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PATENT SPECIFICATION

NO DRAWINGS

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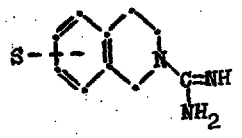
COMPLETE SPECIFICATION

A process for the Manufacture of *Iso*quinoline Derivatives

We, F. HOFFMANN-LA ROCHE & Co. Aktiengesellschaft, a Swiss Company, of 124—184 Grenzacherstrasse, Basle, Switzerland, 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 relates to a process for the manufacture of *iso*quinoline derivatives; more particularly, the invention is concerned with a process for the manufacture of *iso*quinoline derivatives many of which are novel and with said novel derivatives *per se*.

The derivatives obtained by carrying out the process of the invention are compounds of the general formula



wherein S denotes 6- or 7-(lower alkoxy), 6,7-di(lower alkoxy) or 6,7-(methylenedioxy or ethylenedioxy) substitution and the broken line denotes that the substitutents attached thereby are optional, and acid addition salts thereof. Both the compounds of the foregoing formula and their pharmaceutically acceptable acid addition salts are useful as hypotensives. More particularly, they are useful as hypotensive adrenergic blocking agents. They are especially suitable in that they they exhibit of low incidence of side effects (e.g. diarrhoea) common to other hypotensive adrenergic blocking agents. Moreover, they do not deplete catechol amines (e.g. epinephrine and norepinephrine). Thus, they do not deplete endogenous catechol amines from the adrenal glands or from peripheral storage sites. They are also useful as inhibitors of *Trichomonas vaginalis* and may be used for treating infections caused by this organism.

Both the compounds of the foregoing formula and their pharmaceutically acceptable acid addition salts can be administered orally or parenterally with dosage adjusted to individual requirements. They can be administered therapeutically (for example, orally or parenterally) by incorporating a therapeutic dosage in a conventional dosage form such as tablets, capsules, elixirs, suspensions or solutions. They can be administered in admixture with conventional pharmaceutical carriers or excipients, for example, corn starch, calcium stearate, magnesium carbonate, calcium silicate, dicalcium phosphate, talc or lactose. Moreover, they can be administered in the presence of buffers or agents used to adjust isotonicity and the pharmaceutical dosage forms can, if desired, be subjected to conventional pharmaceutical practices such as, for example, sterilization. As stated earlier, the dosage can be adjusted to individual requirements. When administered to a higher mammal in order to produce a hypotensive effect, the average daily dose is ~~suitably~~ suitably between about 10 mg and 180 mg per day, preferably between about 40 mg and 80 mg per day. The dosage can be taken at one time or in separate dosages at different times during the day. On a body-weight basis a dosage of about 1 to 5 mg/kg per day is appropriate in lower mammals, whereas lower body-weight dosages suffice in higher mammals. The foregoing dosages are given by way of example since there can, of course, be individual cases where higher or lower dosage ranges are required.

It will be appreciated that the invention also includes a process for providing economically useful animals free from infections of *Trichomonas vaginalis*, which process comprises treating said animals suffering from or subject to such infections with one or more of the compounds formulated hereinbefore or one or more acid addition salts thereof or with a composition containing same.

The term "lower-alkoxy" is used in this

[*Price 4s. 6d.*]

description and in the claims appended hereto to mean alkoxy groups containing from one to four carbon atoms. Similarly, the term "lower-alkyl" is used in this description and in the claims appended hereto to mean alkyl groups containing from one to four carbon atoms.

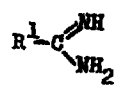
According to the process provided by the invention, the derivatives aforesaid are manufactered by reacting an amine of the formula



(wherein S and the broken lines have the significance given earlier), or an acid addition salt thereof, with cyanamide or with a compound containing a labile amidino group and, if desired, converting the product, if an acid addition salt, into the free base or into another acid addition salt or, if a base, into an acid addition salt.

