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PATENT SPECIFICATION

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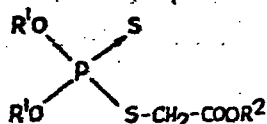
International Classification:—A01n. C07f.

COMPLETE SPECIFICATION

Substituted O,O-Dialkyl-Dithiophosphorylacetic Esters and Process for their Preparation

We, MONTECATINI SOCIETA GENERALE PER L'INDUSTRIA MINERARIA E CHIMICA, a Body Corporate organised and existing under the laws of Italy, of 18, Via Filippo Turati, Milan, Italy, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

- 5 The present invention refers to organic esters of dithiophosphoric acid useful as insecticides, rodenticides and, generally, as agents for the control of parasites of plants and houses, as well as to the process for their preparation.
- 10 Previous experiments which we have performed have shown that O,O - dialkyl - dithiophosphorylacetic esters, corresponding to the general formula

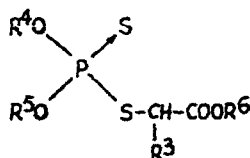


(I)

- 20 (wherein R^1 is a lower alkyl radical, such as methyl or ethyl, and R^2 is a saturated or unsaturated, straight or branched chain alkyl radical which may contain Cl, Br, I, OH or SCN, or an unsubstituted or substituted aryl or arylalkyl radical), possess an anti - parasitic activity.

Through further laboratory experiments it has now been observed that modifications of the above formula give rise to products which sometimes possess clearly a higher insecticidal activity. This occurs above all with O,O - dialkyl - dithiophosphorylacetic esters corresponding to the general formula

[Price 3s. 6d.]

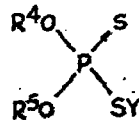


(II)

(wherein R^4 , R^5 and R^6 are like or different and each is a saturated or unsaturated, straight or branched chain alkyl radical, and R^3 is a substituted or unsubstituted aryl radical).

Particular members of this group of compounds are those in which R^3 is a naphthyl radical or a substituted aryl radical, and also those esters in which at least one of R^4 , R^5 or R^6 is a saturated branched - chain radical.

The products of the present invention are prepared by reacting a salt of an O,O-dialkyl-dithiophosphoric ester of the general formula



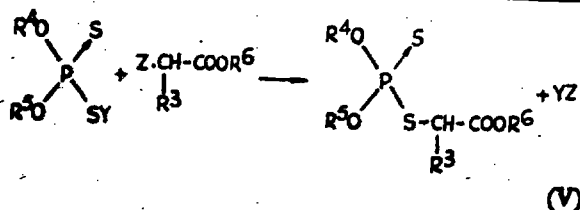
(III)

(wherein R^4 and R^5 are as defined and Y is ammonium or an alkali metal or an alkaline-earth metal) with an ester of an α - halogen- α -arylacetic acid, of the general formula



(wherein R^7 and R^8 are as above defined and Z is Cl, Br or I) in the presence of a solvent for either or both reactants according to the scheme

Price 4s. 6d.



A modification of this process consists in using, instead of said salt (III), the corresponding free acid (i.e. (III), wherein $\text{Y}=\text{H}$) and a base which is sufficiently basic to neutralise said acid, such as an alkali, or alkaline-earth metal, hydroxide, carbonate or bicarbonate, for example, Na_2CO_3 , K_2CO_3 , BaCO_3 , NaOH , KOH , NaHCO_3 or KHCO_3 .

The reaction is carried out in the presence of a solvent for either or both reactants. As solvents the following materials may be used: water, alcohols, ketones, esters, dioxane, or aromatic hydrocarbons (such as benzene, toluene or xylene).

The process is particularly applicable to the preparation of compounds in which R^3 is a naphthyl radical or a substituted aryl radical and also to the preparation of those compounds in which at least one of R^4 , R^5 or R^6 is a saturated branched-chain alkyl radical.

Also included in the invention is a disinfecting composition comprising one or more esters according to the invention, either as sole

active substances or in admixture with one or more of the known disinfecting compounds, such as insecticides, and/or fungicides, and/or in admixture with one or more nutritive substances for plants, and/or fertilisers.

