can undergo conjugation.

LITERATURE CITED

Barnett, J. R.; Dorough, H. W. *J. Agric. Food Chem.* **1974**, *22*, 612.
Bevenue, A.; Hylin, J. W.; Kawano, Y.; Kelley, T. W. *Pestic. Monit. J.* **1972**, *6*, 56.
Blus, L. J.; Neely, B. S.; Lamont, T. G.; Mulhern, B. *Pestic. Monit. J.* **1977**, *11*, 41.
Bugg, J. C., Jr.; Higgins, J. E.; Robertson, E. A., Jr. *Pestic. Monit. J.* **1967**, *1*, 9.
Burns, B. G.; Peach, M. E.; Stiles, D. A. *Pestic. Monit. J.* **1975**, *9*, 35.
Brimfield, A. A.; Street, J. C.; Futrell, J.; Chatfield, D. A. *Pestic. Biochem. Physiol.* **1978**, *9*, 84.
Brooks, G. T. "Chlorinated Insecticides", Vol. I and II; CRC Press: Cleveland, OH, 1974.
Casper, V. L. *Pestic. Monit. J.* **1967**, *1*, 13.
Feroz, M.; Khan, M. A. Q. *J. Agric. Food Chem.* **1979a**, *27*, 95.
Feroz, M.; Khan, M. A. Q. *J. Agric. Food Chem.* **1979b**, *27*, 108.
Feroz, M.; Khan, M. A. Q. *Arch. Environ. Contam. Toxicol.* **1979c**, *8*, 519.
Gackstatter, J. H. Ph.D. Thesis, University of North Carolina at Chapel Hill, Chapel Hill, NC, 1966.
Glooschenko, V.; Lott, J. N. A. *Can. J. Bot.* **1977**, *55*, 2866.
Godsil, P. J.; Johnson, W. C. *Pestic. Monit. J.* **1968**, *1*, 21.
Hamelink, J. L. *Ann. Rev. Pharmacol. Toxicol.* **1977**, *17*, 167.
Johnson, D. W. In "Environmental Pollution by Pesticides", Edwards, C. A., Ed.; Plenum Press: New York, 1973; Chapter 5.
Kenaga, E. E. In "Environmental Toxicology of Pesticides"; Matsumura, F., Boush, G. M., Misato, T., Ed.; Academic Press: New York, 1972.
Kerr, S. R.; Vass, W. P. In "Environmental Pollution by Pesticides", Edwards, C. A., Ed.; Plenum Press: New York, 1973; Chapter 4.
Law, M. L.; Goerlitz, D. F. *Pestic. Monit. J.* **1974**, *8*, 33.
Lawrence, J. H.; Barrow, R. P.; Chen, J. Y.; Lombardo, P.; Benson, W. R. *J. Assoc. Off. Anal. Chem.* **1970**, *53*, 261.
Lichtenberg, J. J.; Eichelberger, J. W.; Dressman, R. C.; Longbottom, J. E. *Pestic. Monit. J.* **1970**, *4*, 71.
Macek, K. J. In "The Biological Impact of Pesticides in the Environment", Gillete, J. W., Ed.; Oregon State University Press, 1971; pp 17–21.
Mattraw, H. C., Jr. *Pestic. Monit. J.* **1975**, *9*, 106.
Metcalf, R. L. In "Pesticides in Aquatic Environments", Khan, M. A. Q., Ed.; Plenum Press: New York, 1977; pp 127–144.
Miles, J. R. W.; Harris, C. R. *Pestic. Monit. J.* **1973**, *6*, 363.
Moore, R.; Toro, E.; Stanton, M.; Khan, M. A. Q. *Arch. Environ. Contam. Toxicol.* **1977**, *6*, 411.
Podowski, A. A.; Banerjee, B. C.; Feroz, M.; Dudek, M. A.; Willey, R. L.; Khan, M. A. Q. *Arch. Environ. Contam. Toxicol.* **1979**, *8*, 509.
Polen, P. B.; Hester, M.; Benziger, J. *Bull. Environ. Contam. Toxicol.* **1971**, *5*, 521.
Poonawalla, N. H.; Korte, F. *Life Sci.* **1964**, *3*, 1497.
Poonawalla, N. H.; Korte, F. *J. Agric. Food Chem.* **1971**, *19*, 467.
Saha, J. G.; Lee, Y. W. *Bull. Environ. Contam. Toxicol.* **1969**, *4*, 285.
Sanborn, J. R.; Metcalf, R. L.; Bruce, W. N.; Lu, P. Y. *Environ. Entomol.* **1976**, *5*, 533.
Schwemmer, B.; Cochrane, W. P.; Polen, P. B. *Science* **1970**, *169*, 1087.
Street, J. C.; Blau, S. E. *J. Agric. Food Chem.* **1972**, *20*, 395.
Tanita, R.; Johnson, J. M.; Chun, M.; Maciolek, J. *Pestic. Monit. J.* **1976**, *10*, 24.
Tashiro, S.; Matsumura, F. *J. Agric. Food Chem.* **1977**, *25*, 872.
Velsicol Chemical Corporation, "Methods of Analysis of Residues from Technical Chlordane", 1972.

