EP. 0032948

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 3:	A1	(11) International Publication Number: WO 81/00406
C07D 263/04, 277/04		(43) International Publication Date: 19 February 1981 (19.02.81)

(21) International Application Number: PCT/US80/00941

(22) International Filing Date: 28 July 1980 (28.07.80)

(31) Priority Application Number: 063,635

(32) Priority Date: 3 August 1979 (03.08.79)

(33) Priority Country: US

(71) Applicant: STAUFFER CHEMICAL COMPANY [US/US]; Westport, CT 06880 (US).

(72) Inventor: TEACH, Eugene, G.; 1929 Downey Place, El Cerrito, CA 94530 (US).

(74) Agents: PACINI, Harry, A. et al.; Stauffer Chemical Company, 1200 South 47th Street, Richmond, CA 94804 (US).

(81) Designated States: AT (European patent), AU, BR, CH (European patent), DE (European patent), DK, FR (European patent), GB (European patent), HU, JP, NL (European patent), NO, RO, SE (European patent), SU.

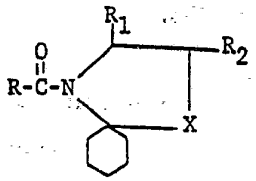
Published

With international search report
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments

(54) Title: SPIROOXAZOLIDINES AND THIAZOLIDINES AS HERBICIDE ANTIDOTES

(57) Abstract

N-haloacyl oxazolidines or thiazolidines substituted in the 2-position with the cyclohexyl spiro group included in a two-part herbicide system comprising a first-part of one or more thiolcarbamate herbicides or haloacetanilide herbicides and a second-part of an effective oxazolidine or thiazolidine antidote compound of the formula



in which X is oxygen or sulfur, R is lower haloalkyl, R_1 is hydrogen or lower alkyl and R_2 is hydrogen or phenyl and the methods of use.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	**KP**	Democratic People's Republic of Korea
AU	Australia	**LI**	Liechtenstein
BR	Brazil	**LU**	Luxembourg
CF	Central African Republic	**MC**	Monaco
CG	Congo	**MG**	Madagascar
CH	Switzerland	**MW**	Malawi
CM	Cameroon	**NL**	Netherlands
DE	Germany, Federal Republic of	**NO**	Norway
DK	Denmark	**RO**	Romania
FI	Finland	**SE**	Sweden
FR	France	**SN**	Senegal
GA	Gabon	**SU**	Soviet Union
GB	United Kingdom	**TD**	Chad
HU	Hungary	**TG**	Togo
JP	Japan	**US**	United States of America

SPIROOXAZOLIDINES AND THIAZOLIDINES AS HERBICIDE ANTIDOTES

Background of the Invention

While many herbicides are immediately toxic to a large number of weed pests, it is known that the effect of many herbicides upon important plant cultivations is either non-selective or not adequately selective. Thus, many herbicides damage not only the weeds to be controlled, but to a greater or lesser extent, the desirable cultivated plants as well. This holds true for many herbicidal compounds which have been commercially successful and are commercially available. These herbicides include types such as triazines, urea derivatives, halogenated acetanilides, carbamates, thiolcarbamates and the like. Some examples of these compounds are described in U.S. Patent Nos. 2,913,237, 3,037,853, 3,175,897, 3,185,720, 3,198,786, 3,442,945, 3,582,314, 3,780,090 and 3,952,056.

The side effect of injury to a cultivated crop by various herbicides is particularly inconvenient and unfortunate. When used in the recommended amounts in the soil to control broadleaf weeds and grasses, serious malformation or stunting of the crop plants sometimes result. This abnormal growth in the crop plants results in loss of crop yield. The search continues for good selective herbicides.

Previous attempts are described to overcome this problem. The treatment of the crop seed with certain "hormonal" antagonistic agents prior to planting is described, see U.S. Patents 3,131,509 and 3,564,768. The protective agents, as well as the herbicide, in these prior processes are largely specific to certain cultivated plant species or in the nature of the antagonistic agents. The prior antagonistic agents have not been notably successful. The aforementioned patents specifically exemplify and

BUREAU OMPI WIPO INTERNATIONAL

describe the treatment of seeds employing compounds of a different chemical class, not suggestive of the present invention.

U.S. Patents 3,859,292 and 3,881,908 disclose cartain N-haloacyl(2-spirocycloaliphatic) oxazolidines useful as herbicides. There is no teaching or disclosure of herbicidal antidote activity. The monochloro acetyl compounds are specifically disclosed.

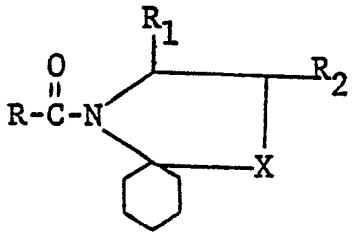
U.S. Patents 3,959,304, 3,989,503, 4,072,688 and 4,124,372 disclose certain substituted oxazolidine and thiazolidine compounds. However, none of these references anticipate or make obvious the particular compounds or the utility of the particular compounds as herbicidal antidotes for thiolcarbamate herbicides, in particular for S-n-propyl N,N-di-n-propyl thiolcarbamate, S-ethyl di-n-propyl thiolcarbamate, S-isopropyl 1-(5-ethyl-2-methylpiperidine) carbothioate, S-ethyl N,N-diisobutyl thiolcarbamate or haloacetanilides, such as 2-chloro-2',6'-diethyl-N-(methoxymethyl) acetanilide, 2-chloro-2'-methyl,6'-ethyl-N-(methoxypropyl-(2)) acetanilide, 2-chloro-2'-methyl,6'-ethyl-N-(ethoxymethyl) acetanilide, 2-chloro-2',6'-dimethyl-N-(methoxymethyl) acetanilide, 2-chloro-N-isopropyl acetanilide, 2-chloro-2',6'-diethyl-N-(n-butyoxymethyl) acetanilide and 2-chloro-N-carbethoxymethyl-2',6'-diethyl acetanilide. None of the references anticipate or make obvious the herbicidal compositions for use employing N-haloacyl oxazolidines substituted in the 2-position with the spiro cyclohexyl moiety.

