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BIS-IMINOPYRROLINES

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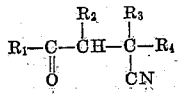
14 Claims. (Cl. 260—313)

This invention is concerned with specific bis-iminopyrrolines as new compositions of matter. It also deals with a method for the preparation of these bis-iminopyrrolines.

The compounds of this invention are prepared by reacting a cyanoketone having the formula

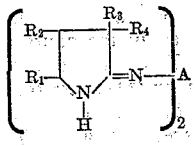


with a diprimary amine having the formula

$$NH_2—A—NH_2$$

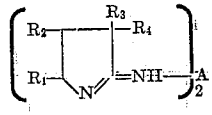
in a molecular ratio of substantially two of the former to one of the latter, to be more fully explained hereinafter. The bis-iminopyrrolines produced may be represented by the formula

(I)



Actually, the compound represented by Formula I is, in varying degrees depending principally on reaction conditions and the values of A, R_1, R_2, R_3, and R_4, in tautomeric relationship with the compounds having the following structures

(II)



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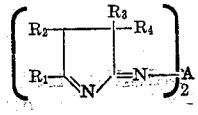

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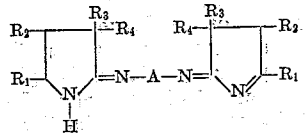


It is believed that the predominant tautomeric product is that represented by Formula I but appreciable amounts of II, III, and IV are undoubtedly present, based on the best experimental and analytical evidence. In the present instance, Formula I will be referred to as the most probably form of the four possible tautomeric structures (I, II, III, and IV), but such reference is meant to include all four of the tautomeric forms.

The symbol R_1 represents hydrocarbon groups of one to ten carbon atoms, preferably alkyl, aralkyl, cycloalkyl, aryl, and alkaryl. The symbol R_2 represents a

hydrogen atom or an alkyl group of one to four carbon atoms. The symbols R_3 and R_4 may be hydrogen atoms or hydrocarbon groups containing from one to ten carbon atoms including alkyl, aralkyl, cycloalkyl, aryl, and alkaryl groups. In addition, R_1 and R_2 taken together with the carbon atoms to which they are joined may form a carbocyclic ring containing five to six carbon atoms which in turn may have alkyl substituents containing a total of no more than four additional carbon atoms. In addition, R_2 and R_3 taken together with the carbon atoms to which they are joined may form a carbocyclic ring containing five to six carbon atoms which in turn may have alkyl substituents containing a total of no more than four additional carbon atoms. In addition, R_3 and R_4 taken together with the carbon atoms to which they are joined may form a carbocyclic ring containing five to six carbon atoms which in turn may have alkyl substituents containing a total of no more than four additional carbon atoms. The total number of carbon atoms in the cyanoketone should not exceed twenty-four. The preferred embodiments are those in which R_1 and R_4 are alkyl groups, R_2 is a hydrogen atom, and R_3 is a methyl group. R_1, R_3, and R_4 may typically individually represent methyl, butyl, octyl, benzyl, phenylbutyl, cyclopentyl, cyclohexyl, phenyl, naphthyl, butylphenyl groups, and the like.