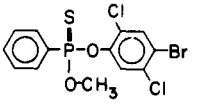
Received for review April 7, 1978. Accepted June 20, 1979. The study was supported by a USPHS Grant No. ES-01479 from the National Institute of Environmental Health Sciences. Part of the paper was presented at the 174th National Meeting of the American Chemical Society, Division of Pesticide Chemistry (Paper No. 30), Chicago, IL, Aug 28, 1977.

Delayed Neurotoxicity of *O*-Alkyl *O*-Aryl Phenylphosphonothioate Analogues Related to Leptophos Administered Orally to the Hen

J. Gary Hollingshaus, Sameer Abu-El-Haj, and T. Roy Fukuto*

Analogues of leptophos [*O*-(4-bromo-2,5-dichlorophenyl) *O*-methyl phenylphosphonothioate] were examined for acute toxicity to mice and houseflies and for delayed neurotoxic activity in adult hens following adminstration of a single oral dose. Development of ataxia after recovery from acute poisoning was the criterion for delayed neurotoxic acitivity. All mono- and dichlorophenyl analogues were delayed neurotoxic, the 2,5-dichlorophenyl analogue being the most potent delayed neurotoxic compound tested. Substitution for the methyl by an ethyl group abolished delayed neurotoxic activity in both leptophos and the 2,5-dichlorophenyl analogue at doses of 1000 mg/kg. The propyl and butyl analogues of the latter were also nondelayed neurotoxic at 500 and 333 mg/kg, respectively. Substitution of methyl for ethyl in EPN [*O*-*p*-nitrophenyl *O*-ethyl phenylphosphonothioate] did not alter its delayed neurotoxicity.

The discovery of the potential of some organophosphorus compounds to cause an insidious neuropathic anomaly, termed delayed neurotoxicity, has necessitated careful screening of potential organophosphorus pesticides for such delayed neurotoxic activity (Johnson, 1975). A recent incidence of delayed neurotoxicity involved the use of leptophos [Phosvel or *O*-(4-bromo-2,5-dichlorophenyl) *O*-methyl phenylphosphonothioate] for control of cotton



pests in Egypt. In this instance, some 1300 water buffalo were paralyzed and later six people were discovered to have

Division of Toxicology and Physiology, Department of Entomology, University of California, Riverside, California 92521.

0021-8561/79/1427-1197$01.00/0

symptoms of delayed neurotoxic poisoning with traces of leptophos found in their tissues (Shea, 1974). Abou-Donia and Preissig (1976a,b), and Sanborn et al. (1977) have conclusively demonstrated that leptophos, leptophos oxon, and desbromoleptophos are capable of producing delayed neurotoxicity in hens.

Previous work with substituent effects and structural isomers of TOCP has shown that minor changes in a molecule will sometimes abolish delayed neurotoxic activity (Bondy et al., 1960; Hine et al., 1956; and Henschler, 1958).

