EUROPEAN QUALIFYING EXAMINATION 1992

PAPER A
CHEMISTRY

This paper comprises:

INSTRUCTIONS TO CANDIDATES

You are to assume that you have received the annexed letter from your client including a description of an invention for which he wishes you to obtain a European patent together with references to the most pertinent prior art known to your client.

You should accept the facts given in the paper and base your answers upon such facts. Whether and to what extent these facts are used is your responsibility.

You should not use any special knowledge you may have of the subject-matter of the invention, but are to assume that the prior art given is in fact exhaustive.

Your task is to draft an independent claim (or claims) offering the applicant the broadest protection possible while at the same time having a good chance of succeeding before the EPO. In drafting your claim(s) you should bear in mind the need for inventive activity over the prior art indicated, the requirements of the Convention as to the form of claims, other requirements of the Convention and the recommendations made in the Guidelines for Examination in the EPO. Dependent claims should be kept to a reasonable number and so drafted as to enable you to fall back upon them should the independent claim(s) fail.

You are also expected to draft an introduction, i.e. that part of the description which precedes the examples or the explanation of the drawings. The introduction should be sufficient to provide support for all claims. In particular, you should consider the advisability of mentioning advantages of the invention in the introduction.

You are expected to draft claims and an introduction for one European patent application only. If you find that the requirements of the Convention as to unity would in practice cause you to make any of these claims the subject of a separate patent application, you should indicate that separately without further elaboration in this respect.

In addition to your elaborated solution, you may - but this is not mandatory - give, on a separate sheet of paper, the reasons for your choice of solution, for example, why you selected a particular form of claim, a particular feature for an independent claim, a particular piece of prior art as starting point or why you rejected or preferred some piece of prior art. Any such statement should however be brief.

It is assumed that you have studied the examination paper in the language in which you have given your answer. If this is not so, please indicate on the front page of your answer in which language you have studied the examination paper. This always applies to candidates who - after having filed such a request when enrolling for the examination - give their answer in a language other than German, English or French.

Different sets of claims for those states which have made reservations under Article 167 (2) EPC are not required.

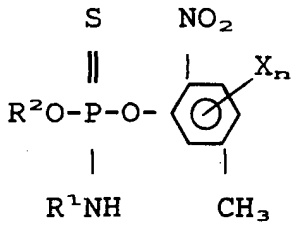
Client's letter

Our researches into weed control, which is one of the areas we operate in, have led to the development of new herbicides containing amido thionophosphoric acid esters. We therefore ask you to file an application for a European patent in respect of our invention described below.

A known compound of this type used until now to control unwanted vegetable growth is, for example, O-methyl-N-isopropylamido-O-(2,4-dichlorophenyl)-thionophosphoric acid ester (see Document I). Chlorine-containing compounds of this type have the disadvantage of being toxic to useful plants.

Another substance with a similar structure - O-methyl-N-isopropylamido-O-(4-nitrophenyl)-thionophosphoric acid ester - which is described in Document II and has also already been used for weed control, displays this disadvantage to a far lesser degree but in order to be properly effective has to be used in relatively concentrated form.

The novel herbicides developed by us are compounds represented by the following formula:



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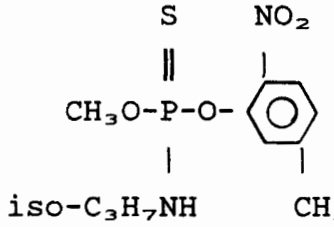
wherein R^1 is a C_3-C_4 alkyl group, R^2 is a C_1-C_4 alkyl group, X a methyl group, and n an integer from 0 to 3.

Our investigations have shown that these compounds display a ve low phytotoxicity to crop plants and unlike many other herbicides are not toxic to mammals. Another very important factor is that the new compounds are extremely effective even at low concentrations and, compared with known substances, can therefore be applied in smaller quantities in herbicide compositions. They have been found to be effective in quantities as low as 0.5 to 5 kg/ha of active ingredient.

