

PATENT SPECIFICATION

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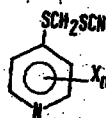
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(54) HALOPYRIDYLTHIOALKYL THIOCYANATES

(71) We, THE DOW CHEMICAL COMPANY, a Corporation organised and existing under the laws of the State of Delaware, United States of America, of Midland, County of Midland, State of Michigan, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention is directed to halopyridylthioalkyl thiocyanates of the formula



wherein each X is the same and is either chloro or bromo and n is 2, 3 or 4.

The halopyridylthioalkyl thiocyanates of the present invention are crystalline solids or oils which are of low solubility in water and of moderate solubility in common organic solvents. These compounds have low phytotoxicity and are useful as bactericides and fungicides.

The compounds of the present invention can be prepared by the reaction of an appropriate halo substituted 4-(chloromethylthio)pyridine with an alkali metal thiocyanate in the presence of an inert solvent. This reaction can be represented as follows:

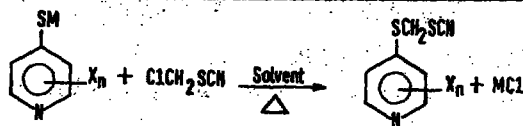


wherein X and n are as hereinbefore defined and M is an alkali metal, i.e. sodium, lithium, potassium caesium, or rubidium.

Suitable inert solvents include dimethylformamide, hexamethylphosphoramide, and 4-formylmorpholine. The reaction is preferably carried out at room temperature, although temperatures of from 0° to 100°C can be employed. The reaction is usually carried out at atmospheric pressure. While the reaction consumes the reactants in equimolar amounts, it is preferred that a 10 to 150 percent excess of the alkali metal thiocyanate be employed.

The reactants are maintained together, under agitation, until the reaction is complete. The required reaction time is usually between 30 minutes and 4 hours. Upon completion of the reaction, the reaction mixture is diluted with cold water to precipitate out any solid product. The solid product can be purified, if desired, by recrystallization from benzene, hexane, pentane, or mixtures thereof.

An alternative procedure for the preparation of the halopyridylthioalkyl thiocyanates involves the reaction of an appropriate halo substituted alkali metal thiopyridine with chloromethyl thiocyanate in the presence of a reaction medium or solvent, preferably ethanol. This reaction can be represented as follows:



wherein X, n, and M are as hereinbefore defined.

In carrying out this reaction, the alkali metal thiopyridine can be prepared *in situ* by the reaction of a halomercaptopyridine with an alkali metal in a solvent. This *in situ* preparation is usually carried out by first dissolving the alkali metal in an alkanol and admixing this, at room temperature, with a solution of the halomercaptopyridine in an alkanol. The chloromethyl thiocyanate can thereafter be added directly to the alcoholic solution of the halo alkali metal thiopyridine and this mixture refluxed until the completion of the reaction, usually from 30 minutes to 2 hours. After the completion of the reaction, the reaction mixture is filtered to remove the alkali metal chloride salt by-product. The alcohol is thereafter removed by evaporation under reduced pressure. The purified product can be recovered from the residue by crystallization from a solvent such as benzene, hexane or mixtures thereof.

We have found that compositions comprising the halopyridylthioalkyl thiocyanates in admixture with an inert carrier can be employed as bactericides or fungicides. The compounds of the present invention or compositions containing them as toxic constituents can be included in and on plaster, ink, wallboard, textiles, paper, adhesives, soaps, synthetic detergents, cutting oils, polymeric materials, embalming fluids, oil paints and latex paints to prevent the attack of various fungal pests and the subsequent economic loss due to the degradation of such products by micro-organisms. Also, the compounds can be distributed in textiles or cellulosic materials to preserve and protect such products from the attack of the organisms of rot, mold and decay.

The exact concentration of the toxicant to be employed in the treating compositions is not critical and may vary considerably. The concentration of toxicant in liquid compositions generally is from 0.0001 to 50 percent by weight. Concentrations up to 95 percent by weight are often conveniently employed, particularly in concentrate compositions. In dusts, the concentrations of the toxicant can be from 0.1 to 95 percent by weight. In compositions to be employed as concentrates, the toxicants can be present in a concentration of from 5 to 98 percent by weight. For use as a spray, it is often convenient to prepare the compounds as wettable powders.