Description of the Invention

It has been discovered that cultivated crop plants can be protected against injury by thiolcarbamate-type herbicides or haloacetanilide-type herbicides, and said injury can be decreased when the thiolcarbamate-type herbicides or haloacetanilide-type herbicides, each alone or in mixtures or combination with other compounds, are applied in a variety of ways. Further, as an alternative effect,

BUREAU OMPI WIPO INTERNATION

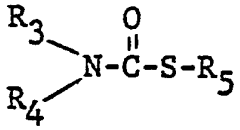
the tolerance of the plants, to these herbicides, can be substantially increased by adding to the soil an antidote compound of the type N-haloacyl oxazolidine or thiazolidine substituted in the 2-position with the spiro cyclohexyl group. Therefore, the present invention also includes a two-part herbicide system comprising a first-part of one or more thiolcarbamate herbicides or haloacetanilide herbicides and a second-part of an effective antidote compound therefore, said antidote compounds corresponding to the following formula



in which X is oxygen or sulfur, R is lower haloalkyl having 1 to 6 carbon atoms, inclusive, and halo is at least one of chlorine, fluorine or bromine, R_1 is hydrogen or lower alkyl having 1 to 6 carbon atoms, inclusive, and R_2 is hydrogen or phenyl.

Those compounds in which R is haloalkyl having at least two halogens, especially chlorine, are new compositions of matter.

By thiolcarbamate herbicides the present invention includes compounds of the formula



in which

R_3 is selected from the group consisting of alkyl 1-6 carbon atoms and alkenyl 2-6 carbon atoms;

R_4 is selected from the group consisting of alkyl 1-6 carbon atoms, alkenyl 2-6 carbon atoms, cyclohexyl, phenyl and benzyl; or

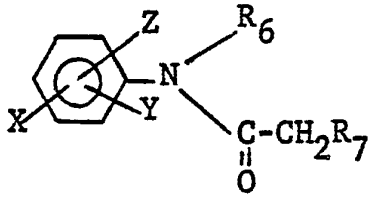
R_3 and R_4 taken together with the nitrogen atom to which they are attached form an alkylene ring substituted

BUREAU OMPI WIPO INTERNATIONAL

and unsubstituted 2-9 carbon atoms; and

R_5 is selected from the group consisting of alkyl 1-6 carbon atoms, haloalkyl 1-6 carbon atoms, alkenylene ring 5-10 carbon atoms, phenyl, substituted phenyl, benzyl and substituted benzyl.

By haloacetanilide herbicides the present invention includes compounds of the formula



in which

X, Y and Z are independently selected from the group consisting of hydrogen, alkyl 1-4 carbon atoms and alkoxy 1-4 carbon atoms;

R_6 is selected from the group consisting of alkyl 1-6 carbon atoms, alkylalkoxy 2-10 carbon atoms, acetoxy 2-6 carbon atoms and dioxane; and

R_7 is selected from the group consisting of chlorine, bromine and iodine.

The unacylated oxazolidine and thiazolidine intermediates for preparing the subject compounds can be synthesized conveniently by reacting substituted amino alkanols or mercaptans with a suitable aldehyde or with ketone. A substantial list of these compounds is given in the review article "THE OXAZOLIDINES", E. D. Bergman, Chem. Rev., 53; 309 (1953). Usually, the amino alcohol or mercaptan and the ketone or aldehyde are heated together in an inert hydrocarbon solvent, and by-product water is separated from the condensed azeotropic mixture of hydrocarbon and water in a Dean-Stark water separator. The solvent is then evaporated and the product purified by distillation under reduced pressure. Suitable reaction solvents are water immiscible hydrocarbons such as benzene, toluene and the like. A preferred solvent is benzene because of its low boiling point.

BUREAU OMPI WIPO INTERNATIONAL

The N-haloacyl oxazolidines and thiazolidines of this invention can be synthesized by reacting the corresponding intermediate oxazolidine or thiazolidine with the desired haloalkylcarbonyl chloride (also described as a haloacyl chloride) at a temperature in the range of about 50°C. in the presence of an acid-acceptor. The reaction is preferably carried out in an organic solvent, inert under the conditions of the reaction. For example, acetonitrile, benzene, xylene and the like; hydrocarbon solvents are generally preferred. The acid-acceptor is generally a basic substance which forms water soluble by-products easily separable from the main reaction product. Although the acid-acceptor can sometimes be an alkali metal salt of a weak acid, such as sodium or potassium carbonate, or acetate, it is preferable to use a tertiary amine. Useful and common tertiary amines are, for example, triethylamine and pyridine; frequently the crystalline hydrohalide formed as a by-product is insoluble in the reaction solvent and easily removed by filtration. When a hydrocarbon solvent is used the product is frequently completely soluble in the reaction solvent and workup is conveniently carried out by filtering the by-product amine hydrohalide, washing the remaining organic phase with water, and removing the reaction solvent by evaporation or distillation. Thereafter, the product can usually be purified by conventional distillation procedures including ones at subatmospheric pressure.

The compounds of the present invention and their preparation are more particularly illustrated by the following examples. Following the examples of preparation is a table of compounds which are prepared according to the procedures described herein. Compound numbers have been assigned to them and are used for identification throughout the balance of the specification.

EXAMPLE 1

Preparation of 2,2-Spirocyclohexyl-N-dichloroacetyl thiazolidine

BUREAU OMPI WIPO INTERNATIONAL

2-2-Spirocyclohexyl thiazolidine (4.7 grams) was combined in methylene chloride (50 milliliters) with triethylamine (3.5 grams). The solution was cooled in an ice water bath and dichloroacetyl chloride (4.4 grams) was added dropwise with vigorous stirring and maintained at less than 15°C. The mixture was washed with 100 milliliters water, separated, dried over magnesium sulfate and the solvent stripped.

The residue was further extracted with a benzene cyclohexane solution, decanted, washed with dilute hydrochloric acid, dried over magnesium sulfate and the solvent stripped under reduced pressure. The yield was 4.4 grams of an oil which crystallized to a waxy solid. The structure was confirmed by infrared analysis.

