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UREA AND THIOUREA COMPOUNDS

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The present invention is concerned with organic compounds wherein one terminal position is occupied by a polyhalogenopolycycloalkenyl radical and the other terminal position is occupied by a urea or thiourea radical. These compounds have been found to possess significant toxicity toward and inhibition of a wide variety of fungi.

The need for efficient and economical fungicidal and fungistatic compositions has long been manifest. In spite of this fact, however, a vast number of the compounds employed as fungicides have generally been found lacking in one or more of the basic requirements of a satisfactory fungicide. In order to be commercially useful a fungicidal composition must be compatible with adjuvants and other active ingredients; it must be economical; it should be soluble in common solvents and stable; and most important, it must not be toxic to the plants to which it is applied or to animal life. A prohibitive degree of phytotoxicity under the conditions utilized for fungus control and toxicity toward warm blooded animals are among the most common shortcomings of present fungicides.

It is, consequently, the principal object of the present invention to provide new and novel compounds which are effective as fungicides yet do not manifest prohibitive phytotoxicity or toxicity toward warm blooded animals such as man.

Another object of the present invention is to provide new and novel fungicidal compounds which can be economically prepared, distributed and applied to plants.

Yet another object of the present invention is to provide economical and stable fungicidal compositions containing these compounds.

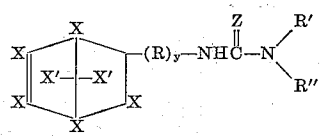
Still another object of the present invention is to provide a method of combating fungi by applying these compositions to plants.

Other objects, features and advantages will be apparent from the following description read in conjunction with the appended claims.

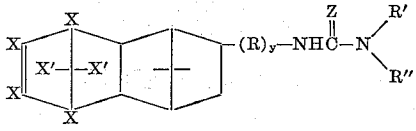
Generally speaking, the present invention is concerned with organic compounds wherein one terminal position is occupied by a polyhalogenocycloalkene such as hexachlorobicyclo(2.2.1)hept-5-ene and the other terminal position is occupied by a urea or thiourea radical.

The cycloalkene portion of the molecule may be attached directly to the urea or thiourea radical or alternatively, the terminal positions of the molecule may be separated by alkyl, aryl, or aralkyl radicals.

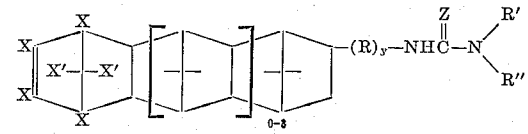
Of the polyhalogenopolycycloalkenes which occupy one terminal position of the compounds of the present invention, halogenated bicyclo(2.2.1)hept-5-ene rings as shown in the following structural formula are preferred:



Of equal interest is the dimethanonaphthalene ring structure shown in the following structural formula:



The present invention also encompasses the polycyclic structures shown in the following general formula:



The basic skeleton consists of not more than five linearly fused five membered rings.

In these formulae R represents a straight chain, branched chain or cyclic alkylene group of 1–10 carbon atoms, an arylene group such as phenylene, tolylene, naphthylene and anthrylene, or an aralkylene group wherein the alkylene portion contains 1–10 carbon atoms and the aryl portion is chosen from such groups as phenyl, benzyl, tolyl, naphthalenyl, and anthracenyl. Y is 0 to 10. Z is oxygen or sulfur, preferably oxygen.

X represents hydrogen or a halogen (preferably chlorine) and X′ represents hydrogen, a halogen (preferably chlorine) or an alkoxy (preferably methoxy) group. At least one X is preferably a halogen.

R′ and R″ individually represent hydrogen, aliphatic groups of 1–10 carbon atoms, saturated and unsaturated, both substituted and unsubstituted, aromatic groups such as phenyl, benzyl, tolyl, naphthalenyl and anthracenyl or aralkyl groups wherein the alkyl portions contain 1–10 carbon atoms and the aryl portions are chosen from such groups as phenyl, benzyl, tolyl, naphthalenyl and anthracenyl. R′ and R″ may also individually represent a polyhalogenocycloalkene of the type already described and illustrated. These cycloalkenes may be attached directly to a nitrogen atom as in 1,3-bis(1,2,3,4-tetrachloro-7-oxobicyclo(2.2.1)hept-5-en-2-yl)-2-thiourea tetramethyl diacetal or separated by an aliphatic group of 1–10 carbon atoms as in 1,3-bis(1,2,3,4-tetrachloro-7-oxobicyclo-(2.2.1)hept-5-en-2-ylmethyl)-2-thiourea tetramethyl diacetal. The compounds of the present invention may thus be considered as ureas and thioureas having substituted therein halogenated polycyclic structures such as polyhalopolycyclic alkenyl radical or a halogenated 1,4,5,8-dimethanonaphthyl radical.