The potential continued use of leptophos for pest control by many countries prompted a systematic study of pesticidal activity vs. delayed neurotoxic potential of structural analogues of leptophos (House Subcommittee Report, 1978). In addition, the toxic properties of several known impurites (WHO, 1976) and metabolic products of these compounds were examined.

MATERIALS AND METHODS

Chemicals. Technical leptophos, provided by the Velsicol Chemical Co., Chicago, IL, was purified by repeated recrystallization from benzene. Analytical grade EPN (**14**) was provided by E. I. duPont deNemours and Co., Wilmington, DE.

The leptophos analogues generally were prepared by a four-step sequence of reactions described as follows. Phenylphosphonothioic dichloride (Aldridge Chemical Co.) was converted to the corresponding phenylthionophosphine sulfide, mp 217–223 °C, according to Newallis et al. (1962). The phenylthionophosphine sulfide was treated with the appropriate alcohol to give the corresponding *O*-alkyl phenylphosphonodithioic acid, which was converted to the respective *O*-alkyl phenylphosphonochloridothioate by reaction with chlorine or sulfuryl chloride (Chupp and Newallis, 1962). The *O*-alkyl phenylphosphonochloridothioates used to prepare the final products were purified by vacuum distillation: (alkyl, bp) methyl, 68 °C (0.08 mm); ethyl, 86 °C (0.15 mm); propyl, 90 °C (0.15 mm); butyl, 110 °C (0.025 mm). The structures of the phenylphosphonochloridothioates were verified by NMR analysis.

The *O*-aryl *O*-alkyl phenylphosphonothioates (leptophos analogues) were prepared in the usual manner by overnight refluxing of a mixture consisting of equimolar amounts of the appropriate chloridothioate and sodium salt of the substituted phenol in 2-butanone solvent. The reaction mixture was filtered through Celite, the solvent was removed, and the residue was taken up in benzene–ether (1:1) and washed repeatedly with water. Crystalline products were purified by recrystallization from hexanes, unless otherwise specified. Liquid compounds were purified by silicic acid column chromatography (Silic AR CC-7 Special) or by preparative TLC (Silica Gel 60 PF-254) using hexane–benzene (2:1). Purity was verified by TLC using hexane–benzene (2:1) and hexane–ethyl acetate (9:1). Spots were located by ultraviolet detection and by 0.5% 2,6-dibromoquinone-4-chloroimide (DBQ) in ether as a spray reagent (Menn et al., 1957). Structures of all final compounds were verified by ^{1}H NMR and infrared spectroscopy and by elemental analysis. NMR spectra were obtained with a Varian T-60 or EM-390 spectrometer in chloroform-*d* using tetramethylsilane as the internal standard. A Beckman IR 4240 spectrophotometer was used to obtain infrared spectra, and elemental analyses were carried out by C. F. Geiger, Ontario, CA. Physical properties and elemental analyses of the leptophos analogues are presented in Table I.

O,O-Dimethyl phenylphosphonate (**16**) was prepared by heating at reflux for 3 h a mixture of sodium methoxide and phenylphosphonic dichloride in methanol. *O,O*-Bis(2,5-dichlorophenyl) phenylphosphonate (**17**) was similarly prepared from sodium 2,5-dichlorophenoxide and phenylphosphonic dichloride and *O,O*-bis(4-bromo-2,5-dichlorophenyl) phenylphosphonothioate (**18**) from sodium 4-bromo-2,5-dichlorophenoxide and phenylphosphonothioic dichloride, using 2-butanone as the solvent.