EXAMPLE 2

Preparation of 2,2-Spirocyclohexyl-N-dichloroacetyl oxazolidine

2,2-Spirocyclohexyl oxazolidine (4.2 grams) was combined in methylene chloride (50 milliliters) with triethylamine (3.5 grams). The solution was cooled in an ice water bath and dichloroacetyl chloride (4.4 grams) was added dropwise with vigorous stirring and maintained at less than 15°C. The mixture was washed with 100 milliliters of water, separated, dried over magnesium sulfate and stripped under reduced pressure. There was obtained a yield of 4.2 grams of the title compound, a solid, m.p. 82-85°C. The structure was confirmed by infrared analysis.

EXAMPLE A

Intermediate Preparation:
Preparation of cyclohexanespiro-2'-(4'-ethyl-1',3'-oxazolidine)

Cyclohexanone (20.6 grams, 0.21 mole) and 2-amino-butanol-1 (17.8 grams, 0.2 mole) in 130 milliliters of toluene were stirred and refluxed at 400 to 500 millimeters under a Dean-Stark apparatus until about 3.8 milliliters of

BUREAU OMPI WIPO INTERNATIONAL

water were collected. The toluene solution was dried over sodium sulfate and its volume adjusted to 190 milliliters. It was calculated to contain 0.178 grams/milliliter of the spiro oxazolidine which was not isolated.

EXAMPLE B

Intermediate Preparation:
Preparation of cyclohexanespiro-2'-(5'-phenyl-1',3'-oxazolidine)

Cyclohexanone (10.8 grams, 0.11 mole) and 2-amino-1-phenylethanol (13.7 grams, 0.10 mole) in 100 milliliters of toluene were stirred and refluxed at about 280 millilimeters under a Dean-Stark appartus until no further water was collected. The solution was treated with sodium sulfate. Its final volume was 150 milliliters and it was calculated to contain 0.145 grams/milliliter of the spiro oxazolidine.

EXAMPLE 3

Preparation of Cyclohexanespiro-2'[3'-(chloroacetyl)-4'-ethyl-1',3'-oxazolidine]

To 32.3 milliliters of the toluene solution of cyclohexanespiro-2'-(4'-ethyl-1',3'-oxazolidine) (0.034 mole) was added dropwise at -10° to -5°C, a solution of chloroacetyl chloride (2.39 milliliters, 0.03 mole) in 10 milliliters of toluene followed by triethylamine (4.4 milliliters, 0.032 mole) stirred overnight at room temperature. The mixture was washed with 100 milliliters water, twice with 100 milliliters saturated sodium bicarbonate solution, with 50 milliliters saturated NaCl, and dried over $MgSO_4$.

The remaining solvent was removed under vacuum giving 5.7 grams of product n_D^{30} 1.5030 (77%). Structure confirmed by infrared and nuclear magnetic resonance.

EXAMPLE 4

Preparation of Cyclohexanespiro-2'-[3'(dichloroacetyl)-4'-ethyl-1',3-oxazolidine]

BUREAU OMPI WIPO INTERNATIONAL

The reaction was carried out on the same molar scale as in Example 3 except that the triethylamine was added to the oxazolidine stock solution before the addition of dichloroacetyl chloride (2.89 milliliters, 0.03 mole) in 10 milliliters of toluene. The product was worked up as in Example 3. The product was a low-melting solid. Yield: 7.2 grams (85.7%). Structure confirmed by infrared and nuclear magnetic resonance.

EXAMPLE 5

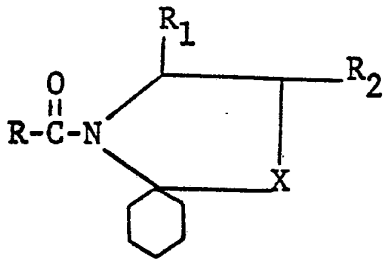
Preparation of Cyclohexanespiro-2'-[3'-(dichloroacetyl)-5'-phenyl-1',3'-oxazolidine]

To 40.4 milliliters of the toluene stock solution of cyclohexanespiro-2'-(5'-phenyl-1',3'-oxazolidine) (0.02 mole) and 3.5 milliliters (.025 mole) triethylamine, was added a solution of dichloroacetyl chloride (2.2 milliliters, 0.023 mole) in 10 milliliters of toluene as described in Example 3 above. The product was worked up in the same manner as in Example 3. There was obtained a yellow oil, n_D^{30} 1.5514 yield: 7.2 grams (96%). Structure confirmed by infrared and nuclear magnetic resonance.

Table I is a list of compounds prepared according to the above procedures and are representative of compounds embodied in the present invention.

BUREAU OMPI WIPO INTERNATIONAL

TABLE I



Compound Number	R	X	R_1	R_2	Physical Constant
1	Cl_2CH	S	H	H	Waxy solid
2	Cl_2CH	O	H	H	m.p. 82-85°C
3	$ClCH_2$	S	H	H	Semi-solid
4	$ClCH_2$	S	C_2H_5	H	n_D^{30} 1.5035
5	Cl_2CH	O	C_2H_5	H	Low-melting solid
6	$Cl(CH_2)_3$	O	H	H	n_D^{30} 1.4926
7	$ClCH_2$	O	H	Ø	n_D^{30} 1.5482
8	Cl_2CH	O	H	Ø	n_D^{30} 1.5514
9	ClC_2H_4	O	H	Ø	n_D^{30} 1.5435

It is clear that the classes of herbicidal agents described and illustrated herein are characterized as effective herbicides exhibiting such activity. The degree of this herbicidal activity varies among specific compounds and among combinations of specific compounds within the classes. Similarly, the degree of activity to some extent varies among the species of plants to which a specific herbicidal compound or combination may be applied. Thus, selection of a specific herbicidal compound or combination to control undesirable plant species readily may be made. Within the present invention the prevention of injury to a desired crop species in the presence of a specific compound or combination may be achieved. The beneficial plant

BUREAU OMPI WIPO INTERNATIONAL

species which can be protected by this method is not intended to be limited by the specific crops employed in the examples.

