United States Patent Office 2,938,919 Patented May 31, 1960

2,938,919

THIOPHOSPHORIC ACID ESTERS AND A PROCESS FOR THEIR MANUFACTURE

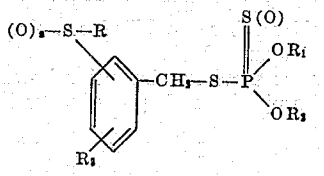
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No Drawing. Filed Jan. 27, 1959, Ser. No. 789,259

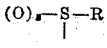
Claims priority, application Germany July 10, 1956

14 Claims. (Cl. 260—461)

This invention relates to and has as its objects new and useful thiophosphoric acid esters and their production. Generally the new inventive esters may be represented by the following formula

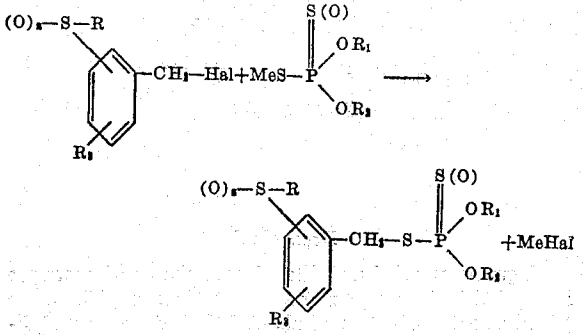


wherein R, R_1 and R_2 stand for alkyl radicals, R_3 stands for hydrogen or an alkyl radical, the alkyl radicals being especially lower alkyl radicals containing 1 to 4 carbon atoms, z stands for zero or a whole number up to two, and the group



stands either in an o- or p-position to the —CH_2-group, attached to the benzene nucleus.

These new thio- and dithiophosphoric acid esters, which are valuable insecticides and plant protecting agents, may be obtained by reacting the corresponding alkyl-mercapto- (or alkyl-sulfoxyl)- or alkyl-sulfonyl-)-halomethyl-(alkyl)-benzenes with salts of O.O-dialkylthiol- or thionothiol-phosphoric acids. This reaction may be shown by the following formulae



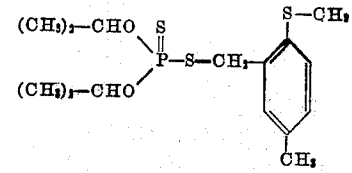
The starting materials, if they are 1-alkyl-mercapto-2-halomethyl-4-alkylbenzenes are easily obtainable from the corresponding 1-alkyl-mercapto-4-alkylbenzenes with formaldehyde and hydrochloric acid as it is described e.g. in the German patent specification No. 569,569. These alkyl mercapto compounds furthermore may be oxidized by known methods to the corresponding sulfoxides or sulfones. The first may be obtained by oxidizing the sulfides in glacial acetic acid with molar amounts of hydrogen peroxide at lower temperatures, whereas the sulfones are obtained by using an excess of hydrogen peroxide (at least 2 mols) at higher temperatures. The oxidation may also be carried out after the condensation with the 1-alkyl-mercapto-phenyl-thiophosphoric acid esters has taken place.

The starting materials, if they are 1-alkyl-mercapto-4-halomethylbenzenes, are known from the literature. Their oxydation products, namely the sulfoxides and sulfones are partially known, too, or may be obtained according to well known processes as described above.

The reaction between the O.O-dialkylthiol- or -thionothiolphosphates and the alkyl-mercapto-(or alkyl-sulfoxyl- or alkyl-sulfonyl-)-halomethyl-(alkyl)-benzenes preferably may be carried out at slightly elevated temperatures, say between about 20 and 80° C. and in the presence of an inert solvent. Suitable inert solvents in the sense of this invention are e.g. lower aliphatic alcohols, such as methanol or ethanol, lower aliphatic ketones, such as acetone or methylethyl ketone, or aromatic hydrocarbons, such as benzene, toluene, and the like. As salts of the O.O-dialkylthiol- or -thionothiolphosphoric acids which are especially suitable for the inventive reaction, there may be named the alkali metal salts or ammonium salts. As halomethyl-(alkyl)-phenylthio ethers (or their corresponding sulfoxides or sulfones), especially the chloromethyl compounds may be used.

