United States Patent

Nikles

[15] **3,676,486**

[45] **July 11, 1972**

[54] AMINOPHENYLCARBAMATES

[72] Inventor: **Erwin Nikles**, Liestal, Switzerland

[73] Assignee: **Ciba-Geigy AG**, Basel, Switzerland

[22] Filed: **Oct. 20, 1969**

[21] Appl. No.: **867,862**

[30] **Foreign Application Priority Data**

Oct. 25, 1968 Switzerland 16003/68
Oct. 31, 1968 Switzerland 16212/68

[52] **U.S. Cl.** ..... **260/479 C**, 260/463, 260/574, 424/300

[51] **Int. Cl.** **C07c 125/06**

[58] **Field of Search** ..... 260/479 C

[56] **References Cited**

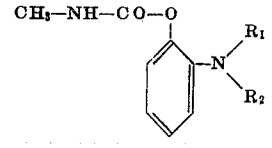
OTHER PUBLICATIONS

Heiss et al. Chem. Abstracts, Vol. 59 (1963), page 2120 C.
Metcalf et al., Agricult. and Food Chem., (1965), pp. 221–225.

Primary Examiner—James A. Patten
Attorney—Harry Goldsmith, Joseph G. Kolodny and Mario A Monaco

[57] **ABSTRACT**

New aminophenylcarbamates of the formula

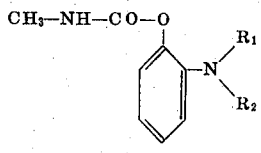


wherein R_1 represents an alkyl residue containing not more than three carbon atoms and R_2 an alkyl residue containing two to four carbon atoms, have very good properties in combating insects and members of the order Acarina, but they possess especially outstanding properties in destroying blood-sucking arthropodes. These carbamates may be used as active ingredients in pesticidal preparations.

10 Claims, No Drawings

AMINOPHENYLCARBAMATES

The present invention relates to preparations for combating blood-sucking arthropodes which contain, as the active component, at least one compound of general formula

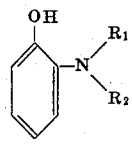


(I)

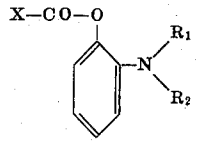
as the free base or in the form of one of its salts, wherein R_1 represents an alkyl residue containing not more than three carbon atoms and R_2 an alkyl residue containing two to four carbon atoms, together with a carrier. As suitable carriers there may be mentioned solvents, diluents, dispersing agents, wetting agents, emulsifiers, thickeners as well as further known pesticides.

The present invention also provides carbamates of the above formula (I) and their salts, on which the agents are based.

The present invention also provides a process for preparing the carbamates of the above formula (I), which comprises reacting a phenol of formula



with methylisocyanate or methylcarbamic acid chloride or by reacting an aminophenylcarbonate or aminophenylchlorocarbonate of formula



with methylamine, in which formulae R_1 and R_2 have the meanings given above or represent substituents which can be converted into these quoted substituents by post-alkylation, X represents a halogen atom, preferably a chlorine atom.

The phenols required as intermediate products can be manufactured by a method known per se. It is, for example, possible to alkylate o-aminophenol in the amino group by means of an alkyl sulphate or dialkyl sulphate, alkyl tosylate or alkyl halide, during which an acid-binding agent may be added. A further method consists in the reductive alkylation of o-nitrophenol or o-aminophenol with an aldehyde or ketone and catalytically activated hydrogen. If R_1 and R_2 are not identical, the alkylation reactions have to be carried out in two stages with different alkylating agents. Especially pure o-monoalkylaminophenols are obtained by alkylation and subsequent hydrolysis from 1,3-benzoxazol-2-one.

The sequence of the synthesis stages hitherto described, up to the final product, can also be changed and suited to the specific properties of the carbamates. For example, it is possible first to manufacture o-nitrophenyl-carbonate or o-nitrophenyl-N-methylcarbamate and then to reduce and alkylate these. In the latter case the new carbamates are directly obtained, and in the former case a reaction with methylamine is still required.

The active component can be present not only as the free base but also in the form of a salt. Inorganic and organic acids can be used for the salt formation, for example, sulphuric acid, hydrochloric acid, hydrobromic acid, nitric acid, phosphoric acid, oxalic acid, citric acid, methanesulphonic acid, toluenesulphonic acid, maleic acid, monochloracetic, dichloracetic and trichloractic acid and many others. Acid salts, for example, the acid sulphate, are distinguished by good stability.

Those active substances of formula (I) in which R_1 represents a methyl, ethyl or propyl residue and R_2 an ethyl, propyl, isopropyl, butyl or sec. butyl residue are preferred.

