

PATENT SPECIFICATION

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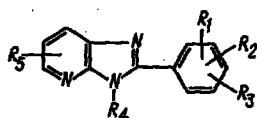
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(54) IMIDAZO[4,5-b]PYRIDINES

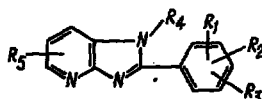
(71) We, [DR.] KARL THOMAE
 G.M.B.H. a German Body Corporate of
 Biberach an der Riss, Germany, do hereby
 declare the invention for which we pray that
 a patent may be granted to us, and the
 method by which it is to be performed, to
 be particularly described in and by the
 following statement:—

The present invention relates to new
 imidazo[4,5-b]pyridines having interesting
 physiological properties.

According to one feature of the present in-
 vention there are provided compounds of
 general formula



and isomers thereof of general formula



[wherein R_1 , R_2 and R_3 , which may be the
 same or different, each represents a hydrogen
 or halogen atom; a hydroxy, alkyl, allyloxy,
 benzyloxy, alkylthio, alkylsulfinyl or alkylsul-
 fonyl group; and amino group optionally sub-
 stituted by one or two alkyl groups; a
 morpholino or a piperazino group optionally

substituted in the 4-position by a phenyl
 group or an alkyl group containing from 1
 to 3 carbon atoms or an alkoxy group con-
 taining from 1 to 4 carbon atoms, optionally
 substituted by a halogen atom or by a
 hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkyl-
 sulfonyl, alkylamino, dialkylamino, piperidino,
 morpholino, thiomorpholino, thiomorpho-
 lino - S - oxide, thiomorpholino - S,S - di-
 oxide, 4 - alkylpiperazino, 4 - phenylpiper-
 azino, 4 - dimethoxyphenylpiperazino, 4 -
 phenylethylpiperazino, phenylethylamino, N -
 methyl - phenylethylamino or N - methyl-
 dimethoxy - phenylethylamino group with
 the proviso that if any two of the
 groups R_1 , R_2 and R_3 represent hydro-
 gen atoms then the other group is
 other than a hydrogen or halogen
 atom, or a methyl or unsubstituted amino
 group; or two of the groups R_1 to R_3 together
 represent a methylenedioxy group and the
 remaining R_1 , R_2 or R_3 group is as hereinbe-
 fore defined each of the above mentioned
 alkyl groups containing from 1 to 4 carbon
 atoms

R_4 represents a hydrogen atom; an alkyl
 group optionally substituted by a hydroxy,
 dialkylamino, phenyl, dimethoxyphenyl,
 piperidino, morpholino, 4-methylpiperazino
 or 4-phenylpiperazino group, each of the
 above mentioned alkyl groups containing
 from 1 to 4 carbon atoms, or a phenyl group
 optionally substituted by one or more halogen
 atoms or methoxy groups with the proviso
 that where R_4 represents a hydrogen atom at
 least one of the groups R_1 to R_3 is other
 than hydrogen; and

R_s represents a hydrogen atom, a halogen atom or an alkyl group containing from 1 to 3 carbon atoms] and the corresponding imidazo[4,5 - b]pyridine - N - oxides and isomers thereof and acid addition salts thereof.

In general the compounds of general formula I and isomers thereof of general formula Ia possess valuable physiological properties, in particular an activity on the blood pressure and heart force, a positive inotropic effect, an antiulcus activity, a platelet aggregation inhibiting effect and a prolonging activity on the bleeding time.

Preferred compounds according to the invention by virtue of their particular favourable physiological properties are those (wherein R_1 , R_2 and R_3 represent hydrogen atoms and R_4 and R_5 , which may be the same or different, each represents a halogen atom or a methyl, methoxy, ethoxy, alkylthio, alkylsulfinyl, dialkylaminoalkoxy, morpholinoalkoxy, thiomorpholinoalkoxy 4-methylpiperazinoalkoxy, 4-phenylpiperazinoalkoxy or alkylsulfinylalkoxy group (wherein each alkyl group contains from 1 to 3 carbon atoms and each alkoxy group contains 2 or 3 carbon atoms) and physiologically compatible acid addition salts thereof. Particularly preferred are the following compounds:—

2 - (2,4 - Dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine and physiologically compatible acid addition salts thereof,

2 - (2 - Methoxy - 4 - methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine and physiologically compatible acid addition salts thereof,

2 - (2 - Methoxy - 4 - methylsulfinyl - phenyl) - 1H - imidazo[4,5 - b]pyridine and physiologically compatible acid addition salts thereof.