Examples of specific compounds encompassed by the present invention follow:

1-(1,4,5,6,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylmethyl)-2-thiourea

3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylmethyl)-1,1-dimethyl-2-thiourea

1-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylmethyl)-3-isopropyl-2-thiourea

1,1-diallyl-3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylmethyl)-2-thiourea

3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylmethyl)-1,1-bis(2-hydroxyethyl)-2-thiourea

1,1-di-sec-butyl-3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)-hept-5-en-2-ylmethyl)-2-thiourea

3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylmethyl)-1,1-dimethylurea

3-(bicyclo(2.2.1)hept-5-en-2-ylmethyl)-1,1-dimethyl-2-thiourea

1,3-bis(1,2,3,4-tetrachloro-7-oxobicyclo(2.2.1)hept-5-en-2-ylmethyl)-2-thiourea tetramethyl diacetal.

(10-(1,4,5,6,7,7-hexabromobicyclo(2.2.1)hept-5-en-2-yl)decyl)urea

1-(1,4,5,6,7,7-hexafluorobicyclo(2.2.1)hept-5-en-2-ylbenzyl)-3-isopropyl-2-thiourea

1,1-diallyl-3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-yltolyl)-2-thiourea

3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylnaphthyl)-1,1-bis(2-hydroxyethyl)-2-thiourea

3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylanthryl)-1,1-didecylurea

3-(10-((bicyclo(2.2.1)hept - 5 - en - 2 - yl)decyl)phenyl)-1,1-dimethyl-2-thiourea

1-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept - 5 - en - 2-yl-2-thiourea

1-(5,6,7,8,9,9 - hexachloro - 1,2,3,4,4a,5,8,8a - octahydro-1,4,5,8-dimethano-2-naphthalen-2-yl)-2-thiourea

1-(10-(5,6,7,8,9,9 - hexabromo - 1,2,3,4,4a,5,8,8a - octahydro-1,4,5,8 - dimethanonaphthalen - 2 - yl)decyl) - 2-thiourea

3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept - 5 - en - 2-ylmethyl)-1-benzyl-1-tolyl-2-thiourea

3-(3-(1,4,5,6,7,7 - hexabromobicyclo(2.2.1)hept - 5 - en-2-yl)propyl)-1-naphthyl-1-anthryl-2-thiourea

3 - (bicyclo(2.2.1)hept-5-en-2-ylmethyl) - 1,1 - di(decylphenyl)-2-thiourea

1-(5,6,7,8,9,9 - hexachloro - 1,2,3,4,4a,5,8,8a - octahydro-1,4,5,8-dimethanonaphthalen-2-yl)-2-thiourea

Generally speaking the thiourea of the present invention may be prepared by reacting the corresponding polyhalogenopolycycloalkene isothiocyanate with the appropriate amine. These isothiocyanates can be prepared as adduction products as in the reaction of hexachlorocyclopentadiene with allyl isothiocyanate to form hexachlorobicycloheptenylmethyl isothiocyanate. The ureas of the present invention may, if desired, be prepared by reacting the appropriate polyhalogenopolycycloalkene amine with an alkylcarbamoyl chloride. The preparation of the amines is described in co-pending application Serial Number 705,781, filed December 30, 1957.

