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N-(1-HALO-1-NITROALKYLTHIO)
DICARBOXIMIDES

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3 Claims

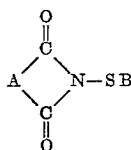
ABSTRACT OF THE DISCLOSURE

N-(1-halo-1-nitroalkylthio) dicarboximides wherein the alkyl group contains 2 to 6 carbon atoms and the halogen is of atomic number 17 to 35. Typical dicarboximides are N-(1-chloro-1-nitroethylthio) phthalimide, N-(1-halo-1-nitropropylthio) - 5,5 - dimethyl hydantoin, N,N-di-(1-chloro-1-nitropropylthio) uracil and 1,1-bis-(chloro-1-nitropropylthio) parabanic acid. These carboximides are fungicidal.

This invention concerns a new class of dicarboximides and their use as biocides. More particulaly, it relates to N-(1-halo-1-nitroalkylthio) dicarboximides and their use as fungicides.

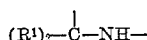
The compounds of this invention are N-(1-halo-1-nitroalkylthio) compounds wherein the nitrogen is attached to two carbonyl groups. The carbonyl groups are in turn attached to a divalent moiety to form either a mono- or bicyclic dicarboximide.

Structurally, the compounds of this invention have the generic formula

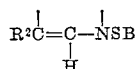


wherein A is one of the following groups:

- (1) 1,2-hexacarbocyclic group having from 0-3 sites of olefinic (aromatic) unsaturation;

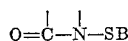


wherein R¹ is hydrogen or lower alkyl of from 1 to 6 carbons;



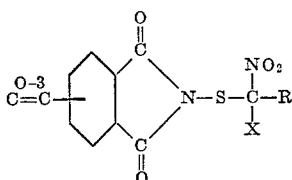
and

- (4)



wherein R² is hydrogen or lower alkyl, i.e., from 1 to 6 carbons, and B is a 1-halo-1-nitroalkyl group in which the halogen is of atomic number 17 to 35 and the alkyl is of from 2 to 6 carbons, i.e., ethyl through hexyl.

The compounds in which A is hexacarbo-cyclic may be more explicitly described by the formula:



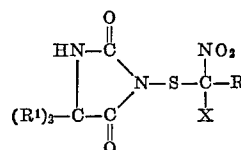
wherein X is halogen of atomic number 17 to 35, R is alkyl of from 1 to 5 carbons and the 1,2-cyclohexylene ring has from 0 to 3 sites of olefinic unsaturation, i.e., 1,2-phenylene, 1,2-dihydrophenylene, 1,2-tetrahydrophenylene and 1,2-hexahydrophenylene. Alternatively, the ring may be considered as phthalimide and derivatives thereof. In this case the ring could be phthalimide, dihydrophthalimide, tetrahydrophthalimide and hexahydrophthalimide. The ring may be unsubstituted or singly substituted with a chloro, bromo, nitro or alkyl group such as methyl, ethyl, butyl, amyl, etc.

The dihydro derivatives, that is, dihydrophthalimide, may be 1,3-, 1,4-, 2,4-, 3,5-, etc. The tetrahydro derivative may be 1-, 2-, 3-, or 4-. Preferred compounds are phthalimide and Δ^4 -tetrahydrophthalimide.

Specific illustration of hexacarboxylic compounds included within the above formula are:

- N-(1-chloro-1-nitroethylthio)-phthalimide,
N-(1-bromo-1-nitrobutylthio)-phthalimide,
N-(1-chloro-1-nitropropylthio)-1,3-dihydrophthalimide,
N-(1-bromo-1-nitrohexylthio)-1,4-dihydrophthalimide,
N - (1-chloro-1-nitroamylthio) - cis- Δ^4 -tetrahydrophthalimide,
N - (1-chloro-1-nitroethylthio) - cis- Δ^4 -tetrahydrophthalimide,
N-(1-bromo-1-nitropropylthio)-3,5-dihydrophthalimide,
N - (1-bromo-1-nitrobutylthio) - cyclohexane-1,2-dicarboximide,
N - (1-bromo-1-nitroethylthio) - cyclohexane-1,2-dicarboximide,
4-nitro-N-(1-chloro-1-nitrobutylthio)-phthalimide,
3 - methyl - N-(1-bromo-1-nitroethylthio)-cyclohexane-1,2-dicarboximide,
4-chloro-N-(1-bromo-1-nitropropylthio)-phthalimide,
3 - bromo - N-(1-chloro-1-nitroamylthio)-cis- Δ^4 -tetrahydrophthalimide, etc.

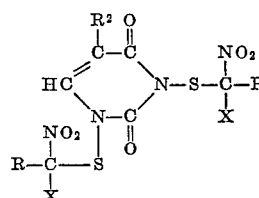
The hydantoin compounds of this invention may be more rigorously represented by the formula



wherein X is halogen of atomic number 17 to 35, i.e., chlorine or bromine, R is alkyl of from 1 to 5 carbons and R¹ is hydrogen or lower alkyl. Included among the lower alkyl groups are, methyl, ethyl, propyl, butyl, amyl and hexyl. Preferred compounds are the 3-(1-halo-1-nitro-alkyl) hydantoins.

Illustrative examples of some of the hydantoin compounds included in this invention are: 3-(1-chloro-1-nitroethylthio) hydantoin, 3-(1-bromo-1-nitrobutylthio) hydantoin, 3-(1-chloro-1-nitrohexylthio) hydantoin, 3-(1-chloro - 1-nitropropylthio)-5,5-dimethylhydantoin, 3-(1-bromo-1-nitroamylthio)-5-methylhydantoin, 3-(1-chloro-1 - nitroethylthio)-5-ethylhydantoin, 3-(1-chloro-1-nitrobutylthio) - 5 - butylhydantoin, 3-(1-bromo-1-nitroethylthio) 5,5-dipropylhydantoin, etc.

Also, the pyrimidine compounds of this invention may be further defined by the structure



wherein X is halogen of atomic number 17 to 35, R is alkyl of from 1 to 6 carbons and R² is hydrogen or methyl. As derivatives of pyrimidine, these compounds may be termed 2,6 - dioxypyrimidine or methyl-dioxypyrimidine, i.e., uracil or thymine.

Illustrative of the compounds in this grouping are: N,N - di - (1-chloro-1-nitroethylthio) uracil, N,N-di-(1-bromo-1-nitrobutylthio) uracil, N,N-di-(1-chloro-1-nitrohexylthio) uracil, N,N - di-(1-bromo-1-nitropropylthio) thymine, N,N - di - (1 - chloro-1-nitroethylthio) thymine, N,N-di-(1-chloro-1-nitrohexylthio) thymine, etc.

Examples of the di-(1-halo-1-nitroalkylthio) substituted parabanic acids of this invention are 1,3-bis-(1-chloro-1-nitroethylthio) parabanic acid, 1,3-bis-(1-bromo-1-nitrobutylthio) parabanic acid, 1,3-bis-(1-chloro-1-nitrohexylthio) parabanic acid, etc.

The preparation of the unique N-(1-halo-1-nitroalkyl) dicarboximides of this invention may be carried out by reacting an alkali metal salt of the corresponding imide with a 1-halo-1-nitroalkylsulfenyl halide. The imide may be contained in a suitable inert medium, such as an aromatic solvent, e.g., benzene, toluene, etc., an alcohol, e.g., methanol, ethanol, etc. or water. Furthermore, the imide may be used directly in the form of its alkali metal salt or the salt may be formed in situ.

The solution or suspension of the alkali metal salt of the imide is vigorously stirred, preferably at low temperature while the sulfenyl halide is added. The sulfenyl halide may be contained in a suitable inert solvent, such as petroleum ether or mixed hexanes, if desired. After a sufficient reaction period the product is isolated by filtration or by stripping off the solvent. The product then may, if desired, be recrystallized from a suitable solvent, such as methanol or an aromatic solvent.