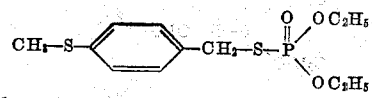
The compounds of the present invention are generally valuable insecticides and plant-protecting agents. They kill pests such as aphids, flies and mites and exhibit a very remarkable systemic action. They are especially valuable contact insecticides with a remarkably low toxicity against mammals. The special advantage of the inventive compounds consists also in their acaricidal activity and in that they are especially active against the eggs of red mites. The application of these compounds should be carried out according to the use of other known phosphorous insecticides, i.e. in dilution or solution with solid or liquid carriers, such as chalk, talc, bentonite, water, alcohols, liquid hydrocarbons, etc. The inventive compounds may further be used in combination with other known insecticides or pesticides, etc. Effective concentrations of the compounds may vary also; generally concentrations of 0.0001% to 1.0% kill pests effectively. The combinations of the compounds may be sprayed or dusted or otherwise brought in contact with pests or plants to be protected. They may also be used as aerosols.

As a special example for the utility of the inventive compounds the O.O-diisopropyl-S-[2-(methyl-mercapto)-4-methylphenyl-(1)]-methyl-dithiophosphate of the following formula



has been tested against black bean aphids, and the toxicity has been determined on rats orally. The above ester is mixed with the same amount of dimethyl formamide; to this solution 50% by weight of a commercial emulsifier consisting of a benzyl hydroxy diphenyl polyglycol ether is added. This mixture is diluted with water to an emulsion containing 0.01% of active ingredient, and that composition kills black bean aphids completely when infected plants are sprayed with this solution. Poisoned baits when fed to rats are well tolerated up to an amount of 1 g. active ingredient per kg. animal.

The activity of the following compound



was tested on dwarf beans (*Phaseolus vulgaris*). Plants, heavily infested with spider mites of the type *Tetranychus althae* Hanst. were sprayed to the run off with aqueous

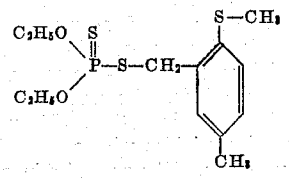
emulsions prepared as described above. After 48 hours 0.01% solutions killed spider mites completely and 0.001% solutions still killed the pests to 60%.

This application is a continuation-in-part application of the copending application Serial No. 669,427, filed July 2, 1957, now abandoned.

The following examples are given by way of illustration only, without, however, limiting the present invention thereto.

Example 1

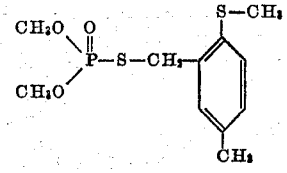
58 grams of the ammonium salt of O.O-diethylthiol-phosphoric acid are dissolved in 200 ccm. of methylethyl ketone. At a temperature of about 40° C., 58 grams of 4-methyl-2-chloromethyl-thioanisol in 50 ccm. methylethyl ketone are added while stirring. The reaction product is kept at a temperature of about 75° C. for 75 minutes while stirring. Then it is cooled and the ammonium chloride is filtered off with suction. The solvent is removed by distillation in vacuo. The residue is taken up in ether, washed with water and the etherical solution is dried over sodium sulfate. There are obtained 87 grams of the new ester of the formula

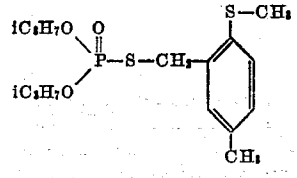


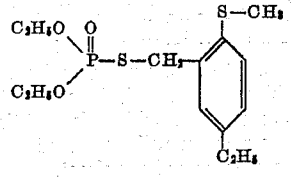
At a pressure of 0.01 mm. the new ester distills at a temperature of about 144° C.

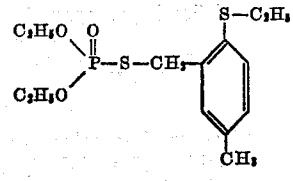
The new ester shows a medium toxicity of about 100 mg./kg. on rats orally. Spider mites are killed completely at concentrations of 0.01%.