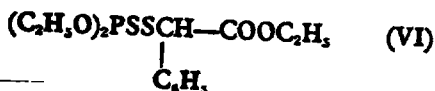
The following Examples are given by way of illustration, but without limitation, of the present invention:

EXAMPLE 1

20 g. O,O - diethyl - dithiophosphoric acid dissolved in 100 cc acetone are neutralised with about 6 g. anhydrous sodium carbonate. After stirring for half an hour at room temperature, 25 g. ethyl α -phenyl- α -bromoacetate are added. After one night, the greatest part of the solvent is distilled slowly at normal pressure. The residue is cooled and shaken with water and a 5% NaHCO_3 solution to pH 7. The mixture is dried over MgSO_4 and distilled, collecting the fraction which boils at about 149–150° C. at 0.05 mm Hg. About 20 g. of a straw-coloured oil are obtained, having

b.p., 145–150° C; n_D^{20} 1.5371; D_{20}^{20} 1.1790

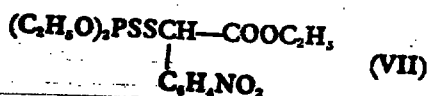
The analysis confirms that this product is the ethyl ester of O,O - diethyl - dithiophosphoryl-phenylacetic acid, which has the formula



EXAMPLE 2

11.5 g. O,O - diethyl - dithiophosphoric acid dissolved in 100 cc acetone are neutralised with 3.3 g. anhydrous sodium carbonate. After stirring for half an hour, 16 g. ethyl α -p-nitrophenyl - α -bromoacetate, dissolved in 60 cc acetone, are added dropwise. The mixture is heated under reflux for 2 hours and the acetone is distilled off. After cooling, the mixture is treated with ice-water and extracted with CCl_4 ; the tetrachloride solution is shaken with NaHCO_3 (5% solution) to pH 7. The solution is dried over MgSO_4 and the solvent is removed under vacuum on a boiling water bath. The residue is a dark red oil, having n_D^{20} : 1.5351; D_{20}^{20} : 1.3244

The analysis confirms that this product is the ethyl ester of O,O - diethyl - dithiophosphoryl - p - nitrophenylacetic acid, which has the formula

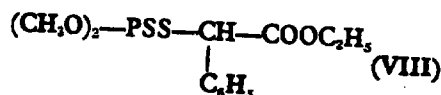


EXAMPLE 3

38 g. crude O,O-dimethyl - dithiophosphoric acid dissolved in 150 cc acetone are neutralised with 13 g. anhydrous sodium carbonate. After stirring for half an hour, 48.6 g. ethyl α -phenyl - α -bromoacetate are added. The mixture is heated under reflux for 1 hour and the greatest part of the acetone is distilled off at normal pressure on a boiling water bath. After cooling, the mass is treated with ice-water and extracted with carbon tetrachloride. The organic solution is shaken with a 5% NaHCO_3 solution to pH 7. It is then dried over MgSO_4 and the solvent is removed under vacuum on a boiling water bath. The residue consists of 49 g. of a yellow oil, having

n_D^{20} 1.5449; D_{20}^{20} : 1.2635

The analysis confirms that this product is the ethyl ester of O,O - dimethyl - dithiophosphoryl - phenylacetic acid, having the formula



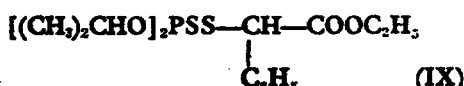
EXAMPLE 4

35 g O,O - diisopropyl - dithiophosphoric acid dissolved in 100 cc acetone are neutralised with 9.3 g. anhydrous sodium carbonate. The solution is stirred for half an hour and 36 g.

ethyl α - phenyl - α - bromoacetate are added. After one night, the acetone is slowly distilled off. The mass is cooled to room temperature and treated with ice-water. The oil thus obtained is separated and shaken with a 5% NaHCO_3 solution to pH 7. The mixture is dried over MgSO_4 and filtered. 43 g. of a yellow oil are obtained having

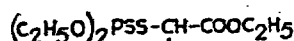
$$n_D^{20} : 1.5269; D_{20}^{20} : 1.1355$$

- 10 The analysis confirms that this product is the ethyl ester of O,O - diisopropyl - dithiophosphoryl - phenylacetic acid, having the formula



- 30 b.p._{0.05} 158—160° C. $n_D^{20} : 1.5470$ D_{20}^{20} 1.2381

The analysis confirms that this product is the ethyl ester of O,O - diethyl - dithiophosphoryl - *p* - chlorophenyl - acetic acid, having the formula



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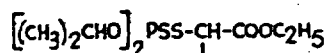
(X)