Examples of specific preparations of compounds encompassed by the present invention follow:

EXAMPLE I. — 1 - (1,4,5,6,7,7 - HEXACHLOROBICYCLO(2.2.1)HEPT - 5 - EN - 2- YLMETHYL) - 2-THIOUREA

To a solution of 8 grams of anhydrous ammonia in 175 ml. of anhydrous ethanol was added 50 grams of 1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept - 5 - en - 2 - ylmethyl isothiocyanate. After standing at room temperature over night the solvent was stripped to give a viscous dark oil which could not be crystallized immediately. Upon standing for about 3 months partial crystallization occurred. The solid was dissolved in ethanol and reprecipitated by addition of ether. The tan flocculent material, 35 grams, was recrystallized several times from ether to give 28 grams of a pure white material, M.P. 75° with decomposition.

Analysis.—Calcd. for $C_9H_8Cl_6N_2S$: Cl, 54.8; N, 7.2; S, 8.2. Found: Cl, 53.0; N, 6.9; S, 7.4.

EXAMPLE II.—3 - (1,4,5,6,7,7 - HEXACHLOROBICYCLO(2.2.1)HEPT - 5 - EN - 2 - YLMETHYL)-1,1-DIMETHYL-2-THIOUREA

A solution of 20 grams of dimethylamine in about 20 ml. of ethanol was added to a solution of 55.8 grams of 1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept - 5 - en - 2 - ylmethyl isothiocyanate in 150 ml. of ether at 0°. The mixture was stored in a refrigerator at 2° overnight. The resulting white solid was collected on a Büchner funnel and washed well with cold ether; 58 grams, M.P. 158–160°. Upon recrystallization from 95% ethanol a first crop, 37 grams, melted at 160–161°.

Analysis.—Calcd. for $C_{11}H_{12}Cl_5N_2S$: Cl, 51.1; N, 6.7; S, 7.7. Found: Cl, 50.8; N, 6.1; S, 7.3.

EXAMPLE III. — 1-(1,4,5,6,7,7-HEXACHLOROBICYCLO(2.2.1)HEPT - 5 - EN - 2 - YLMETHYL)-3-ISOPROPYL-2-THIOUREA

A solution of 0.2 mole (73.6 grams) of 1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylmethyl isothiocyanate in 10 ml. of ethanol was reacted with 12 grams (0.2 mole) of isopropylamine at 40° for one half hour, then kept at room temperature overnight. The mixture was poured into water; the solid was collected, M.P. 145–152°. It was recrystallized from a mixture of benzene-

hexane to give 27 grams of pure product, M.P. 154–156°.

Analysis.—Calcd. for $C_{12}H_{14}Cl_6N_2S$: Cl, 49.5; N, 6.5. Found: Cl, 49.2, 49.4; N, 6.3.

EXAMPLE IV. — 1,1 - DIALLYL-3-(1,4,5,6,7,7-HEXACHLOROBICYCLO(2.2.1)HEPT - 5 - EN - 2 - YLMETHYL)-2-THIOUREA

To a solution of 75 grams of 1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylmethyl isothiocyanate in 200 ml. of ether was added a solution of 20 g. of diallylamine in 100 ml. of ether over a period of 20 minutes. When no solid had formed after 3 days hexane was added and most of the ether was boiled off. On cooling 90 grams of solid was obtained. 40 grams of this was recrystallized to give a first crop of 26 grams, M.P. 131.5–132.5°.

Analysis.—Calcd. for $C_{15}H_{16}Cl_6N_2S$: Cl, 45.5; N, 6.0. Found: Cl, 45.4; N, 5.9.

EXAMPLE V.—3 - (1,4,5,6,7,7 - HEXACHLOROBICYCLO(2.2.1)HEPT-5-EN-2-YLMETHYL) - 1,1 - BIS-(2-HYDROXYETHYL)-2-THIOUREA

A solution of 21 grams of diethanolamine in 100 ml. of methanol was added to 74 grams of 1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2 - ylmethyl isothiocyanate in 200 ml. of methanol. After standing at 30° for 24 hours the solvent was removed under vacuum leaving a viscous syrup which was soluble in benzene. After standing, the oil became a glassy solid, M.P. 75–100°.

Analysis.—Calcd. for $C_{12}H_{15}N_2SO_2Cl_6$: Cl, 44.7. Found: Cl, 44.9.