O-Methyl *O,P*-2,2′-biphenylene phosphonothioate (**20**) was prepared by the following procedure. A mixture of 9.5 g of sodium 2-phenylphenoxide and 8.5 g of phosphorus thiochloride in benzene was heated at reflux overnight to give *O*-2-phenylphenyl phosphorothioic dichloride. The excess phosphorus thiochloride and benzene were removed in vacuo, the residue was dissolved in carbon disulfide and 1.75 equiv of aluminum chloride was slowly added while stirring vigorously. The mixture was heated to reflux in a warm water bath for 3 h until evolution of HCl ceased. The reaction was cooled in ice and 1 equiv of phosphorus oxychloride was added dropwise. The mixture was filtered and washed with three 50-mL portions of petroleum ether. *O,P*-2,2′-Biphenylene phosphonothioic chloride crystallized from the benzene–petroleum ether and was recrystallized from petroleum ether, mp 136–138 °C (45–50% yield). This chloridate was refluxed overnight with 1 equiv of sodium methoxide in methanol. The mixture was filtered and the solvent removed in vacuo. The product was crystallized from ethyl acetate and recrystallized from benzene: mp 79–80 °C; ^{1}H NMR (chloroform-*d*, Me_4Si), δ 7.0–8.3 (m, 8 H, aromatic protons), 3.66 (d, 3h, OCH_3, J = 7 Hz); IR (CS_2 or CCl_4) 1431, 1200, 1178, 1037, 751, 715, and 617 cm^{-1}.

Appropriate caution should be taken in preparing and handling these compounds as leptophos has been implicated in cases of delayed neurotoxicity in man (Report of the Leptophos Advisory Committee, 1976).

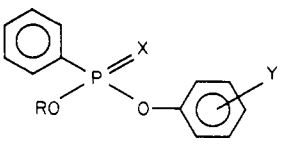
Acute Toxicity. Insecticidal activity was determined using female houseflies, susceptible S_{NAIDM} strain, as described by March and Metcalf (1949). Treated flies were held at 60 °F and the mortality was estimated after 24 h. Mammalian toxicity was determined with 25–35-g female Swiss white mice obtained from Simonson Laboratories, Gilroy, CA. Solutions of the toxicants in corn oil were administered orally at 0.25 mL/mouse to animals fasted for 6 h before treatment. LD_{50} values were based on 24-h mortality using five–seven mice per dose and at least five different doses per compound.

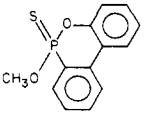
Delayed Neurotoxicity. Adult white leghorn hens, 1.3–1.8 kg in weight, were used to determine a minimum effective dose causing ataxia. Toxicants were administered orally in gelatin capsules to paired hens for each dose. Control birds were given corn oil. Paired birds were caged together and given standard layers mash and water ad libitum, accessible even when paralyzed. Birds were examined by two independent observers twice weekly for 30 days for signs of ataxia as described by Davies and Holland (1972). The minimum effective dose was determined as the lowest dose administered that produced any visually detectable ataxia. Hens showing symptoms of acute cholinergic poisoning were given intramuscular injections of 20 mg/kg of atropine sulfate in saline at 1, 8, and 16 h posttreatment as needed for survival. Three injections were the maximum number given; however, most of the compounds produced no acute symptoms at the doses used and no atropine was administered in those cases.

RESULTS AND DISCUSSION

Leptophos and its analogues were conveniently prepared by the reaction (Newallis et al., 1962; Chupp and Newallis,

