MICRO-SYNTHESIS OF RADIOLEPTOPHOS LABELLED AT FIVE DIFFERENT SITES*

S.M.A.D. Zayed, M. Farghaly**, I.M.I. Fakhr** and A. Hassan
(M.E. Regional Radioisotope Centre - Dokki, Cairo, Egypt)

ABSTRACT

The micro-procedure involved interaction of benzene with phosphorus trichloride followed by addition of sulphur. Phenyl dichlorophosphine sulphide was condensed with methanol to form O-methyl phenylthiophosphonochloridate which was allowed to react with the sodium salt of 4-bromo-2,5-dichlorophenol to yield leptophos [O-(4-bromo-2,5-dichlorophenyl) O-methyl phenyl phosphonothioate]. Five radioactive leptophos compounds were prepared by substituting the cold chemicals with the appropriate radioactive precursor ($^{32}PCl_3$, 1-^{14}C-benzene, ^{35}S, ^{14}C-methanol or tritiated 4-bromo-2,5 dichlorophenol).

KEY WORDS

Insecticides; leptophos; synthesis, organic sulphur compounds; phosphonic acid esters.

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** National Research Centre - Dokki, Cairo, Egypt.

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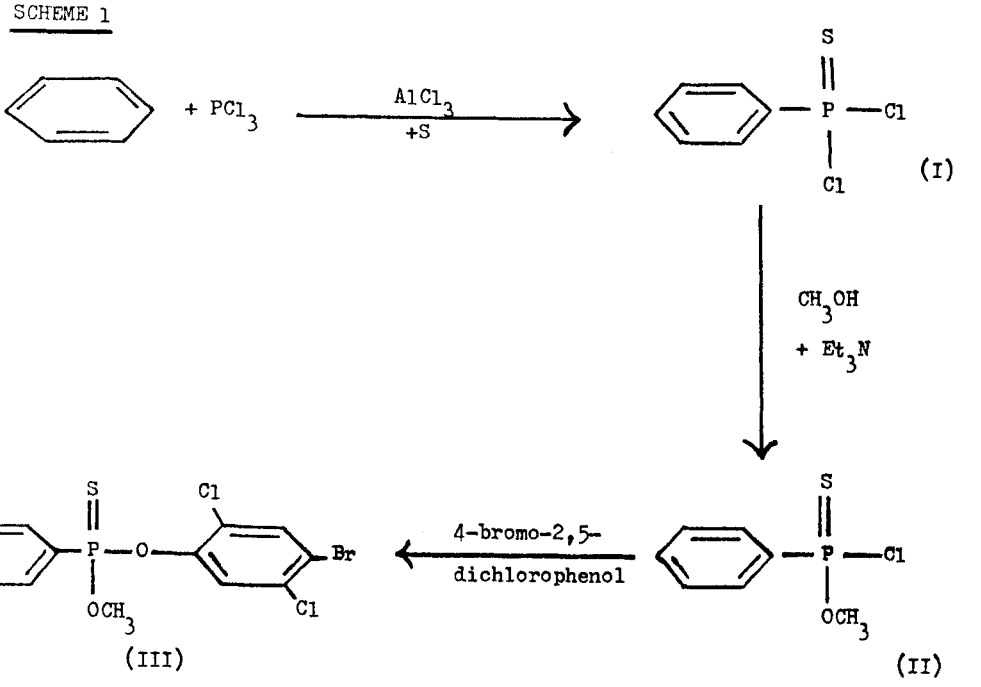
Leptophos (O-4-bromo-2,5-dichlorophenyl) O-methyl phenyl phosphonothioate was produced by Velsicol Chemical Corporation, U.S.A., and marketed under the name "Phosvel". The chemical possesses a broad spectrum of activity towards several insect species (1,2,3,4). The wide use of leptophos in the Middle and Far East for controlling cotton pests prompted us to conduct a series of studies on the chemistry and toxicology of this insecticide. For some of these investigations the use of radiolabelled leptophos proved to be highly advantageous (5,6,7). The present paper describes the synthesis of leptophos labelled at five different sites. The preparation of ^{32}P-labelled leptophos (5) and ^{14}C-phenyl-labelled leptophos (6) were previously reported.

The general procedure presented in scheme 1 proved to be suitable for the preparation of the five radiolabelled leptophos compounds. This method involved the condensation of benzene with phosphorus trichloride in presence of aluminium chloride and subsequent addition of sulphur to give phenyl dichlorophosphine sulphide (I). For the preparation of O-methyl phenyl thiophosphonochloridate (II), equimolecular amounts of I and methanol were allowed to react in presence of triethylamine. O-methyl phenyl thiophosphonochloridate condensed readily with an equimolecular amount of the sodium salt of 4-bromo-2,5-dichlorophenol to give leptophos (III). This method gives an overall yield of 75% based on the amount of benzene used. The crude product was purified by column chromatography on silica gel using petroleum ether 40-60°-chloroform (6:1) for elution. Further crystallization from hexane gave colourless crystals, m.p. 72°.

