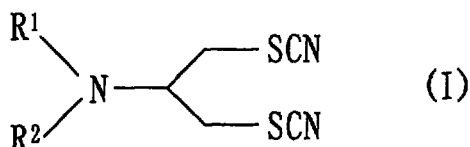


DESCRIPTION

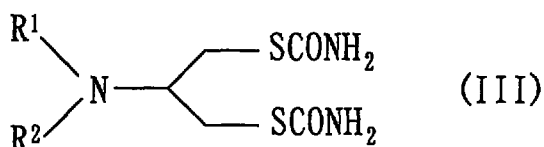
Production of Thiolcarbamate and Thiocyanate Compounds

5 Technical Field

It is described that a compound represented by the formula:



wherein R^1 and R^2 independently represent a hydrocarbon group,
10 or R^1 and R^2 form a nitrogen-containing 5- or 6-membered
heterocyclic group together with the adjacent nitrogen atom,
(hereinafter, sometimes abbreviated as "compound (I)") or
a salt thereof itself has a strong pesticidal activity in
JP-B-42177/1976. Also, it is described that it is an
15 important intermediate for synthesis of a thiolcarbamate
derivative (III) represented by the formula:



wherein each symbol has the same meaning as defined above,
(hereinafter, sometimes abbreviated as "compound (III)") or
20 a salt thereof, which has a further stronger pesticidal
activity in JP-B-10969/1967.

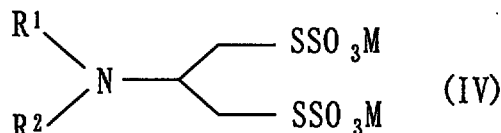
With respect to production methods of the compound (I)
or a salt thereof, a method of reacting corresponding
dihalide compound with thiocyanate, a method of reacting
25 corresponding thiosulfate (hereinafter sometimes
abbreviated as "bunte salt") with a cyanide, a method of
reacting the corresponding dithiol compound with a halogen
cyanide (cyanogen halide), and a method of reacting the
corresponding bissulfonate compound with prussiate (salt
30 with prussic acid) were reported in JP-B-18012/1964, JP-

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B-19524/1969, JP-A-34316/1972 and JP-B-28905/1988 respectively.

It is described that a compound represented by the formula (IV):



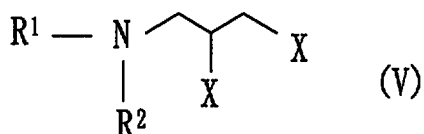
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wherein R^1 and R^2 have the same meanings as defined above, and M is a metal or ammonium (hereinafter, sometimes abbreviated as "compound (IV)") or a salt thereof itself has a strong pesticidal activity and it is an important intermediate for synthesis of the thiolcarbamate (III) which has a further stronger pesticidal activity in JP-B-17404/1970.

With respect to a production method of the compound (IV) or a salt thereof, a method of reacting corresponding dihalide compound with thiosulfate (salt with thiosulfuric acid) is reported in JP-B-17404/1970.

However, according to the prior art, it is hard to handle waste water, and there are also problems of low yield. Further, there is no use of crystallization filtrate (waste) yielded during the production steps of thiolcarbamate (III) which has an excellent pesticidal activity, and therefore it has been treated by incineration. Because the above waste contains thiolcarbamate derivative, it has been a serious environmental problem in view of saving resources.

Further, according to the method described in JP-B-18012/1964 or JP-B-17404/1970, there is a problem of lower yield because of yield, as a by-product, of a compound (V) represented by the formula:



wherein X represents a group of SCN or SSO_3M (wherein M represents a metal or ammonium), and other symbols have the

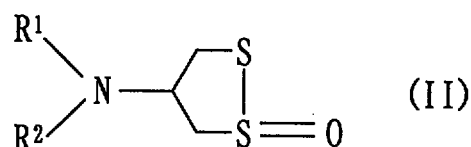
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same meanings as defined above, such as S,S'-
(dimethylaminomethyl)ethylene di(sodium thiosulfate) and
dimethylaminomethylethyl di(thiocyanate), each of which is
an isomer of the desired product.

5

Disclosure of Invention

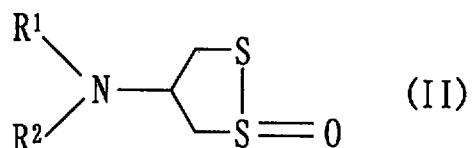
The present inventors have made intensive research on
methods for production of compound (I), (III) or (IV) or a
salt thereof in high yield with smoothly handling of waste
water, and recycling of waste yielded during production steps
of thiolcarbamate derivatives. As a result, the inventors
have found surprisingly that, when a compound represented
by the formula:



wherein R^1 and R^2 independently represent a hydrocarbon group,
or R^1 and R^2 form a nitrogen-containing 5- or 6-membered
heterocyclic group together with the adjacent nitrogen atom,
or a salt thereof is reacted with prussic acid or a salt
thereof, dithiolane ring of the compound (II) is cleaved to
give a compound (I) or a salt thereof in a high yield.

20

Further, the inventors have found surprisingly that ,
when a compound represented by the formula:



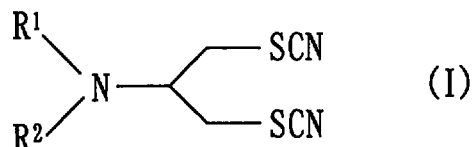
wherein each symbols has the same meaning as defined above,
or a salt thereof is reacted with sulfurous acid or a salt
thereof, dithiolane ring of the compound (II) is cleaved to
give a compound (IV) or a salt thereof in high yield and high
purity. Also, this compound (IV) or a salt can be reacted
with prussic acid or a salt thereof to give a compound (I)
or a salt thereof.

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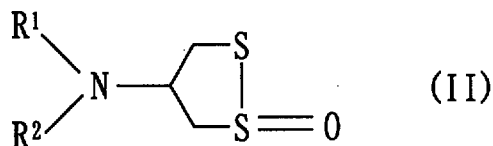
Further, the present inventors have made intensive research based on such knowledge, thus completing the present invention.