Typical cyanoketone reactants include

4-oxopentanonitrile,
3-methyl-4-oxopentanonitrile,
2,2-dimethyl-4-oxopentanonitrile,
2-methyl-2-ethyl-4-oxopentanonitrile,
2,4,8-trimethyl-4-cyano-6-nonanone,
2-methyl - 2 - (2,2,4,4-tetramethylpentyl)-4-oxopentanonitrile,
2-methyl-2-ethyl-4-oxoheptanonitrile,
2-methyl-2-hexyl-4-oxodecanonitrile,
2-isobutyl-2,6-dimethyl-4-oxoheptanonitrile,
2-methyl-2-neopentyl-4-oxopentanonitrile,
2-methyl-2,4-diphenyl-4-oxobutanonitrile,
2-(1-cyanocyclohexyl)-cyclohexanone,
2-methyl-2,4-dicyclohexyl-4-oxobutanonitrile,
5-methyl-2-(1-methyl-1-cyanoethyl)-cyclohexanone,
1,3,3-trimethyl-5-oxocyclohexane-carbonitrile,
2-acetyl-1-methylcyclopentanecarbonitrile,
1-butyl-2-methyl-3-oxocyclopentanecarbonitrile,
1-(2-oxocyclopentyl)-cyclohexanecarbonitrile,
1-(1-pentyl-2-oxooctyl)-cyclopentanecarbonitrile,
1-octyl-2-methyl-3-oxocyclohexanecarbonitrile,
3,3-dimethyl - 2 - (2-oxopropyl)-bicyclo[2,2,1]heptane-2-carbonitrile,
2-benzoyl-1-methylcyclopentanecarbonitrile, and
2-butyl-2-naphthyl-4-oxobutanonitrile.

The symbol A represents a chain, cyclic or acyclic, of at least four carbon atoms, A is usually hydrocarbon in content but may very well include a secondary or tertiary amino group, an ether oxygen atom, a thioether sulfur atom, and the like. While the upper limit of carbon atoms in A is not especially critical about 24 is considered the practical upper limit. In addition to the carbon atoms there may be one or more nitrogen, oxygen, or sulfur atoms present as previously mentioned. With regard to the reactant $NH_2—A—NH_2$ it is necessary that there be at least four carbon atoms between the two primary amino groups. It is also necessary that each of the primary amino groups be attached to a carbon atom that in turn is attached to no more than two carbon atoms. In other words, the carbon atom to which each of the primary amino groups is attached must bear at least one hydrogen atom, otherwise the reaction is not consummated probably because of interfering steric conditions.

Illustrative reactants having the formula

$$NH_2—A—NH_2$$

include the following:

$NH_2CH_2CH_2NHCH_2CH_2NH_2$

$NH_2(CH_2)_6NH_2$

$NH_2(CH_2)_{10}NH_2$

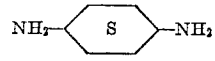
$(NH_2CH_2CH_2CH_2)_2NH$

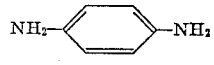
$(NH_2CH_2CH_2CH_2)_2O$

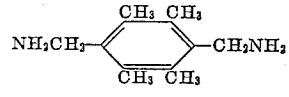
$(NH_2CH_2CH_2CH_2CH_2CH_2CH_2)_2O$

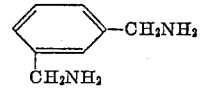
$(NH_2CH_2CH_2CH_2)_2S$

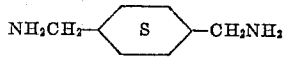
$(NH_2CH_2CH_2CH_2NHCH_2)_2$

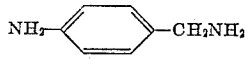


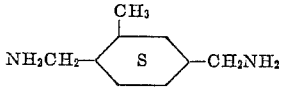




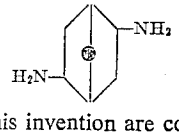








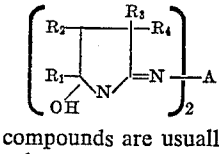
and



The reactants of this invention are compounds that are known or prepared by known methods.

It has been previously stated that the product of this invention is a specific bis-iminopyrroline having the Formula I. However, if the reactants of this invention are mixed and allowed to stand at room temperature or at temperatures up to about 75° C. over prolonged periods of time, a product is formed having the formula

(V)



The Formula V compounds are usually crystalline solids which, when heated to a range approaching that required for distillation, lose water and are converted to a Formula I product.