Table I. Physical Properties and Elemental Analyses of Leptophos Analogues



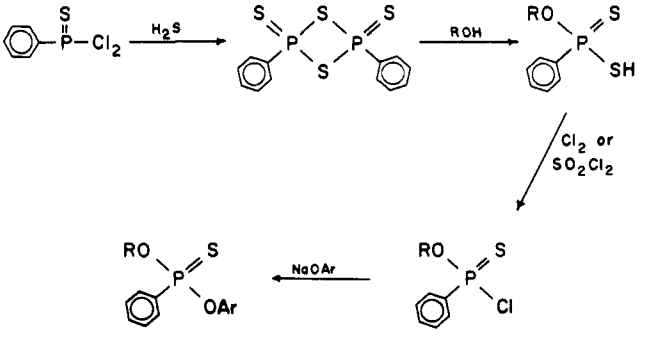
compd	X	R	Y	mp, °C (n^{23}_D)	analysis calcd	analysis found
leptophos	S	CH_3	2,5-Cl_2-4-Br	71-72	C, 37.89 H, 2.45	C, 37.68 H, 3.41
1	S	CH_3	2,6-Cl_2	53-56	C, 46.80 H, 3.30	C, 46.38 H, 2.96
2	S	CH_3	2,5-Cl_2	48-49	C, 46.80 H, 3.30	C, 46.84 H, 3.26
3	S	CH_3	2,4-Cl_2	(1.6059)	C, 46.80 H, 3.30	C, 46.90 H, 2.96
4	S	CH_3	2,3-Cl_2	(1.6065)	C, 46.80 H, 3.30	C, 46.20 H, 3.80
5	S	CH_3	2-Cl	(1.5975)	C, 52.26 H, 4.06	C, 52.59 H, 4.31
6	S	CH_3	3-Cl	(1.5951)	C, 52.26 H, 4.06	C, 52.85 H, 4.43
7	S	CH_3	4-Cl	(1.5867)	C, 52.26 H, 4.06	C, 52.31 H, 4.12
8	S	CH_3	3,4-Cl_2	(1.6089)	C, 46.80 H, 3.30	C, 46.88 H, 3.84
9	S	CH_3	3,5-Cl_2	(1.6027)	C, 46.80 H, 3.30	C, 46.46 H, 3.66
10	S	CH_3	H	(1.5938)	C, 59.09 H, 4.92	C, 59.25 H, 4.83
11	S	C_2H_5	2,5-Cl_2	(1.5784)	C, 48.42 H, 3.75	C, 48.73 H, 4.03
12	S	C_3H_7	2,5-Cl_2	(1.5790)	C, 49.86 H, 4.16	C, 49.79 H, 4.15
13	S	C_4H_9	2,5-Cl_2	(1.5781)	C, 51.20 H, 4.53	C, 51.54 H, 4.75
14	S	C_2H_5	4-NO_2	36-37	C, 52.01 H, 4.33	C, 52.40 H, 4.69
15	S	CH_3	4-NO_2	31-32	C, 50.48 H, 3.88	C, 50.86 H, 4.17
16	O	CH_3	same as R	(1.5070)	C, 51.61 H, 5.91	C, 51.88 H, 5.97
17	O	2,5-$Cl_2C_6H_3$	same as R	89-91	C, 48.24 H, 2.46	C, 48.21 H, 2.33
18	S	2,5-Cl_2-4-BrC_6H_2	same as R	120-122	C, 34.74 H, 1.45	C, 34.22 H, 1.27
19	S	C_2H_5	2,5-Cl_2-4-Br	62-64	C, 39.45 H, 2.82	C, 39.25 H, 2.74
20				79-80	C, 59.54 H, 4.20	C, 58.73 H, 4.20

1962) shown in Scheme I. This method was used because it proved to be superior to the procedure which employs stepwise substitution of the chlorine atoms in phenylphosphonothioic dichloride by an alkoxy and aryloxy moiety (Velsicol patent). Excellent yields and high purity products were obtained.

Data for the acute toxicity of the various leptophos analogues to houseflies and white mice, and delayed neurotoxicity to hens are given in Table II. Several compounds were highly toxic to houseflies; the most toxic were EPN (14) an its methoxy analogue (15). These two compounds also were acutely highly toxic to mice and hens, and both produced severe ataxia in hens when their acute toxicity was counteracted by three intramuscular injections of atropine.

The paralytic effects produced in the hen with EPN have been reported to develop immediately after dosing with EPN (Durham et al., 1956; Witter and Gaines, 1963; Gaines, 1969) and therefore differ from the classical,

Scheme I



delayed symptoms noted with TOCP. However, Ohkawa et al. (1977) reported that hens had completely recovered from the acute effects of EPN poisoning prior to the development of ataxic symptoms 10–14 days after treatment. Ohkawa administered 15 mg/kg of atropine