By exactly the same procedure but using instead of the ammonium salt of O.O-diethylthiol-phosphoric acid, the corresponding amount of the ammonium salts of O.O-dimethyl- or O.O-diisopropyl-thiolphosphoric acid, and instead of the 4-methyl-2-chloro-methylthioanisol, also exactly the corresponding molecular amount of 4-ethyl-2-chloro-methylthionanisol or 4-methyl-2-chloro-methylthiophenetole there are obtained the following compounds:



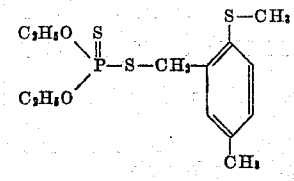






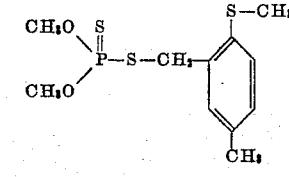
Example 2

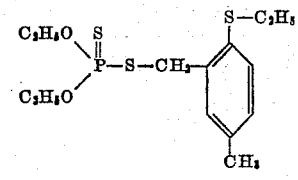
42 grams of dried and filtered potassium carbonate are suspended in 180 ccm. of methylethyl ketone. There are added at a temperature of about 50° C. 47 grams of diethyl-dithiophosphoric acid. Furthermore there are added while stirring at a temperature of 60° 48 grams of 4-methyl-2-chloromethyl-thioanisol (dissolved in 70 ccm. methylethyl ketone). After a reaction time of 4 hours at a temperature of 65–70° C. the mixture is cooled to room temperature and the potassium chloride is filtered off with suction. The solvent is then removed by distillation. The residue is taken up in 100 ccm. of ether and washed with water. After drying the etherical solution the ether is evaporated in vacuum. There are obtained 85 grams of the new ester of the formula

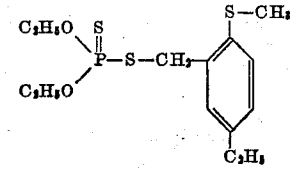


At a pressure of 0.01 mm. the new ester boils at 127–130° C. Spider mites are killed completely with concentrations of about 0.01%.

By exactly the same way but using instead of O.O-diethyl-dithiophosphoric acid potassium salt, the corresponding molecular amount of the corresponding dimethyl ester and instead of the 4-methyl-2-chloromethyl-thioanisol, exactly the corresponding molecular amount of 4-ethyl-2-chloromethyl-thioanisol or 4-methyl-2-chloromethylthiophenetole there are obtained the following compounds:

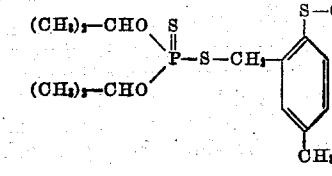






Example 3

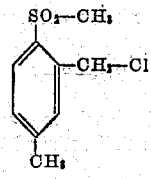
42 grams of dried and filtered potassium carbonate are suspended in 140 ccm. of methylethyl ketone. There are added at a temperature of about 50° C. 54 grams of diisopropyl-dithiophosphoric acid. Thereafter there is added a solution of 48 grams 4-methyl-2-chloromethyl-thioanisol in 70 ccm. of methylethyl ketone during 20 minutes. The reaction product is kept for 3 hours at a temperature of about 65° C. and then is worked up as described in Example 2. There are obtained 87.5 grams of the new ester of the formula



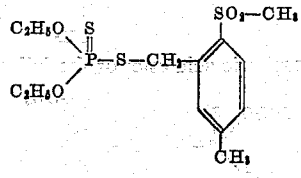
Yield: 96% of the theoretical. Even in high vacuum the new ester is not distillable without decomposition. The new ester shows a toxicity LD_{50} of 500–1000 mg./kg. on rats orally. 0.01% solutions kill black bean aphids completely.

Example 4

40 grams of the ammonium salt of O.O-diethylthiol-phosphoric acid are dissolved in 150 ccm. of methylethyl ketone. There is added at a temperature of about 30° C. a solution of 44 grams of the sulfone of the following formula dissolved in 100 ccm. methylethyl ketone:



The reaction product is warmed for 3 hours (while stirring) at 50° C. and then worked up in the usual manner. There are obtained 57 grams of the new ester of the following formula

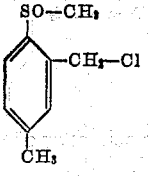


Yield: 81% of the theoretical. After a short period the raw product is crystallized; M.P. 63° C. The new ester shows a toxicity of 100 mg./kg. (LD_{50}) on rats orally. Spider mites are killed completely with concentrations of about 0.1%.

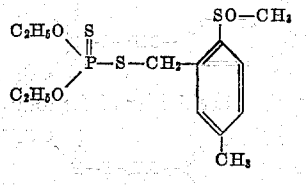
The above shown sulfone may be prepared as follows: 95 grams of 2-chloromethyl-4-methylthio-anisol are dissolved in 240 ml. of glacial acetic acid. At a temperature of 50° C. there are added 250 ml. of hydrogen peroxide (concentration 35%) within 15 minutes. The reaction is completed by standing for another hour and a half at 65° C. While cooling the sulfone crystallizes and may be recrystallized (if necessary) from benzene; M.P. 84° C.