According to one embodiment of the process, the derivatives aforesaid are manufactured by reacting an amine of the foregoing formula, or an acid addition salt thereof, with cyanamide. It is preferably to carry out this reaction in a substantially non-polar inert solvent such as toluene or xylene. The solvent acts as a diluent and is added to an approximately equimolar mixture of the starting materials to moderate the reaction when the components are heated. Without a solvent, a vigorous reaction occurs at about 150°—170°C. If the components are suspended in a solvent, it has been found preferable to carry out the reaction at an elevated temperature (e.g. at the reflux temperature of the solvent). Time is not critical, but it has been found, for example, that when the components are suspended in toluene and the mixture is heated under reflux for 2 hours, a substantially complete reaction occurs.

According to a further, and preferred, embodiment of the process, the derivatives aforesaid are manufactured by reacting an amine of the foregoing formula with an acid addition salt of a urea derivative of the formula



wherein R^1 stands for an alkylmercapto, alkoxy, pyrazolyl-(1) or alkyl-substituted pyrazolyl-(1) group, and, if desired, converting the resulting acid addition salt into the free base or into another acid addition salt.

The preferred acid addition salts of the urea derivatives are acid addition salts of S - (lower alkyl) - *iso*thioureas, O - (lower alkyl) - *pseudo*ureas, 2 -~~amino~~ - pyrazole or a 2-amidino-pyrazole which contains one or more lower-alkyl groups in the pyrazole ring. The preferred substituted-pyrazole is a 3,5-di-(lower alkyl)-pyrazole.

The reaction of the amine with the acid addition salt of the urea derivative leads to the corresponding acid addition salt of the compound of the first formula hereinbefore. The success of the reaction is not dependent on temperature and it can be carried out at room temperature or at temperatures above or below room temperature. The reaction can also be carried out at atmospheric pressure or at reduced or elevated pressure. When using an acid addition salt of an O-(lower alkyl)-*pseudo*urea, the reaction is suitably carried out at atmphospheric pressure between about room temperature and 100°C (preferably between about 50°C and 80°C). When using an acid addition salt of 2-amidino-pyrazole or an alkyl substituted derivative thereof the reaction is suitably carried out at atmospheric pressure between about room temperature and 100°C (preferably between about 70°C and 100°C. The reaction should be carried out in a medium which serves as a solvent for the reactants. Any suitable conventional solvent medium can be used; for example, an aqueous medium, an aqueous-alcoholic medium or an aqueous medium containing a water-miscible organic solvent.

As stated earlier, any acid addition salt obtained may be converted into the free base or into another acid addition salt. These conversions can be carried out by conventional methods.

The compounds of the first formula hereinbefore are basic and form the acid addition salts with both inorganic and organic acids. Thus, they form pharmaceutically acceptable acid addition salts with inorganic acids such as hydrochloric acid, hydrobromic acid, hydroiodic acid, hydrofluoric acid, sulphuric acid, nitric acid and phosphoric acid and with organic acids such as alkanesulphonic acids (e.g. methanesulphonic acid), monoaryl sulphonic acids, (e.g. *para*toluenesulphonic acid, benzenesulphonic acid) acetic acid, tartaric acid, maleic acid, citric acid, benzoic acid, salicyclic acid and ascorbic acid.

The novel *iso*quinoline derivatives referred to earlier are the acid addition salts of the compounds of the first formula hereinbefore and those compounds of the first formula hereinbefore in which S is present, and it will be appreciated that these novel derivatives also form part of the invention. The preferred novel derivatives are acid addition salts of 2 -amidino - 1,2,3,4 - tetrahydro - *iso*quinoline with pharmaceutically acceptable acids (especially the sulphate and the hydrochloride) and 2 - amidino - 6,7 - dimethoxy-1,2,3,4 - tetrahydro - *iso*quinoline and its acid addition salts.