Table II. Acute and Delayed Neurotoxicity of Leptophos Analogues to Houseflies, Mice, and Hen Chickens

compd	acute toxicity: housefly LD_{50}, μg/g	acute toxicity: mouse (oral) LD_{50}, mg/kg	neurotoxicity, hen MED,[a] mg/kg
leptophos	13	65	+250-275
1	430	105	+40-50
2 (desbromo-leptophos)	10	95	+23-26
3	30	240	+160-175
4	34	>500	+100-175
5	270	165	+300-325
6	100	>500	+275-300
7	>500	>500	+385-480
8	32	100	+100-175
9	5	200	+175-225
10	>500	>500	-500
11	12	153	-1000[b]
12	>500	>500	-500
13	>500	>500	-333
14	1	16	+100-125[b]
15	2	12	+100-125[b]
16	>500	>500	-500
17	>500	>500	-500
18	>500	>500	-500
19	9	75	-1000[b]
20	>500	>500	-515

[a] Minimum effective dose producing ataxia. [b] Atropinized.

sulfate subcutaneously in saline 6 and 24 h after treatment while in the earlier studies 15 mg/kg of atropine sulfate was given orally 15 min before treatment. Our results are in agreement with Ohkawa's findings in that the acute symptoms of poisoning had ceased for several days prior to the development of ataxia.

All of the monochloro and dichlorophenyl *O*-methyl phenylphosphonothioate analogues (**1–9**) caused ataxia in hens. Compared to leptophos the dichlorophenyl esters were more delayed neurotoxic while the monochlorophenyl esters (**5–7**) were less delayed neurotoxic. The unsubstituted phenyl ester (**10**) was not delayed neurotoxic at a single oral dose of 500 mg/kg. The 2,5-dichlorophenyl ester (**3** or desbromoleptophos), with a single minimum effective dose of 23–26 mg/kg, was the most delayed neurotoxic analogue examined. This compound has been reported to be one of the major photolytic conversion products of leptophos (Metcalf and Sanborn, 1975).

Substitution of the *O*-methyl group of leptophos by *O*-ethyl gave an analogue (**19**) which was essentially devoid of delayed neurotoxic activity, i.e., symptoms of delayed neurotoxicity were not observed at a single oral dose as high as 1000 mg/kg. Similarly, the *O*-ethyl analogue (**11**) of desbromoleptophos also was not delayed neurotoxic at 1000 mg/kg. In this case, the reduction in activity was substantially more significant owing to the greater delayed neurotoxicity of desbromoleptophos compared to leptophos. The *O*-propyl (**12**) and *O*-butyl (**13**) analogues of desbromoleptophos were not delayed neurotoxic at single oral doses of 500 and 333 mg/kg, respectively, the highest doses tested.

Examination of housefly toxicity data show that the ethyl analogues of leptophos (**19**) and desbromoleptophos (**11**) were as effective as leptophos against houseflies. Further, **19** and **11**, with mouse oral LD_{50} values of 75 and 153 mg/kg, were both less toxic to mice than leptophos. In a separate study, **19** has been reported to be nearly as effective as leptophos against the bollworm, *Heliothis zea*, and tobacco budworm, *Heliothis virescens* (Wolfenbarger, 1969). Although further testing is necessary, the *O*-ethyl analogue of leptophos may be a possible replacement for leptophos.

Compound **18** is a reported impurity of technical leptophos (WHO, 1976), and compounds **16** and **17** are potential photolytic oxidation products of reported impurities. None of these compounds caused acute or delayed toxic symptoms in any of the test animals at 500 mg/kg.

UV irradiation of leptophos in acetone solution is reported to result in two major products, desbromoleptophos and another compound believed to be *O*-methyl *O,P*-(5-chloro-2,2′-biphenylene) phosphonothioate (Report of the Leptophos Advisory Committee, 1976). The structural similarity between the latter product and the potent saligenin phosphate metabolite of TOCP (Eto et al., 1962) suggests the possibility of similar delayed neurotoxic activity. Compound **20**, the deschloro analogue of the proposed compound, showed no acute nor delayed neurotoxic activity at 515 mg/kg. Several attempts to synthesize the proposed photochemical product were unsuccessful.