EXAMPLE VI.—1-DI - SEC - BUTYL - 3 - (1,4,5,6,7,7-HEXACHLOROBICYCLO(2.2.1)HEPT - 5 - EN - 2-YLMETHYL)-2-THIOUREA

Thirteen grams of di-sec-butylamine was added to 37 grams of 1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylmethyl isothiocyanate in 10 ml. of benzene. After the exothermic reaction subsided 200 ml. of hexane was added and the solution cooled to give 29 grams of product, M.P. 106–108°, and concentration of the mother liquor gave 7 grams more solid, M.P. 103–106°.

Analysis.—Calcd. for $C_7H_{24}Cl_6N_2S$: Cl, 42.4. Found: Cl, 42.5, 42.6.

EXAMPLE VII.—3 - (1,4,5,6,7,7-HEXACHLOROBICYCLO(2.2.1)HEPT - 5 - EN - 2 - YLMETHYL-1,1-DIMETHYL UREA

A solution of 33 grams of 1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-ene-2-methylamine, 10.8 grams of dimethylcarbamoyl chloride, 8 grams of pyridine and 100 ml. of toluene was stirred at steam bath temperature for 16 hours. It was then poured on ice and the product was taken up in benzene. The benzene solution was washed with dilute HCl and then with water. After drying the benzene solution, the solvent was removed and the oily residue was recrystallized from ether to give 3 grams of product, M.P. 170–173°. The combined crops were recrystallized from a chloroform-ether mixture to give 6.4 grams of pure product, M.P. 175–6°.

Analysis. — Calcd. for $C_{11}H_{12}Cl_6N_2O$: Cl, 53.1. Found: Cl, 53.1, 53.3.

EXAMPLE VIII.—3 - (BICYCLO(2.2.1)HEPT-5-EN-2-YLMETHYL)-1,1-DIMETHY-2-THIOUREA

A solution of about 20 ml. of dimethylamine in 50 ml. of ether was added to a solution of 17 grams of bicyclo-(2.2.1)hept-5-en-2-ylmethyl isothiocyanate in 50 ml. of ether at 0°. After 2 hours the solid, 20.5 grams, was collected, combined with 20 grams obtained from a similar run and recrystallized from ether to give a first crop, M.P. 92–93°, 30 grams.

Analysis.—Calcd. for $C_{11}H_{18}N_2S$: N, 13.3. Found: N, 12.9.

EXAMPLE IX.—1,3-BIS(1,2,3,4 - TETRACHLORO-7-OXOBICYCLO(2.2.1)HEPT - 5-EN-2-YLMETHYL)-2-THIOUREA TETRAMETHYL DIACETAL

A mixture of 21 grams of 1,2,3,4-tetrachloro-7-oxobicyclo(2.2.1)hept-5-en-2-ylmethyl isothiocyanate dimethyl acetal and 800 ml. of 2% sodium hydroxide solution was refluxed with stirring for 16 hours. After cooling the crude solid was collected and recrystallized from benzene-hexane mixture to give 15 grams of product, M.P. 194–196°.

Analysis.—Calcd. for $C_{21}H_{24}Cl_8N_2O_4S$: C, 36.9; H, 3.5; Cl, 41.6; S, 4.7. Found: C, 36.6; H, 3.8; Cl, 41.7, 41.8; S, 5.1.

EXAMPLE X.—1-(5,6,7,8,9,9-HEXACHLORO-1,2,3,4,-4a,5,8,8a-OCTAHYDRO - 1,4,5,8 - DIMETHANONAPHTHALEN-2-YL)-2-THIOUREA

A two-phase system consisting of 92 g. (1.0 mole) of bicyclo(2.2.1)hepta-2,5-diene, 76 g. of ammonium thiocyanate, and 75 ml. of water in a 500 ml. flask was stirred on the steam bath while 100 g. of concentrated hydrochloric acid was added dropwise over a period of one hour. After cooling, the mixture was diluted with ether and the ether phase was separated, washed with water, and dried over anhydrous sodium sulfate. Distillation, and redistillation gave 92 g. (61% yield) of water-white product, B.P. 63.5–65° (0.1 mm.); $n^{28.5}D$ 1.5602, bicyclo-(2.2.1)hept-5-en-2-yl isothiocyanate.

Analysis.—Calcd. for C_8H_9NS: N, 9.28; S, 21.2; mol. wt. 151. Found: N, 9.16; S, 20.9; mol. wt. 156.