Namely, the present invention relates to:

- 5 [1] a method for producing a compound represented by the formula:



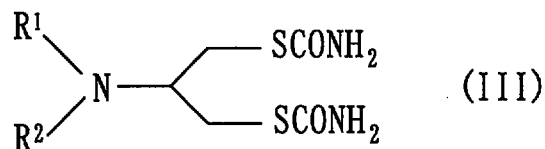
- wherein R^1 and R^2 independently represent a hydrocarbon group, or R^1 and R^2 form a nitrogen-containing 5- or 6-membered heterocyclic group together with the adjacent nitrogen atom, or a salt thereof, which comprises reacting a compound represented by the formula:



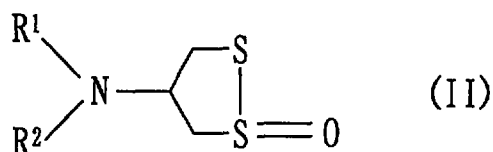
- wherein each symbol has the same meaning as defined above, or a salt thereof, with prussic acid or a salt thereof,

- 15 [2] the method as described in [1] above, wherein R^1 and R^2 independently represent an alkyl group,
[3] the method as described in [1] above, wherein both R^1 and R^2 represent a methyl group,

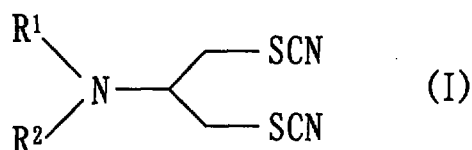
- 20 [4] a method for producing a compound represented by the formula:



- wherein R^1 and R^2 independently represent a hydrocarbon group, or R^1 and R^2 form a nitrogen-containing 5- or 6-membered heterocyclic group together with the adjacent nitrogen atom, or a salt thereof, which comprises reacting a compound represented by the formula:



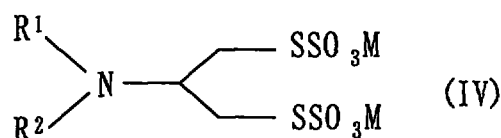
wherein each symbol has the same meaning as defined above, or a salt thereof, with prussic acid or a salt thereof to provide a compound represented by the formula:



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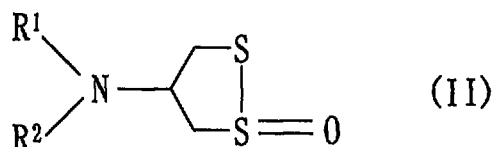
wherein each symbol has the same meaning as defined above, or a salt thereof, and then subjecting the resulting compound to a hydrolysis reaction or a reaction with a lower alcohol in the presence of a hydrogen halide,

10 [5] a method for producing a compound represented by the formula:



15

wherein R^1 and R^2 independently represent a hydrocarbon group, or R^1 and R^2 form a nitrogen-containing 5- or 6-membered heterocyclic group together with the adjacent nitrogen atom, and M is a metal or ammonium, or a salt thereof, which comprises reacting a compound represented by the formula:



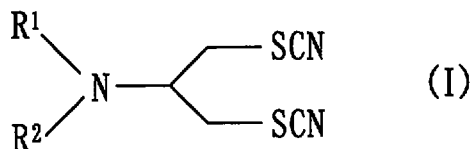
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wherein each symbol has the same meaning as defined above, or a salt thereof, with sulfurous acid or a salt thereof,

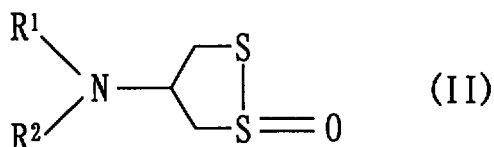
[6] the method as described in [5] above, wherein R^1 and R^2 independently represent an alkyl group,

[7] the method as described in [5] above, wherein both R^1 and R^2 represent a methyl group,

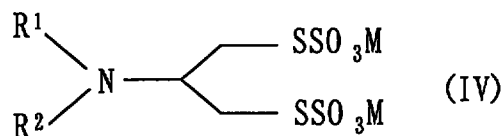
[8] a method for producing a compound represented by the formula:



wherein R^1 and R^2 independently represent a hydrocarbon group,
 5 or R^1 and R^2 form a nitrogen-containing 5- or 6-membered heterocyclic group together with the adjacent nitrogen atom, or a salt thereof, which comprises reacting a compound represented by the formula:

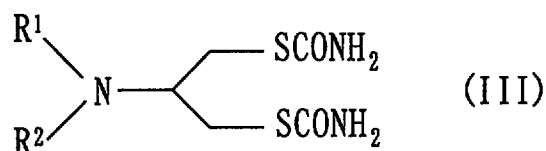


10 wherein each symbol has the same meaning as defined above, or a salt thereof, with sulfurous acid or a salt thereof to provide a compound represented by the formula:



15 wherein M is a metal or ammonium and the other symbols have the same meanings as defined above, or a salt thereof, and then reacting the resulting compound with prussic acid or a salt thereof, and

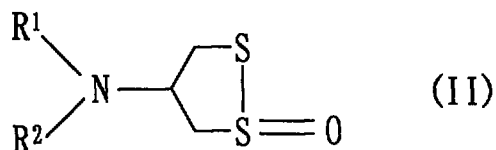
[9] a method for producing a compound represented by the formula:



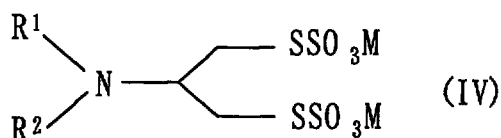
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wherein R^1 and R^2 independently represent a hydrocarbon group, or R^1 and R^2 form a nitrogen-containing 5- or 6-membered heterocyclic group together with the adjacent nitrogen atom, or a salt thereof, which comprises:

(i) reacting a compound represented by the formula:

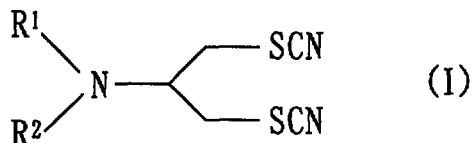


wherein each symbol has the same meaning as defined above, or a salt thereof, with sulfurous acid or a salt thereof to provide a compound represented by the formula:



wherein M is a metal or ammonium and the other symbols have the same meanings as defined above, or a salt thereof,

(ii) reacting the resulting compound with prussic acid or a salt thereof to provide a compound represented by the formula:



wherein each symbol has the same meaning as defined above, or a salt thereof, and

(iii) subjecting the resulting compound to a hydrolysis reaction or a reaction with a lower alcohol in the presence of a hydrogen halide.

Best Mode for Carrying Out the Invention

The hydrocarbon group for R^1 and R^2 includes a straight-chained, branched or cyclic aliphatic hydrocarbon group which can have double bonds or triple bonds, an aryl group or an aralkyl group. Specifically, an alkyl group, an alkenyl group, an alkynyl group, an aryl group or an aralkyl group can be used. Among them, a C_{1-19} hydrocarbon group is preferable.