The development of delayed neurotoxic symptoms appears to involve a threshold phenomenon. In a series of dosages, every hen receiving a dose above a certain level developed severe ataxia, some becoming completely paralyzed in the legs, while none of the hens given a small-increment lower dose developed any symptoms. It is possible, however, that histological examination would reveal pathological lesions at doses lower than those producing ataxia.

It is apparent that minor molecular changes have a pronounced effect on the delayed neurotoxic potential of some organophosphorus compounds. Although activity appears to be associated with the methoxy group of *O*-halophenyl *O*-methyl phenylphosphonothioates tested in this experiment and not with the higher alkoxy derivatives, this trend apparently does not apply when nonhalogen substituents are present in the phenoxy moiety, e.g., EPN. Careful testing must therefore be conducted in evaluating the delayed neurotoxic potential of new phosphonate pesticides.

LITERATURE CITED

Abou-Donia, M. B., Preissig, S. H., *Toxicol. Appl. Pharmacol.* **35**, 269 (1976a).
Abou-Donia, M. B., Preissig, S. H., *Toxicol. Appl. Pharmacol.* **38**, 595 (1976b).
Bondy, H. F., Field, E. J. Worden, A. N., Hughes, J. P., *Br. J. Ind. Med.* **17**, 190 (1960).
Chupp, J. P., Newallis, P. E., *J. Org. Chem.* **27**, 3832 (1962).
Davies, D. R., Holland, P., *Biochem. Pharmacol.* **21**, 3145 (1972).
Durham, W. F., Gaines, T. B., Hayes, W. J., Jr., *AMA Arch. Ind. Health* **13**, 326 (1956).
Eto, M., Casida, J. E., Eto, T., *Biochem. Pharmacol.* **11**, 337 (1962).
Gaines, T. B., *Toxicol. Appl. Pharmacol.* **14**, 515 (1969).
Henschler, D., *Klin. Wschr.* **36**, 663 (1958).
Hine, C. H., Dunlap, M. K., Rice, E. G. Coursey, M. M., Gross, R. M., Anderson, H. H., *J. Pharmacol. Exp. Ther.* **116**, 227 (1956).
House Subcommittee on Commerce, Consumer, and Monetary Affairs, "Report on Export of Products Banned by U.S. Regulatory Agencies", No. 95–1686, 95th Congress, 2nd Session, U.S. Government Printing Office, Washington, DC, 1978.
Johnson, M. K., *CRC Crit. Rev. Toxicol.* **3**, 289 (1975).
March, R. B., Metcalf, R. L., *Calif. Dep. Agric. Bull.* **38**, 1 (1949).
Menn, J. J., Erwin, W. R., Gordon, H. T., *J. Agric. Food Chem.* **5**, 601 (1957).
Metcalf, R. L., Sanborn, J. R., *Ill. Natl. Hist. Survey Bull.* **31**, 381 (1975).
Newallis, P. E., Chupp, J. P., Groenweghe, C. D., *J. Org. Chem.* **27**, 3829 (1962).

Ohkawa, H., Mikami, N., Okuno, Y., Miyamoto, J., *Bull. Environ. Contam. Toxicol.* **6**, 23 (1977).
Report of the Leptophos Advisory Committee to The Administrator United States Environmental Protection Agency, Washington, DC Oct 1976.
Sanborn, J. R., Metcalf, R. L., Hansen, L. G., *Pestic. Biochem. Physiol.* **7**, 142 (1977).
Shea, K. P., *Environment* **16**, 6 (1974).
WHO, World Health Organization, Technical Report Series No. 592, Geneva, 1976.
Witter, R. F., Gaines, T. B., *Biochem. Pharmacol.* **12**, 1377 (1963).
Wolfenbarger, D. A., *Texas Agric. Exp. Sta.* PR-2670-2674, 9 (1969).