The following Examples illustrate the process of the invention:

amidino

EXAMPLE 1

13 g of 1,2,3,4 - tetrahydro - *iso*quinoline and 17 g S - ethyl - *iso*thiourea hydrobromide were dissolved in about 50 ml of water. A clear solution formed on shaking and was heated to 80°C for 3 hours. The resulting mixture was distilled to dryness *in vacuo* at 50°—60°C, leaving a crystallized residue which was triturated with acetone and filtered, yielding crystals which, upon recrystallization from about 100 ml of water, gave 2 - amidino - 1,2,3,4 - tetrahydro - *iso*quinoline hydrobromide melting at 170—171°C (uncorrected).

EXAMPLE 2

A) *The reaction*

27 g of 1,2,3,4 - tetrahydro - *iso*quinoline were added at *ca* 20°C to a solution of 28 g of S - methyl - *iso*thiourea sulphate in 80 ml of water. The resulting mixture was kept at *ca* 20°C with occasional shaking. After a short time methyl-mercaptan began to escape and the mixture warmed up slightly. Upon standing for 24 hours, crystals formed. They were filtered off and rinsed with ice-cold water. Recrystallization from approximately 100 ml of water yielded 2 - amidino - 1,2,3,4-tetrahydro-*iso*quinoline sulphate melting at 278°—280°C (uncorrected).

Another batch prepared in the same manner melted at 284°—285°C due to a minute difference in moisture content.

B) *The conversion into the free base*

44.85 g of 2 - amidino - 1,2,3,4 - tetrahydro - *iso*quinoline sulphate were dissolved at *ca* 20°C in 1000 ml of water and 18.94 g of finely ground barium hydroxide monohydrate were added thereto. The resulting mixture was shaken on a shaking machine for 24 hours. The precipitated barium sulphate was filtered off and the clear filtrate distilled to dryness *in vacuo*. There remained a colourless viscous oil which slowly solidified to a soft crystalline mass of the free base, 2-amidino - 1,2,3,4 - tetrahydro - *iso*quinoline. It was very soluble in water and in alcohols. It dissolved sparingly in ether and was insoluble to ligroin. When left standing exposed to the air, it took up carbon dioxide and formed the carbonate.

C) *The conversion into the hydrochloride*

10 g of 2 -amidino - 1,2,3,4 - tetrahydro-*iso*quinoline sulphate were dissolved in 200 ml of water on a steam-bath and a solution of 5.45 g of barium chloride dihydrate in 30 ml of water was added thereto. The mixture was warmed for 0.5 hour and the precipitated barium sulphate filtered off. The clear filtrate was distilled to dryness, leaving a practically colourless viscous residue which was dissolved in a small amount of absolute alcohol and cautiously diluted with anhydrous ether until a slight turbidity remained. On standing for several hours, crystals formed. They were filtered off, washed with ether and dried, yileding 2 - amidino - 1,2,3,4 - tetrahydro-*iso*quinoline hydrochloride melting at 179°C (uncorrected).

D) *The conversion into the carbonate*

2 g of 2 - amidino - 1,2,3,4 - tetrahydro *iso*quinoline sulphate were dissolved in a small amount of water. The resulting solution was cooled with ice-water and an excess of sodium hydroxide added thereto. The resulting alkaline mixture was repeatedly extracted with ether, the combined ether extracts were dried over potassium carbonate and filtered. Carbon dioxide gas was introduced into the filtered clear solution causing 2 - amidino - 1,2,3,4-tetrahydro - *iso*quinoline carbonate to crystallize. The carbonate melted at 136°—138°C (uncorrected).

E) *The conversion into the nitrate*

10 g of 2 -amidino - 1,2,3,4 - tetrahydro-*iso*quinoline sulphate was slowly added to an ice-cold solution of 10 g of potassium hydroxide in 10 ml of water. The mixture was then extracted repeatedly with ether and the resulting ether solution cautiously neutralized with nitric acid, whereupon 2-amidino-1,2,3,4-tetrahydro - *iso*quinoline nitrate precipitated. It melted at 146°—148°C (uncorrected).