Tests have shown that the presence of the 2-nitro and 5-methyl groups on the phenyl group are for the most part essential to obtain the excellent herbicidal activity.

Below we give examples, numbered (I) to (V), of amido thiono-phosphoric acid esters of the above formula which produced good results when used to control weeds, i.e. those which always include the 2-nitro group and a 5-methyl group.

(I)



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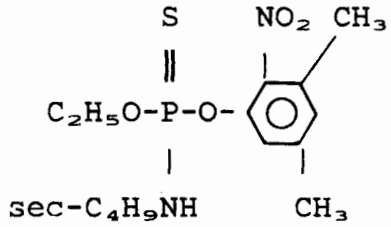

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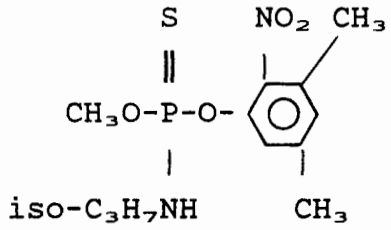

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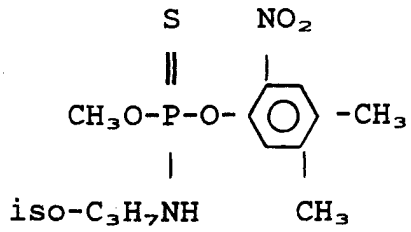

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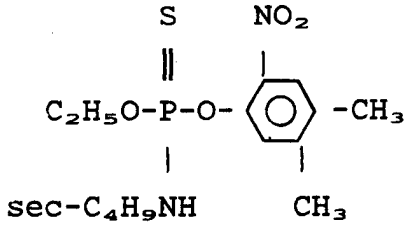
(V)



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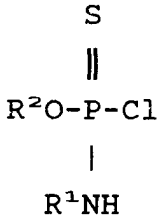
Of these compounds, compounds IV and V show particularly high herbicidal activity.

Amido thionophosphoric acid esters of the type described above, in which the phenyl group is substituted not only by a nitro group but also by an alkyl group (Document III), are, by the way, already known. However, these compounds are used for purposes quite different to our own.

Our compounds may be suitably prepared by reacting a thionophosphoric acid chloride of the formula



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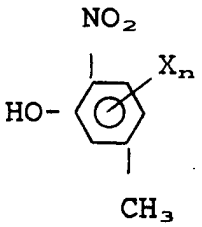
wherein R^1 and R^2 are the same as in the above formula, with a nitrophenol of the formula



(X and n are as indicated above). The reaction is carried out in an organic solvent in the presence of an acid-binding agent.

Many aliphatic or aromatic hydrocarbons or other polar aprotic solvents such as benzene, toluene, dichloromethane and dioxane are suitable as organic solvents. However, lower aliphatic nitriles, preferably those with a boiling point of up to 100°C such as acetonitrile and propionitrile, have been found to be particularly satisfactory. As acid-binding agents both inorganic compounds, such as potassium carbonate, and organic bases, such as triethylamine or pyridine, may be used.

The reaction is normally carried out at a temperature ranging from room temperature to 120°C, preferably at temperatures from 40-70°C. Depending on the temperature chosen, the reaction takes approximately two to five hours. If one wants to obtain a product which is solvent-free, the solvent is removed by distillation under reduced pressure once the reaction has been carried out. The resulting crude product which is an oil can then be purified by repeated washing, for example with benzene and with water and by subjecting it to column chromatography using active aluminium oxide.

Our compounds can be used without restriction to treat agricultural areas and display strong herbicidal activity against a wide range of weeds.

They are especially suitable for selective weed control, particularly when the herbicide is applied to the agricultural areas before the emergence of the crop plants or before the emergence of the weeds.

Weeds which can be successfully controlled with our herbicide compositions are grass family weeds such as barnyard grass (echinochloa crus-galli), large crabgrass (digitaria sanguinalis) and green foxtail (setaria viridis), and also such broad-leaved weeds as common purslane (portulaca oleracea), common lambsquarter (chenopodium album), monochoria and chickweed (stellaria media).