The alkyl group includes a straight-chained or a branched C_{1-6} alkyl group or a C_{3-14} cyclic alkyl group, for

example includes a C₁₋₆ alkyl group or a C₃₋₁₄ cycloalkyl group such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, sec-pentyl, isopentyl, neopentyl, cyclopropyl, cyclopentyl, n-hexyl, isohexyl or cyclohexyl.

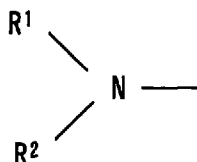
The alkenyl group includes a straight-chained or branched C₂₋₆ alkenyl group or a C₃₋₁₄ cyclic alkenyl group, for example includes a C₂₋₆ alkenyl group or a C₃₋₁₄ cycloalkenyl group such as allyl, isopropenyl, isobutenyl, 2-pentenyl, 2-hexenyl or 2-cyclohexenyl.

The alkynyl group includes a C₂₋₆ alkynyl group such as propargyl, 2-butyne, 3-butyne, 3-pentyne or 3-hexyne.

The aryl group includes a C₆₋₁₄ aryl group such as phenyl, naphthyl or anthryl.

The aralkyl group includes a C₇₋₁₉ aralkyl group such as a phenyl-C₁₋₄ alkyl (e.g. benzyl, phenethyl, phenylpropyl, etc.), benzhydryl or trityl.

In the group represented by the formula:



, the 5- or 6-membered nitrogen-containing heterocyclic group, which R¹ and R² may form together with an adjacent nitrogen atom includes pyrrolidino, piperidino, piperadino, morpholino, thiomorpholino or thiazolidinyl.

R¹ and R² is preferably a straight-chained or branched lower alkyl group having a carbon number of 1 to 4. Among them, methyl group is particularly preferable.

The salts of the compound (I) include salts with inorganic acids such as hydrochloric acid, sulfuric acid and phosphoric acid or salts with organic acids such as benzenesulfonic acid, p-toluenesulfonic acid and oxalic acid.

The compound (I) or a salt thereof can be produced by

reacting a compound (II) or a salt thereof with prussic acid or a salt thereof under a weakly acidic to weakly basic condition, specifically in the range of pH 5 to 9, preferably pH 7 to 9.

5 The prussic acid or a salt thereof as used in the present invention includes solid alkaline metal salts of prussic acid such as sodium cyanide and potassium cyanide which are available on the market or prussic acid gas, and if necessary, ammonium salts or alkaline earth metal salts
10 (e.g. calcium salt, magnesium salt, etc.), salts of heavy metal (e.g. iron, copper, zinc, etc.) can be used. As the preferable prussic acid or a salt thereof, sodium cyanide (sodium prussiate) and potassium cyanide (potassium prussiate) are used.

15 The salts of compound (II) include the same ones as mentioned in the above salts of compound (I).

 Since this reaction proceed quantitatively in a short period, 2 moles of prussic acid or a salt thereof will be sufficient based on 1 mole of compound (II)
20 stoichiometrically. If necessary, an excess amount of prussic acid or a salt thereof can be used, but it is not desirable in view of saving resources and handling of waste yielded after the reaction.

 As a solvent to be used in the reaction, a solvent which
25 can dissolve each or both of compound (II) or a salt thereof and prussic acid or a salt thereof can be preferably used, however this reaction will proceed enough even if solvent can not dissolve both of them well. However, the solvent of which pH inclines toward extremely acidic or basic side is
30 not desirable in consideration of the properties of reagents, compound (I) and compound (II) or a salt thereof. Therefore, if a solvent is almost neutral, any solvent which does not interfere the reaction can be employed. Such a solvent includes lower aliphatic alcohols such as methanol, ethanol,
35 isopropanol, etc.; lower aliphatic ketones such as acetone, methyl ethyl ketone, methyl isobutyl ketone, etc.; lower

chained or a cyclic aliphatic ethers such as diethyl ether, tetrahydrofuran, dioxane, etc.; lower aliphatic carboxylic acid derivatives such as ethyl acetate, acetonitrile, dimethylformamide, etc.; lower chained or a cyclic aliphatic sulfur compounds such as carbon disulfate, dimethylsulfoxide, tetramethylene sulfone, etc. If necessary, water or a lower aliphatic halogenated hydrocarbon such as methylene chloride, chloroform or carbon tetrachloride; or an aromatic hydrocarbon such as benzene, toluene, xylene or chlorobenzene can be used. These solvent can be used alone or two or more kinds of them (preferably, not more than three kinds of them) may be mixed in an appropriate proportion. Further, when the reaction mixture is not homogeneous, for example in case of water and an aromatic hydrocarbon or an aliphatic halogenated hydrocarbon, the reaction system becomes two-phase system, however under such a circumstance, a little amount of phase transfer catalyst such as a quaternary ammonium salt, a sulfonium salt, or a phosphonium salt may be added preferably. Two solvents such as water and a solvent which is not miscible with water (e.g. toluene or benzene) may be used preferably, because separating operation will be easily conducted.

In the method of the present invention, the reaction starts immediately by contacting the compound (II) or a salt thereof with prussic acid or a salt thereof in an appropriate solvent. The reaction may proceed exothermically. The resulting compound (I) is not stable against heat in a form of free base, and therefore the reaction temperature desirably may be kept at below 40°C, generally room temperature or not more. If necessary, the reactor can be cooled down from outside. The reaction temperature is preferably 0 to 20 °C.

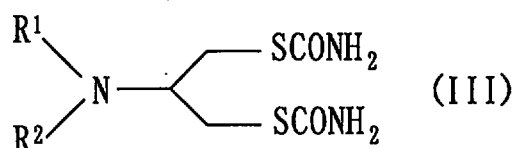
Also, the reaction in the method of the present invention proceeds smoothly under the above mentioned conditions to complete for a period of 1 hour to several hours generally, but however according to circumstances it can be

completed for several minutes or tens of minutes.

Since the compound (I) or a salt thereof lacks stability against an alkaline, in case a reaction time is extended for unnecessarily long time and resulting compound (I) is contacted with an excess amount of a cyanide ion for a long time, it may cause coloring or lower yield. Therefore, it is desirable to separate the desired substance from the reaction system via extraction and redistribution toward a soluble solvent (e.g. toluene, benzene, etc.) with cooling immediately after completion of the reaction.