EXAMPLE 3

3 g of 6,7 - dimethoxy - 1,2,3,4 - tetrahydro-*iso*quinoline were dissolved in 25 ml of methanol and a solution of 2.2 g of S -methyl - *iso*thiourea sulphate in 15 ml of water was added thereto. The mixture was allowed to stand at *ca* 20°C for 1 day and was then warmed to 60°—70°C for 5 hours. The solution was then evaporated *in vacuo* and the solid residue triturated with absolute alcohol and filtered. The crystals thus obtained were recrystallized from 90% alcohol, yielding 6,7 - dimethoxy - 1,2,3,4 - tetrahydro-*iso*quinoline sulphate melting at 259°—261°C (uncorrected).

EXAMPLE 4

13.5 g of 1,2,3,4 - tetrahydro - *iso*quinoline and 12 g of O - methyl - *pseudo*urea sulphate were dissolved in 100 ml of water. After standing at *ca* 20°C for 24 hours, the solution was heated under reflux for 20 hours, and then cooled in ice for several hours. Crystals separated and were filtered off. The filtrate was distilled to dryness and the mixture stirred with alcohol and filtered. The crystals were recrystallized from water, yielding 2 - amidino - 1,2,3,4 - tetrahydro - *iso*quinoline sulphate melting at 266°—268°C.

EXAMPLE 5

13.3 g of 1,2,3,4 - tetrahydro - *iso*quinoline and 20 g of 1 - amidino - 3,5 - dimethylpyrazole nitrate were heated under reflux for *ca* 16 hours in 200 ml of absolute alcohol. The solvent was removed by distillation *in vacuo*, leaving a crystalline mass. On triturating with 60 ml of alcohol at *ca* 20°C, part of the material dissolved. The mixture was filtered and the crystals were washed with ice-cold alcohol, yielding 2-amidino-1,2,3,4-tetrahydro-*iso*quinoline nitrate melting at 144°—146°C. A mixed melting point with a sample of the nitrate prepared from the sulphate according to Example 2 (E) showed no depression.

EXAMPLE 6

8.5 g of 1,2,3,4 - tetrahydro - *iso*quinoline hydrochloride and 2 g of cyanamide were suspended in about 50 ml of toluene. The mixture was stirred and heated to reflux temperature for about 5—6 hours. It was then allowed to cool to *ca* 20°C and kept at this temperature for about 15 hours. Crystals separated and were filtered off by suction. They were recrystallized from about 30 ml of alcohol, yielding 2 - amidino - 1,2,3,4 - tetrahydro-*iso*quinoline hydrochloride of melting point 179°—181°C.

The following Examples illustrate pharmaceutical preparations containing the novel derivatives provided by the invention and the manner in which said preparations may be made up.

EXAMPLE A

A solid pharmaceutical composition was prepared as follows: 26.11 g of 2-amidino-1,2,3,4 - tetrahydro - *iso*quinoline sulphate, 7.00 g of pregelatinized corn starch, 32.00 g of corn starch and 32.875 g of dicalcium phosphate were thoroughly blended and passed through a suitable size screen. 0.015 g of F.D. & C. Blue dye No. 1 dissolved in water was used to granulate the foregoing screened composition containing the active ingredient. The wet granulated composition was then passed through a suitable size screen, dried at 43°C and again passed through a suitable size screen. 2 g of calcium stearate were then added to the mixture, the resulting composition blended well and compressed to tablets each containing 40 mg (base equivalent) of the active ingredient.