The herbicidal compounds employed in the utility of this invention are active herbicides of a general type. That is, the members of the classes are herbicidally effective against a wide range of plant species with little or no discrimination between desirable and undesirable species. The method of controlling vegetation comprises applying an herbicidally effective amount of the herein described herbicidal compounds to the area or plant locus where control is desired.

An herbicide as used herein means a compound which controls or modifies the growth of vegetation or plants. Such controlling or modifying effects include all deviations from natural development; for example, killing, retardation, defoliation, desiccation, regulation, stunting, tillering, stimulation, dwarfing and the like. By "plants" it is meant germinant seeds, emerging seedlings, and established vegetation, including the roots and above-ground portions.

The terms herbicide antidote or antidotal amount, is meant to describe that effect which tends to counteract the normal injurious herbicidal response that the herbicide might otherwise produce. Whether it is to be termed a remedy, interferant, protectant, or the like, will depend upon the exact mode of action. The mode of action is varied, but the effect, which is desirable, is the result of the method of treating the seed, soil or furrow in which a crop is planted. Hitherto, there have been no systems employing the antidotes of the present invention which have been satisfactory for this purpose.

As alternative modes of action, the compounds of this invention may interfere with the normal herbicidal action of the thiolcarbamate-type or haloacetanilide-type or other herbicides to render them selective in their action. The observation noted with the presence of the herein described antidote is a decrease in phytotoxicity with respect

BUREAU OMPI OMPI INTELLECTUAL

to various crops. The phytotoxicity is otherwise observed when various thiolcarbamate or haloacetanilide herbicides are used for weed control. Whichever mode of action is present, the corresponding beneficial and desirable effect is the continued herbicidal effect of the thiolcarbamate or haloacetanilide against weed species present with the crop, with the accompanying selective decreased herbicidal effect on desired crop species. This advantage and utility will become more apparent hereinafter.

Corn Seed Treatment Test

Small flats were filled with Felton loamy sand soil. Soil incorporated herbicides were applied at this time. The soil from each flat was placed into a five-gallon cement mixer where the soil was mixed as the herbicides were applied using a predetermined amount of a stock solution containing 936 milligrams of 75.5% active ingredient to 100 milliliters of water. One milliliter of stock solution was applied to the soil in a volumetric pipet for each pound of herbicide desired. One milliliter of stock solution contained 7 milligrams of herbicide which equals 1 pound per acre when applied to the soil in the flats. After the herbicide incorporation, the soil was placed back into the flats.

Flats of herbicide-treated and untreated soil were then ready to be planted. A pint sample of soil was removed from each flat and placed next to each flat for later use in covering up the seeds. The soil was leveled and rows one-half inch deep were made for planting seeds. Alternating rows of treated and untreated crop seeds were sown. In each test, six PAG 344T field corn seeds were planted in each row. Rows were approximately 1 1/2 inches apart in the flat. Seeds were treated by either (1) placing 50 milligrams of the antidote compound with 10 grams of corn seed in a suitable container and shaking them until the seeds were uniformly covered with the compound; or (2) preparing a stock solution by dissolving 50 milligrams of the

BUREAU OMPI WIPO INTERNATIONAL

antidote compound in 5 milliliters of acetone, then using 0.5 milliliters of the solution to treat 10 grams of corn seed (0.05% w/w). Antidote compounds were also applied as liquid slurries and powders or dusts. In some cases, acetone was used to dissolve powdered or solid compounds so they could be more effectively applied to the seeds.

After the flats were seeded, they were covered with the one pint of soil which had been removed just prior to planting. Flats were placed on greenhouse benches where temperatures ranged from 70°-90°F. Flats were watered by sprinkling as needed to assure good plant growth. Percent control ratings were taken 2, 3 and 4 weeks after the treatments were applied.

In each test, the herbicide was applied alone, in combination with the seed protectant, and the seed protectant was applied alone to check for phytotoxicity. The untreated adjacent row was employed to observe any beneficial lateral movement of the antidote compound through the soil. The degree of the effect was noted by comparison with the control.

From the above seed treatment test, compound number 1 reduced injury to corn from 80 percent to 30 percent; and compound number 2 reduced injury to corn from about 80 percent to 20 percent.

When compound number 3 was used at 5 lb/A preplant incorporated with EPTC at 1/2 lb/A preplant incorporated, barley was reduced in injury from 50 percent to 10 percent. When compound number 3 was used at 5 lb/A preplant incorporated and EPTC at 5 lb/A preplant incorporated, injury to oil seed rape was reduced from 75 percent to 30 percent.

When compound number 9 was used at 5 lb/A preplant incorporated and the thiolcarbamate herbicide VERNAM® (S-propyl N,N-dipropyl thiolcarbamate) was used at 6 lb/A preplant incorporated, corn injury was reduced from 90 percent to 75 percent.

BUREAU OMPI WIPO INTERNATIONAL

Testing

Stock solutions of the herbicides were prepared by diluting the requisite amount of each herbicide in water. The solution concentrations and application rates and times are summarized as follows:

Herbicide Stock Solutions

Herbicide Name	Concentration		Application	
	Herbicide (mg)	Water (ml)	ml/flat	lb/acre
VERNAM®	427	400	5	1.00
S-propyl N,N-dipropyl thiol-carbamate	2560	400	5	6.00

Stock solutions of each antidote compound were prepared at the desired concentrations by diluting the requisite amounts of each antidote in acetone. The concentrations and rates for each method of application are summarized as follows:

Antidote Stock Solutions

Concentration		Application		
Antidote (mg)	Acetone (ml)	ml/flat	lb/acre	Method*
95	15	1.50		IF

* IF = In-furrow surface application.

All of the soil used in the tests described herein was loamy sand soil treated with 50 parts per million (ppm) each of cis-N[trichloromethyl)-thio]-4-cyclohexane-1,2-dicarboximide, a fungicide sold as Captan®, and an 18-18-18 fertilizer, which contains 18% by weight equivalent each of nitrogen, phosphorus pentoxide, and potassium oxide.