In a representative operation, 2,6-dichloro-4-(thiocyanatomethylthio)pyridine when employed in a nutrient agar at a concentration of 10 parts by weight of the compound per million parts of agar was found to give 100 percent kill of the organisms *Staphylococcus aureus*, *Candida albicans*, *Mycobacterium phlei*, *Bacillus subtilis*, *Trichophyton mentagrophytes*, *Candida pelliculosa*, *Pullularia pullveans*, *Cephaloascus fragans*, *Ceratocystis ips*, *Trichoderma* sp. Madison P-42, *Rhizopus nigricans*, and *Aspergillus terreus*.

In an additional operation, 2,3,5-trichloro-4-(thiocyanatomethylthio)pyridine was found to give 100 percent kill of the organisms *Staphylococcus aureus*, *Candida albicans*, *Trichophyton mentagrophytes*, *Bacillus subtilis*, *Aspergillus terreus*, *Candida pelliculosa*, *Pullularia pullulans*, *Mycobacterium phlei*, *Ceratocystis ips*, *Cephaloascus fragans*, *Trichoderma* sp. Madison P-42, and *Rhizopus nigricans*, when employed in a nutrient agar at a concentration of 10 parts by weight of the compound per million parts of agar.

In another operation, 2,3,5,6-tetrachloro-4-(thiocyanatomethylthio)pyridine was found to give 100 percent kill and control of the organisms *Mycobacterium phlei*, *Trichophyton mentagrophytes*, *Cephaloascus fragans*, *Aspergillus terreus*, *Ceratocystis ips* and *Trichoderma* sp. Madison P-42, when employed in a nutrient agar at a concentration of 10 parts by weight of the compound per million parts of agar.

The following examples illustrate the present invention.

Example 1

To a solution of 5.0 grams (0.0219 mole) 2,6-dichloro-4-(chloromethylthio)pyridine in 15 milliliters of dimethylformamide was added, at room temperature with stirring, a solution of 3.19 grams (0.0329 mole) of potassium thiocyanate in 15 milliliters of dimethylformamide. The mixture was stirred at room temperature for about one hour, heated to 60–80°C, and stirred at a temperature within this range for about one hour. At the completion of this reaction, the product was filtered to remove the potassium chloride by-product and the resultant mother liquor poured into ice water. The water was decanted off and fresh water added to the sticky solid which remained.

Upon washing in the water, a waxy solid was obtained and recovered by filtration. The solid was taken up in benzene and dried with sodium sulfate. The benzene was removed and the solid was recrystallized in hexane. 2,6-Dichloro-4-(thiocyanatomethylthio)pyridine was recovered as a fluffy yellow-tan solid. The product was recovered in a yield of 3.0 grams (55%) and melted at 55°C. The product was found to have chlorine and sulfur contents of 27.84 and 25.48 percent respectively, as compared with the theoretical contents of 28.23 and 25.53 percent respectively.

Example 2

A solution was prepared by dissolving 0.77 grams (0.023 mole) of sodium metal in 25 milliliters of 28 absolute ethanol. This solution was slowly added to a solution of 5 grams (0.023 mole) of 2,3,5-trichloro-4-mercaptopyridine in hot ethanol. This mixture was refluxed for 45 minutes, and 2.7 grams (0.025 mole) of chloromethylthiocyanate was added thereto. This mixture was refluxed for one hour. The sodium chloride which formed was removed by filtration followed by the removal of the ethanol by evaporation under reduced pressure. The oil which remained as a residue was washed with a mixture of benzene and hexane. The solvent mixture was removed. The residue was allowed to stand and crystals started to form. Hexane was added and the hexane removed. The residue was cooled and filtered to recover 2,3,5-trichloro-4-(thiocyanatomethylthio)pyridine. The product melted at 96°C. and was found to have carbon, hydrogen, chlorine, nitrogen, and sulfur contents of 29.8, 1.3, 36.9, 9.4, and 22.2 percent respectively, as compared with the theoretical contents of 29.5, 1.1, 37.3, 9.8, and 22.5 percent respectively.

Example 3

To a stirred solution of 10.0 grams (0.34 mole) of 2,3,5,6-tetrachloro-4-(chloromethylthio)pyridine in 50 milliliters of dimethylformamide was added at room temperature 3.4 grams (0.035 mole) of potassium thiocyanate in 25 milliliters of dimethylformamide. The mixture was allowed to stir for 1 hour at room temperature. The temperature of the mixture was raised to 40°C and then to 100°C and the mixture stirred at this temperature for 1 hour. After completion of the reaction, the reaction mixture was poured into cold water. The yellow-tan solid which precipitated was recovered by filtration. The crude solid was taken up in benzene and dried with sodium sulfate. A portion of the benzene was evaporated off and hexane was added. The mixture was cooled and 2,3,5,6-tetrachloro-4-(thiocyanatomethylthio)pyridine was recovered by filtration and thereafter recrystallized from hexane. The product melted at 118—120°C and was recovered in a yield of 4.8 grams (45%). The product was found to have carbon, hydrogen, chlorine, nitrogen, and sulfur contents of 26.44, 0.73, 44.42, 8.77, and 19.86 percent respectively, as compared with the theoretical contents of 26.23, 0.63, 44.25, 8.76, and 20.00 percent respectively.