EXAMPLE B

A solid pharmaceutical composition was prepared as follows: 17.406 g of 2-amidino-1,2,3,4 - tetrahydro - *iso*quinoline sulphate, 6.667 g of pregelatinized corn starch, 36.667 g of corn starch and 37.2597 g of dicalcium phosphate were thoroughly blended and passed through a suitable size screen. 0.0003 g of F.D. & C. Blue No. 1 dissolved in water was used to granulate the screened composition containing the active ingredient. The wet granulated composition was then passed through a suitable size screen, ~~dried~~ at 43°C and again passed through a suitable size screen. 2 g of calcium stearate were then added to the mixture, the resulting composition blended well and compressed to tablets each containing 20 mg (base equivalent) of the active ingredient.

EXAMPLE C

The following injectable formulation was prepared: 25.5 g of 2-amidino-1,2,3,4-tetrahydro-*iso*quinoline sulphate (with 2% excess), 1.0 g of disodium hydrogen citrate, 4.5 g of anhydrous phenol, 4.0 g of sodium chloride and 100.0 mg of disodium dihydrogen ethylenediamine tetraacetate were dissolved in about 700 ml of water for injection and the pH of the solution was adjusted to 5.0±0.2 using dilute sodium hydroxide or dilute sulphuric acid as needed. The solution was then adjusted to 1 litre and filtered through a filter candle and filled under nitrogen gas into 1 and 2 ml amber glass ampoules containing 25.0 and 50.0 mg of active substance respectively. A similar injectable solution was prepared using a mixture of 0.3 g of citric acid and 0.7 g of trisodium citrate in place of the disodium hydrogen citrate.

EXAMPLE D

Tablets were prepared containing:

2-amidino-1,2,3,4-tetrahydro-*iso*-quinoline hydrobromide	16.4 g
Corn starch	43.3 g
Dicalcium phosphate	36.5 g
Calcium stearate	2.0 g

The active ingredient was blended with part of the corn starch and all the dicalcium phosphate. A corn starch paste was then made by mixing in the remainder of the corn starch and, as described in Examples A and B, a wet granulation was prepared by granulating this paste with a dye solution. The wet granulated composition was then passed through a hammer mill and dried for *ca* 16 hours at 43°C. The dry granules were screened through a suitable size screen and the calcium stearate added. The mixture was then blended well and compressed to tablets each containing 20 mg (base equivalent) of active ingredient.

EXAMPLE E

Tablets were prepared containing:

2-amidino-1,2,3,4-tetrahydro-*iso*-quinoline hydrochloride	14.7 g
Corn starch	43.3 g
Dicalcium phosphate	40.0 g
Calcium stearate	2.0 g

The active ingredient was blended with

part of the corn starch and all the dicalcium phosphate. A corn starch paste was then made by mixing in the remainder of the corn starch and, as described in Examples A and B, a wet granulation was prepared by granulating this paste with a dye solution. The wet granulated composition was then passed through a hammer mill and dried for *ca* 16 hours at 43°C. The dry granules were screened through a suitable size screen and the calcium stearate added. The mixture was then blended well and compressed to tablets each containing 20 mg (base equivalent) of active ingredient.

EXAMPLE F

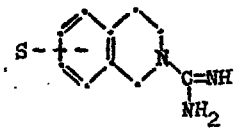
Tablets were prepared by dissolving 21 g of 2 -amidino - 1,2,3,4 - tetrahydro - *iso*-quinoline in alcohol (15% w/v) and absorbing the solution on 150 g of calcium silicate. This was then mixed with 29 g of pre-gelatinized corn starch, 50 g of dicalcium phosphate and 50 g of corn starch. The mixture was granulated by the addition of distilled water. It was then dried at 37°C, passed through a suitable size screen, blended with 3 g of talc and 3 g of calcium stearate and mixed well. The resulting mixture was then compressed to tablets each containing 20 g of the active ingredient.