Depending on the concentration applied, herbicide compositions containing one of the new compounds as an active ingredient can control completely the growth of the weed species mentioned above without any significant phytotoxicity to crops such as rice, soy bean, pea or cotton. As already mentioned, the substances are most effective when applied before germination of the weeds in the quantities indicated above.

Our compounds may be used as such or preferably in the form of suitable preparations (formulations) such as wettable powders, granulates, oil sprays and emulsifiable concentrates in particular. These preparations are formed by mixing the active substance with additives, such as solid carriers and/or solvents. Advantageously surface active agents, dispersants and emulsifiers are used in addition. The solid carriers may, for example, be ground kaolin or fine-grained clay. Examples of solvents are benzene and toluene, and in particular cyclohexanone.

Such preparations are, of course, adapted to the purpose and method of application. It is moreover possible to use the herbicidal active agent or a formulation containing such an agent in admixture with fungicides, insecticides and also fertilisers. Formulating the herbicide as an emulsifiable concentrate, that can be diluted with water, has proved particularly advantageous.

Such an emulsifiable concentrate is prepared by dissolving the compounds in one of the aforementioned solvents and mixing them with an emulsifier. Examples of such emulsifiers which can be added to the liquid mixture are polyethylene glycol ether or a mixture of polyethoxylated fatty acid and polyethoxylated alkylphenol.

The composition of an emulsifiable herbicidal concentrate, which can be advantageously used as a liquid preparation, is as follows:

10 to 30% by weight of active ingredient in the form of a compound according to the aforementioned formula,
50 to 70% by weight of cyclohexanone as solvent and
10 to 20% by weight of polyethylene glycol ether as emulsifier.

To ensure that the active ingredient is properly dispersed it is advisable to add spreading agents to the preparation. As spreading agents, fatty alcohols or fatty acid esters may be used. Isopropyl myristate and isopropyl palmitate have been found to be particularly effective as spreading agents. They are preferably added in quantities of 5 to 10% by weight relative to the emulsifiable concentrate.

In certain circumstances the presence of a significant amount of spreading agent in the preparation may, however, lead to stability problems, causing the preparations to decompose to a lesser or greater extent on storage. This can be avoided, preferably by adding a stabiliser such as methane sulphonic acid, benzene sulphonic acid, tetrapropylene benzene sulphonic acid, and in particular 2-nitrobenzoic acid. Where appropriate, 0.5 to 1% by weight of stabiliser is added to the emulsifiable concentrate.

Such a stabilised concentrate is particularly beneficial in weed control in crops of transplanted or wet-sown rice since even undiluted concentrate can be applied directly to the water surface.

The examples which follow illustrate the excellent herbicidal effect of compounds of formulae I to V set out above.

Example 1

Seeds of barnyard grass, large crabgrass, common purslane, monochoria and radish (raphanus sativus) were individually sown in flower pots and covered with soil. The five test compounds of the above-mentioned formulae I to V were then applied to the soil. All the test compounds were used in the form of an aqueous dilution of an emulsifiable concentrate. The composition of the concentrate was as follows:

20 parts by weight of the test compound
65 parts by weight of cyclohexanone and
15 parts by weight of a polyethylene glycol ether.

The test plants were grown in a greenhouse for twenty days, at the end of which the results were evaluated according to the following scale:

0: no appreciable damage
1: very slight damage
2: minor damage
3: moderate damage
4: badly damaged
5: completely killed.

The results are set out in Table 1.

Example 2 (application under waterlogged conditions)

In further tests, flower pots were filled with paddy-field soil and rice seedlings were transplanted to them. Seeds of the two types of weed indicated in Table 2 were then sown in the pots, which were filled to the top with soil and placed in a water tank. On the

third day after sowing, undiluted emulsifiable concentrates of same composition as in Example 1 were applied in the quantities shown in Table 2. After twenty-five days the effect on the weeds and the phytotoxicity to the rice were evaluated in accordance with the scale given in Example 1. The results are set out in Table 2.