A mixture of 13 g. (0.05 mole) of hexachlorocyclopentadiene and 7.6 g. (0.05 mole) of bicyclo(2.2.1)hept-5-en-2-yl isothiocyanate was heated at 160–170° for 17 hours. The black oily solid was taken up in 150 ml. of dioxane, charcoaled, and filtered. Two volumes of methanol and one of water were added. The precipitate was collected and washed with methanol. The solid was recrystallized from 100 ml. of heptane to give 9.0 g. of product, M.P. 186–188.5°. A second crop of 3 g., M.P. 176–182° was obtained by concentrating the mother liquors. These two crops were combined and recrystallized from ethyl acetate to give 8.0 g. (38% yield) of product as needles, M.P. 188–190°.

Analysis.—Calcd. for $C_{13}H_8NSCl_6$: Cl, 50.2; S, 7.55. Found: Cl, 50.0; S, 7.45.

A mixture of 10 g. of the Diels-Alder adduct of hexachlorocyclopentadiene and bicyclo(2.2.1)hept-5-en-2-yl isothiocyanate, 100 ml. of dioxane and 100 ml. of concentrated ammonium hydroxide was heated on the steam bath with stirring for two hours. Seventy ml. of concentrated ammonium hydroxide and 40 ml. of dioxane were added and heating and stirring were continued. After two hours, another 30 ml. of concentrated ammonium hydroxide was added. After one hour and 20 minutes, the mixture was allowed to cool to room temperature and stand over the weekend. The solid was collected and recrystallized first from methanol and then from benzene to give product as pure white powder, M.P. 209° with decomposition.

Analysis.—Calcd. for $C_{13}H_{12}Cl_6N_2S$: C, 35.4; H, 2.72; Cl, 48.3; S, 7.25. Found: C, 35.5; H, 3.04; Cl, 48.0; S, 7.09.

The compounds of the present invention possess fungicidal activity to a wide variety of plant pathogens. In the foliage fungicide screen, three varieties of bean plants which are hosts for four foliage fungus diseases, were employed. These hosts and pathogens are listed below. The chemicals were screened for general as well as specific test control activity and for phytotoxicity Diseases and hosts are shown below.

Bean hosts	
Phaseolus vulgaris var. Pinto.	*Uromyces phaseoli* var. typica (rust).
P. vulgaris var. Black Valentine.	*Erysiphe polygoni* (powdery mildew).
P. limensis var. Fordhood 242.	*Colletotrichum lindemuthianum* (anthracnose).
	Phytophthora phaseoli (downy mildew).

These four bean pathogens are of economical importance and represent each of the four classes of fungi. *P. phaseoli* is closely allied with *P. infestans,* the important potato and tomato pathogen. Thus, with the above selection, chemicals can be routinely screened for general or specific disease control activity and for phytotoxicity on a moderately susceptible plant type.

The test is carried out according to the following procedure. Test chemicals are prepared as 1% w./v. stock solutions in a solvent. The stock is diluted for spraying using a diluent consisting of distilled water+solvent (1:1) or diluent consisting of distilled water plus two co-solvents. Triton X–155, at 0.005% w. (2:1:1) –0.10% w. is used as a wetting agent for each concentration of toxicant. All chemicals are initially tested at a single concentration of 1000 p.p.m. If acceptable disease control is shown, chemicals are retested at 1000 p.p.m. and the next lowest dilution of 500 p.p.m. Chemicals continuing to show disease control are retested in this fashion until the minimum effective concentration is determined. Phytotoxicity assessments are expressed as the maximum "safe" concentration.

Spray applications are made using a laboratory sprayer. The bean plants are selected for use at a stage when the two primary leaves are about three-quarters expanded. To facilitate deposit, the primary leaves are oriented to a vertical position by pinning them to a small wire staff. Either the upper or lower epidermis of the leaf is exposed to the spray stream, depending on the surface to be inoculated.

With the mist type spray and the diluent mixture which is applied, a drying interval of 1–2 hours is sufficient before inoculation with spore suspensions using a specially constructed atomizer. Inoculations with bean mildew are made by dusting conidia over treated plants in the greenhouse.

After 24 hours incubation at 19° C. and 100% humidity, the plants are removed to the controlled-environment greenhouse for sympton development. Disease control and phytotoxicity assessments are made within 7 days.