The following compounds of the present invention are prepared in accordance with the methods hereinbefore set forth.

2,6-Dibromo-4-(thiocyanatomethylthio)-pyridine having a molecular weight of 340.05;

3,5-Dichloro-4-(thiocyanatomethylthio)-pyridine having a molecular weight of 251.15;

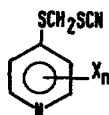
2,3,5-Tribromo-4-(thiocyanatomethylthio)-pyridine having a molecular weight of 418.97;

3,6-Dichloro-4-(thiocyanatomethylthio)-pyridine having a molecular weight of 251.15; and

2,3,5,6-Tetrabromo-4-(thiocyanatomethylthio)-pyridine having a molecular weight of 497.89.

WHAT WE CLAIM IS:—

1. A compound of the formula



wherein each X is the same and is either chloro or bromo and n is 2, 3 or 4.

2. 2,6-Dichloro-4-(thiocyanatomethylthio)-pyridine.

3. 2,3,5-Trichloro-4-(thiocyanatomethylthio)-pyridine.

4. 2,3,5,6-Tetrachloro-4-(thiocyanatomethylthio)-pyridine.



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Upon washing in the water, a waxy solid was obtained and recovered by filtration. The solid was taken up in benzene and dried with sodium sulfate. The benzene was removed and the solid was recrystallized in hexane. 2,6-Dichloro-4-(thiocyanatomethylthio)pyridine was recovered as a fluffy yellow-tan solid. The product was recovered in a yield of 3.0 grams (55%) and melted at 55°C. The product was found to have chlorine and sulfur contents of 27.84 and 25.48 percent respectively, as compared with the theoretical contents of 28.23 and 25.53 percent respectively.

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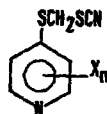
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WHAT WE CLAIM IS:—

1. A compound of the formula



wherein each X is the same and is either chloro or bromo and n is 2, 3 or 4.

2. 2,6-Dichloro-4-(thiocyanatomethylthio)-pyridine.

3. 2,3,5-Trichloro-4-(thiocyanatomethylthio)-pyridine.

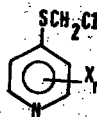
4. 2,3,5,6-Tetrachloro-4-(thiocyanatomethylthio)-pyridine.



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5. A compound as claimed in claim 1 substantially as hereinbefore described in any of the Examples.

6. A process for producing a compound as claimed in claim 1, which comprises reacting a compound of the formula



wherein X and n are as defined in claim 1, with an alkali metal thiocyanate in the presence of an inert solvent.

7. A process as claimed in claim 6 wherein the solvent employed is dimethylformamide.

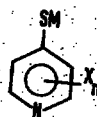
8. A process as claimed in claim 6 or 7 wherein the reaction is carried out at a temperature of from 0 to 100°C.

9. A process as claimed in any one of claims 6 to 8 wherein the alkali metal thiocyanate is employed in an excess of from 10 to 150 percent.

10. A process as claimed in claim 6 substantially as hereinbefore described in Example 1 or Example 3.

11. A compound as claimed in claim 1 whenever prepared by a process as claimed in any one of claims 6 to 10.

12. A process for producing a compound as claimed in claim 1 which process comprises reacting a compound of the formula



wherein M is an alkali metal and X and n are as defined in claim 1, with chloromethyl thiocyanate in the presence of a reaction medium or solvent.

13. A process as claimed in claim 12 wherein the reaction medium or solvent employed is ethanol.

14. A process as claimed in claim 13 wherein the reaction is carried out at reflux temperature.

15. A process as claimed in claim 12 substantially as hereinbefore described in Example 2.

16. A compound as claimed in claim 1 whenever prepared by a process as claimed in any one of claims 12 to 15.

17. A bactericidal or fungicidal composition which comprises a compound as claimed in any one of claims 1 to 5, 11 or 16 in admixture with an inert carrier.

18. Plaster, ink, wallboard, textiles, paper, adhesives, soaps, synthetic detergents, cutting oils, polymeric materials, embalming fluids, oil paints and latex paints comprising a compound as claimed in any one of claims 1 to 5, 11 or 16.

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