1,081,249

PATENT SPECIFICATION

NO DRAWINGS

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Int. Cl.:—C 07 f 9/02 // A 01 n

COMPLETE SPECIFICATION

New Phosphorus-Containing Esters

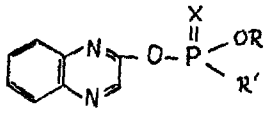
We, FARBENFABRIKEN BAYER AKTIENGESELLSCHAFT, a body corporate organised under the laws of Germany, of Leverkusen, Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention is concerned with new phosphorus-containing esters of 2-hydroxyquinoxaline, which have insecticidal and acaricidal properties, and with the preparation thereof.

Open chain and cyclic quinoxaline-2,3-thiophosphoric acid esters are already known from Patent Specification No. 894,163. These products are obtained by reacting the corresponding 2,3-dimercaptoquinoxalines with alkyl- or arylphosphoric or thionophosphoric acid monoester dihalides or diester monohalides.

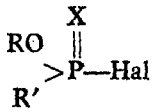
According to this Patent Specification, the compounds in question are characterised by a good insecticidal and acaricidal activity; they have an especially strong action against resistant spider mites. However, the production of this group of active compounds is comparatively difficult, at least on an industrial scale.

We have now found that phosphorus-containing esters of the general formula:—



(I)

are obtained in a smooth reaction and in very good yields, when 2-hydroxy-quinoxaline is reacted with phosphorus-containing ester halides of the general formula:—



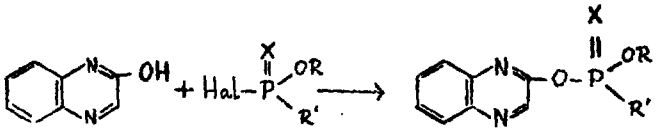
(II)

In the above formulae, R is an alkyl radical containing 1 to 4 carbon atoms, R′ is an alkyl radical containing 1 to 4 carbon atoms, an alkoxy radical having up to four carbon atoms, or a phenyl radical, X is an oxygen or sulphur atom and Hal is a halogen atom.

The new compounds of general formula (I) have strong insecticidal and acaricidal properties. They have an excellent activity against eating and sucking insects, as well as an outstanding activity against spider mites and ticks. The compounds according to the present invention are, in this respect, superior to the known products of analogous

constitution and the same type of activity; therefore they ~~constitue~~ constitute a genuine enrichment of the art.

The process according to the present invention takes place according to the following equation:—



In the above equation, R, R', X and Hal have the same meanings as above.

However, R preferably stands for an alkyl radical containing 1 to 3 carbon atoms, such as a methyl, ethyl, *n*-propyl or isopropyl radical; R' preferably denotes a radical OR or a methyl, ethyl or *n*- or isopropyl radical or a phenyl radical; X is preferably a sulphur atom and Hal is preferably a chlorine atom.

The process according to the present invention is preferably carried out with the concurrent use of suitable solvents or diluents. Practically all inert organic solvents or mixtures thereof can be used for this purpose, such as optionally halogenated hydrocarbons, for example, benzine, benzene, toluene, chlorobenzene and xylene; ethers, for example, diethyl ether, dibutyl ether and dioxan; and ketones, for example, acetone, methyl ethyl ketone, methyl isopropyl ketone and methyl isobutyl ketone. However, low boiling aliphatic alcohols, for example, methanol or ethanol, and, in particular, nitriles, for example, acetonitrile and propionitrile, as well as dimethyl formamide, have proved to be especially suitable for this purpose.

Furthermore, the reaction according to the present invention is preferably carried out in the presence of acid acceptors. Practically all customary acid-binding agents can be used for this purpose. Alkali metal alcoholates and carbonates, such as potassium and sodium methylate and ethylate, and sodium and potassium carbonate, as well as tertiary aromatic and heterocyclic amines, for example, triethylamine, dimethyl aniline and pyridine, have proved especially useful.