EXAMPLE 6

- 23.5 g. O,O - diisopropyl - dithiophosphoric acid dissolved in 100 cc acetone are neutralised with 6.8 g. anhydrous sodium carbonate. 23.2 g. ethyl - α - *p* - chlorophenyl - α - chloroacetate are added. The mixture is heated under reflux for 2 hours and the acetone is distilled off. After cooling, the mass is poured into 400 g. ice; the oil which separates is extracted with ether; the ether extract is neutralised by shaking it with a NaHCO_3 solution and is dried, the solvent is then evaporated under vacuum on a boiling water bath. The residue, amounting to 37.7 g. is a yellow oil, having

- 50 n_D^{20} 1.5332; D_{20}^{20} 1.1914

The analysis confirms that this product is the ethyl ester of O,O - diisopropyl - dithiophosphoryl - *p* - chlorophenylacetic acid, having the formula



55



(XI)

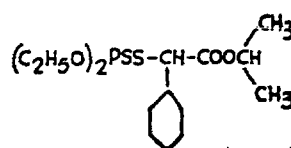
EXAMPLE 5

- 20.4 g. of distilled O,O - diethyl - dithiophosphoric acid dissolved in 100 cc acetone are neutralised with 5.7 g anhydrous sodium carbonate. The excess carbonate is removed by decanting and 23.2 g. ethyl - α - *p* - chlorophenyl - α - chloroacetate are added to the acetone solution. After one night, the mixture is heated under reflux for 2 hours, then the acetone is distilled off. After cooling, the mass is treated with ice-water, neutralised with a small amount of NaHCO_3 and extracted with ether. The ether extract is dried over MgSO_4 and the solvent is distilled off. 32.3 g. of oil are obtained. The oil is distilled at 0.05 mm Hg pressure and has

EXAMPLE 7

- 27 g. O,O - diethyl - dithiophosphoric acid dissolved in 150 cc ethyl alcohol are neutralised with 8 g. anhydrous sodium carbonate. The solution is stirred for half an hour, then is filtered and treated with 33 g. isopropyl α - phenyl - α - bromoacetate. After one night, the mixture is heated under reflux for 2 hours and then treated with water. The oil which separates is shaken with NaHCO_3 solution to pH 7; during this treatment it solidifies almost completely. The mixture is filtered by suction and the product is washed on the filter with water. 38 g. of white crystals are obtained. After recrystallisation from ligroin, the product has m.p. 53° C.

The analysis confirms that this product is the isopropyl ester of O,O - diethyl - dithiophosphoryl - phenylacetic acid, having the formula



(XII)

EXAMPLE 8

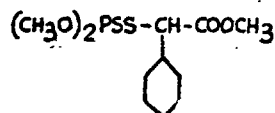
- 29 g. crude O,O - dimethyl - dithiophosphoric acid dissolved in 150 cc dioxane are neutralised with 10 g. anhydrous sodium carbonate. The mixture is stirred for half an hour and 37.5 g. methyl α - phenyl - α - bromoacetate are added. The mass is heated at 70—80° C. for 2 hours. After one night, the NaCl formed is filtered off and the filtrate is diluted with water. The oil which separates is dried over MgSO_4 . 40 g. of a straw-coloured oil are obtained. By distillation at 0.15 mm Hg pressure, this oil yields 75% of a product with b.p. (0.15) = 161° C.

90

The distilled product has

$$n_D^{20} 1.5631 \quad D_{20}^{20} 1.2656$$

- 5 The analysis confirms that this product is the methyl ester of O,O - dimethyl - dithiophosphorylphenylacetic acid, having the formula



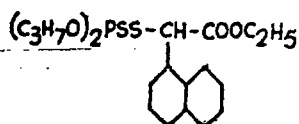
(XIII)

EXAMPLE 9

- 10 9.5 g. O,O - diisopropyl - dithiophosphoric acid dissolved in 50 cc acetone are neutralised with 2.4 g. anhydrous sodium carbonate. The undissolved sodium carbonate is separated by decanting and to the acetone solution 10 g. of ethyl α - naphthyl - α - chloroacetate are added. Sodium chloride separates slowly. The mixture is heated under reflux for 2 hours. The solvent is distilled off, ice-water is added and the mixture is extracted with ether. The ether solution is neutralised with sodium carbonate, shaken with water and dried over anhydrous magnesium sulphate. The solvent is evaporated under vacuum on a boiling water bath. 14.6 g of a dense reddish oil are left, having

$$n_D^{20} 1.5714 \quad D_{20}^{20} 1.1682$$

- 25 The analysis confirms that this product is the ethyl ester of O,O - diisopropyl - dithiophosphorylnaphthylacetic acid, having the formula



(XIV)

- 30 Results of an evaluation of the biological activity of the above Examples. The products of the general formula (II)

have proved to possess interesting biological properties that render them suitable to be used for the control of parasites.