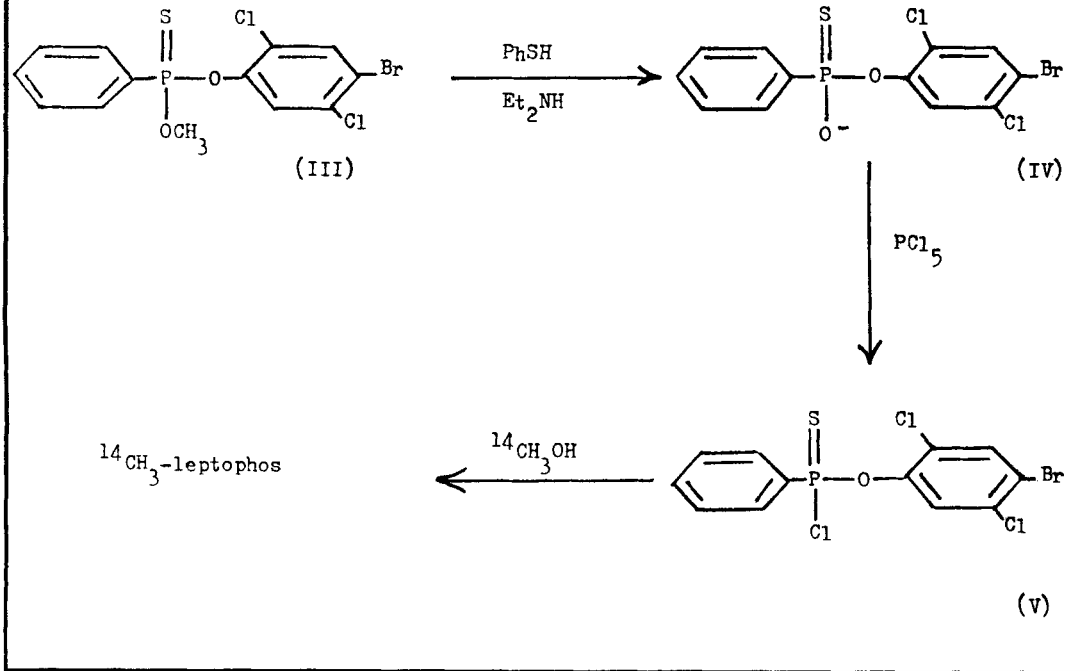
The use of $^{32}PCl_3$, ^{35}S, crystalline rhombic sulphur, $^{14}CH_3OH$ or 1-^{14}C-benzene yielded leptophos labelled at the corresponding moiety. ^{3}H-leptophos was prepared from ^{3}H-4-bromo-2,5-dichlorophenol. The latter was readily obtained by an exchange reaction between the cold phenol and tritiated water at 110°, for 70 hours. The phenol was purified by preparative thin layer chromatography using petroleum ether (60-80°) - benzene (5:1); R_F = 0.14, m.p. 66°.

The preparation of $^{14}CH_3$-leptophos according to scheme 1 is usually associated with a considerable loss of radioactivity due to the formation of

SCHEME 1



SCHEME 2



other ^{14}C-methyl side products, mainly O,O-^{14}C-dimethyl phenylthiophosphonate. An alternative high-yielding method involves the condensation of $^{14}CH_3OH$ with O-(4-bromo-2,5-dichlorophenyl) phenylthiophosphonochloridate (V) (scheme 2). The latter was synthesized from leptophos by reaction with equimolar amounts of diethylamine and thiophenol to yield the dimethyl ammonium salt of IV, which is a crystalline compound (m.p.140-142°) and can be purified by crystallization from absolute ethanol. This reacted readily with phosphorus pentachloride in dry benzene to yield V in almost quantitive yield. The latter was purified by chromatography on Silica gel using chloroform/petroleum ether (1:2) for elution (scheme 2).

The radiochemical purity of III could be determined by TLC radio- and inverse isotope dilution techniques. All radiolabelled compounds were over 99% pure. Typical batches of the labelled insecticide possessed the following specific activities:

^{32}P-leptophos	2.0 - 4.0 mCi/mg
^{14}C-phenyl leptophos	1.5 - 2.5 mCi/mg
^{14}C-methyl leptophos	0.5 - 2.0 mCi/mg
^{35}S-leptophos	2.2 mCi/mg
^{3}H-leptophos	0.18 Ci/mg

REFERENCES

1. Janes, M.J., and Greene, G.L. J. Econ. Entom., 65, 52 (1972).
2. Ward, C.R., Huddleston, Owens, J.C., Hills, T., Richardson, L.G., and Ashdown, D. J. Econ. Entom., 65, 522 (1972).
3. Kaddor, K.N., Rawat, R.R., Luchmann, W.H., and Purohit, M.L. J. Econ. Entom., 65, 902 (1972).
4. Kamel, A.A., and Mitri, S.H. J. Econ. Entom., 63, 609 (1970).
5. Zayed, S.M.A.D., Fakhr, I.M.I., and Hassan, A. Environ. Qual. Safety, Supplement Vol. III, p.713 (1975).
6. Hassan, A., Abdel-Hamid, F.M., and Zayed, S.M.A.D. Environ. Qual. Safety, Supplement Vol. III, p.652 (1975).
7. Hassan, A., Abdel-Hamid, F.M., and Mohammed, S.I. Arch. Environm. Contam. Toxicol., 6, 447 (1977).