The new carbamates of formula (I), according to the invention, show very good biocidal properties in general combating of insects and pests of the order Acarina, in each case in all their stages of development. Thus cicadas are destroyed even by using small amounts of the active substance. Fruit flies are completely killed at concentrations of 2.5 ppm after one hour. The carbamates, however, generally possess exceptional properties in destroying blood-sucking arthropodes.

This group of pests is not so much sub-divided through particular classes or orders but is especially characterized and defined by its behavior as parasites of warm-blooded animals.

Their effect on humans and animals is, alongside pure molestation, that of potential carriers of diseases (vectors), which cause infections or occur as intermediate hosts of excitants of diseases.

As the most important representatives, flies (stinging flies, animal flies, tsetse flies and others), mosquitoes (yellow fever mosquito, malaria mosquito and others), lice, bugs, fleas, and also ticks and mites should be mentioned.

The last-mentioned representatives of the order Acarina assume their greatest importance as ectoparasites for mammals and birds. However, the other groups of pests which have been mentioned also represent a constant and outstanding threat to all animal stocks, whether cattle, sheep, goats, pigs, horses, poultry or other useful animals.

The compounds of formula (I), by themselves or in preparations, show both a contact poison effect and an ingested poison effect in the pests which are to be combatted. For example, 2-(methyl-isopropylamino)-phenyl-N-methyl-carbamate, 2(ethyl-isopropylamino)-phenyl-N-methylcarbamate, 2(methyl-ethyl-amino)-phenyl-N-methylcarbamate, 2-diethyl-amino-phenyl-N-methylcarbamate, 2-(isopropyl-n-propylamino)-phenyl-N-methylcarbamate and 2-(methyl-sec.butylamino)-phenyl-N-methylcarbamate are highly active against bugs such as Rhodnius prolixus or Cimex lectularius, mosquitoes such as Aedes aegypti or Anopheles stephensi, parasitary mites such as Dermanyssus gallinae and ticks such as Boophilus microplus, Amblyomma variegatum. As the bases or in the form of their salts, especially the acid sulphates, the new carbamates are suitable for use as active components in bait mixtures for combating flies.

The new preparations can be employed in the most diverse manner in a solid, liquid or gaseous form, for example, in the form of sprays, dusting powders and emulsions and also in so-called fly plates or flypapers which are impregnated with a solution of at least one of the active substances.

Possible materials for the manufacture of directly sprayable solutions of the compounds of general formula (I) are, for example, mineral oil fractions of high to medium boiling range, for example, Diesel oil or kerosene, coal tar oil and oils of vegetable or animal origin, as well as hydrocarbons, for example, alkylated naphthalenes or tetrahydronaphthalene, optionally using xylene mixtures, cyclohexanols, ketones and also chlorinated hydrocarbons, for example, trichloroethane and tetrachlorethane, trichlorethylene or trichlorobenzenes and tetrachlorobenzenes. Organic solvents of which the boiling point is above 100° C are advantageously used.

Aqueous application forms are especially appropriately manufactured from emulsion concentrates, pastes or wettable spraying powders by adding water. Possible emulsifiers or dispersing agents are non-ionic products, for example, condensation products of aliphatic alcohols, amines or carboxylic acids having a long-chain hydrocarbon residue of about 10 to 20 carbon atoms with ethylene oxide, for example, the condensation product of octadecyl alcohol and 25 to 30 mols of ethylene oxide, or that of technical oleylamine and 15 mols of ethylene oxide or that of dodecylmercaptan and 12 mols of ethylene oxide. Amongst the anionic emulsifiers which can be

employed there may be mentioned: the sodium salt of dodecyl alcohol sulphuric acid ester, the sodium salt of dodecyl-benzenesulphonic acid, the potassium or triethanolamine salt of oleic acid or of abietic acid or of mixtures of these acids, or the sodium salt of a petroleum-sulphonic acid. Possible cationic dispersing agents are quaternary ammonium compounds, for example, cetylpyridinium bromide, or dihydroxyethylbenzyldodecylammonium chloride.

Talc, kaolin, bentonite, calcium carbonate, calcium phosphate, but also charcoal, cork powder, wood flour and other materials of vegetable origin can be employed for the manufacture of dusting agents and scattering agents, for example for combating mites in poultry. The manufacture of the preparations in a granular form is also to be recommended for special uses. The various forms of use can be provided in the usual manner with additions of substances which improve the distribution, the adhesion, the rain resistance or the penetrating power; amongst these there may be mentioned: fatty acids, resin, glue, casein or alginates.

The preparations according to the invention can be employed by themselves or together with customary pesticides, especially insecticides, acaricides, nematocides, bactericides and fungicides.

The concentration of the active ingredient employed can vary within wide limits depending on the nature of the use. It is generally 0.01 percent by weight of 20 percent by weight for more dilute preparations, whilst more concentrated preparations contain 20 percent by weight to 98 percent by weight of active ingredient. Preparations of maximum concentration are, say, used in the so-called ULV technique (ultra-low volume) with minimum amounts of additives. The ULV technique is employed with very finely atomizing spraying equipments, preferably with the aid of aircraft.