The completion of the reaction can be confirmed easily by analysis such as thin layer chromatograph (TLC), high performance liquid chromatograph (HPLC), and so on.

The compound (I) or a salt thereof can be converted to the compound represented by the formula:



wherein each symbol has the same meanings as mentioned above (hereinafter sometimes abbreviated as compound (III)), or a salt thereof, which has an excellent insecticidal activity according to the method described in JP-B-19520/1970 or JP-B-10969/1967.

Namely, the compound (III) or a salt thereof can be produced by subjecting the compound (I) or a salt thereof to a hydrolysis reaction or reacting the compound (I) or a salt thereof with a lower alcohol in the presence of a hydrogen halide as following.

Compound (I) or a salt thereof which is a starting material for this reaction may be used without isolation or purification after the production according to the above-mentioned method of the present invention. As a matter of course, isolated or purified compound (I) or a salt thereof can be used.

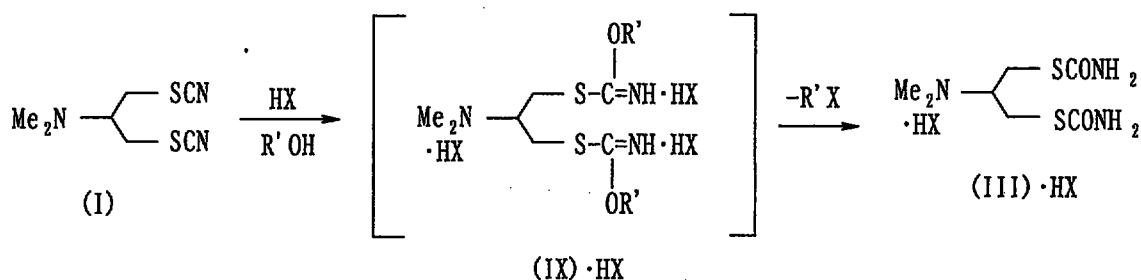
[hydrolysis reaction]

Compound (I) or a salt is hydrolyzed under an acidic condition. Acids to be used include inorganic acids such as hydrochloric acid, sulfuric acid, phosphoric acid,
 5 hydrobromic acid, etc. Especially, hydrochloric acid and sulfuric acid are preferable. The concentration of the acid is preferably 5 to 98%. 5% to saturated hydrochloric acid or 10-60% sulfuric acid may be preferable. The reaction
 10 temperature is preferably 0 to 100°C, especially preferably 20 to 80°C.

This reaction can be proceed in an acidic aqueous solution, and if necessary an organic solvent which is described concerning the reaction for producing a compound
 (I) or a salt thereof from a compound (II) or a salt thereof,
 15 and which does not interfere the reaction, may be added. When the organic solvent which is not miscible with water is used, the phase transfer catalyst described above can be added.

20 [Reaction with hydrogen halide]

Compound (III) or a salt thereof can be produced by reacting a compound (I) or a salt thereof with an lower alcohol (R'OH; R' represents a lower C₁₋₄ alkyl group such as methyl, ethyl, etc.) in the presence of hydrogen halide
 25 gas (HX) such as hydrogen chloride gas and hydrogen bromide gas to give an intermediate (IX) or a salt thereof, and then heating the mixture under reduced pressure or at ordinary pressure without isolation, or leaving the mixture to stand at room temperature to eliminate an alkyl halide (R'X).



30

The reaction toward an intermediate (IX) can be conducted

at a temperature between 0°C to boiling point of lower alcohol to be used, preferably at 0 to 40°C. This reaction may proceed comparatively rapidly, but however it is desirable to continue the reaction for a period of 2 to 12 hours for completion of
5 the reaction. The amount of hydrogen halide is more than 3 equivalents, preferably more than 10 equivalents to the compound (I).

The lower alcohol includes methanol, ethanol and the like. As the hydrogen halide gas, particularly hydrogen
10 chloride gas is preferable.

Salts of compound (III) include the same ones as mentioned in the above salts of compound (I).

The compound (III) or a salt thereof can be isolated and purified by per se known methods such as extraction, pH
15 change, redistribution, concentration, concentration under reduced pressure, crystallization, and recrystallization and the like.

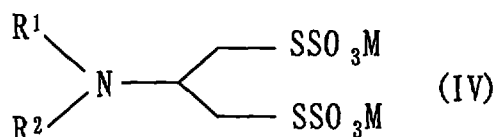
For example, after the completion of the reaction, when the reaction mixture is aqueous solution, extraction is
20 conducted without further operations, and when the reaction mixture contains an organic solvent which can be mixed homogeniously with water, after concentration under reduced pressure, a lower aliphatic halogenated hydrocarbon such as methylene chloride or chloroform, etc. or an aromatic
25 hydrocarbon such as benzene, toluene, xylene or chlorobenzene, etc. which is dissolved hardly in water is added and then extraction is conducted. Thus obtained organic layer is concentrated to obtain a crude compound (III) as a crystal. Compound (III) as separated can be obtained in
30 the form of a salt by crystallization after adding an inorganic acid such as hydrochloric acid, sulfuric acid, phosphoric acid, hydrobromic acid, etc. or an organic acid such as benzenesulfonic acid, p-toluenesulfonic acid, oxalic acid, etc. in ether, toluene, etc.

35 Compound (II) or a salt thereof used in the method of the present invention can be produced according to per se

known methods, for example a method described in Agricultural and Biological Chemistry, 34, 935-940, 1974.

5 The above mentioned compound (I) or a salt thereof can be obtained by using a compound (II) or a salt thereof in accordance with another method which is explained below.

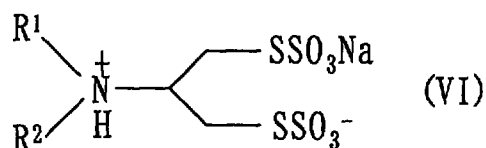
Namely, compound (I) or a salt thereof can be produced by reacting a compound (II) or a salt thereof with sulfurous acid or a salt thereof to provide a compound represented by the
10 formula:



wherein M is a metal or ammonium and the other symbols have the same meanings as defined above, or a salt thereof, and then reacting the resulting compound with prussic acid or a salt thereof.
15

M is a metal (e.g. alkaline metal such as sodium, potassium, etc.; alkaline earth metal such as calcium, magnesium, etc.) or ammonium group. Among them, sodium or potassium is preferable.