The thiolcarbamate herbicides were applied to the soil by preplant incorporation. For in-furrow (IF) antidote applications, a one pint (473 cubic centimeters) sample of soil from each planting flat was removed and retained. After leveling and furrowing the soil, seeds of the crop or weed species were planted 1/2 inch (1.27 centimeters) deep. Each flat was divided in half by a wooden barrier. A stock

BUREAU OMPI WIPO INTERNATIONAL

solution of the antidote was atomized directly onto the exposed seeds and soil in the open furrow on one side of the barrier. The seeds in the entire flat were then covered with the previously removed soil. The antidotally untreated sections of flats were compared for observed differences which would indicate lateral movement of the antidote through the soil.

For the preplant incorporation method the herbicide and the antidote of each test group were incorporated into the soil as a tank mix using a five-gallon rotary mixer.

All flats were placed on greenhouse benches where temperature was maintained between 70 and 90°F. The flats were watered by sprinkling as needed to assure good plant growth.

Control flats contained crops treated with herbicides only at the various rates and method of application.

Injury ratings were taken four weeks after application of the antidote. The effectiveness of the antidote was determined by visual comparison of injuries to crops and weeds in the control and test flats to those in untreated flats.

The treated crops initially screened for reduced herbicidal injury were milo (Ml), wheat (Wh), cotton (Ct), rice (Rc), barley (Ba), corn (Cn) and soybeans (Soy). Those compounds which showed substantial crop injury reduction were further tested at reduced rates.

KEY TO TABLE II

Antidotes

Compound numbers in this table correspond to the numbers and their chemical description in Table I.

Application:

IF - In-furrow surface

PPI - Preplant incorporation of herbicide and antidote as a tank mix

BUREAU ... DES MARQUES

Herbicide

VERNAM® = S-propyl N,N-dipropylthiocarbamate as described in U.S. Patent No. 2,913,324

Rates:

All rates are shown in pounds per acre.

Injury Ratings:

(1) Antidotally untreated; % Injury 4 weeks after herbicide application.

(2) Antidotally treated; % Injury 4 weeks after treatment with herbicide plus antidote compound.

- = Indicates no change from control where no antidote is present.

TABLE II

Antidote Compound Number	lb/A IF Rate	VERNAM 1 lb/A PPI					VERNAM 6 lb/A PPI	
		Ml	Wh	Ct	Rc	Ba	Cn	Soy
4	5	65	60	-	35	55	70	-
5	5	55	60	-	55	60	10	45
6	5	-	-	-	-	-	-	-
7	5	-	-	-	60	-	-	-
8	5	75	-	-	-	60	0	75
Control	0	95	95	40	90	80	90	30

Evaluation with haloacetanilide and thiolcarbamate herbicides:

Acetanilide Herbicides and Stock Solutions

LASSO - 2-chloro-2',6'-diethyl-N-(methoxymethyl) acetanilide

729 mg/50 ml acetone; 2 ml = 3.5 lb/A PES
1250 mg/50 ml acetone; 2 ml = 6 lb/A PES

ANTOR - 2-chloro-2',6'-diethyl-N-(carbethoxymethyl) acetanilide

717 mg/50 ml acetone; 2 ml = 2 lb/A PES
833 mg/50 ml acetone; 2 ml = 4 lb/A PES

BUREAU OMPI WIPO INTERNATIONAL

DUAL - 2-chloro-2'-methyl,6'-ethyl-N-(methoxypropyl (2)) acetanilide

486 mg/50 ml acetone; 2 ml = 3.5 lb/A PES

972 mg/50 ml acetone; 2 ml = 4 lb/A PES

TERIDOX - 2-chloro-2',6'-dimethyl-N-(methoxyethyl) acetanilide

50 mg/50 ml acetone; 2 ml = 0.5 lb/A PES

200 mg/50 ml acetone; 2 ml = 2 lb/A PES

MON 55097 - 2-chloro-2'-methyl,6'-ethyl-N-(ethoxymethyl) acetanilide

175 mg/50 ml acetone; 2 ml = 1 lb/A PES

2105 mg/50 ml acetone; 2 ml = 12 lb/A PES

Thiolcarbamate herbicides:

VERNAM® - vernolate - S-propyl dipropyl thiolcarbamate

EPTAM® - EPTC - S-ethyl-di-n-propyl thiolcarbamate

SUTAN® - butylate - S-ethyl diisobutyl thiolcarbamate

Methods of Application. The antidotes were applied at 5 lb/A preemergence surface tank mixed with the herbicide (PES-TM); 0.5% seed treatment (ST); 5 lb/A in-furrow (IF) and 5 lb/A preplant incorporated tank-mixed with the herbicide (PPI-TM). The herbicides were applied preemergence surface or preplant incorporated.

Flats were filled with sandy loam soil. Premixed or incorporated applications were applied to the soil during incorporation in the soil in a 5-gallon rotary mixer.

After the soil was treated with the appropriate solutions of herbicide and/or antidote, the soil was transferred from the mixer back into the flat where it was prepared for seeding. The initial step in planting was to remove a one pint sample of soil from each flat to be retained and used to cover the seeds after planting. The soil was then leveled and rows 1/4 inch deep were made in each flat. The flats were seeded with the crops

BUREAU OMPI WIPO INTERNATIO

Milo - Ml [Sorghum vulgare]
Wheat - Wh [Triticum aestivum]
Cotton - Ct [Gossypium hirsutum]
Barley - Ba [Hordeium vulgare (L.)]
Soybeans - Soy [Glycine max]
Rice - Rc [Dryza sativa]
or
Corn - Cn [Zea maize]

and with the weed species

Watergrass - Wg [Echinochloa crusgalli]
Foxtail - Ft [Setaria viridis]

The seeds then were covered with the pint soil sample removed prior to seeding.

The flats were placed on greenhouse benches where the temperature was maintained between 70-90°F. The soil was watered by sprinkling to assure good plant growth.

Injury ratings were taken four weeks after treatments were applied. Flats treated with herbicides alone were included to provide a basis for determining the amount of injury reduction provided by the herbicide antidotes. The percent injury was determined by a comparison with the control flats not treated with the antidote compounds and with blank flats with neither herbicide or antidote additive.