The action of the carbamates according to the invention can be further increases by synergistic agents. Sesamine, sesamex, piperonyl-cyclonene, piperonyl-butoxy, piperonal-bis[2-(2-butoxyethoxy)ethyl]acetate, sulphoxides, propyl-isome, N-(2-ethylhexyl)-5-norbornene-2,3-dicarboxamide, octachlorodipropyl-ether, 2-nitrophenyl-propargyl-ether, 4-chloro-2-nitrophenyl-propargyl-ether and 2,4,5-trichlorophenyl- propargyl-ether are, for example, suitable for this purpose.

The following Examples illustrate the invention. The parts denote parts by weight:

Manufacturing Example A

2-(Isopropyl-methyl-amino)-phenol

150 Parts of isopropyl bromide are added in portions at 60° C, in a nitrogen atmosphere, to a stirred mixture of 123 parts of 2-methylaminophenol, 200 parts by volume of dimethylformamide, 130 parts of 2,6-lutidine and 48 parts of potassium iodide. Thereafter the mixture is stirred for 24 hours at 90° C, cooled and poured onto 3000 parts by volume of ice water. The product is extracted with three times 500 parts by volume of toluene. The toluene solution is repeatedly washed with water, dried over anhydrous sodium sulphate, filtered and evaporated. Oily 2-(isopropyl-methyl-amino)-phenol is obtained as the residue.

2-(Isopropyl-methyl-amino)phenyl-N-methylcarbamate (Compound No. 1)

50 Parts of 2-(isopropyl-methyl-amino)phenol are dissolved in 300 parts by volume of carbon tetrachloride, mixed with 0.2 parts of triethylenediamine and, at room temperature, with 19 parts of methylisocyanate added in portions, during which addition the temperature rises. When the exothermic reaction has subsided, the solution is kept for 14 hours at 40° C and is then evaporated, whereupon the final product crystallises out. Melting point 65° to 70° C.

The following compounds can be manufactured analogously:

2. 2-(Isopropyl-ethyl-amino)phenyl-N-methylcarbamate, oil.

3. 2-(Isopropyl-n-propyl-amino)phenyl-N-methylcarbamate, oil.

4. 2-(Sec.butyl-methyl-amino)phenyl-N-methylcarbamate, oil. NMR-spectrum measured in CCl_4 (δ-values):

$m = 0.6 - 1.2$, 6 H ($-\underset{|}{C}H-\underline{CH_3}$, $-CH_2-\underline{CH_3}$),

$m = 1.2 - 1.8$, 2 H ($-\underline{CH_2}-CH_3$),

$s = 2.58$, $d = 2.61$ } 6 H ($N-\underline{CH_3}$ and $-CO-NH-\underline{CH_3}$)

$m = 3.0 - 3.5$, 1 H ($-\underset{|}{\overset{C_2H_5}{C}}H-CH_3$)

$b = 6.0 - 6.5$, 1 H ($-CO-\underline{NH}-$)

$m = 7.7 - 8.2$, 4 H (aromat. H).

5. 2-(Methyl-n-propyl-amino)-phenyl-N-methylcarbamate, oil.

6. 2-(Methyl-n-butyl-amino)-phenyl-N-methylcarbamate, oil.

7. 2-(Ethyl-methyl-amino)-phenyl-N-methylcarbamate, melting point 66° to 68° C.

8. 2-Diethylaminophenyl-N-methylcarbamate, oil. NMR-spectrum measured in CCl_4 (δ-values):
$t = 1.02$, 6 H (two $-CH_2-CH_3$) (J = 7 Hz),
$d = 2.89$, 3 H ($-CO-NH-CH_3$) (J = 5 Hz),
$q = 3.12$, 4 H (two $-CH_2-CH_3$) (J = 7 Hz),
$b = 5.0 - 5.3$, 1 H ($-CO-NH-$),
$m = 6.9 - 7.4$, 4 H (aromat. H).

Manufacturing Example B

Manufacture of the acid sulphate of the compound No. 4

10.2 Parts of 96 percent strength sulphuric acid are diluted with 44.9 parts of water whilst cooling. 23.6 Parts of 2-(sec.butyl-methyl-amino)-phenyl-N-methylcarbamate are introduced whilst stirring, whereupon a clear solution of the acid sulphate is immediately obtained.

Formulation Examples

Dusting agents

Equal parts of an active substance according to the invention and of precipitated silica are finely ground. Dusting agents preferably containing one to six percent of active substance can be manufactured therefrom by mixing with kaolin or talc.