20 When pH is about 4, the compound (IV) may form an inner salt represented by the formula:



wherein each symbol has the same meaning as defined above. Such an inner salt is also involved within the scope of
25 compound (IV). This inner salt shows low water-solubility, thus can be isolated as a crystal. In this case, it often has water of crystallization.

Compound (IV) or a salt thereof can be produced by reacting a compound (II) or a salt thereof with sulfurous
30 acid or a salt thereof under a weakly acidic to weakly basic

condition, preferably in the range of pH 4 to 11, more preferably pH 4 to 8.

Salts of compound (IV) include the same ones as mentioned in the above salts of compound (I).

5 As sulfurous acid or a salt thereof includes alkaline metal salts of sulfurous acid such as sodium sulfite, potassium sulfite, etc.; ammonium sulfite; hydrogensulfite (salts with alkaline metal) such as sodium hydrogensulfite, potassium hydrogensulfite, etc.; alkaline earth metal salts of sulfurous
10 acid such as calcium sulfite, magnesium sulfite, etc.; sulfurous acid gas, and so on.

 Among them, a solid alkaline metal salt of sulfurous acid such as sodium sulfite or potassium sulfite which is available on the market, is preferable.

15 Since this reaction proceeds quantitatively in a short period, 2 moles of sulfurous acid or a salt thereof will be sufficient based on 1 mole of compound (II) stoichiometrically. If necessary an excess amount of about 2 to 4 moles may be allowed.

20 As a solvent to be used in the reaction, a solvent which can dissolve each or both of compound (II) or a salt thereof and sulfurous acid or a salt thereof can be preferably used, however this reaction will proceed enough even if solvent can not dissolve both of them well. However, the solvent of
25 which pH inclines toward extremely acidic or basic side is not desirable in consideration of the properties of the reagents, compound (IV) and compound (II) or salts thereof. Therefore, if a solvent is almost neutral, any solvent which does not interfere the reaction can be employed. Such a
30 solvent includes water which is necessary for dissolving sulfurous acid or a salt thereof, and another solvent for example, includes a lower aliphatic alcohol such as methanol, ethanol, isopropanol, etc.; a lower aliphatic ketone such as acetone, methyl ethyl ketone, methyl isobutyl ketone,
35 etc.; a lower chained or a cyclic aliphatic ether such as diethyl ether, tetrahydrofuran, dioxane, etc.; a lower

aliphatic carboxylic acid derivative such as ethyl acetate, acetonitrile, dimethylformamide, etc.; a lower chained or a cyclic aliphatic sulfur compound such as carbon disulfate, dimethylsulfoxide, tetramethylene sulfone, etc.; a lower
5 aliphatic halogenated hydrocarbon such as methylene chloride, chloroform, carbon tetrachloride, etc.; or an aromatic hydrocarbon such as benzene, toluene, xylene, chlorobenzene etc. These solvents can be used alone or two or more kinds of them (preferably not more than three kinds
10 of them) may be mixed in an appropriate proportion together with water.

In the method of the present invention, the reaction starts immediately by contacting the compound (II) or a salt thereof with sulfurous acid or a salt thereof in an
15 appropriate solvent. The reaction temperature desirably may be kept at below 60°C, generally 50°C or not more. The reaction temperature is preferably 20 to 50 °C.

Also, the reaction in the method of the present invention proceeds smoothly under the above mentioned
20 conditions to complete for a period of 30 minutes to several hours generally.

The completion of the reaction can be confirmed easily by analysis such as thin layer chromatograph (TLC), high performance liquid chromatograph (HPLC), and so on.

25 The compound (IV) or a salt thereof can be converted to the compound (I) or a salt thereof, which has an excellent pesticidal activity itself according to the method described in JP-B-19524/1969.

Further, compound (IV) or a salt thereof can be
30 isolated and purified by per se known methods such as pH change, ion-exchange chromatograph, concentration, concentration under reduced pressure, crystallization, and recrystallization and the like.

For example, when the reaction mixture is an aqueous
35 solution, it is neutralized with an equivalent or a little excess amount of an inorganic acid such as hydrochloric acid,

sulfuric acid, phosphoric acid, or an organic acid such as benzenesulfonic acid, p-toluenesulfonic acid, oxalic acid, without further operations, and when the reaction mixture contains an organic solvent which can be mixed homogeneously with water, after removing the organic solvent by concentration under reduced pressure, the obtained aqueous layer is neutralized as mentioned above, to isolate an inner salt of compound (VI) as a high purified crystal.

The compound (I) or a salt thereof can be produced by reacting compound (IV) or a salt thereof with prussic acid or a salt thereof. This reaction can be conducted by the same conditions as a reaction for producing a compound (I) or a salt thereof from a compound (II) or a salt thereof as mentioned above. Compound (IV) or a salt thereof which is a starting material of this reaction may be used without isolation or purification after the production according to the above-mentioned method of the present invention. As a matter of course, isolated or purified compound (IV) or a salt thereof can be used.

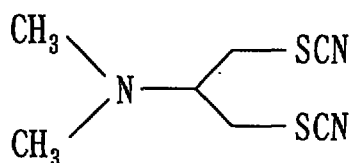
Thus obtained compound (I) or a salt thereof can be introduced to the compound (III) or a salt thereof by the same method as mentioned above.

Examples

The following Examples further illustrate the present invention in detail but are not to be construed to limit the scope thereof.

Example 1

Production of 2-(dimethylamino)trimethylene di(thiocyanate);



2.49 g (purity 98.3%, 0.05 mole) of sodium cyanide

(sodium prussiate) was dissolved in 22.06 g of water, and then the mixture was cooled down to 5°C. 25 mL of toluene was added to the mixture, and then a solution dissolving 5.04 g (0.025 mole) of 4-dimethylamino-1,2-dithiolane-1-oxide hydrochloride in 20.16 g of water was added dropwise for about 1 hour. After the addition, the mixture was stirred for about 1 hour at the same temperature and was separated into a toluene layer and an aqueous layer. This toluene layer was analyzed by HPLC to provide 2.35 g of 2-(dimethylamino)trimethylene di(thiocyanate) (yield: 46.7%) and 0.82 g of 4-dimethylamino-1,2-dithiolane (yield: 21.9%).

Example 2

Production of 2-(dimethylamino)trimethylene di(thiocyanate)

5.04 g (0.025 mole) of 4-dimethylamino-1,2-dithiolane-1-oxide hydrochloride was dissolved in 35 g of water. 25 mL of toluene was added to the mixture, and then the mixture was cooled down to 5 °C. At that time, pH was 2.6.