The Formula I compounds, and these of course encompass types II, III, and IV, as discussed heretofore, are predominantly formed under conditions whereby water as formed in the reaction is removed from the reaction medium. The preferred method is to conduct the reaction in the presence of an inert volatile organic solvent that forms an azeotrope with water. Useful as a solvent in this respect are benzene, toluene, xylene, heptane, hexane, methylene, chloride, chloroform, and the like. The water is removed azeotropically as the reaction progresses, preferably at about 40° C. to 250° C., and very little, if any, of the type V product is formed. The reaction is desirably terminated when the substantially theoretical amount of water is removed. The product may be isolated by distillation under reduced pressure or recrystallization from a solvent, such as isooctane, as desired. If the diprimary amino reactant has been used in excess it has to be separated from the product at the conclusion of the reaction, by conventional methods, or otherwise a diprimary amino addition salt will form.

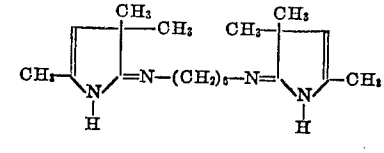
It is probable that in some instances mixtures of products are obtained but this is no deterrent to the present invention. The compounds of this invention, whether of the types corresponding to I or V or mixtures thereof, are valuable for the present purposes. The present compounds are useful as fungicides which are non-injurious to plants upon which they are applied.

These compounds effectively control *Monilinia fructicola* and *Stemphylium sarcinaeforme* when used according to standard techniques in concentrations as low as one to ten parts per million. At the same time the present compounds are non-phytotoxic even in concentrations as high as one-hundred parts per million. Particularly effective in this respect are 1,7-bis(2,4,4-trimethyl-2-pyrrolin-5-ylidene)-1,4,7-triazaheptane and 1,8-bis(2,4,4-trimethyl-2-pyrrolin-5-ylidene)-1,8-diazaoctane.

The compounds of this invention, as well as the methods for their preparation, may be more fully understood from the following examples which are offered by way of illustration and not by way of limitation. Parts by weight are used throughout.

Example 1

Hexamethylenediamine (41 parts of an aqueous 75% solution), and toluene (35 parts) are placed in a boiling flask topped by a water separating head and reflux condenser. Toluene (25 parts) is placed in the water separator initially. The reaction mixture is boiled under reflux in order to separate water azeotropically. Water (11 parts) is removed in the course of this preliminary drying operation. There is added 2,2-dimethyl-4-oxopentanonitrile (62.5 parts) when the water separation is completed. Again the mixture is heated to reflux and water is removed azeotropically. The pot temperature remains in the region 154–160° C., under which conditions the theoretical amount of water (9 parts) separates. The reaction mixture is stripped of low-boiling materials to a pot temperature of 165° C. at 0.2 mm. absolute pressure. The residue (81 parts) is the desired product, 1,8-bis(2,4,4 - trimethyl-2-pyrrolin-5-ylidene)-1,8-diazaoctane having the formula



Calculated for $C_{20}H_{34}N_4$: total nitrogen—17.0%; titratable nitrogen—8.5%. Found: total nitrogen—16.5%; titratable nitrogen—8.3%.

The yield is 98% of the theoretical.

In the same manner, hexamethylenediamine and 2-methyl-2-neopentyl-4-oxopentanonitrile give 1,8-bis(2,4-dimethyl - 4 - neopentyl - 2 - pyrrolin - 5 - ylidene)-1,8-diazaoctane; 1,5 - pentamethylenediamine and 1-(2-oxocyclohexyl) - 1 - cyclohexanecarbonitrile give 1,7-bis(3,3-pentamethylene - 2,3,4,5,6,7 - hexahydroindol-2-ylidene)-1,7 - diazaheptane; hexamethylenediamine and 2,6 - dimethyl - 2-(2-methylpropyl) - 4 - oxoheptanonitrile give 1,8 - bis[4 - methyl - 2,4 - di(2-methylpropyl) - 2 - pyrrolin - 5 - ylidene]-1,8 - diazaoctane; 1,4 - diaminocyclohexane and 2,2-dimethyl-4-oxopentanonitrile give N,N'-bis-(2,4,4-trimethyl - 2 - pyrrolin - 5 - ylidene) - 1,4-diaminocyclohexane; m-xylenylenediamine and 2,2-dimethyl-4-oxopentanonitrile give N,N'-bis-(2,4,4-trimethyl-2-pyrrolin-5-ylidene)-m-xylenylenediamine; and p-phenylenediamine and α,α,4 - trimethyl - 2 - oxocyclohexane-