Spraying powders

In order to manufacture a spraying powder, the following components are for example mixed and finely ground:

50 parts of active substance according to the present invention
20 parts of HISIL (highly adsorbent silica)
25 parts of Bolus alba (kaolin)
3.5 parts of a reaction product of p-tert. octylphenol and ethylene oxide and
1.5 parts of sodium 1-benzyl-2-stearyl-benzimidazole-6,3'-disulphonate.

Emulsion concentrate

Easily soluble active substances can also be formulated as an emulsion concentrate according to the following instruction:

20 parts of active substance
70 parts of xylene and
10 parts of a mixture of a reaction product of an alkylphenol with ethylene oxide and calcium dodecyl-benzenesulphonate are mixed. On dilution with water to the desired concentration a sprayable emulsion is produced.

EXAMPLE 1

Action against female mosquitoes (Aedes aegypti)

a. Concentration experiment

Female mosquitoes are placed for six hours on a coating of the substance to be tested, in Petri dishes of 11 cm diameter. This coating is produced by treating the bottom of the dish with 1 ml of a solution of the substance in acetone and subsequent drying for one hour. Solutions of 1,000, 100, 10 and 1 ppm are employed, corresponding to a concentration of 1, 0.1, 0.01 and 0.001 mg of active substance/dish (1mg/dish ≅ 1 g/9.4 m^2). The mosquitoes are cooled in ice and counted out 10 at a time into the dishes. 4 repeats are run per concentration. The evaluation takes place after 45, 90 and 360 minutes.

b. Time experiment: Test of the minimum exposure time

1.9 ml of a solution of the active substance in acetone, containing 1000 ppm of active substance, are uniformly distributed over a filter paper of size 10 × 19 cm. After drying, the paper is rolled and pushed into a test tube into which 10 female mosquitoes, briefly anaesthetised with CO_2, are introduced, the test tube thereafter being closed.

After an exposure time of 2, 4, 8, 16, 32, 60 or 120 minutes the mosquitoes are again briefly anaesthetised and introduced into a clean Petri dish with fodder (honey water).

An evaluation is made after 24 hours. The minimum exposure time is taken to be the time at which 100 percent mortality can still be observed.

The following results are obtained from the two experiments:

Compound No.	Total mortality (L_c100) at	after	Minimum exposure time
1	0.001 mg/dish	45 mins.	16 mins.
2	0.001 mg/dish	45 mins.	16 mins.
3	0.001 mg/dish	90 mins.	16 mins.
4	0.001 mg/dish	45 mins.	8 mins.
5	0.001 mg/dish	45 mins.	8 mins.
6	0.001 mg/dish	45 mins.	8 mins.
7	0.001 mg/dish	45 mins.	8 mins.
8	0.001 mg/dish	45 mins.	8 mins.

EXAMPLE 2

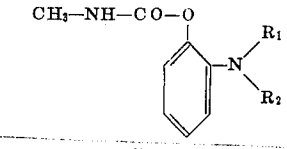
Action against blood-sucking bugs (Rhodnius prolixus)

The experimental arrangement corresponds to that of Example 1 a). One hour after treatment of the Petri dish, 10 bugs of the third larvae stage (L–3) are exposed therein for 24 hours. The action of the active substance coating is ascertained after 45, 90, 360 minutes, and 24 hours. Two repeats are run per concentration.

Compound No.	Total mortality (L_c100) at	after
1	0.01 mg/dish	360 mins.
4	0.01 mg/dish	45 mins.
5	0.01 mg/dish	90 mins.
7	0.01 mg/dish	360 mins.
8	0.01 mg/dish	360 mins.

What we claim is:

1. Compounds of the formula



wherein R_1 represents an alkyl residue containing not more than three carbon atoms and R_2 an alkyl residue containing two to four carbon atoms.

2. Compounds of the formula according to claim 1, wherein R_1 represents a methyl, ethyl, or propyl residue and R_2 an ethyl, propyl, isopropyl, butyl or sec. butyl residue.

3. The compound 2-(isopropyl-ethyl-amino)-phenyl-N-methylcarbamate according to claim 1.

4. The compound 2-(isopropyl-n-propyl-amino)-phenyl-N-methylcarbamate according to claim 1.

5. The compound 2-(sec.butyl-methyl-amino)-phenyl-N-methylcarbamate according to claim 1.

6. The compound 2-(methyl-n-propyl-amino)-phenyl-N-methylcarbamate according to claim 1.

7. The compound 2-(methyl-n-butyl-amino)-phenyl-N-methylcarbamate according to claim 1.

8. The compound 2-(ethyl-methyl-amino)-phenyl-N-methylcarbamate according to claim 1.

9. The compound 2-diethylaminophenyl-N-methylcarbamate according to claim 1.

10. The compound 2-(isopropyl-methyl-amino)-phenyl-N-methylcarbamate according to claim 1.

* * * * *