On the other hand, 2.49 g (purity:98.3%, 0.05 mole) of sodium cyanide (sodium prussiate) was dissolved in 6.86 g of water. This solution was added dropwise to the above obtained mixture for about 1 hour. In the meantime, pH was controlled to be 8 by using 5N hydrochloric acid. After the addition, the reaction mixture was stirred for about 1 hour at the same temperature. After pH was adjusted to 10 by using 4N NaOH, the mixture was separated into a toluene layer and an aqueous layer. This toluene layer was analyzed by HPLC to provide 4.91 g of 2-(dimethylamino)trimethylene di(thiocyanate) (yield: 97.6%). The toluene layer was concentrated under reduced pressure and the resulting residue was recrystallized from methanol to provide crystalline 2-(dimethylamino)trimethylene di(thiocyanate) (melting point: 53-54°C).

Example 3

Production of 2-(dimethylamino)trimethylene di(thiocyanate)

5 13.19 g(0.071 mole) of 1,3-bis(carbamoylthio)-2-(N,N-dimethylamino)propane hydrochloride was dissolved in 250 mL of water. 100 mL of toluene was added to the mixture, and then 28 % sodium hydroxide was added dropwise to be pH=9 under cooling below 45°C since the reaction was exothermic.

10 After the pH was adjusted to be 9, 7.59 g (0.078 mole) of 35% hydrogen peroxide was added dropwise for 1 hour at the same temperature. In the meantime, pH was controlled to be 9 by using 28% sodium hydroxide. After the addition, the reaction mixture was stirred for about 1 hour at the same

15 temperature, then the mixture was separated into a toluene layer and an aqueous layer. 15 mL of water and 17.1 g (0.1645 mole) of 35 % hydrochloric acid were added to the toluene layer, and then the mixture was separated into a toluene layer and an aqueous layer. As a consequence of an analysis of the

20 aqueous layer by HPLC, 12.5 g (0.0675 mole) of 4-(dimethylamino)-1,2-dithiolane hydrochloride was obtained. To this aqueous solution kept at 10°C, 6.56 g (0.0675 mole) of 35 % hydrogen peroxide solution was added dropwise for about 1 hour with stirring. After the addition, the mixture

25 was stirred for about 1 hour at a room temperature. As a consequence of an analysis of the reaction mixture by HPLC, 12.93 g (0.0641 mole) of 4-(dimethylamino)-1,2-dithiolane-1-oxide hydrochloride was obtained. 65 mL of toluene was added to the mixture, and the mixture was cooled

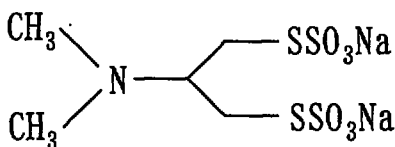
30 down to 5°C, and then a solution prepared by dissolving 6.38 g (purity 98.3%, 0.13 mole) of sodium cyanide (sodium prussiate) in 17.6 g of water, was added dropwise for about 1 hour. In the meantime, pH was controlled not to be more than 7 by using 5N hydrochloric acid. After the addition,

35 the mixture was stirred for about 1 hour at the same temperature, and then pH was adjusted to 10 by using 4N NaOH,

5

Example 4

10



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Example 5

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13.27 g (purity: 95%, 0.10 mole) of sodium sulfite was dissolved in 44.41 g of water. 80 mL of toluene was added to this mixture, and then the pH was adjusted to 7.0 with conc.

hydrochloric acid. After the solution was heated up to 30°C, a solution prepared by dissolving 5.04 g (0.025 mole) of 4-dimethylamino-1,2-dithiolane-1-oxide hydrochloride in 20.16 g of water was added dropwise to the aqueous solution for about 1.5 hours. During the addition, the pH was maintained to 7 with conc. hydrochloric acid. After the mixture was stirred for about 1 hour at the same temperature, pH was adjusted to 9.0 with 28% sodium hydroxide, and then the mixture was separated to obtain an aqueous solution of the titled compound. The aqueous layer was analyzed by HPLC to provide 8.71 g of S,S'-(2-dimethylamino)trimethylene di(sodium thiosulfate) (yield: 98.0%).

Example 6

Production of S,S'-(2-dimethylamino)trimethylene di(sodium thiosulfate)

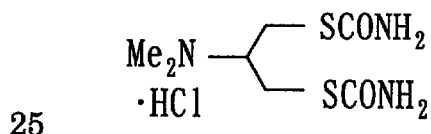
13.19 g(0.071 mole) of 1,3-bis(carbamoylthio)-2-(N,N-dimethylamino)propane hydrochloride was dissolved in 250 mL of water. 100 mL of toluene was added to the mixture, and then 28 % sodium hydroxide was added dropwise to be pH=9 under cooling below 45°C since the reaction was exothermic. After the pH was adjusted to be 9, 7.59 g (0.078 mole) of 35% hydrogen peroxide was added dropwise for 1 hour at the same temperature. In the meantime, pH was controlled to be 9 by using 28% sodium hydroxide. After the addition, the reaction mixture was stirred for about 1 hour at the same temperature, and then the mixture was separated into a toluene layer and an aqueous layer. 15 mL of water and 17.1 g (0.1645 mole) of 35 % hydrochloric acid were added to the toluene layer, and then the mixture was separated into a toluene layer and an aqueous layer. As a consequence of an analysis of the water layer by HPLC, 12.5 g (0.0675 mole) of 4-(dimethylamino)-1,2-dithiolane hydrochloride was obtained. To this aqueous solution kept at 10°C, 6.56 g (0.0675 mole) of 35 % hydrogen peroxide solution was added dropwise for about 1 hour with stirring. After the addition,

the mixture was stirred for about 1 hour at room temperature. As a consequence of an analysis of the reaction mixture by HPLC, 12.93 g (0.0641 mole) of 4-(dimethylamino)-1,2-dithiolane-1-oxide hydrochloride was obtained.