The 1-halo-1-nitroalkylsulfenyl halides used in the preparation of the compounds of this invention may be synthesized by reacting an alkali or alkaline earth metal salt of a primary nitroalkane with sulfur monochloride in the presence of an anhydrous, nonhydroxylic inert medium, such as ether, to form a bis-(1-nitroalkyl) disulfide and cleaving the disulfide with halogen, i.e., chlorine or bromine.

In specific illustration of the compounds of this invention and their method of preparation, the following examples are presented. These examples are offered as representative of the compounds falling within the scope of this invention and are not intended as limiting of the invention herein described.

EXAMPLE I

A 4.2 gm.-portion of the potassium salt of phthalimide mixed with 50 mls. ether was charged to a vessel. To this mixture was added 4.0 gm. 1-chloro-1-nitroethylsulfenyl chloride in ether. This mixture was stirred for 15 minutes after which the solids were filtered from the mixture. The solids were washed with water and dried, to leave 3 gms. N-(1-chloro-1-nitroethylthio) phthalimide. This compound was observed as a white solid which melted at 110–112° C. Its analysis was: percent Cl: theory—12.4, found—12.28; percent S: theory—11.15, found—11.15.

EXAMPLE II

A 5.0 gm.-portion of the sodium salt of cis- Δ^4 -tetrahydrophthalimide was charged to a vessel. To this mixture was added 5.45 gm. 1-chloro-1-nitropropylsulfenyl chloride in ether. The contents were stirred overnight and then filtered. The solids were washed with water and hexane and then dried. The product, N-(1-chloro-1-nitropropylthio)-cis- Δ^4 -tetrahydrophthalimide, was observed as a solid which melted at 104–105° C. Its analysis was: percent Cl: theory—11.64, found—11.68; percent S: theory—10.52, found—10.30.

Using the methods described in Examples I and II, various other 1,2-hexacarbocyclic dicarboximides were

prepared. The analyses of these compounds are contained in Table I.

TABLE I

Compound	Analyses			
	Percent Cl		Percent S	
	Theory	Found	Theory	Found
N-(1-chloro-1-nitropropylthio)-phthalimide	11.78	11.0	10.66	10.22
N-(1-chloro-1-nitroethylthio)-cis- Δ^4 -tetrahydrophthalimide	12.54	12.65	11.02	10.65

EXAMPLE III

A 3.0 gm.-portion of the monopotassium salt of hydantoin in ether was charged to a vessel. To this suspension 3.75 gm. 1-chloro-1-nitropropylsulfenyl chloride were added. The contents were stirred for 1 hour and allowed to stand for 3 days. The mixture was filtered and the solids were slurried with water. The water slurry was filtered and the solids were dried leaving 3.2 gms. 3-(1-chloro-1-nitropropylthio) hydantoin. It was observed as a white solid which melted at 157–160° C. with decomposition. Its analysis was: percent Cl: theory—14.0, found—14.33; percent S: theory—12.65, found—12.20.

EXAMPLE IV

A 5.0 gm.-portion of the sodium salt of uracil in water was charged to a vessel. This mixture was cooled in an ice bath and a hexane solution of 8.5 gms. of 1-chloro-1-nitropropylsulfenyl chloride and 4.3 g. NaOH were added while the mixture was blended in a Waring Blendor. A gluey solid was formed. The water was decanted and the solids were slurried with hexane, filtered and dried, leaving 3.1 gms. product. The product, N,N-di-(1-chloro-1-nitropropylthio) uracil melted at 129–133° C. Its analysis was: percent Cl: theory—16.91, found—14.55; percent S: theory—15.29, found—15.19.