As is clear from table 2, no phytotoxicity could be demonstrated for the compounds used according to the invention against rice, with the result that they are particularly suitable for use in paddy-fields as well.

Table 1

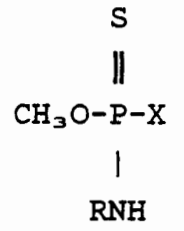
Test compound	Amount of active ingredient (g/are)	Effect on barnyard grass	large crab-grass	portulaca oleracea	mono-choria	radish
I	50	5	5	5	5	0
	22	4	5	4	4	0
	8	3	3	4	3	0
II	50	5	4	5	5	0
	22	5	3	4	5	0
	8	4	3	3	3	0
III	50	5	5	5	5	0
	22	5	4	4	4	0
	8	3	3	3	3	0
IV	50	5	5	5	5	0
	22	5	5	5	5	0
	8	5	5	4	5	0
V	50	5	5	5	5	0
	22	5	5	5	5	0
	8	4	4	4	4	0

Table 2

Test compound	Amount of active ingredient (g/are)	Effect on barnyard grass	Effect on portulaca oleracea	Effect on rice
I	50	5	5	0
	25	4	4	0
	12	4	3	0
II	50	5	5	0
	25	5	4	0
	12	4	3	0
III	50	5	5	0
	25	4	4	0
	12	3	3	0
IV	50	5	5	0
	25	5	5	0
	12	5	5	0
V	50	5	5	0
	25	5	5	0
	12	5	4	0

DOCUMENT I (State of the Art)

Method of controlling weeds with a herbicide composition which contains as an active ingredient a compound of the following general formula



wherein R is hydrogen or a C_1-C_3 alkyl group and X stands for 2,4-dichlorophenyloxy or 2,4,5-trichlorophenyloxy.

The herbicide composition based on one or more compounds of the above formula completely or very largely controls the growth of annual weeds, in particular unwanted species of grass, in useful crops such as cotton and maize. However, it is also particularly suitable for controlling weeds and unwanted species of grass in lawns (permanent grass-grown areas).

The herbicide composition can therefore be used for selective weed control. However, the amount of the herbicide composition in growing useful plant crops must be strictly controlled as too high a dose may slightly damage the plants.

The amount of the herbicide composition to be used will depend on the soil structure and the unwanted vegetation to be controlled. As

a general rule, very effective selective weed control can be obtained with 10 to 17 kg of active ingredient per hectare (kg/ha) of the area to be treated.

The active ingredient may be used in either powder or liquid form. The solid form is generally preferred because the liquid form has only a limited storage life.

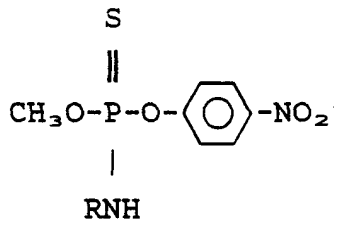
Example

Two aqueous suspensions were prepared from a concentrate of O-methyl-N-isopropylamido-O-(2,4-dichlorophenyl)thionophosphate, one containing 0.02 kg/l and the other 0.015 kg/l of active substance. Each of these suspensions was used to treat an area of Kentucky bluegrass heavily infested with crabgrass. This herbicide composition was applied to the test fields with a commercial atomiser at a rate of 160 and 110 g/ar, respectively. An adjoining field used as a control was left untreated.

After four months, the crabgrass was found to have receded by 98% and 82% respectively on the treated test fields. The Kentucky bluegrass had not suffered but had even grown more profusely than in the control field.

DOCUMENT II (State of the Art)

The invention relates to the preparation of new herbicides containing as an active ingredient a compound of the following structural formula



wherein R is a C_1-C_4 alkyl.

These derivatives of amido thionophosphoric acid with a nitro group as the substituent on the phenyl group have a broader spectrum of activity as herbicides than similar known compounds.