5 Separately, 34.02 g (purity: 95 %, 0.256 mole) of sodium sulfite was dissolved in 113.1 g of water. 205 mL of toluene was added to this mixture, and then pH was adjusted to 7.0 with conc. hydrochloric acid. After the mixture was heated up to 30°C, total amount (12.93 g, 0.0641 mole) of above prepared aqueous
10 solution of 4-dimethylamino-1,2-dithiolane-1-oxide hydrochloride was added dropwise for about 1.5 hours. During the addition, pH was maintained 7.0 with conc. hydrochloric acid. After the mixture was stirred for about 1 hour at the same temperature, pH was adjusted to 9.0 with 28% sodium hydroxide.
15 The separation was conducted to obtain an aqueous solution of the titled compound. As a result of analysis of the aqueous layer by HPLC, 21.64 g of S,S'-(2-dimethylamino)trimethylene di(sodium thiosulfate) (yield: 85.7% based on 1,3-bis(carbamoylthio)-2-(N,N-dimethylamino)propane
20 hydrochloride) was obtained.

Example 7

Production of 1,3-bis(carbamoylthio)-2-(N,N-dimethylamino)propane hydrochloride:

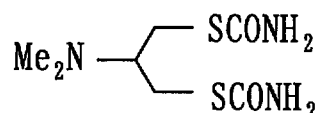


According to the same reaction condition described in Example 2, a toluene solution containing 2-(dimethylamino)trimethylene di(thiocyanate) was provided from 10.09 g (0.05 mole) of 4-dimethylamino-1,2-dithiolane-1-oxide hydrochloride. Hydrogen chloride gas was
30 introduced into a mixture of the residue obtained by concentration of the toluene solution and 30 ml of methanol for 2 hours. The reaction mixture was concentrated under reduced pressure to remove methyl chloride together with

methanol. The residue was recrystallized to provide 12.18 g (89%) of 1,3-bis(carbamoylthio)-2-(N,N-dimethylamino)propane hydrochloride.

5 Example 8

Production of 1,3-bis(carbamoylthio)-2-(N,N-dimethylamino)propane:



10 Hydrogen chloride gas was introduced into a mixture of 20.1 g (0.1 mole) of 2-(dimethylamino)trimethylene di(thiocyanate) obtained according to the same reaction condition as Example 2 and 4 ml of water for 8 hours. The reaction mixture was dissolved in 35 ml of water. This solution was neutralized with sodium hydrogen carbonate.
15 After ice-cooling, crystals precipitated were collected by filtration. The crystals were dried, and recrystallized from ethanol to obtain 12.1 g (51%) of 1,3-bis(carbamoylthio)-2-(N,N-dimethylamino)propane.

20 Example 9

Production of 1,3-bis(carbamoylthio)-2-(N,N-dimethylamino)propane hydrochloride

25 An aqueous solution containing S,S'-(2-dimethylamino)trimethylene di(sodium thisulfate) was obtained from 10.09 g (0.05 mole) of 4-dimethylamino-1,2-dithiolane-1-oxide hydrochloride according to the same method as Example 5.

30 4.90 g (0.10 mole) of sodium cyanide was added portionwise to this aqueous solution, and then the mixture was stirred under ice-cooling for 30 minutes. The precipitated crystals were collected by filtration to obtain 8.56 g of 2-(dimethylamino)trimethylene di(thiocyanate). (yield: 85% based on 4-dimethylamino-1,2-dithiolane-1-oxide hydrochloride)

Hydrogen chloride gas was introduced into a mixture of thus obtained compound and 30 ml of methanol for 2 hours. The reaction mixture was concentrated under reduced pressure to remove methyl chloride together with methanol. The residue
5 was recrystallized from methanol to provide 11.46 g of 1,3-bis(carbamoylthio)-2-(N,N-dimethylamino)propane hydrochloride. (yield: 83% based on 4-dimethylamino-1,2-dithiolane-1-oxide hydrochloride).

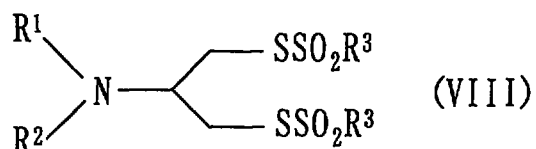
10 Industrial Applicability

According to the method of the present invention to produce compound (I) from compound (II), water-soluble inorganic salts is given as by-product, so that a lipophilic compound (I) which is a desired product can be easily
15 separated after the completion of the reaction. For example, in case of using water and an organic solvent which separates from water as reaction solvent, a thiocyanate compound can be collected quantitatively as a highly purified product by separation into an aqueous layer containing inorganic salts
20 and an organic layer containing the desired product. Therefore, waste yielded by the method of the present invention can be handled smoothly, and it is an extremely useful method in view of measures against environmental pollution.

25 Such a compound (I) or a salt thereof can be also produced via compound (IV) or a salt thereof. According to the method for producing the compound (I) and compound (IV) of the present invention, an isomer such as compound (V) is not yielded as a by-product, thus compound (I) and compound
30 (IV) can be obtained in high yield.

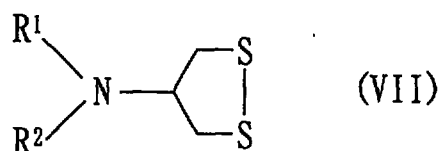
Further, the compound (I) or a salt thereof obtained according to the method of the present invention is useful as an intermediate for synthesis of thiolcarbamate derivatives (e.g. 1,3-bis(carbamoylthio)-2-(N,N-
35 dimethylamino)propane) indicated by compound (III) which have strong insecticidal activity.

In addition, compound (IV) or a salt thereof can be introduced to thiol-sulfonate derivatives represented by the formula:



5 wherein R^1 and R^2 have the same meanings as defined above, and R^3 is a lower alkoxy group; a lower alkyl group which may have saturated heterocyclic group containing oxygen atom as the hetero atom; 10-campharyl group; a phenyl group which may have an alkyl group, a lower alkoxy group, a lower
10 alkylthio group, halogen or an acylamino group as its substituents; or a naphthyl group, which have strong insecticidal activities as described in JP-B-13755/1971. Therefore, compound (IV) or a salt thereof is useful as an intermediate for synthesis of compounds which have an
15 excellent insecticidal activity. Above mentioned compound (VIII) can be produced according to the method described in JP-B-32350/1988.