EXAMPLE V

In the manner described in Example IV, N,N-di-(1-chloro-1-nitroethylthio) uracil was prepared. It melted at 145–146° C. with decomposition and had the following analysis: percent Cl: theory—19.12, found—18.63; percent S: theory—16.4, found—15.51.

EXAMPLE VI

A 5.0 gm.-portion of the dipotassium salt of parabanic acid dissolved in ether was charged to a vessel. To this mixture was added 10.0 gm. 1-chloro-1-nitropropylsulfenyl chloride. The contents were stirred for 1 hour and allowed to stand for 3 days. The solids were filtered off and the ether was stripped from the filtrate. The stripped filtrate was further distilled to 60° C. at 1.0 mm. Hg to give 4 gms. 1,3-di-(1-chloro-1-nitropropylthio) parabanic acid. This product was observed to be a viscous orange oil.

These new compounds find use in the control and killing of fungi. A number of the invention compounds were evaluated for fungicidal effectiveness by means of the mycelial drop test. This test is designed to measure the fungitoxic activity of fungicidal chemicals in terms of their degree of inhibition upon mycelial growth. Each compound to be tested was dissolved in acetone in dilutions as indicated in Table II. Paper discs previously inoculated by impregnation with equal amounts of particular fungus mycelium placed on potato dextrose agar medium were treated by applying a precise and equal volume of each of these fungicidal solutions to their center. Following treatment with the fungitoxic chemical, the discs were incubated along with inoculated but untreated control discs at ambient temperatures until such time that these untreated control discs were filled with mycelial growth. Activity of the fungitoxic chemical tested was determined by comparative measurements of radii of mycelial growth away from the edge of the disc in treated and untreated samples. From this comparison a percent

inhibition of growth area was determined. The results of this test for various compounds of this invention on the particular fungus mycelium are indicated in Table II.

lesions on the primary leaves. These counts were compared with a similarly inoculated but unsprayed control series to determine the percentage of fungus control

TABLE II

Compound	Concen- tration, p.p.m.	Fungus Mycellim Percent Inhibition			
		Pyth- ium	Fusar- ium	Rhi- zoctonia	Verti- cillium
N-(1-chloro-1-nitroethylthio) phthalimide.....	500	-----	-----	50	98
N-(1-chloro-1-nitropropylthio) phthalimide.....	500	97	98	97	-----
N-(1-chloro-1-nitropropylthio) cis-Δ ⁴ -tetrahydrophthalimide.....	500	100	98	-----	-----
N-(1-chloro-1-nitroethylthio)-cis-Δ ⁴ -tetrahydrophthalimide.....	500	100	61	-----	-----
3-(1-chloro-1-nitropropylthio) hydantoin.....	500	100	40	-----	-----
N,N-di-(1-chloro-1-nitropropylthio) uracil.....	500	100	-----	-----	-----
1,3-di-(1-chloro-1-nitropropylthio) parabanic acid.....	500	100	-----	50	70

A number of the compounds were also tested for effectiveness against spores by means of "The Standard Spore Slide-Germination Method for Determining Fungicidal Activity," described in the American Phytopathological Society Journal, volume 33, pages 627-632, (1943). The method is designed to measure the fungitoxic activity of fungicidal chemicals, their activity being expressed in terms of percent inhibition of germination of fungus spores.

Each compound to be tested was dissolved in acetone to a concentration of 10 p.p.m. These solutions were then pipetted into the wells of depression slides and allowed to dry. The wells were filled with a spore suspension of the specified test organism and incubated in a moist chamber overnight. A group of 100 spores was examined and the number of spores germinated and not germinated was counted and recorded to show the biological activity in terms of the percentage germination inhibition. Table III reports the results of this testing.

effected by the fungitoxic chemical. The results appear in Table IV.