EXAMPLE G

Tablets were prepared by dissolving 21 g of 2 - amidino - 1,2,3,4 - tetrahydro - *iso*-quinoline in alcohol (15% w/v) and absorbing the solution on 150 g of magnesium carbonate. This was then mixed with 29 g of pre-gelatinized corn starch, 50 g of dicalcium phosphate and 50 g of corn starch. The mixture was granulated by the addition of distilled water. It was then dried at 37°C, passed through a suitable size screen, blended with 3 g of talc and 3 g of calcium stearate and mixed well. The resulting mixture was then compressed to tablets each containing 20 mg of the active ingredient.

WHAT WE CLAIM IS:—

1) A process for the manufacture of compounds of the general formula



wherein S denotes 6- or 7-(lower alkoxy), 6,7-di(lower alkoxy) or 6,7-(methylenedioxy or ethylenedioxy) substitution and the broken line denotes that the substituents attached thereby are optional, and acid addition salts thereof, which process comprises reacting an amine of the formula

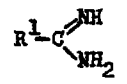


(wherein S and the broken lines have the signficance given earlier in this claim), or an acid addition salt thereof, with cyanamide or with a compound containing a labile amidino group and, if desired, converting the product, if an acid addition salt, into the free base or into another acid addition salt or, if a base, into an acid addition salt.

2) A process in accordance with claim 1, wherein the reaction with cyanamide is carried out in the presence of a non-polar inert solvent.

3) A process in accordance with claim 2, wherein said solvent is toluene or xylene and the reaction is carried out at reflux temperature.

4) A process in accordance with claim 1, wherein an amine of the formula given in that claim is used and the compound containing the labile amidino group is an acid addition salt of a urea derivative of the formula



in which R^1 stands for an alkylmercapto, alkoxy, pyrazolyl-(1) or alkyl-substituted pyrazolyl-(1) group.

5) A process in accordance with claim 4, wherein said urea derivative is an S-(lower alkyl)-*iso*thiourea.

6) A process in accordance with claim 4, wherein said urea derivative is an O-(lower alkyl)-*pseudo*urea.

7) A process in accordance with claim 4, wherein said urea derivative is a 2-amidino-3,5-di(lower alkyl)-pyrazole.

8) A process in accordance with any one of claims 1 to 7 wherein the amine starting material is 1,2,3,4 - tetrahydro - *iso*quinoline or 6,7 - dimethoxy - 1,2,3,4 - tetrahydro-*iso*quinoline.

9) A process for the manufacture of the compounds of the first formula given in claim 1, and acid addition salts thereof, substantially as described with reference to Examples 1 to 6.

10) Compounds of the first formula given in claim 1, and acid addition salts thereof, when manufactured by the process claimed in any one of claims 1 to 9 inclusive.

11) Acid addition salts of the compounds of the first formula given in claim 1.

12) Acid addition salts of 2-amidino-1,2,3,4 - tetrahydro - *iso*quinoline with pharmaceutically acceptable acids.

part of the corn starch and all the dicalcium phosphate. A corn starch paste was then made by mixing in the remainder of the corn starch and, as described in Examples A and B, a wet granulation was prepared by granulating this paste with a dye solution. The wet granulated composition was then passed through a hammer mill and dried for *ca* 16 hours at 43°C. The dry granules were screened through a suitable size screen and the calcium stearate added. The mixture was then blended well and compressed to tablets each containing 20 mg (base equivalent) of active ingredient.

EXAMPLE F

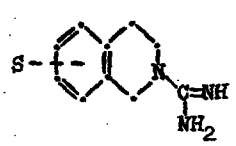
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EXAMPLE G

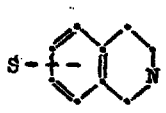
Tablets were prepared by dissolving 21 g of 2 - amidino - 1,2,3,4 - tetrahydro - *iso*-quinoline in alcohol (15% w/v) and absorbing the solution on 150 g of magnesium carbonate. This was then mixed with 29 g of pre-gelatinized corn starch, 50 g of dicalcium phosphate and 50 g of corn starch. The mixture was granulated by the addition of distilled water. It was then dried at 37°C, passed through a suitable size screen, blended with 3 g of talc and 3 g of calcium stearate and mixed well. The resulting mixture was then compressed to tablets each containing 20 mg of the active ingredient.