BUREAU OMPI WIPO INTERNATIONAL

TABLE III

Herbicide: VERNAM

Herbicide Applied PPI

Control* - 1 lb/A		Ml	Wh	Ct	Rc	Ba	6 lb/A	Cn	Wg	Ct	Ft	Soy
Antidote	Method of Application	90	95	60	100	80		85	100	85	100	25
1	IF/5	75	-	-	90	60		0	-	-	90	-
2	IF/5	60	-	-	90	65		0	-	-	90	15
1	PPI-TM/5	80	-	-	-	65		0	-	-	-	-
2	PPI-TM/5	65	-	-	-	70		0	-	-	-	-
1	ST/0.5%	80	-	50	90	70		0	-	-	-	15
2	ST/0.5%	70	-	-	85	60		0	-	-	-	10

Herbicide: EPTC

Herbicide Applied PPI

Control* - 0.75 lb/A		Ml	Wh	Ct	Rc	Ba	5 lb/A	Cn	Wg	Ct	Ft	Soy
Antidote	Method of Application	80	85	50	95	60		50	100	85	100	50
1	IF/5	65	75	-	90	50		0	-	-	90	-
2	IF/5	70	75	-	90	50		0	-	-	90	70
1	PPI-TM/5	70	70	-	-	40		0	90	-	-	-
2	PPI-TM/5	60	70	30	90	40		0	90	-	-	-
1	ST/0.5%	70	75	40	85	20		0	-	-	-	-
2	ST/0.5%	35	60	-	70	20		0	-	-	-	-

Herbicide: SUTAN

Herbicide Applied PPI

Control* - 1.5 lb/A		Ml	Wh	Ct	Rc	Ba	18 lb/A	Cn	Wg	Ct	Ft	Soy
Antidote	Method of Application	65	75	0	60	80		25	100	55	100	75
1	IF/5	-	-	-	-	70		0	-	-	-	-
2	IF/5	50	-	-	-	80		0	-	-	-	-
1	PPI-TM/5	-	-	-	-	-		0	-	35	-	-
2	PPI-TM/5	-	-	-	-	-		0	-	-	-	-
1	ST/0.5%	50	-	-	-	65		0	-	20	-	-
2	ST/0.5%	35	65	-	-	65		0	-	25	-	-

BUREAU OMPI WIPO

Herbicide: TERIDOX

Herbicide Applied PES

Control* - 0.5 lb/A		Cn 70	Wh 65	Rc 100	Ba 65	M1 95	2 lb/A	Cn 99	Wg 100	Ct 80	Ft 100	Soy 65
Antidote	Method of Application											
1	IF/5	20	35	-	40	-		85	-	-	-	-
2	IF/5	0	45	-	40	-		55	-	70	-	55
1	PES-TM/5	15	30	-	30	90		85	-	-	-	-
2	PES-TM/5	0	0	-	30	-		65	-	70	-	-
1	ST/0.5%	10	15	-	15	85		85	-	-	-	-
2	ST/0.5%	15	30	-	20	80		55	-	70	-	50

Herbicide: MON 097

Herbicide Applied PES

Control* - 1 lb/A		Cn 0	Wh 85	Rc 100	Ba 80	M1 98	12 lb/A	Cn 35	Wg 100	Ct 85	Ft 100	Soy 80
Antidote	Method of Application											
1	IF/5	-	15	-	40	85		15	-	-	-	65
2	IF/5	-	-	-	70	85		-	-	-	-	70
1	PES-TM/5	-	75	-	50	70		0	-	-	-	90
2	PES-TM/5	-	65	-	20	45		-	-	-	-	90
1	ST/0.5%	-	50	-	25	70		15	-	75	-	-
2	ST/0.5%	-	65	-	20	45		-	-	-	-	-

Herbicide: LASSO

Herbicide Applied PES

Control* - 3.5 lb/A		Cn 0	Wh 70	Rc 100	Ba 80	M1 97	6 lb/A	Cn 0	Wg 100	Ct 60	Ft 100	Soy 35
Antidote	Method of Application											
1	IF/5	-	25	-	60	-		-	-	50	-	-
2	IF/5	-	45	-	65	50		-	-	-	-	-
1	PES-TM/5	-	60	-	40	85		-	-	-	-	-
2	PES-TM/5	-	45	-	40	50		-	-	-	-	-
1	ST/0.5%	-	40	-	30	75		-	-	30	-	25
2	ST/0.5%	-	30	-	20	45		-	-	20	-	20

BUREAU OMPI WIPO INTERNATIONAL

Herbicide: DUAL

Herbicide Applied PES

Control* - 3.5 lb/A		Cn	Wh	Rc	Ba	Ml		Cn	Wg	Ct	Ft	Soy
		0	90	100	90	97	7 lb/A	0	100	60	100	40
Antidote	Method of Application											
1	IF/5	-	80	-	-	-		-	-	55	-	20
2	IF/5	-	60	-	80	90		-	-	55	-	-
1	PES-TM/5	-	50	-	75	90		-	-	50	-	40
2	PES-TM/5	-	30	-	70	65		-	-	-	-	-
1	ST/0.5%	-	50	95	60	95		-	-	45	-	-
2	ST/0.5%	-	30	-	40	70		-	-	35	-	30

Herbicide: ANTOR

Herbicide Applied PES

Control* - 2 lb/A		Cn	Wh	Rc	Ba	Ml		Cn	Wg	Ct	Ft	Soy
		85	70	100	75	100	4 lb/A	95	100	30	100	40
Antidote	Method of Application											
1	IF/5	15	-	-	50	-		0	-	-	-	-
2	IF/5	10	50	-	50	-		0	-	-	-	-
1	PES-TM/5	0	55	90	35	90		0	-	20	-	-
2	PES-TM/5	0	35	-	25	85		0	-	20	-	-
1	ST/0.5%	0	50	-	45	-		0	-	0	-	15
2	ST/0.5%	0	40	-	25	-		0	-	20	-	20

* = Flats treated with herbicide alone, no antidote treatment.
- = No change in injury compared to the control.