The following examples will serve to better illustrate these properties without limiting however, in any way, the scope of the present invention. 35

Musca domestica

By topical application, by means of a micro-syringe, of acetone solutions of the products under examination, to five days old flies, the average per cent mortalities indicated in Table 1 were obtained after 20 hours. 40

On tarsal absorption, by introducing five days old female flies into beakers previously treated with controlled amounts of benzene solutions of the active substances under examination, and leaving the flies in contact with these substances for 20 hours, the mortalities indicated in Table 2 were observed. 45 50

Aphis fabae

By nebulizing a population of aphides, apterous virginoparous females, on bean plants under standardized conditions with suitably formulated aqueous dispersions of the compounds under examination, the average mortalities indicated in Table 3 were obtained after 24 hours. 55

Tetranychus telarius

By nebulizing a mixed population of mites in various stages of growth on bean plants under standardized conditions with suitably formulated aqueous dispersions of the substances under examination, the average mortalities indicated in Table 4 were obtained after 24 hours. 60 65

Nebulization of mite eggs gave the average mortalities indicated in Table 5.

Moreover, the LD 50 and LD 95 expressed in various units of measurement were determined by the same technique for the various applications and the results are listed in Table 6. 70

TABLE I

γ /fly	50	10	2	0.4	Example
% mortality after 20 hours					
Ethyl O,O-diethyl-dithiophosphoryl-phenylacetate	—	—	—	100	1
Ethyl O,O-diethyl-dithiophosphoryl-4-nitrophenylacetate	—	—	100	96	2
Ethyl O,O-dimethyl-dithiophosphoryl-phenylacetate	—	—	100	100	3
Ethyl O,O-diisopropyl-dithiophosphoryl-phenylacetate	—	100	100	0	4
Ethyl O,O-diethyl-dithiophosphoryl-4-chlorophenylacetate	—	—	—	100	5
Isopropyl O,O-diethyl-dithiophosphoryl-phenylacetate	—	—	—	100	7
Methyl O,O-dimethyl-dithiophosphoryl-phenylacetate	—	—	100	91	8
Ethyl O,O-diisopropyl-dithiophosphorylnaphthylacetate	—	17	1	0	9

TABLE 2

gr/m ²	0.005	0.025	0.125	Example
	% mortality after 20 hours			
Ethyl O,O-diethyl-dithiophosphoryl-phenylacetate	100	—	—	1
Ethyl O,O-diethyl-dithiophosphoryl-4-nitrophenylacetate	100	—	—	2
Ethyl O,O-dimethyl-dithiophosphoryl-phenylacetate	100	—	—	3
Ethyl O,O-diisopropyl-dithio-phosphorylphenylacetate	45	100	—	4
Ethyl O,O-diethyl-dithiophosphoryl-4-chlorophenylacetate	99	100	—	5
Isopropyl O,O-diethyl-dithio-phosphorylphenylacetate	100	—	—	7
Methyl O,O-dimethyl-dithio-phosphorylphenylacetate	100	—	—	8
Ethyl O,O-diisopropyl-dithio-phosphorylnaphthylacetate	0	9	97	9

TABLE 3

conc. % active substance	0.5	0.1	0.02	Example
	% mortality after 24 hours			
Ethyl O,O-diethyl-dithio- phosphorylphenylacetate	—	—	100	1
Ethyl O,O-diethyl-dithiophosphoryl- 4-nitrophenylacetate	98	60	10	2
Ethyl O,O-dimethyl-dithio- phosphorylphenylacetate	100	97	60	3
Ethyl O,O-diisopropyl-dithio- phosphorylphenylacetate	45	15	0	4
Ethyl O,O-diethyl-dithiophosphoryl- 4-chlorophenylacetate	100	90	10	5
Isopropyl O,O-diethyl-dithio- phosphorylphenylacetate	—	—	100	7
Methyl O,O-dimethyl-dithio- phosphorylphenylacetate	100	92	20	8
Ethyl O,O-diisopropyl-dithio- phosphorylnaphthylacetate	16	3	0	9