Also, the filtrate containing crystal of thiolcarbamate derivatives yielded during production steps
20 of those can be introduced to compound (II) or a salt thereof by the following steps. The filtrate was hydrolyzed under an alkaline condition, and then oxidized to provide a compound (VII) represented by the formula:

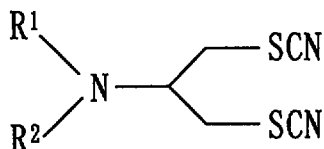


25 wherein each symbol has the same meanings as defined above, or a salt thereof (here, the salt includes the same ones as mentioned in the salt of compound (I)), and then the resulting compound is oxidized under an acidic condition to obtain a compound (II) or a salt thereof. Further, compound (I) or
30 a salt thereof can be obtained from compound (II) or a salt

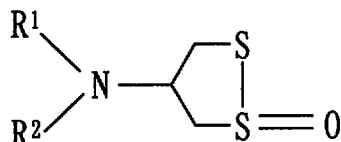
thereof according to the method of the present invention, and therefore, it is possible to recycle as an intermediate for the synthesis of compound (II) or a salt thereof. These processes are considered as extremely useful ones in view
5 of saving resources because of the possibility of use as an intermediate for agrochemicals again via collecting from waste.

CLAIMS

1. A method for producing a compound represented by the formula:



5 wherein R^1 and R^2 independently represent a hydrocarbon group, or R^1 and R^2 form a nitrogen-containing 5- or 6-membered heterocyclic group together with the adjacent nitrogen atom, or a salt thereof, which comprises reacting a compound represented by the formula:



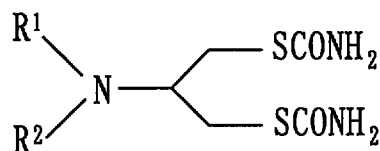
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wherein each symbol has the same meaning as defined above, or a salt thereof, with prussic acid or a salt thereof.

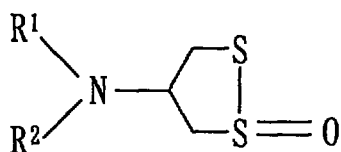
15 2. The method as claimed in claim 1, wherein R^1 and R^2 independently represent an alkyl group.

3. The method as claimed in claim 1, wherein both R^1 and R^2 represent a methyl group.

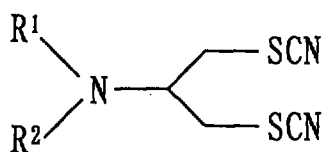
20 4. A method for producing a compound represented by the formula:



25 wherein R^1 and R^2 independently represent a hydrocarbon group, or R^1 and R^2 form a nitrogen-containing 5- or 6-membered heterocyclic group together with the adjacent nitrogen atom, or a salt thereof, which comprises reacting a compound represented by the formula:



wherein each symbol has the same meaning as defined above, or a salt thereof, with prussic acid or a salt thereof to provide a compound represented by the formula:

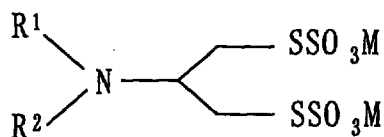


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wherein each symbol has the same meaning as defined above, or a salt thereof, and then subjecting the resulting compound to a hydrolysis reaction or a reaction with a lower alcohol in the presence of a hydrogen halide.

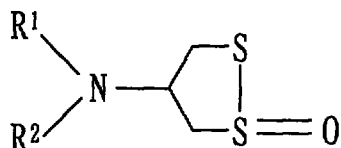
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5. A method for producing a compound represented by the formula:



15

wherein R^1 and R^2 independently represent a hydrocarbon group, or R^1 and R^2 form a nitrogen-containing 5- or 6-membered heterocyclic group together with the adjacent nitrogen atom, and M is a metal or ammonium, or a salt thereof, which comprises reacting a compound represented by the formula:



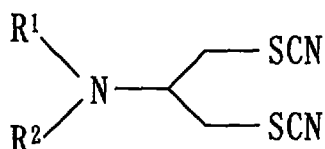
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wherein each symbol has the same meaning as defined above, or a salt thereof, with sulfurous acid or a salt thereof.

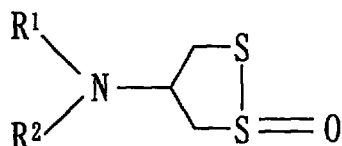
6. The method as claimed in claim 5, wherein R^1 and R^2 independently represent an alkyl group.

7. The method as claimed in claim 5, wherein both R^1 and R^2 represent a methyl group.

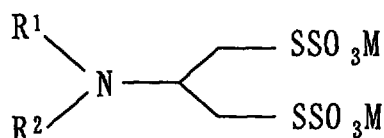
5 8. A method for producing a compound represented by the formula:



wherein R^1 and R^2 independently represent a hydrocarbon group, or R^1 and R^2 form a nitrogen-containing 5- or 6-membered heterocyclic group together with the adjacent nitrogen atom, or a salt thereof, which comprises reacting a compound
10 represented by the formula:

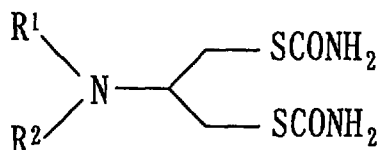


wherein each symbol has the same meaning as defined above, or a salt thereof, with sulfurous acid or a salt thereof to provide
15 a compound represented by the formula:



wherein M is a metal or ammonium and the other symbols have the same meanings as defined above, or a salt thereof, and then reacting the resulting compound with prussic acid or
20 a salt thereof.

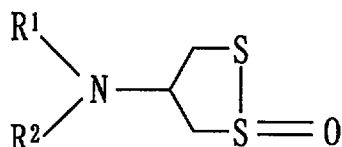
9. A method for producing a compound represented by the formula:



wherein R^1 and R^2 independently represent a hydrocarbon group,

or R^1 and R^2 form a nitrogen-containing 5- or 6-membered heterocyclic group together with the adjacent nitrogen atom, or a salt thereof, which comprises:

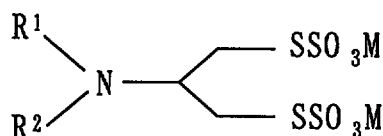
(i) reacting a compound represented by the formula:



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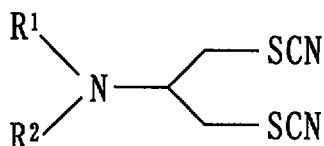


wherein each symbol has the same meaning as defined above, or a salt thereof, with sulfurous acid or a salt thereof to provide a compound represented by the formula:



10 wherein M is a metal or ammonium and the other symbols have the same meanings as defined above, or a salt thereof,

(ii) reacting the resulting compound with prussic acid or a salt thereof to provide a compound represented by the formula:



15 wherein each symbol has the same meaning as defined above, or a salt thereof, and

(iii) subjecting the resulting compound to a hydrolysis reaction or a reaction with a lower alcohol in the presence of a hydrogen halide.