The reaction temperature may be varied within a fairly wide range. In general, the reaction is carried out between 20 and 120°C. (or the boiling point of the reaction mixture), preferably at 40 to 80°C.

The starting materials and the auxiliaries (acid-binding agents) are generally used in stoichiometric quantities. After the starting components have been mixed together, it is advantageous to continue heating the reaction mixture for some time (about 1 to 3 hours), possibly with stirring, in order to complete the reaction. By this method, the products of the present process are obtained in excellent yields and with a high degree of purity.

Some of the esters according to the invention are colourless crystals with a sharp melting point; if necessary, these can easily be further purified by recrystallisation from conventional solvents. In most cases, however, the compounds are colourless to yellow coloured, viscous, water-insoluble oils which cannot be distilled ~~with~~ without decomposition but can be freed from the last volatile components and purified in this way by a so-called "partial distillation", i.e. by prolonged heating at moderately elevated temperatures under reduced pressure. Determination of the refractive index may serve for a more specific characterisation.

As has already been mentioned above, the products of the present process are characterised by an outstanding insecticidal and acaricidal activity. At the same time, they have only a low toxicity towards warm-blooded animals and a low phytotoxicity. The effect appears rapidly and is long-lasting. The compounds according to the present invention can, therefore, be used with good results in plant protection for combating noxious sucking and eating insects and *Diptera* and in this field, as well as in veterinary medicine, against mites (Acarina). The excellent activity of the new compounds against strains of spider mites which are resistant to phosphoric acid esters is to be especially emphasised.

The sucking insects essentially include aphids, such as the peach aphid (*Myzus persicae*) and the black bean aphid (*Doralis fabae*); coccids, such as *Aspidiotus hederae*, *Lecanium hesperidum* and *Pseudococcus maritimus*; *Thysanoptera*, such as *Hercinothrips femoralis*; and bugs, such as the beet bug (*Piesma quadrata*) and the bed bug (*Cimex lectularius*).

The eating insects essentially include butterfly larvae, such as *Plutella maculipennis* and *Lymantria dispar*); beetles, such as grain weevils (*Sitophilus granarius*) and the Colorado beetle (*Leptinotarsa decemlineata*); and also species living in the soil, such

as wire worms (*Agriotes sp.*) and cockchafer larvae (*Melolontha melolontha*); cockroaches, such as the German cockroach (*Blatella germanica*); *Orthoptera,* such as the cricket (*Gryllus domesticus*); termites, such as *Reticulitermes*; and *Hymenoptera,* such as ants.

The *Diptera* mainly comprise the flies, such as the fruit fly (*Drosophila melanogaster*), the Mediterranean fruit fly (*Ceratitis capitata*) and the house fly (*Musca domestica*); gnats, such as the mosquito (*Aedes aegypti*); bluebottle flies, such as the gold fly (*Lucilia sericata*); and blowflies (*Chrysomya chloropyga*).

Among the mites, the spider mites (*Tetranychidae*) are of special importance, such as the common spider mite (*Tetranychus urticae*) and the fruit tree spider mite (*Paratetranychus pilosus*); gall mites, such as the red currant gall mite (*Eriophyes ribis*) and tarsonemides, such as *Tarsonemus pallidus*; and also ticks, such as *Boöphilus microplus* and scab mites.

For use as plant protective and pest control agents, the active compounds according to the present invention can be converted into the usual formulations, such as solutions, emulsions, suspensions, powders, pastes and granulates. These are produced in known manner, for example, by mixing the active compounds with extenders, i.e. liquid and solid diluents and carriers, optionally with the use of surface-active agents and/or dispersion agents. In the case of the use of water as an extender, organic solvents, can, for example, also be used as auxiliary solvents.

As liquid diluents or carriers, there are preferably used aromatic hydrocarbons, such as xylenes or benzene, chlorinated aromatic hydrocarbons, such as chlorobenzenes, paraffins, such as mineral oil fractions, alcohols, such as methanol or butanol, and strongly polar solvents, such as dimethyl formamide or dimethyl sulphoxide, as well as water.