The antidote compounds and compositions of the present invention can be used in any convenient form. Thus, the antidote compounds can be formulated into emulsifiable liquids, emulsifiable concentrates, liquid, wettable powder, powders, granular or any other convenient form. In its preferred form, a non-phytotoxic quantity of an herbicidal antidote compound is admixed with a selected herbicide and incorporated into the soil prior to or after planting the seed. It is to be understood, however, that the herbicides can be incorporated into the soil and thereafter the

BUREAU OMPI INTERNATIONAL

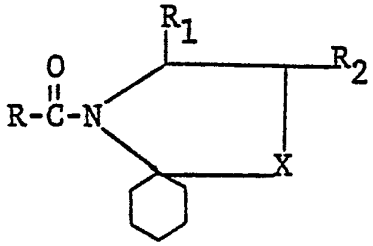
antidote compound can be incorporated into the soil. Moreover, the crop seed itself can be treated with a non-phytotoxic quantity of the compound and planted into the soil which has been treated with herbicides, or untreated with the herbicide and subsequently treated with the herbicide. The addition of the antidote compound does not effect the herbicidal activity of the herbicides except to render the activity selective with respect to beneficial crops.

The amount of antidote compound present can range between about 0.01 to about 30 parts by weight of antidote compound described herein per each part by weight of herbicide. The exact amount of antidote compound will usually be determined on economic ratios for the most effective amount usable. It is understood that a non-phytotoxic quantity of antidote compound will be employed in the herbicidal compositions described herein.

BUREAU OMPI WIPO INTERNATIONAL

WHAT IS CLAIMED IS:

1. A compound having the formula



in which X is oxygen or sulfur, R is lower haloalkyl having 1 to 6 carbon atoms, inclusive and halo is at least two of chlorine, fluorine or bromine, R_1 is hydrogen or lower alkyl having 1 to 6 carbon atoms, inclusive, and R_2 is hydrogen or phenyl.

2. A compound according to Claim 1 in which R is chloroalkyl, R_1 is lower alkyl, and R_2 is hydrogen.

3. A compound according to Claim 2 in which X is oxygen, R is dichloromethyl, and R_1 is ethyl.

4. A compound according to Claim 1 in which R is dichloroalkyl, R_1 is hydrogen, and R_2 is hydrogen.

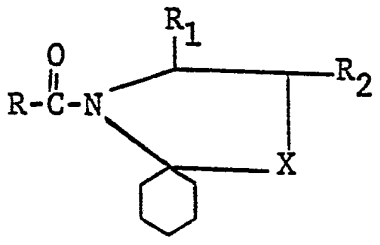
5. A compound according to Claim 4 in which R is dichloromethyl and X is sulfur.

6. A compound according to Claim 5 in which R is dichloromethyl and X is oxygen.

7. A compound according to Claim 1 in which R is chloroalkyl, R_1 is hydrogen, and R_2 is phenyl.

8. A compound according to Claim 7 in which R is dichloromethyl and X is oxygen.

9. In the method of controlling weeds wherein at least one thiolcarbamate or haloacetanilide herbicide is applied to the habitat of said weeds, the improvement comprising applying to the habitat thereof from about 0.01 to about 30 parts by weight for each part by weight of the herbicide an antidote compound corresponding to the formula



BUREAU OMPI WIPO NATION

in which X is oxygen or sulfur, R is lower haloalkyl having 1 to 6 carbon atoms, inclusive and halo is at least two of chlorine, fluorine or bromine, R_1 is hydrogen or lower alkyl having 1 to 6 carbon atoms, inclusive, and R_2 is hydrogen or phenyl.

10. In the method according to Claim 9 in which said antidote has the formula wherein R is chloroalkyl, R_1 is lower alkyl, and R_2 is hydrogen.

11. In the method according to Claim 10 in which X is oxygen, R is dichloromethyl, and R_1 is ethyl.

12. In the method according to Claim 10 in which X is sulfur, R is chloromethyl, and R_1 is ethyl.

13. In the method according to Claim 9 in which R is chloroalkyl, R_1 is hydrogen, and R_2 is hydrogen.

14. In the method according to Claim 13 in which R is dichloromethyl and X is sulfur.

15. In the method according to Claim 13 in which R is dichloromethyl and X is oxygen.

16. In the method according to Claim 13 in which R is chloromethyl and X is sulfur.

17. In the method according to Claim 13 in which R is ω-chloro-n-propyl and X is oxygen.

18. In the method according to Claim 9 in which R is chloroalkyl, R_1 is hydrogen, and R_2 is phenyl.

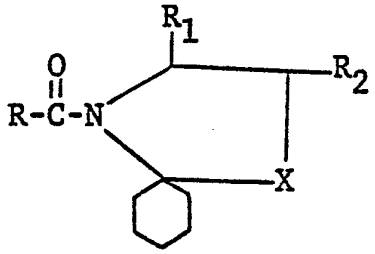
19. In the method according to Claim 18 in which R is chloromethyl and X is oxygen.

20. In the method according to Claim 18 in which R is dichloromethyl and X is oxygen.

21. In the method according to Claim 18 in which R is β-chloroethyl and X is oxygen.

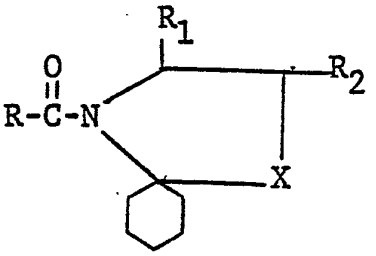
22. The method of protecting a crop from injury due to at least one thiolcarbamate or haloacetanilide herbicide, comprising applying to the crop seed prior to planting, a non-phytotoxic antidotally effective amount of a compound corresponding to the formula

BUREAU OMPI WIPO INTERNATIONAL



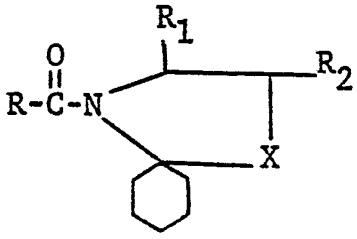
in which X is oxygen or sulfur, R is lower haloalkyl having 1 to 6 carbon atoms, inclusive and halo is at least two of chlorine, fluorine or bromine, R_1 is hydrogen or lower alkyl having 1 to 6 carbon atoms, inclusive, and R_2 is hydrogen or phenyl.