Received for review April 9, 1979. Accepted July 2, 1979. This investigation was supported from Federal Funds from the Environmental Protection Agency under Grant R804345. The contents do not necessarily reflect the views and policies of the Environmental Protection Agency, nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

Equilibrium and Kinetics of Desorption of Picloram and Parathion in Soils

Max W. Cheung,[1] Uri Mingelgrin,[2] and James W. Biggar*

The desorption of picloram from Palouse silt, parathion from Panoche clay loam, and parathion from Palouse silt loam was investigated using a flow system. The desorption–kinetic reaction constant, k_0', was calculated from the specific desorption, $(x/m)_d$, as a function of time. The k_0' values at 25 °C are 0.457, 0.099, and 0.011 for the above three soil–pesticide systems, respectively. Activation parameters for each system were evaluated. The activation energy, E_a, is 8.6, 8.2, and 3.0 kcal/mol for these three systems, respectively. The standard enthalpy for the equilibrium adsorption is compared with the enthalpies of activation for the kinetic adsorption and desorption processes. The interpretation of the activation parameters for each system was supplemented by X-ray diffraction data. Hypotheses concerning the mechanisms involved in the desorption process for these chemicals in these soils are discussed.

Parathion (*O,O*-diethyl *O*-(*p*-nitrophenyl) phosphorothioate) is a very effective insecticide and larvacide. A concentration of 0.01 ppm is sufficient to control mosquito larvae (Yasuno et al., 1966). Depending on the method of application, a good portion of the insecticide deposits on the soil. Residues in soil are subjected to desorption by water and lead to contamination of other components in the ecosystem. Nicholson et al. (1962) recovered 1.7 ppm parathion by weight from a soil in a peach orchard 9 months after the last application and 1.9 ppm was recovered from the bottom soil of a pond located in this orchard, yet a maximum concentration of 3 ppb is recommended for reservoir water (Malov, 1957). Using a batch technique, Saltzman et al. (1972) examined the adsorption and desorption of parathion in soil. The authors found that organic matter played an important role in retaining the parathion.

The utilization of picloram (4-amino-3,5,6-trichloropicolinic acid) as a potent herbicide has been recognized (Laning, 1963; Hamaker et al., 1963; Hoffman, 1971). Its resistance to degradation in the environment ranks next to the chlorinated hydrocarbons (Hiltbold, 1974) and could pose some environmental danger even though it is relatively nontoxic to many animal species (Lynn, 1965). Davidson and Chang (1972) investigated the movement of picloram in soil as related to soil bulk density, particle size, and pore-water velocity.

Since the behavior of pesticides in soil is largely a dynamic phenomenon, a study of the interaction parameters associated with adsorption and desorption is instructive. Often the rates of adsorption and desorption are more important in predicting the movement of a pesticide in soil than the equilibrium adsorption behavior. The present work examines the desorption of picloram and parathion from two soils employing a flow-type kinetic method. Desorption reaction constants were calculated from the experimental results, and their variation with temperature was used to calculate the activation energy and other activation parameters. The activation parameters are compared with the thermodynamic equilibrium parameters for the various systems. The thermodynamic data obtained were used to gain insight into the mechanisms of interaction of pesticides in soil.

EXPERIMENTAL SECTION

Materials. All chemicals used were reagent or analytical grade. Solutions of picloram and parathion were prepared by procedures described in a previous paper (Biggar et al., 1978). The eluting or desorption solution was 0.01 M calcium chloride.

Methods. The apparatus and collection procedures of the desorption kinetic experiments were described elsewhere (Biggar et al., 1978). At the end of the kinetic adsorption experiment, the delivery tube–syringe assembly was separated from the upper fritted-glass top. The pesticide solution in the top was quickly emptied out and the top was rinsed twice and then filled up with the desorption solution. The pesticide solution retained by the soil did not flow out, and because of the fritted-glass

Department of Land, Air and Water Resources, University of California, Davis, California 95616.
[1] Present address: CIBA-GEIGY Corporation, Greensboro, NC 27409.
[2] Present address: Agricultural Research Organization, The Volcanie Center, Institute of Soils and Water, Bet-Dagan, Israel.

0021-8561/79/1427-1201$01.00/0