As solid diluents or carriers, there are preferably used ground natural minerals, such as kaolins, clays, talc and chalk, and ground synthetic minerals, such as highly-dispersed silicic acid and silicates.

Preferred examples of emulsifying agents include non-ionic and anionic emulsifiers, such as polyoxyethylene-fatty acid esters, polyoxyethylene-fatty alcohol ethers, for example, alkyl aryl polyglycol ethers, alkyl sulphonates and aryl sulphonates; and preferred examples of dispersing agents include lignin, sulphite waste liquors and methyl cellulose.

The active compounds according to the present invention can be present in the formulation in admixture with known active ingredients.

In general, the formulations contain between 0.1 and 95, preferably between 0.5 and 90, per cent by weight of active compound.

The active compounds can be used as such, in the form of their formulations or of the preparations made therefrom for application, such as solutions, emulsifiable concentrates, emulsions, suspensions, spray powders, pastes, soluble powders, dusts and granules ready for use. Application is carried out in the usual manner, for example, by watering, spraying, atomising, fumigating, scattering, dusting, or vaporising.

Thus, according to the present invention there are also provided insecticidal and acaricidal compositions, comprising a compound of general formula (I) in admixture with a solid or liquid diluent or carrier.

There is also provided, according to the present invention, a method of combating insects and acarids, wherein there is applied to an insect or acarid habitat a compound of general formula (I), alone or in admixture with a solid or liquid diluent or carrier.

The outstanding insecticidal and acaricidal activity of the new compounds of the present invention can be seen from the following Examples:—

EXAMPLE A

Doralis test (contact action)

Solvent: 3 parts by weight acetone

Emulsifier: 1 part by weight alkylaryl polyglycol ether

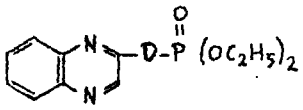
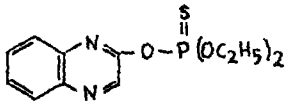
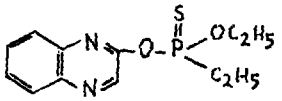
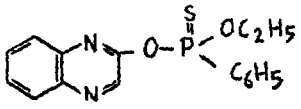
To produce a suitable preparation of active compound, 1 part by weight of the active compound is mixed with the stated amount of solvent containing the stated amount of emulsifier, and the concentrate is diluted with water to the desired concentration.

Bean plants (*Vicia faba*) which have been heavily infested with black bean aphids (*Doralis fabae*) are sprayed with the preparation of the active compound until dripping wet.

After the specified periods of time, the degree of destruction is determined as a percentage: 100% means that all the aphids are killed, whereas 0% means that none are killed.

The active compounds, their concentrations, the evaluation times and the results obtained can be seen from the following Table:

TABLE
(plant damaging insects)

Active compound	Concentration of active compound %	Degree of destruction after 24 hours %
	0.01 0.001	100 20
	0.001	100
	0.001 0.0001	100 95
	0.1 0.01 0.001	100 98 60

EXAMPLE B
Tetranychus test

Solvent: 3 parts by weight acetone
Emulsifier: 1 part by weight alkylaryl polyglycol ether.

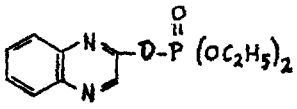
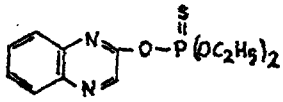
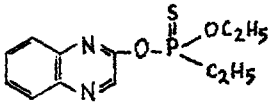
To produce a suitable preparation of active compound 1 part by weight of the active compound is mixed with the stated amount of solvent containing the stated amount of emulsifier, and the concentrate is diluted with water to the desired concentration.

Bean plants (*Phaseolus vulgaris*), which have a height of approximately 10—30 cm., are sprayed with the preparation of the active compound until dripping wet. The bean plants are heavily infested with common spider mites (*Tetranychus urticae*) in all stages of development.