The following table summarizes the results of screening.

Table 1.—Foliage fungicide screen

Chemical compound	Disease control (min. effective conc. p.p.m.)				Phytotoxicity, max. "Safe" (conc. p.p.m.)		
	P.p.[a]	*E.p.*	*U.a.*	*C.l.*	L[b]	P.	B.V.
3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)-hept-5-en-2-ylmethyl)-1,1-dimethyl-2-thiourea	250	1,000–2,000	500	500	>2,000	500	1,000–2,000
1,1-diallyl-3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylmethyl)-2-thiourea	>1,000	>1,000	>1,000	>1,000	>1,000	>1,000	>1,000
3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylmethyl)-1,1-bis(2-hydroxyethyl)-2-thiourea	1,000	1,000	1,000	500–1,000	1,000	1,000	>1,000
3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylmethyl)-1,1-dimethyl-urea	>1,000	>1,000	>1,000	>1,000	>1,000	>1,000	>1,000

[a] *P.p.*=*Phytophthora phaseoli* (downy mildew of lima bean); *E.p.*=*Erysiphe polygoni* (bean powdery mildew); *U.a.*=*Uromyces phaseoli* (bean rust); *C.l.*=*Colletotrichum Lindemuthianum* (bean anthracnose).

[b] L=Lima bean; P=Pinto bean; BV=Black Valentine bean.

The effectiveness of the present compounds as fungicides is further evidenced by the following tests.

To obtain expanded disease control data, chemicals were sprayed mainly as emulsible concentrates using concentrations of 0.24% w., 0.12% w., and 0.06% w. These correspond respectively to 2, 1 and 0.5 lbs. toxicant per 100 gallons of spray. Plants were sprayed to the run-off stage, dried for 24 hours, and inoculated with test fungus spores. After inoculation, the plants were held for 24–48 hours in a humidified incubation chamber at 19° C. They were then removed to the greenhouse for disease and phytotoxicity development.

Crops and diseases used were tomato or potato blight (*Phytophthora infestans*), celery blight (*Septoria apii-graveolentis*), bean mildew (*Erysiphe polygoni*), bean rust (*Uromyces appendiculatus*), and cucumber anthracnose (*Colletotrichum langenarium*).

From four replicated plants per concentration, a percentage disease control figure was obtained, which was based upon the improvement shown over the untreated checks as follows:

$$100 \times \frac{\text{Disease rating of untreated check} - \text{disease rating of treatment or standard}}{\text{Disease rating of untreated check}}$$

The percent disease control for a treatment was next compared with the percent control for the standard fungicide (captan at 0.24% w. of formulated chemical) as follows:

$$\text{Foliage-fungicide activity index (F-F.A.I.)} = \frac{\text{Percent control for treatment}}{\text{Percent control for standard}} \times 100$$

Where the disease control for the test chemical and standard was equivalent, the index value was unity, 100. Values above 100 indicated superiority. It will be understood however that compounds showing index values substantially below 100 may also be of considerable value.

In most cases comparisons were made at the 0.24% w. (2 lbs./100 gal.) concentration.

Readings for plant injury were obtained on tomatoes, beans, celery and cucumber. Both chronic toxicity (yellowing, distortion, etc.) and acute toxicity (tissue death) were recorded. The scale used was from 0–400. "0" represented no visible poisoning and 400 was the most severe manifestation.

The following table summarizes the results of these tests:

The active compounds of the present invention may be used alone or in combination with other fungicidal, viriciadal, insecticidal, or acaricidal materials, the action on which may be either internal or external, with plant nutritives, plant hormones and the like. Wetting agents, and if necessary or desirable, stickers such as the heavy hydrocarbon oils with a minimum viscosity of 10° Engler at 50° C. can be present. Any conventional wetting agent which will not react with the toxicant for example, alkyl sulfate salts, alkyl aryl sulfonate salts, sulfosuccinate salts, ethers from polyethylene glycols and alkylated phenols, and the like can be employed. If the toxic agents are employed in the form of emulsions or suspensions, for example, in water, solvents such as oils, emulsifiers, emulsion stabilizers, and the like may be added. Materials which suppress phytotoxic action may also be added if desired. For example, glucose is known to protect tomato plants against damage by certain substances having a phytotoxic effect when employed in concentrated form.