TABLE 4

conc. % active substance	0.5	0.1	0.02	Example
% mortality after 24 hours				
Ethyl O,O-diethyl-dithio-phosphorylphenylacetate	—	100	98	1
Ethyl O,O-diethyl-dithiophosphoryl-4-nitrophenylacetate	—	100	98	2
Ethyl O,O-dimethyl-dithio-phosphorylphenylacetate	—	—	100	3
Ethyl O,O-diisopropyl-dithio-phosphorylphenylacetate	100	15	0	4
Ethyl O,O-diethyl-dithiophosphoryl-4-chlorophenylacetate	—	100	98	5
Isopropyl O,O-diethyl-dithio-phosphorylphenylacetate	—	—	100	7
Methyl O,O-dimethyl-dithio-phosphorylphenylacetate	—	—	100	8
Ethyl O,O-diisopropyl-dithio-phosphorylnaphthylacetate	100	76	2	9

TABLE 5

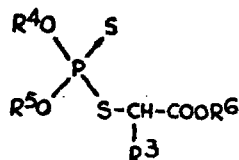
conc. % Active substance	0.5	0.25	0.125	Example
% mortality after 6 days				
Ethyl O,O-diethyl-dithio-phosphorylphenylacetate	100	98	75	1
Ethyl O,O-diethyl-dithiophosphoryl-4-nitrophenylacetate	99	91	87	2
Ethyl O,O-dimethyl-dithio-phosphorylphenylacetate	—	—	100	3
Ethyl O,O-diisopropyl dithiophosphorylphenylacetate	100	98	45	4
Ethyl O,O-diethyl-dithiophosphoryl-4-chlorophenylacetate	—	100	92	5
Isopropyl O,O-diethyl-dithio-phosphorylphenylacetate	—	—	100	7
Methyl O,O-dimethyl-dithio-phosphorylphenylacetate	87	65	15	8
Ethyl O,O-diisopropyl-dithio-phosphorylnaphthylacetate	80	22	2	9

TABLE 6

Formula	Activity <i>Musca domestica</i>		Activity on <i>A. fabae</i> , LD 95 in % active substance	Activity on <i>T. telarius</i> LD 95 in % active substance	Activity on eggs of <i>T. telarius</i> LD 95 in % active substance	Example
	Topical, LD 50 in γ active substance/fly	Tarsal, LD 50 in gr. active substance/sq. m.				
Ethyl O,O-diethyl-dithio-phosphorylphenylacetate	0.092	0.00038	0.02	0.0005	0.17	1
Ethyl O,O-diethyl-dithio-phosphoryl-4-nitrophenylacetate	0.22	0.0024	0.20	0.0015	0.14	2
Ethyl O,O-dimethyl-dithio-phosphorylphenylacetate	0.02	0.0009	0.055	0.0004	0.25	3
Ethyl O,O-diethyl-dithio-phosphoryl-4-chlorophenylacetate	0.22	0.0014	0.16	0.00065	0.1	5

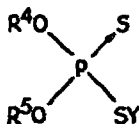
WHAT WE CLAIM IS:—

1. A process for the preparation of an O,O-dialkyl - dithiophosphorylacetic ester, having the general formula



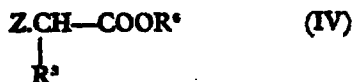
(II)

(wherein R⁴, R⁵ and R⁶ are like or different and each is a saturated or unsaturated, straight- or branched-chain alkyl radical, and R³ is a substituted or unsubstituted aryl radical), which comprises reacting a salt of an O,O-dialkyl-dithiophosphoric ester, having the general formula



(III)

(wherein R⁴ and R⁵ are as defined and Y is ammonium or an alkali metal, or an alkaline-earth metal), with an α-halogeno - α - aryl-acetic ester, having the general formula



(wherein R⁷ and R⁸ are as defined and Z is Cl, Br or I) in the presence of a solvent for either or both reactants.

2. A modification of the process according to Claim 1, wherein the α-halogeno - α - aryl-acetic ester (IV) is reacted with the free acid of the O,O-dialkyl - dithiophosphoric ester (i.e. (III), wherein Y=H) in the presence of a solvent for either or both reactants and in the additional presence of a base sufficiently basic to neutralise said acid.

3. A process according to Claim 2, wherein the base employed is an alkali or alkaline-earth metal hydroxide, carbonate or bicarbonate.

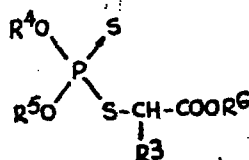
4. A process according to any one of Claims 1 to 3 in which R³ is a naphthyl radical or a substituted aryl radical.

5. A process according to any one of Claims 1 to 3 in which at least one of R⁴, R⁵ and R⁶ is a saturated branched chain radical.