After the specified periods of time, the effectiveness of the preparation of active compound is determined by counting the dead mites. The degree of destruction is expressed as a percentage: 100% means that all the spider mites are killed, whereas 0% means that none are killed.

The active compounds, their concentrations, the evaluation times and the results obtained can be seen from the following Table:

TABLE
(plant damaging mites)

Active compound	Concentration of active compound %	Degree of destruction after 48 hours %
	0.1 0.01	100 60
	0.1 0.001	100 40
	0.01	100

EXAMPLE C
Plutella test

Solvent: 3 parts by weight acetone
Emulsifier: 1 part by weight alkylaryl polyglycol ether.

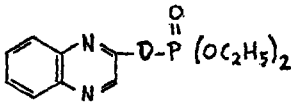
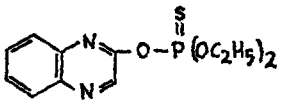
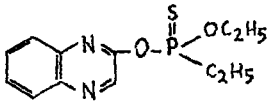
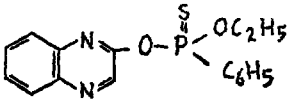
To produce a suitable preparation of active compound, 1 part by weight of the active compound is mixed with the stated amount of solvent containing the stated amount of emulsifier, and the concentrate is diluted with water to the desired concentration.

Cabbage leaves (*Brassica oleracea*) are sprayed with the preparation of the active compound until dew moist, and are then infested with caterpillars of the diamond-back moth (*Plutella maculipennis*).

After the specified periods of time, the degree of destruction is determined as a percentage: 100% means that all the caterpillars are killed, whereas 0% means that none are killed.

The active compounds, their concentrations, the evaluation times and the results obtained can be seen from the following Table:

TABLE
(plant damaging insects)

Active compound	Concentration of active compound %	Degree of destruction after 4 days %
	0.001 0.0001	100 80
	0.0001	100
	0.0001 0.00001	100 20
	0.001 0.0001	100 75

EXAMPLE D
Boophilus test

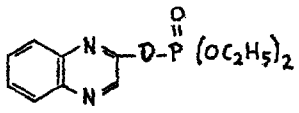
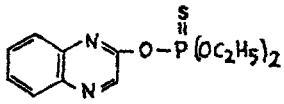
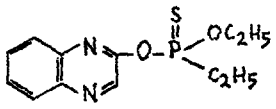
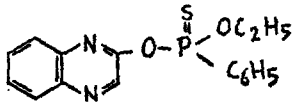
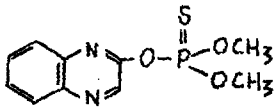
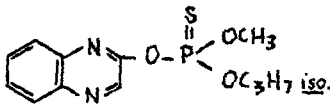
Solvent: 3 parts by weight acetone
Emulsifier: 1 part by weight alkylaryl polyglycol ether

To produce a suitable preparation of active compound, 1 part by weight of the active compound is mixed with the stated amount of the solvent, the stated amount of emulsifier is added, and the concentrate diluted with water to the desired concentration.

Ten female ticks (*Boöphilus microplus*) are placed on a small cotton pad which is subsequently immersed in the preparation of active compound. After one minute, the cotton pad is removed from the solution and placed in a glass disc containing filter paper. The ticks are removed from the cotton pad and placed on dry filter paper. After the specified periods of time, the degree of destruction is determined as a percentage: 100% means that all the ticks are killed, whereas 0% means that none are killed.