The application of a moderately large dose of the active ingredient - approximately 6 to 8 kg/ha - utilising the herbicide composition according to the invention will severely restrict the growth of many broad-leaved weeds and grass species, without any damage to crop plants such as rice, soy bean, pulses and cotton being observed. Approximately 10 to 15 kg/ha of active ingredient needs to be used to control completely the growth of weed species and eradicate every single weed. Since this may give rise to some phytotoxicity to useful plants it is preferable to apply such a relatively concentrated dosage at the pre-emergence stage.

The herbicide compositions according to the invention are generally

most effective when applied before the weed germinates. The norm germination of the weed seeds is then prevented.

The active ingredient represented by the above formula may be applied in the form of dusts, granulates or in aqueous form, and as a solution or dispersion.

Example 1

20 parts by weight of the compound according to the invention, O-methyl-N-isopropylamido-O-(4-nitrophenyl)-thionophosphoric acid ester, were mixed and ground together with 75 parts by weight of bentonite and 5 parts by weight of sodium alkylbenzene sulphonate to obtain a wettable powder, which is mixed with water and then applied.

Example 2

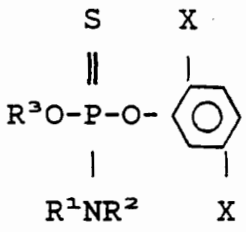
200g of the same compound as in Example 1 were dissolved with heating in xylene. The solution was then sprayed onto clay granules to obtain a granulate with 10% active ingredient.

Example 3

Greenhouse experiments were conducted with the herbicide composition prepared in accordance with Examples 1 and 2. Using a dose of 6 to 7 kg/ha of active ingredient, the growth of weeds such as spring wild-oat (avena fatua), white mustard (sinapsis alba) - and to a somewhat lesser extent millet - was found to be significantly inhibited whilst the crop plants maize and soy bean were undamaged.

DOCUMENT III (State of the Art)

The invention relates to derivatives of amido thionophosphoric acid of the general structural formula



wherein R^1 is hydrogen or a methyl group, R^2 a C_1-C_3 alkyl group, R^3 a C_1-C_4 alkyl group and one of the groups X is a nitro group and the other group X is hydrogen or a methyl group.

The compounds according to the invention are prepared by reacting a phenol substituted in the 2 or 5 position by a nitro group and, where appropriate, additionally substituted by a methyl group in the 2 or 5 position not occupied by the nitro group with a phosphorus thiochloride. The intermediate product obtained is reacted in two successive stages, firstly with a lower aliphatic alcohol and then with a primary or secondary amine.

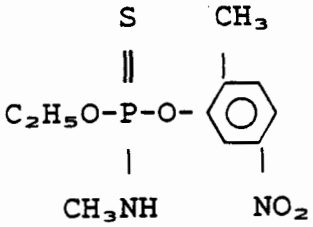
The compounds thus obtained are used in particular to modify synthetic resins and as an additive to high-pressure oils.

It was found, furthermore, that compounds of the above general

formula carrying a methyl group in the 5 position on the phenyl group are less suitable for the above uses.

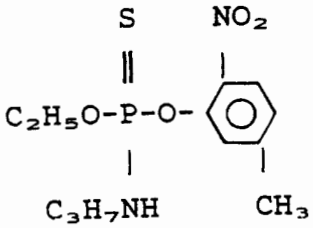
Example 1

1 mole of 2-methyl-5-nitrophenol was reacted with 1 mole of phosphorus thiochloride to give O-(2-methyl-5-nitrophenyl)-thionophosphoric dichloride, which was then esterified with two moles of ethanol before being amidised with one mole of methylamine to give the product of the following formula:



Example 2

Example 1 was repeated with the difference that 2-nitro-5-methylphenol was substituted for the phenol and propylamine was substituted for methylamine. The product thus obtained had the following formula



Example 3

Example 1 was repeated with the difference that 2-nitrophenol was used as the starting compound. The product thus obtained had the following formula