6. A process according to any of the preceding Claims, wherein the solvent employed

is water, an alcohol, a ketone, an ester, dioxane, or an aromatic hydrocarbon.

7. As a novel product, an O,O - dialkyl-dithiophosphorylacetic ester, having the general formula



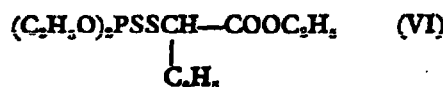
(II)

(wherein R⁴, R⁵ and R⁶ are like or different and each is a saturated or unsaturated, straight- or branched-chain alkyl radical and R³ is a substituted or unsubstituted aryl radical).

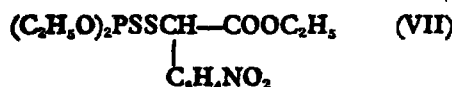
8. An O,O - dialkyl - dithiophosphorylacetic ester according to Claim 7, in which R³ is a naphthyl radical or a substituted aryl radical.

9. An O,O - dialkyl - dithiophosphorylacetic ester according to Claim 7, in which at least one of R⁴, R⁵, R⁶ is a saturated branched-chain radical.

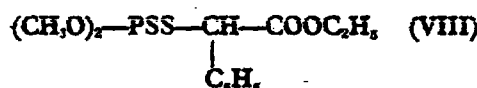
10. As a novel product, the ethyl ester of O,O - diethyl - dithiophosphorylphenylacetic acid having the formula



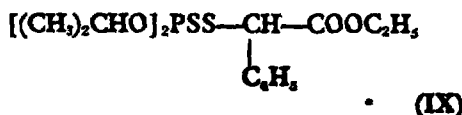
11. As a novel product, the ethyl ester of O,O-diethyl dithiophosphoryl - p - nitrophenyl acetic acid, having the formula



12. As a novel product, the ethyl ester of O,O - dimethyl - dithiophosphorylphenylacetic acid, having the formula

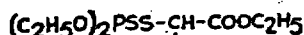


13. As a novel product, the ethyl ester of O,O - diisopropyl - dithiophosphorylphenylacetic acid, having the formula



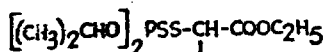
14. As a novel product, the ethyl ester of O,O - diethyl - dithiophosphoryl - p - chlorophenylacetic acid, having the formula





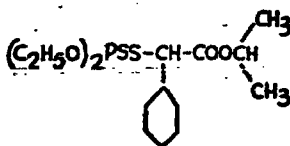
(X)

15. As a novel product, the ethyl ester of O,O - diisopropyl - dithiophosphoryl - *p*-chlorophenylacetic acid, having the formula



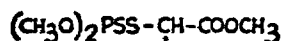
(XI)

16. As a novel product, the isopropyl ester of O,O - diethyl - dithiophosphorylphenyl - acetic acid, having the formula



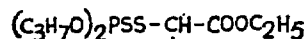
(XII)

17. As a novel product, the methyl ester of O,O - dimethyl - dithiophosphorylphenylacetic acid, having the formula



(XIII)

18. As a novel product, the ethyl ester of O,O - diisopropyl - dithiophosphorylnaph - thylacetic acid, having the formula



(XIV)

19. The process for the preparation of an O,O - dialkyl - dithiophosphorylacetic ester, substantially as described in any of the foregoing Examples 1—9.

20. An O,O - dialkyl - dithiophosphorylacetic ester, whenever prepared or produced by the process claimed in any of Claims 1—6 or Claim 19, or its obvious chemical equivalent.

21. A disinfecting composition comprising one or more esters as claimed in any of Claims 7—18 or Claim 20, either as sole active substances or in admixture with one or more of the known disinfecting compounds, such as insecticides, and/or fungicides, and/or in admixture with one or more nutritive substances for plants, and/or fertilisers.

ERIC POTTER & CLARKSON,

Chartered Patent Agents,
317 High Holborn, London, W.C.1.

Reference has been directed, in pursuance of Section 8 of the Patents Act, 1949, to Specification 803,441.

ERRATA

SPECIFICATION NO. 834,814

Page 1, Heading for "a - Substituted" read "q - Substituted"

Page 1, line 35, for "R⁶ and R⁵" read "R⁵ and R⁶"

Page 9, line 14, for "wherein" read "(wherein"

Page 9, line 65, after "diethyl" insert "-"

THE PATENT OFFICE,
14th June, 1960.

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