The ureas and thiourea compounds of the present invention may be applied by means of spraying. Spraying of the plants to be treated may be performed with aqueous emulsions, solutions or suspensions of the active agents. The spray liquid is generally applied at a rate of from about 75 to 150 gallons per acre. If spraying is effected with smaller quantities of liquid as in low volume spraying, high concentrations of the active agents should be employed. If desired, a minor amount of the order of about 0.01 to about 0.05% by weight, of a wetting agent may be added to aid in forming a suspension of the salt in the aqueous medium. Any of the conventional wetting agents can be employed. Particularly suitable wetting agents are the sodium salts of a mixture of secondary heptadecyl sulfates, sold commercially under the name of "Teepol" and polyethylene glycol ethers of alkyl phenols sold under the trade name of "Triton X–100" and "Triton X–155." Preferable concentrate compositions comprising an active compound of the present invention and a suitable wetting agent are prepared, and the concentrate is then dispersed in water prior to use.

A further form in which the fungicidal compounds of the present invention may be applied consists of solutions of the active ingredient in suitable inert liquid or semi-solid diluents, in which the active ingredient is present in molecularly dispersed form. The form in which the agents to be employed are applied to the objects treated

Table 2–Foliage fungicide test

FOLIAGE-FUNGICIDE ACTIVITY INDEX

Chemical compound	Activity index at 0.24% conc. (upper figure and percent control at 0.06% (lower figure)						Phytotoxicity at 0.24% (upper figure) and 0.06% conc. (lower figure) respectively				
	P.i.[a]	*S.a.*	*E.p.*	*U.a.*	*C.l.*	Combined index	T[b]	C	B	Cu	Combined
1-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)-hept-5-en-2-ylmethyl)-2-thiourea	100	73	25	100	68	73	100	100	100	100	100
	100	64	10	50	63	57	0	0	0	0	0
3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)-hept-5-en-2-ylmethyl)-1,1-dimethyl-2-thiourea.	137	100	82	109	-----	-----	75	75	100	350	150
	85	67	50	100	63	73	0	0	50	175	56
1-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylmethyl)-3-isopropyl-2-thiourea.	67	106	50	108	66	79	0	0	75	0	19
	67	81	30	75	57	62	0	0	50	0	13
1,1-diallyl-3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylmethyl)-2-thiourea.	33	0	100	82	54	53	0	0	0	0	0
	33	44	95	65	46	59	0	0	0	0	0
3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylmethyl)-1,1-bis(2-hydroxyethyl)-2-thiourea.	100	78	5	66	61	61	100	100	125	125	113
	100	46	0	50	61	51	50	0	100	100	63
1,1-di-sec-butyl-3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylmethyl)-2-thiourea.	100	73	100	83	26	75	0	0	0	0	0
	67	54	80	100	0	60	0	0	0	0	0
3-(1,4,5,6,7,7-hexachlorobicyclo(2.2.1)hept-5-en-2-ylmethyl)-1,1-dimethyl-urea.	78	0	100	156	-----	-----	100	0	175	400	169
	50	0	35	100	-----	-----	75	0	100	400	144
3-[bicyclo(2.2.1)hept-5-en-2-yl-methyl]-1,1-dimethyl-2-thiourea	100	100	-----	-----	-----	-----	325	200	375	375	319
	100	100	50	50	86	77	200	100	100	100	125
1,3-bis(1,2,3,4-tetrachloro-7-oxobicyclo(2.2.1)hept-5-en-2-ylmethyl)-2-thiourea tetramethyl diacetal.	0	0	25	67	16	27	0	0	50	0	13
	0	0	0	58	0	12	0	0	0	0	0

[a] *P.p.* = *Phytophthora phaseoli* (downy mildew of lima bean); *E.p.* = *Erysiphe polygoni* (bean powdery mildew); *U.a.* = *Uromyces phaseoli* (bean rust) *C.l.* = *Colletotrichum Lindemuthianum* (bean anthracnose).

[b] T=tomato; C=celery; B=bean; Cu=cucumber.

depends on the nature of the object and the purpose of the application.