23. The method of protecting a crop from injury due to at least one thiolcarbamate or haloacetanilide herbicide, comprising preplant incorporation in the soil in which said crop is to be planted, a non-phytotoxic antidotally effective amount of a compound corresponding to the formula



in which X is oxygen or sulfur, R is lower haloalkyl having 1 to 6 carbon atoms, inclusive and halo is at least two of chlorine, fluorine or bromine, R_1 is hydrogen or lower alkyl having 1 to 6 carbon atoms, inclusive, and R_2 is hydrogen or phenyl.

24. The method of protecting a crop from injury due to at least one thiolcarbamate or haloacetanilide herbicide, comprising applying to the seed and soil in which said crop is to be planted, a non-phytotoxic antidotally effective amount of an antidote compound corresponding to the formula



BUREAU OMPI WIPO INTERNATION

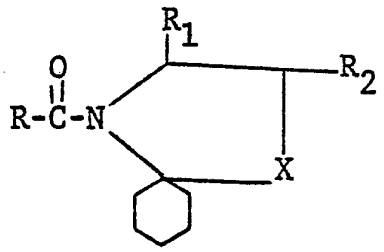
in which X is oxygen or sulfur, R is lower haloalkyl having 1 to 6 carbon atoms, inclusive and halo is at least two of chlorine, fluorine or bromine, R_1 is hydrogen or lower alkyl having 1 to 6 carbon atoms, inclusive, and R_2 is hydrogen or phenyl.

25. In the method according to Claim 24 in is chloroalkyl, R_1 is lower alkyl, and R_2 is hydrogen.

26. In the method according to Claim 24 in which R is chloroalkyl, R_1 is hydrogen, and R_2 is hydrogen.

27. In the method according to Claim 24 in which R is chloroalkyl, R_1 is hydrogen, and R_2 is phenyl.

28. An herbicidal composition comprising at least one thiolcarbamate or haloacetanilide active herbicide and an antidote compound therefor corresponding to the formula



in which X ix oxygen or sulfur, R is lower haloalkyl having 1 to 6 carbon atoms, inclusive and halo is at least two of chlorine, fluorine or bromine, R_1 is hydrogen or lower alkyl having 1 to 6 carbon atoms, inclusive, and R_2 is hydrogen or phenyl.

29. The herbicidal composition of Claim 28 in which R is chloroalkyl, R_1 is lower alkyl, and R_2 is hydrogen.

30. The herbicidal composition of Claim 29 in which X is oxygen, R is dichloromethyl, and R_1 is ethyl.

31. The herbicidal composition of Claim 29 in which X is sulfur, R is chloromethyl, and R_1 is ethyl.

32. The herbicidal composition of Claim 28 in which R is chloroalkyl, R_1 is hydrogen, and R_2 is hydrogen.

33. The herbicidal composition of Claim 32 in which R is dichloromethyl and X is sulfur.

34. The herbicidal composition of Claim 32 in which R is dichloromethyl and X is oxygen.

BUREAU OMPI WIPO INTERNATIONAL

35. The herbicidal composition of Claim 32 in which R is chloromethyl and X is sulfur.

36. The herbicidal composition of Claim 32 in which R is ω-chloro-n-propyl and X is oxygen.

37. The herbicidal composition of Claim 28 in which R is chloroalkyl, R_1 is hydrogen, and R_2 is phenyl.

38. The herbicidal composition of Claim 37 in which R is chloromethyl and X is oxygen.

39. The herbicidal composition of Claim 37 in which R is dichloromethyl and X is oxygen.

40. The herbicidal composition of Claim 37 in which R is β-chloroethyl and X is oxygen.

BUREAU OMPI WIPO INTERNATIONAL

INTERNATIONAL SEARCH REPORT

International Application No PCT/US80/00941

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [3]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int. Cl.[3] C07D 263/04, 277/04
U.S. Cl. 548/147, 216; 71/88,90

II. FIELDS SEARCHED

Minimum Documentation Searched [4]

Classification System	Classification Symbols
US	548/147, 216; 71/88,90

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [5]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [14]

Category *	Citation of Document, [16] with indication, where appropriate, of the relevant passages [17]	Relevant to Claim No. [18]
X	US,A, 3,881,908, published 6 May 1975, See Column 1, lines 63-65, Dorschner et al	1-40
X	US,A, 3,859,292, published 7 January 1975, See Column 1, lines 63-65, Dorschner et al	1-40
A	US,A, 4,072,688, published 7 February 1978, Teach	1-40
A	US,A, 4,124,372, published 7 November,1978, Pallos et al	1-40
A	US,A, 3,989,503, published 2 November,1976 Pallos et al	1-40
A	US,A, 3959,304, published 25 May 1976 Teach	1-40
X	US,A, 3,185,720, published 25 May 1965, Tilles et al	9-40
X	US,A, 3,442,945, published 6 May 1969,Olin	9-40

* Special categories of cited documents: [15]

"A" document defining the general state of the art

"E" earlier document but published on or after the international filing date

"L" document cited for special reason other than those referred to in the other categories

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but on or after the priority date claimed

"T" later document published on or after the international filing date or priority date and not in conflict with the application, but cited to understand the principle or theory underlying the invention

"X" document of particular relevance

IV. CERTIFICATION

Date of the Actual Completion of the International Search [2]	Date of Mailing of this International Search Report [2]
12 December 1980	17 DEC 1980
International Searching Authority [1]	Signature of Authorized Officer [20]
ISA/US	Catherine L. Mills

Form PCT/ISA/210 (second sheet) (October 1977)

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

V. ☐ OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE [10]

This International search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. ☐ Claim numbers _____, because they relate to subject matter [12] not required to be searched by this Authority, namely:

2. ☐ Claim numbers _____, because they relate to parts of the International application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out [13], specifically:

VI. ☒ OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING [11]

This International Searching Authority found multiple inventions in this international application as follows:

I. Compounds: Claims 1-8

II. Two component compositions and methods of use: Claims 9-40

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the International application.

2. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the International application for which fees were paid, specifically claims:

3. ☒ [illegible]

Remark on Protest

☐ The additional search fees were accompanied by applicant's protest.

☐ No protest accompanied the payment of additional search fees.