TABLE IV.—IN VIVO, BEAN RUST

Compound	Percent control
N-(1-chloro-1-nitroethylthio) phthalimide.....	69
N-(1-chloro-1-nitropropylthio) phthalimide.....	80
N-(1-chloro-1-nitroethylthio)-cis-Δ ⁴ -tetrahydrophthalimide.....	88
N-(1-chloro-1-nitropropylthio)-cis-Δ ⁴ -tetrahydrophthalimide.....	85
3-(1-chloro-1-nitropropylthio) hydantoin.....	98
N,N-di-(1-chloro-1-nitropropylthio) uracil.....	53
1,3-di-(1-chloro-1-nitropropylthio) parabanic acid.....	99

TABLE III

Compound	Organism Percent Inhibition		
	<i>Monolinia fructicola</i>	<i>Alternaria solani</i>	<i>Fusarium solani</i>
N-(1-chloro-1-nitroethylthio) phthalimide.....	98	-----	100
N-(1-chloro-1-nitropropylthio) phthalimide.....	100	61	-----
N-(1-chloro-1-nitropropylthio)-cis-Δ ⁴ -tetrahydro-phthalimide.....	70	-----	97
N-(1-chloro-1-nitroethylthio)-cis-Δ ⁴ -tetrahydro-phthalimide.....	97	-----	100
3-(1-chloro-1-nitropropylthio) hydantoin.....	30	-----	-----
N,N-di-(1-chloro-1-nitropropylthio) uracil.....	-----	-----	100

Additionally, a similar sampling of the compounds of this invention were tested for fungicidal activity in vivo. In these tests, the chemicals were tested for the control of bean rust. According to this procedure, three replicate pinto bean plants growing in a standard University of California soil mix, in the 3-triplicate state and approximately 5 inches tall were sprayed at 15 p.s.i. with an acetone solution of each of the compounds to be tested at a concentration of 500 p.p.m. These suspension made uniform by means of an inert wetting agent and suitable filler. The plants were dried at ambient greenhouse temperatures and then inoculated with a spray of approximately 30,000 urediospores per mil. of *Uromyces phasecoli typica*, the fungus causing bean rust. The plants were immediately incubated in a moist room for 24 hours at 72-73° F. and a relative humidity of 99-97%, after which they were removed to a room with ambient temperatures in the range of 75-80° F. and a relative humidity of 85-90% for 12 days. At the end of this incubation period, disease readings were made by counting the local

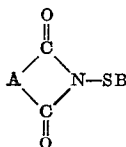
Aside from the specific formulation and application of the class of compounds of the invention as represented by the foregoing tests, these compounds may be dispersed in or upon other inert liquid and solid carriers, such as inert clay, xylenes, etc. The solid carriers may be in the form of a dust, or used in conjunction with a suitable wetting agent to form a wettable powder. The fungi-toxic compounds of the invention may also be formulated with other solvent, dispersing agents, or emulsifying agents. Further, these compounds may not only be applied alone or in mixtures with other compounds of the disclosed class, but may also be used in combination with other active toxicants in the formulation of fungicidal compositions.

The compounds may be applied to any environmental area which is a host to fungus or susceptible to fungus attack. For example, the fungicidal compositions may be sprayed or otherwise applied directly to a plant or other host, may be applied to the plant seed, sprayed upon the soil or other plant environment, or used in similar ways so as to effect the control of fungus and fungus diseases.

7

We claim:

1. Compound of the formula



wherein A is a 1,2-cyclohexylene ring having 0 to 3 sites of olefinic unsaturation substituted with 0 to 1 chloro, bromo, nitro or lower alkyl and B is a 1-halo-1-nitroalkyl group in which the halogen is of atomic number 17 to 35 and the alkyl is of from 2 to 6 carbon atoms.

8

2. N - (1 - halo - 1 - nitroalkylthio) - cis - Δ^4 - tetrahydrophthalimide wherein the alkyl group is of 2 to 6 carbon atoms.

3. N-(1-halo-1-nitroalkylthio)phthalimide wherein the alkyl group is of 2 to 6 carbon atoms.

References Cited

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260—260, 309.5; 424—251, 263, 274