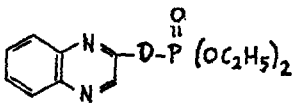
The active compounds, their concentrations and the results obtained can be seen from the following Table:

TABLE
(plant damaging insects)

Active compound	Concentration of active compound %	Degree of destruction after 72 hours %
	0.5 0.05	100 25
	0.0025 0.0005	100 50
	0.0005 0.00025	100 65
	0.001 0.00025	100 55
	1.0	100
	0.0005 0.00025	100 50

The following Examples are given for the purpose of illustrating the present invention: —

EXAMPLE 1



59 grams (0.4 mol) 2-hydroxyquinoxaline are heated under reflux, together with an equimolar amount of dried, finely sieved potassium carbonate, in 350 ml. acetonitrile for 15 minutes, while stirring, and 69 g. O,O-diethylphosphoric acid ester chloride are subsequently added dropwise to the reaction mixture at 50 to 55°C.

The reaction mixture is stirred for a further 2 hours at 75°C., allowed to cool, mixed with 500 ml. benzene and the soluble components are washed out by shaking several times with water. The organic phase is dried over sodium sulphate and the solvent evaporated under reduced pressure, finally using a so-called "partial distillation" at 70°C. and 0.1 mm Hg.

In this way, 94 g. (83.5% of theory) O,O-diethylphosphoric acid-O-[quinoxalyl-(2)] ester are obtained in the form of a yellowish oil which cannot be distilled without decomposition and has refractive index n_{25}^{D} 1.5383.

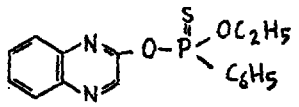
Analysis:

Calculated for $C_{12}H_{15}N_2O_4P$ (molecular weight 282.2):

N 9.92% P 10.97%

N 10.15% P 11.12%

EXAMPLE 2



44 grams (0.3 mol) 2-hydroxyquinoxaline are stirred with 750 ml. dimethyl formamide and an equivalent amount of a methanolic sodium methylate solution is added to this mixture, which is then concentrated under reduced pressure to a volume of 200 ml.

The resultant solution is mixed dropwise at 60°C. with 66 g. phenyl-thionophosphonic acid-O-ethyl ester chloride and subsequently further stirred at 75 to 80°C. for two hours. Working up of the reaction mixture as in Example 1 gives 85 g. (86% of theory) phenyl-thionophosphonic acid-O-ethyl-O-[quinoxalyl-(2)] ester in the form of white crystals which melt at 142°C., after recrystallisation from benzene/ligroin.

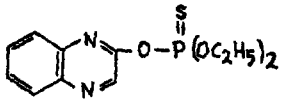
Analysis:

Calculated for $C_{16}H_{15}N_2O_3PS$ (molecular weight 330.4):

P 9.39% S 9.71%

Found P 9.75% S 9.89%.

EXAMPLE 3:



51 grams (0.35 mol) of 2-hydroxyquinoxaline are stirred into 400 ml. acetonitrile and briefly boiled with 36 g. triethylamine. 66 grams O,O-diethyl-thionophosphoric acid ester chloride are added dropwise to this mixture, which is subsequently stirred for a further two hours, while boiling under reflux. Working up of the reaction mixture is carried out in the manner described in Example 1. 85 grams (81.5% of theory) O,O-diethyl-thionophosphoric acid-O-[quinoxalyl-(2)]ester are obtained in the form of a dark-yellow oil of refractive index n_{25}^{D} 1.5624, which decomposes when distilled. The oil crystallizes upon standing for a longer time. The solid production be recrystallized from ligroin and melts at 35 to 36°C.

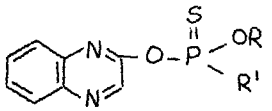
Analysis:

Calculated for $C_{12}H_{15}N_2O_3PS$ (molecular weight 298.3):

P 10.38% S 10.75%

Found: P 10.56% S 10.75%

EXAMPLE 4:
The following compounds of the general formula:—

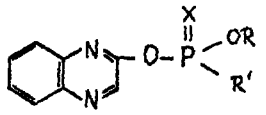


are obtained in a manner analogous to that described in Examples 1 to 3.