Example 5

34 grams of dried and filtered potassium carbonate are suspended in 120 ccm. of methylethyl ketone. At a temperature of about 20° C. there are added 37.6 grams of diethyl-dithiophosphoric acid. Then while stirring and at a temperature of about 50° C. there is added a solution of 40 grams of the sulfoxide of the following formula dissolved in 70 ccm. of methylethyl ketone:



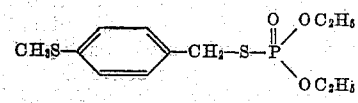
The reaction mixture is kept for 5 hours at a temperature of 60° C. and then it is worked up in the usual manner. There are obtained 73 grams of the new ester of the following formula



The new ester shows a medium toxicity of 1000 mg./kg. on rats orally. Mosquito larvae are killed completely with concentrations of about 0.0001%.

The above shown sulfoxide may be prepared as follows: 95 grams of 2-chloro-methyl-4-methyl-thioanisol are dissolved in 240 ml. of glacial acetic acid. At 0° C. there are added within 1 hour 120 ml. of hydrogen peroxide (concentration 35%). The reaction is completed within 2½ hours and the acetic acid and water is distilled off in vacuum. The sulfoxide remains as an oil and is pure enough for being further reacted according to the above example.

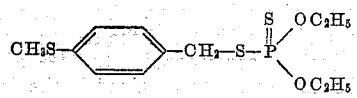
Example 6



52 grams (0.3 mol) of 4-methylmercapto-benzyl-chloride of B.P. 96–98° C./2 mm. Hg are added dropwise at 40–50° C. to a suspension of 67 grams (0.33 mol) of diethyl-thiolphosphoric acid ammonium salt in 150 ccm. of acetone. The mixture is heated for a further hour to 50–60° C. to complete the reaction. The precipitated ammonium chloride is filtered off with suction, and the filtrate poured into water. The oil is taken up in benzene, washed with water and a sodium bicarbonate solution, dried and distilled. 77 grams of thiolphosphoric acid-O.O-diethyl-S-4-methylmercapto-benzyl ester are obtained in the form of a yellow, thinly liquid oil of B.P. 124° C./0.01 mm. Hg. Yield: 81.3% of the theoretical.

The ester shows a toxicity (LD_{50}) of 10 mg./kg. on rats per os. Spider mites are killed to 60% even with dilutions of 1:100.000.

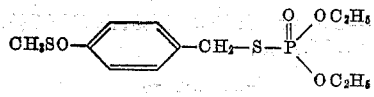
Example 7



30.5 grams (0.2 mol) of 4-methylmercapto-benzyl-chloride are added dropwise to a solution of 44 grams (0.22 mol) of diethyl-thionothiol-phosphoric acid ammonium salt in 100 ccm. of acetone starting at a temperature of 20° C. After the slightly exothermic reaction subsides, the solution is heated to 50–60° C. for one hour, the reaction product is then poured into water, the oil is taken up in benzene, washed and dried. By distillation 56 grams of thionothiolphosphoric acid-O.O-diethyl-S-4-methylmercapto-benzyl ester of B.P. 125° C./0.01 mm. Hg are obtained in the form of a pale yellow, almost colorless oil. Yield: 87% of the theoretical.

The ester shows a toxicity (LD_{50}) of 50 mg./kg. on rats per os. 0.001% solutions kill spider mites to 100%.

Example 8

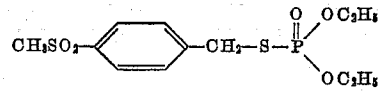


30.6 grams of the ester obtained according to Example 6 are dissolved in 75 ccm. of methanol and treated with 0.5 ccm. of 50% sulfuric acid. The calculated amount of a high-percent hydrogen peroxide is added dropwise with cooling at 40–50° C., the solution is stirred for one hour during which it cools. After the addition of water, the oil is taken up in benzene, washed with water and dried; the solvent is distilled off; 29.5 grams of thiolphosphoric acid-O.O-diethyl-S-4-methyl-sulfinyl-benzyl ester are obtained in the form of a pale yellow, water-insoluble oil which is not distillable.

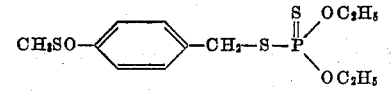
The toxicity (LD_{50}) of the ester lies at 20 mg./kg. on rats per os. At a concentration of 0.01% the ester still shows a 100% action against the eggs of the red spider.

