradical phosphorus oxythionate similar to **D.**

Pathway I. Loss of sulfur yields the oxon. Peracid oxidation of (−)-menthyl methylphenylphosphinothioate to its oxon diastereomers occurs with a high degree of retention of configuration using MCPBA but with predominant inversion using PTFAA, suggesting that the form of the phosphorus oxythionate decomposing to the oxon varies with the acidity or polarity of the reaction mixture. Use of this phosphinothioate (or another optically active one with less easily oxidized alkyl groups) in microsomal oxidation systems and determination of the optical activity of the oxon formed would help to relate the mechanism of enzymatic oxidation to either the MCPBA or PTFAA systems.

Pathway II. Cleavage products are formed either by scission of the P-X bond (when X is N, O, or S) and then nucleophilic attack by water on the P of the positively charged cyclic intermediate (Figure 1) or by direct attack of water on the phosphorus oxythionate, in either case yielding the phosphorothioic acids. The oxygen retained in the phosphorothioic acid may be that from water rather than from the peracid if the mechanism of the oxidation is similar to that occurring with microsomal oxidation systems. The cleavage products are potential sources of the phosphinothioyl derivatives, of the non-P-containing disulfides when X is S, and of various pyrophosphorus compounds by reaction of the phosphorothiolate fragment with other reactive species in the peracid-containing mixture.

Pathway III. Intramolecular rearrangement to the phosphinothioyl derivative is observed with certain compounds in which X is N or S. In other cases this derivative may not be sufficiently stable for detection or isolation.

The present study shows that *S*-phosphinothioyl derivatives may also form intermolecularly by MCPBA oxidation of the appropriate thioic acid and thiol. Several products can be generated on degradation of the *N*- or *S*-phosphinothioyl derivatives, with possible catalysis by water or appropriate phosphorus acids; these include the corresponding phosphorothioic and phosphoric acids, pyrophosphorus compounds, sulfur, and non-P-containing disulfides (Fahmy and Fukuto, 1972; McBain *et al.*, 1971b). While it is possible that cleavage of the phosphinyl disulfides could yield R′SS as well as R′S fragments capable of forming tri- and tetrasulfides on combination with other fragments or molecules likely to be present in the mixture, the experimental results do not require this interpretation. Pathway III may be involved in the photodecomposition of some thionophosphorus insecticides. Phoxim undergoes photosensitized isomerization and also forms tepp and *O,O,O,O*-tetraethyl monothionopyrophosphate (Dräger, 1971). This could result from photooxidation, leading to the corresponding phosphorus oxythionate and then combination of its S with the oxime N. Other phosphorothionates also undergo photosensitized isomerization (Menzie, 1969) in which a phosphorus oxythionate might be the important intermediate.

The products ultimately formed on monooxygenation of thionophosphorus compounds are dependent on the nature of the attacking oxygen species, the medium or reaction environment, and the strengths of each bond in the P–S–O moiety of the various possible phosphorus oxythionate intermediates, which in turn are influenced by the other substituents bonded to the phosphorus (*i.e.*, R,R′,XR″ in Figure 1). The following generalizations are appropriate for the compounds examined but must be considered on this restricted basis. Pathway I is the predominant or only pathway with phosphine sulfides and phosphinothionates. Pathways I and II are involved in varying degrees in oxidation of phosphonothionates and phosphorothionates, with pathway II being more important with some phosphorothionates than with phosphonothionates. All three pathways come into play with *S*-phenyl phosphonodithioates. Pathway III is involved with some phosphoramidothionates such as a *N*-(dimethoxyphosphinothioyl)carbamate ester but not others, while this pathway is not involved with the phosphorodithioates in the present investigation.

The products of MCPBA oxidation ultimately isolated are dependent not only on the mechanism of rearrangement of the phosphorus oxythionate but also on the procedures used for their isolation and characterization with the attendant structural alterations and decomposition involved. Thus, several intermediates are too reactive to be demonstrated directly with the techniques that have been employed, and many of the early products may undergo further oxidation, hydrolysis, or varying types of additions or recombinations. While this feature of the reactions is inconvenient in mechanistic considerations, it is useful in preparing many derivatives for comparison with metabolites and photoproducts of the thionophosphorus compounds.

Phosphates do not react with MCPBA but phosphoramidothiolates are readily oxidized in the cases examined. The rapid cleavage of monitor and related compounds and the ultimate formation of the appropriate S-esters of substituted sulfonic acids might be initiated by formation of the phosphoramidothiolate sulfoxides followed by cleavage, recombination, and further oxidation in an undetermined sequence. The sulfoxide of fonfos is not a product of fonfos oxidation with MCPBA, suggesting either that the thionate sulfur is much more easily oxidized than the thiolate sulfur or that the sulfoxide is not sufficiently stable to be isolated from the reaction mixture.

This system may be useful as an easy chemical method to obtain some of the possible metabolites and photoproducts of S-containing organophosphorus insecticide chemicals and in gaining an understanding of the chemistry of microsomal oxidations and photodegradation of the thionophosphorus grouping.

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