R	R'	Empirical formula	Molecular weight	Analysis		Yield % of theory	Physical constants
				calc.	found		
CH_3	OCH_3	$C_{10}H_{11}N_2O_3PS$	270.2	P 11.46%	P 11.73%	71 n^D_{25}	1.5573
				S 11.87%	S 12.60%		
i—C_3H_7	OCH_3	$C_{12}H_{15}N_2O_3PS$	298.1	P 10.38%	P 9.56%	82 n^D_{25}	1.5603
				S 10.70%	S 9.99%		
C_2H_5	CH_3	$C_{11}H_{13}N_2O_2PS$	268.2	P 11.60%	P 13.10%	69 n^D_{25}	1.5768
				S 11.90%	S 13.40%		
C_2H_5	C_2H_5	$C_{12}H_{15}N_2O_2PS$	282.3	P 10.90%	P 11.7%	78 n^D_{25}	1.5802
				S 11.36%	S 11.25%		

WHAT WE CLAIM IS:—

1. Phosphorus-containing esters of the general formula:—



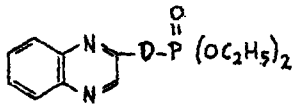
wherein

R is an alkyl radical containing 1 to 4 carbon atoms,

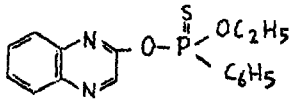
R′ is an alkyl radical containing 1 to 4 carbon atoms, an alkoxy radical having up to 4 carbon atoms, or a phenyl radical, and

X is an oxygen or sulphur atom.

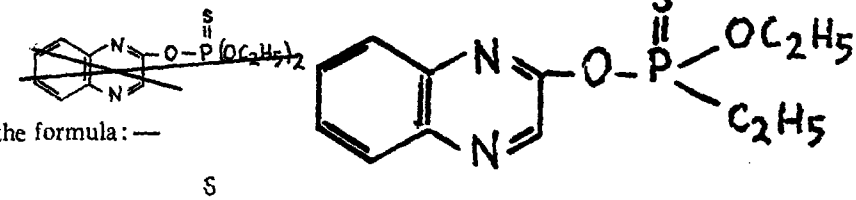
2. The compound of the formula:—



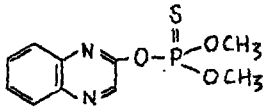
3. The compound of the formula:—



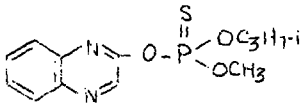
4. The compound of the formula:—



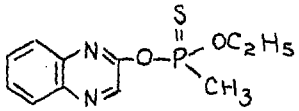
5. The compound of the formula:—



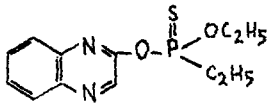
6. The compound of the formula:—



7. The compound of the formula:—



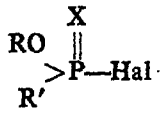
8. The compound of the formula:—



9. Process for the preparation of compounds of the general formula given in claim 1, wherein 2-hydroxy-quinoxaline is reacted with an ester halide of the general formula:—

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* C L M S *



in which R, R′ and X have the same meanings as in claim 1 and Hal is a halogen atom.

10. Process according to claim 9, wherein the reaction is carried out in a solvent or diluent.

11. Process according to claim 9 or 10, wherein the reaction is carried out in the presence of an acid acceptor.

12. Process according to any of claims 9—11, wherein the reaction is carried out at a temperature between 20 and 120°C.

13. Process according to claim 12, wherein the reaction is carried out at a temperature between 40 and 80°C.

14. Process for the preparation of compounds of the general formula given in claim 1, substantially as hereinbefore described and exemplified.

15. Compounds of the general formula given in claim 1, whenever prepared by the process according to any of claims 9—14.

16. Insecticidal and acaricidal compositions comprising, as active ingredient, a compound of the general formula given in claim 1, in admixture with a solid or liquid diluent or carrier.

17. Method of combating insects and acarids, wherein there is applied to an insect or acarid habitat a compound of the general formula given in claim 1, alone or in admixture with a solid or liquid diluent or carrier.

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