If the ester obtained according to Example 6 is oxidized with the calculated amount of potassium permanganate in

diluted sulfuric acid there is obtained the ester of the following formula



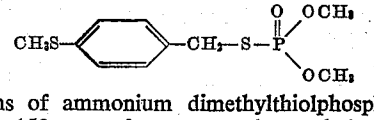
Example 9



As described in Example 8, 25 grams of the ester obtained according to Example 7 are oxidized in 50 ccm. of methanol in the presence of a small amount of dilute sulfuric acid with the calculated quantity of hydrogen peroxide. After working up in conventional manner 25 grams of thionothiol-phosphoric acid-O.O-diethyl-S-4-methyl-sulfinyl-benzyl ester are obtained. The colorless to pale yellow ester is water-insoluble and not distillable.

The toxicity (LD_{50}) of the ester lies between 10 to 20 mg./kg. on rats per os. With concentrations of 1:100.000 spider mites and their eggs are completely killed.

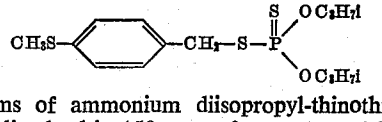
Example 10



45 grams of ammonium dimethylthiolphosphate are dissolved in 150 ccm. of acetone, and p-methyl-mercapto-benzyl-chloride of B.P. 59° C./0.01 mm. Hg is added dropwise at 40–35° C. The solution is subsequently heated to 60° C. for a half hour. After cooling, the salt is filtered off and the solution is diluted with benzene and shaken out twice with water. The benzene solution is dried over sodium sulfate and the solvent removed in vacuum. 41 grams (corresponding to 74% of the theoretical) of the new ester are obtained in the form of an almost colorless oil.

Analysis.—Calculated: P = 11.13%; S = 23.03%. Found: P=9.76%; S=22.85%.

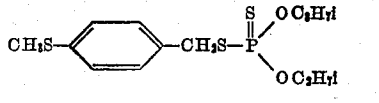
Example 11



56 grams of ammonium diisopropyl-thinothiol-phosphate are dissolved in 150 ccm. of acetone, and 35 grams of p-methylmercapto-benzyl chloride of B.P. 59° C./0.01 mm. Hg are added dropwise at 40° C. Working up is carried out as indicated in Example 10. 66 grams of the new ester are obtained in the form of a pale yellow oil which is clear soluble in cyclohexane. Yield: 99% of the theoretical.

Analysis.—Calculated: P=9.26%; S=28.77%. Found: P=8.73%; S=26.73%.

Example 12

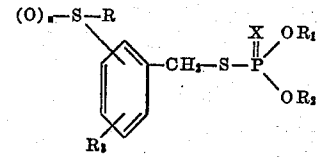


53 grams of ammonium diisopropyl-thiolphosphate are dissolved in 150 ccm. of acetone, and 35 grams of p-methyl-mercapto-benzyl chloride of B.P. 59° C./0.01 mm. Hg are added dropwise at 50° C. The reaction mixture is heated to the boil under reflux on a water bath for 1 hour. Working up is carried out as described in Example 10. The new ester is obtained in the form of a pale yellow oil. Yield: 63 grams corresponding to 99% of the theoretical.

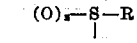
Analysis.—Calculated: P=9.73%; S=20.15%. Found: P=8.94%; S=17.32%.

We claim:

1. A thiophosphoric acid ester of the following formula

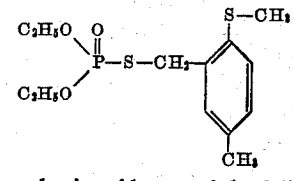


in which X is a chalcogen having an atomic weight between 16 and 33, R, R_1 and R_2 stand for lower alkyl radicals up to 4 carbon atoms, R_3 stands for a member selected from the group consisting of hydrogen and a lower alkyl radical up to 4 carbon atoms, *z* stands for a member selected from the numbers 0, 1 and 2, and the group

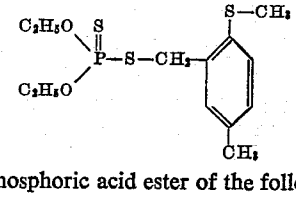


stands in a position selected from *o* and *p*.