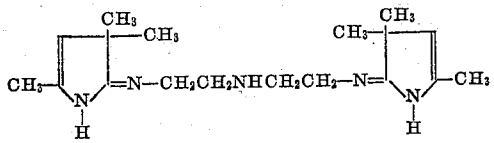
acetonitrile give N,N'-bis - (3,3,6 - trimethyl - 2,3,4,5,6,7-hexahydroindol - 2 - ylidene) - p - phenylenediamine.

Example 2

Diethylenetriamine (72 parts), 2,2-dimethyl - 4 - oxopentanonitrile (125 parts), and benzene (40 parts) are charged to a reactor fitted with a water separator and capped by a reflux condenser. The reaction mixture is boiled under reflux and water is separated azeotropically. When the theoretical amount of water (18 parts) separates, the material is stripped under reduced pressure and finally to 90° C. at 0.1 mm. absolute pressure.

Calculated for $C_{18}H_{31}N_5$: total nitrogen—22.0%; titratable nitrogen—13.2%. Found: total nitrogen—21.2%; titratable nitrogen—12.1%.

The product is 1,7-bis(2,4,4 - trimethyl-2-pyrrolin-5-ylidene)-1,4,7-triazaheptane and has the following structure



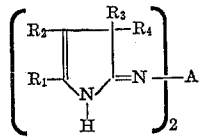
In a similar fashion 1,5,8,12-tetrazadodecane and 2,2-dimethyl - 4 - oxopentanonitrile give 1,12-bis(2,4,4-trimethyl - 2 - pyrrolin - 5 - ylidene) - 1,5,8,12 - tetrazadodecane; 1,9 - diaza - 5 - oxanonane and 1-(2-oxocyclohexyl) - cyclohexanecarbonitrile give 1,9 - bis(3,3-pentamethylene - 2,3,4,5,6,7 - hexahydroindol - 2 - ylidene)-1,9 - diaza - 5 - oxanonane; 1,9 - diaminodiaza - 5 - thianonane and 2 - acetyl - cyclohexanecarbonitrile give 1,9 - bis(3 - methyl - 2,4,5,6,7,7a - hexahydroisoindol - 1-ylidene) - 1,9 - diaza - 5 - thianonane; and 1,15 - diaza-8-oxapentadecane and 3-methyl-4-oxapentanonitrile give 1,15-bis(2,3-dimethyl - 2 - pyrrolin - 5 - ylidene) - 1,15-diaza-8-oxapentadecane.

Example 3

Xylene (30 parts), 1,10-diaminodecane (17.2 parts), and 2-methyl - 2,4 - diphenyl - 4 - oxobutanonitrile (50 parts) are refluxed for twenty-four hours until the theoretical amount of water (3.6 parts) separates. The reaction mixture is stripped under reduced pressure to give the product 1,12 - bis(4 - methyl - 2,4 - diphenyl - 2 - pyrrolin-5-ylidene)-1,12-diazadodecane, in high yield. In a similar fashion there are prepared N,N'-bis(3,3-pentamethylene - 2,3,4,5,6,7 - hexahydroindol - 2 - ylidene)-2,5 - diaminobicyclo(2.2.1)heptane from 1 - (2-oxocyclohexyl) - cyclohexanecarbonitrile and 2,5-diaminobicyclo (2.2.1)heptane; N,N' - bis(4 - methyl - 2,4 - dihexyl - 2-pyrrolin - 5 - ylidene) - 1,4-di(aminomethyl) - cyclohexane from 1,4-di(aminomethyl-cyclohexane and 2 - methyl-2-hexyl-4-oxodecanonitrile; and 1,10-bis(2,4,4-trimethyl-2 - pyrrolin - 5 - ylidene) - 1,4,7,10 - tetrazadecane from triethylenetetramine and 2,2-dimethyl - 4 - oxopentanonitrile.