Suitable inert solvents for the manufacture of liquid preparations should not be readily inflammable, as odorless as possible and without any toxic effect on humans and animals when properly used. Neither should they have a corrosive effect on the components of the preparations or the material of the storage vessel. Examples of suitable solvents are high boiling oils, e.g. oils of vegetable origin such as castor oil, etc., and lower-boiling solvents with a flash point of at least 30° C., such as carbon tetrachloride, ethylene dichloride, hydrated naphthalene, alkylated naphthalene, sorbent naphtha, etc. Mixtures of solvents may also be used.

The active compounds of the present invention may also be applied in the form of dusts utilizing as the inert vehicle such materials as tricalcium phosphate, precipitated chalk, bentonite, kaolin, kieselguhr, etc.

These compounds may also be employed in the form of aerosols. For this purpose the active ingredient is dissolved or dispersed in a solvent boiling below room temperature at atmospheric pressure.

We claim as our invention:

1. 1 - (1,4,5,6,7,7 - hexachlorobicyclo(2.2.1)hept - 5-en-2-ylmethyl)-2-thiourea.

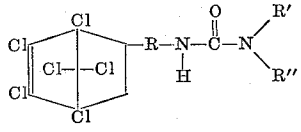
2. 1 -(1,4,5,6,7,7 - hexachlorobicyclo(2.2.1)hept - 5-en-2-ylmethyl)-3-isopropyl-2-thiourea.

3. 1,1 - diallyl - 3 - (1,4,5,6,7,7 - hexachlorobicyclo (2.2.1)hept-5-en-2-ylmethyl)-2-thiourea.

4. 3 - (1,4,5,6,7,7 - hexachlorobicyclo(2.2.1)hept - 5-en-ylmethyl)-,1-bis(2-hydroxyethyl)-2-thiourea.

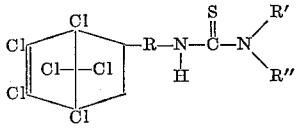
5. 1,1 - di - sec - butyl - 3-(1,4,5,6,7,7 - hexachlorobicyclo(2.2.1)-hept-5-en-2-ylmethyl)-2-thiourea.

6. A compound of the formula



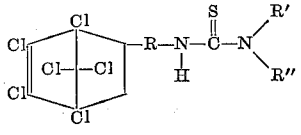
wherein R is alkylene of from 1 to 10 carbon atoms and R′ and R″ are each alkyl of from 1 to 10 carbon atoms.

7. A compound of the formula



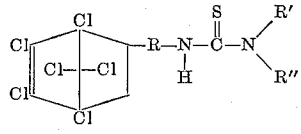
wherein R is alkylene of from 1 to 10 carbon atoms and R′ and R″ are each alkenyl of from 1 to 10 carbon atoms.

8. A compound of the formula



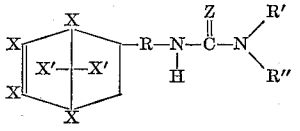
wherein R is alkylene of from 1 to 10 carbon atoms and R′ and R″ are each alkyl of from 1 to 10 carbon atoms.

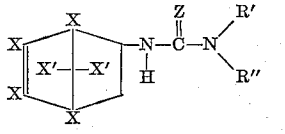
9. A compound of the formula

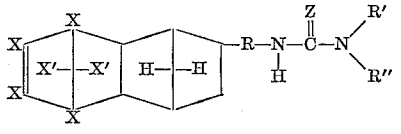


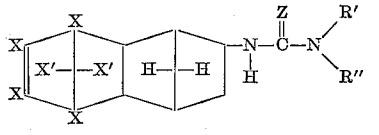
wherein R is alkylene of from 1 to 10 carbon atoms and R′ and R″ are each alkenyl of from 1 to 10 carbon atoms.

10. A compound of the formula selected from the group consisting of









wherein X is halogen, X′ is selected from the group consisting of hydrogen, halogen and lower alkoxy, R is alkylene of from 1 to 10 carbon atoms, Z is selected from the group consisting of oxygen and sulfur, and R′ and R″ are individually selected from the group consisting of hydrogen, alkyl of from 1 to 10 carbon atoms, alkenyl of from 1 to 10 carbon atoms and hydroxyethyl.

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