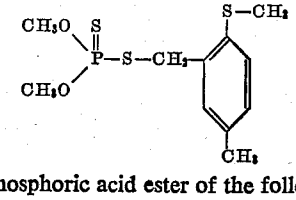
2. A thiophosphoric acid ester of the following formula



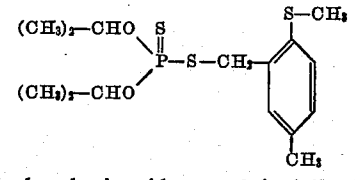
3. A thiophosphoric acid ester of the following formula



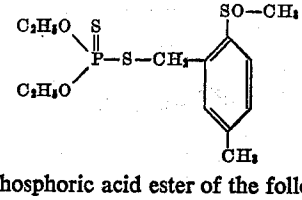
4. A thiophosphoric acid ester of the following formula



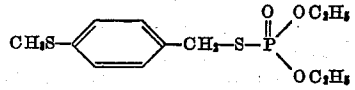
5. A thiophosphoric acid ester of the following formula



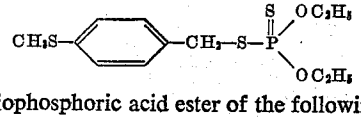
6. A thiophosphoric acid ester of the following formula



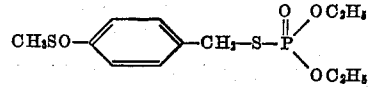
7. A thiophosphoric acid ester of the following formula



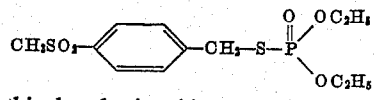
8. A thiophosphoric acid ester of the following formula



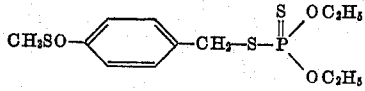
9. A thiophosphoric acid ester of the following formula



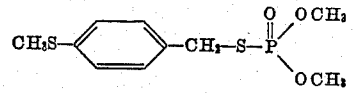
10. A thiophosphoric acid ester of the following formula



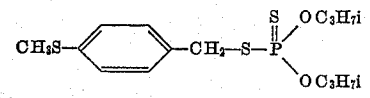
11. A thiophosphoric acid ester of the following formula



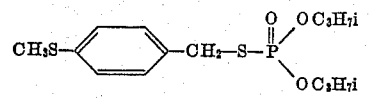
12. A thiophosphoric acid ester of the following formula



13. A thiophosphoric acid ester of the following formula



14. A thiophosphoric acid ester of the following formula



References Cited in the file of this patent

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2,803,580 Metivier ---------- Aug. 20, 1957

UNITED STATES PATENT OFFICE

CERTIFICATE OF CORRECTION

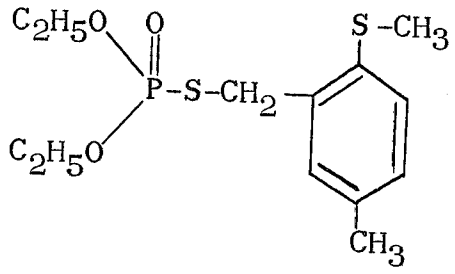
Patent No. 2,938,919

May 31, 1960

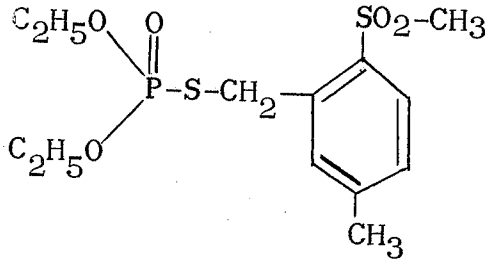
Walter Lorenz et al.

It is hereby certified that error appears in the printed specification of the above numbered patent requiring correction and that the said Letters Patent should read as corrected below.

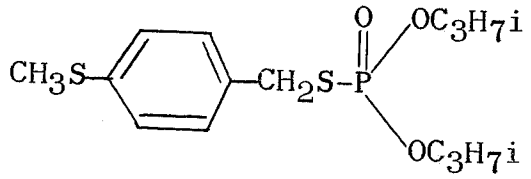
Column 3, lines 25 to 31, the formula should appear as shown below instead of as in the patent:



column 5, lines 25 to 31, the formula should appear as shown below instead of as in the patent:



column 7, line 49, for "-thinothiol-" read -- -thionothiol- --; same column 7, lines 60 to 64, the formula should appear as shown below instead of as in the patent:



Signed and sealed this 10th day of January 1961.

(SEAL)
Attest:

KARL H. AXLINE
Attesting Officer

ROBERT C. WATSON
Commissioner of Patents