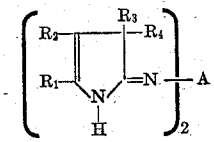
We claim:

1. A member from the group consisting of the compound whose principal tautomeric form is represented by the formula



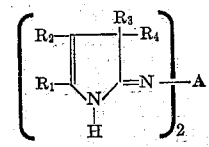
and the pharmaceutically acceptable acid addition salts thereof, in which A represents a member of 4 to 24 carbon atoms from the group consisting of alkylene, cycloalkylene, phenylene, alkylene - phenylenealkylene, alkylenealkyl substituted phenylenealkylene, phenylenealkylene, alkylenecycloalkylenealkylene, bicycloalkylene, and an alkylene interrupted by at least one member of the class consisting of an amino group, an alkylamino group, an ether oxygen atom, and a thioether sulfur atom, provided that there are at least 2 carbon atoms between the members of said class, R_1 taken individually represents a member from the class consisting of alkyl, phenylalkyl, cycloalkyl, phenyl, naphthyl, and alkylphenyl groups of no more than 10 carbon atoms, R_2 taken individually represents a member from the class consisting of a hydrogen atom and an alkyl group of 1 to 4 carbon atoms, R_3 and R_4 taken individually represent members from the class consisting of alkyl, cycloalkyl, phenylalkyl, phenyl, naphthyl, and alkylphenyl groups of no more than 10 carbon atoms, R_1 and R_2 taken collectively with the carbon atoms to which they are joined form a member from the class consisting of a carbocyclic ring of 5 to 6 carbon atoms and one olefinic bond, and said ring having alkyl substituents consisting of a total of no more than 4 carbon atoms, R_2 and R_3 taken collectively with the carbon atoms to which they are joined from a member from the class consisting of a saturated carbocyclic ring of 5 to 6 carbon atoms and said ring having alkyl substituents consisting of a total of no more than 4 carbon atoms, and R_3 and R_4 taken collectively with the carbon atoms to which they are joined from a member from the class consisting of a saturated carbocyclic ring of 5 to 6 carbon atoms and said ring having alkyl substituents consisting of a total of no more than 4 carbon atoms.

2. The compound whose principal tautomeric form is represented by the formula



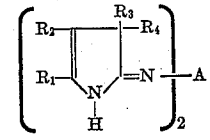
in which A represents an alkylene chain of 4 to 24 carbon atoms, R_1 is an alkyl group of 1 to 10 carbon atoms, R_2 is a hydrogen atom, R_3 is an alkyl group of 1 to 10 carbon atoms and R_4 is an alkyl group of 1 to 10 carbon atoms.

3. The compound whose principal tautomeric form is represented by the formula



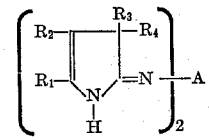
in which A represents an alkylene chain of 4 to 24 carbon atoms, R_1 and R_4 are alkyl groups of 1 to 10 carbon atoms, R_2 is a hydrogen atom, and R_3 is a methyl group.

4. The compound whose principal tautomeric form is represented by the formula



in which A represents an alkylene chain of 4 to 24 carbon atoms, R_1 and R_2 taken collectively with the carbon atoms to which they are joined represent a carbocyclic ring of 5 to 6 carbon atoms having one olefinic bond and R_3 and R_4 are alkyl groups of 1 to 10 carbon atoms.

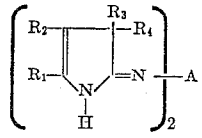
5. The compound whose principal tautomeric form is represented by the formula



in which A represents an alkylene chain of 4 to 24 carbon atoms, R_1 is an alkyl group of 1 to 10 carbon atoms, R_2 and R_3 taken collectively with the carbon atoms to

which they are joined form a saturated carbocyclic ring of 5 to 6 carbon atoms and R_4 is an alkyl group of 1 to 10 carbon atoms.