WHAT WE CLAIM IS:—

1) A process for the manufacture of compounds of the general formula



wherein S denotes 6- or 7-(lower alkoxy), 6,7-di(lower alkoxy) or 6,7-(methylenedioxy or ethylenedioxy) substitution and the broken line denotes that the substituents attached thereby are optional, and acid addition salts thereof, which process comprises reacting an amine of the formula

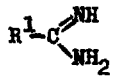


(wherein S and the broken lines have the signficance given earlier in this claim), or an acid addition salt thereof, with cyanamide or with a compound containing a labile amidino group and, if desired, converting the product, if an acid addition salt, into the free base or into another acid addition salt or, if a base, into an acid addition salt.

2) A process in accordance with claim 1, wherein the reaction with cyanamide is carried out in the presence of a non-polar inert solvent.

3) A process in accordance with claim 2, wherein said solvent is toluene or xylene and the reaction is carried out at reflux temperature.

4) A process in accordance with claim 1, wherein an amine of the formula given in that claim is used and the compound containing the labile amidino group is an acid addition salt of a urea derivative of the formula



in which R^1 stands for an alkylmercapto, alkoxy, pyrazolyl-(1) or alkyl-substituted pyrazolyl-(1) group.

5) A process in accordance with claim 4, wherein said urea derivative is an S-(lower alkyl)-*iso*thiourea.

6) A process in accordance with claim 4, wherein said urea derivative is an O-(lower alkyl)-*pseudo*urea.

7) A process in accordance with claim 4, wherein said urea derivative is a 2-amidino-3,5-di(lower alkyl)-pyrazole.

8) A process in accordance with any one of claims 1 to 7 wherein the amine starting material is 1,2,3,4 - tetrahydro - *iso*quinoline or 6,7 - dimethoxy - 1,2,3,4 - tetrahydro-*iso*quinoline.

9) A process for the manufacture of the compounds of the first formula given in claim 1, and acid addition salts thereof, substantially as described with reference to Examples 1 to 6.

10) Compounds of the first formula given in claim 1, and acid addition salts thereof, when manufactured by the process claimed in any one of claims 1 to 9 inclusive.

11) Acid addition salts of the compounds of the first formula given in claim 1.

12) Acid addition salts of 2-amidino-1,2,3,4 - tetrahydro - *iso*quinoline with pharmaceutically acceptable acids.

13) 2 - Amidino - 1,2,3,4 - tetrahydro-*iso*quinoline sulphate.

14) 2 - Amidino - 1,2,3,4 - tetrahydro-*iso*quinoline hydrochloride.

15) Acid addition salts of 2-amidino-6,7 - dimethoxy - 1,2,3,4 - tetrahydro - *iso*-quinoline.

16) Compounds of the first formula given in claim 1, wherein S is present.

17) 2 - Amidino - 6,7 - dimethoxy - 1,2,3,4-tetrahydro-*iso*quinoline.

18) A composition of matter comprising one or more of the compounds of the first formula given in claim 1 or one or more acid addition salt thereof in association with a compatible pharmaceutical or veterinary carrier.

19) A composition as claimed in claim 18, wherein said compound is 2-amidino-1,2,3,4-tetrahydro - *iso*quinoline and said salt is 2 - amidino - 1,2,3,4 - tetrahydro - *iso*-quinoline sulphate.

20) A process for rendering economically useful animals free from infections of *Trichomonas vaginalis*, which process comprises treating said animals suffering from or subject to such infections with one or more of the compounds of the first formula given in claim 1 or one or more acid addition salt thereof or with a composition as set forth in claim 18.

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Aktiengesellschaft.

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