6. The compound whose principal tautomeric form is represented by the formula



in which A represents an alkylene chain of 4 to 24 carbon atoms, R_1 is an alkyl group of 1 to 10 carbon atoms, R_2 is an alkyl group of 1 to 4 carbon atoms and R_3 and R_4 taken collectively with the carbon atoms to which they are joined form a saturated carbocyclic ring of 5 to 6 carbon atoms.

7. As a composition of matter, 1,8-bis(2,4,4-trimethyl-2-pyrrolin-5-ylidene)-1,8-diazaoctane.

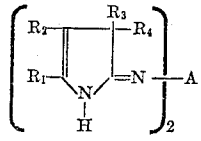
8. As a composition of matter, 1,8-bis(2,4-dimethyl-4-neopentyl-2-pyrrolin-5-ylidene)-1,8-diazaoctane.

9. As a composition of matter, 1,7-bis(3,3-pentamethylene-2,3,4,5,6,7-hexahydroindol-2-ylidene)-1,4,7-triazaheptane.

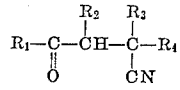
10. As a composition of matter, 1,7-bis(2,4,4-trimethyl-2-pyrrolin-5-ylidene)-1,4,7-triazaheptane.

11. As a composition of matter, 1,12-bis(2,4,4-trimethyl-2-pyrrolin-5-ylidene)-1,5,8,12-tetraazadodecane.

12. A method for the preparation of a compound having the formula



in which A represents a member of 4 to 24 carbon atoms from the group consisting of alkylene, cycloalkylene, phenylene, alkylenephenylenealkylene, alkylenealkyl substituted phenylenealkylene, phenylenealkylene, alkylenecycloalkylenealkylene, bicycloalkylene, and an alkylene interrupted by at least one member of the class consisting of an amino group, an alkylamino group, and an ether oxygen atom, and a thioether sulfur atom, provided that there are at least 2 carbon atoms between the members of said class, R_1 taken individually represents a member from the class consisting of alkyl, phenylalkyl, cycloalkyl, phenyl, naphthyl, and alkylphenyl groups of no more than 10 carbon atoms, R_2 taken individually represents a member from the class consisting of a hydrogen atom and an alkyl group of 1 to 4 carbon atoms, R_3 and R_4 taken individually represent members from the class consisting of alkyl, cycloalkyl, phenylalkyl, phenyl, naphthyl, and alkylphenyl groups of no more than 10 carbon atoms, R_1 and R_2 taken collectively with the carbon atoms to which they are joined form a member from the class consisting of a carbocyclic ring of 5 to 6 carbon atoms and one olefinic bond, and said ring having alkyl substituents consisting of a total of no more than 4 carbon atoms, R_2 and R_3 taken collectively with the carbon atoms to which they are joined form a member from the class consisting of a saturated carbocyclic ring of 5 to 6 carbon atoms and said ring having alkyl substituents consisting of a total of no more than 4 carbon atoms, and R_3 and R_4 taken collectively with the carbon atoms to which they are joined form a member from the class consisting of a saturated carbocyclic ring of 5 to 6 carbon atoms and said ring having alkyl substituents consisting of a total of no more than 4 carbon atoms, which comprises reacting at temperatures from 40° to 250° C., a compound having the formula



with one having the formula

$$NH_2—A—NH_2$$

in which there are at least 4 carbon atoms between the two primary amino groups and in which each of the primary amino groups is attached to a carbon atom that bears at least one hydrogen atom.

13. A method according to claim 12 in which the reaction is conducted in the presence of an inert volatile organic solvent that forms an azeotrope with water.

14. A method according to claim 12 in which the reaction is conducted in the presence of an inert organic volatile solvent that forms an azeotrope with water and the water formed in the reaction is removed azeotropically as the reaction progresses.

References Cited in the file of this patent

UNITED STATES PATENTS

2,417,046	Brooks et al.	Mar. 11, 1947
2,469,830	Knott	May 10, 1949
2,580,738	De Benneville	Jan. 1, 1952

FOREIGN PATENTS

669,037	Germany	Nov. 25, 1940