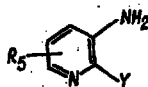
2 - (2 - Methoxy - 4 - methyl - phenyl) - 1H - imidazo[4,5 - b]pyridine and physiologically compatible acid addition salts thereof,

2 - (2 - Methoxy - 5 - methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine and physiologically compatible acid addition salts thereof, and

2 - (2 - Ethoxy - 4 - methyl - phenyl) - 1H - imidazo[4,5 - b]pyridine and physiologically compatible acid addition salts thereof.

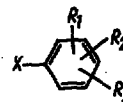
The new compounds of general formula I and isomers thereof of general formula Ia as hereinbefore defined may be prepared by either of the following processes, which processes constitute further features of the invention:—

a) Reaction of a compound of formula



(II)

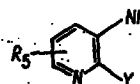
[wherein R_s is as hereinbefore defined and Y represents a group of formula R_4NH — wherein R_4 is as hereinbefore defined] with a compound of formula



(III)

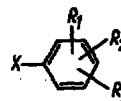
(wherein R_1 to R_3 are as hereinbefore defined and X represents a carboxyl, thiocarboxyl or dithiocarboxyl group) or a functional derivative thereof, for example an acid halide, anhydride, ester or orthoester; and

b) Reaction of a compound of formula



(II)

(wherein R_s is as hereinbefore defined and Y represents a halogen atom) with a compound of formula



(III)

[wherein R_1 to R_3 are as hereinbefore defined and X represents an appropriate $-NR_4$ containing group (wherein R_4 is as hereinbefore defined) which is derived from a carboxyl, thiocarboxyl or dithiocarboxyl group, for example, a nitrile, amide, imido ester, imido thioester, imido halide or amidine group].

In each case the reaction is preferably carried out in the presence of a solvent, suitable solvents including for example benzene, pyridine, glycol, toluene, acetone, diethylene glycol and triethylamine. However the reaction may also be performed in the absence of a solvent. The reaction temperature used is determined by the reactivity of the group X in the compound of formula III used but generally the reaction is effected at temperatures from -20 to 250°C . If desired the reaction may be effected in the presence of an acid binding agent, such as pyridine or triethylamine, or in the presence of a catalytic quantity of an acid, such as *p*-toluenesulfonic acid, or in the presence of a dehydrating agent, such as phosphorus oxychloride or thionyl chloride.

If for example a compound of formula III wherein X represents a carboxyl or amide group is used the reaction is conveniently carried out in the presence of phosphorus oxychloride or thionyl chloride, if desired in the presence of a tertiary organic base such as pyridine or triethylamine, preferably at temperatures from -20°C up to the boiling point of the solvent used, e.g. at 120°C .

If for example a compound of formula III wherein X represents a nitrile group is used, the reaction is conveniently performed in the presence of a catalytic quantity of an acid, such as p-toluenesulfonic acid, preferably at temperatures from 120 to 180°C, e.g. at 160°C, optionally in the presence of a solvent.

If for example a compound of formula III wherein X represents a thioamide group is used, the reaction is conveniently affected in the presence of a solvent, such as glycol, and preferably at temperatures from 100 to 150°C, e.g. at 130°C.

If a compound of formula II wherein Y represents a halogen atom, e.g. a chlorine atom is used, the reaction is preferably carried out via the corresponding amidine, which is cyclized at elevated temperature, e.g. at temperatures from 100 to 200°C, optionally without previous isolation.

The compounds of general formula I and isomers thereof of general formula Ia containing a reactive halogen atom obtained according to the processes of the present invention may, if desired, be subsequently converted into the corresponding amino compounds with amines, and/or compounds of general formula I and isomers thereof of general formula Ia containing reactive hydrogen atoms, may if desired be subsequently alkylated by means of an alkylating agent in the presence of a base.

In addition a compound of formula I or an isomer thereof of formula Ia may if desired be converted into the corresponding N - oxide, S - oxide, or S,S - oxide compound by means of an oxidizing agent. Finally a compound of formula I or an isomer thereof of formula Ia may if desired be converted into an acid addition salt thereof, preferably into a physiologically compatible acid addition salt. Suitable acids include for example hydrochloric acid, hydrobromic acid, sulfuric acid, lactic acid, citric acid, tartaric acid, maleic acid and fumaric acid.

The starting compounds used for the processes according to the invention are known from the literature, or they may be prepared according to known processes (see Examples).

As already mentioned above, the new compounds of general formula I and isomers thereof of general formula Ia in general show valuable pharmacological properties, those which have been tested showing especially an activity on the blood-pressure, a positive inotropic activity, an antiulcus activity, a platelet aggregation inhibiting effect and a prolonging activity on the bleeding time.

The following compounds have been tested with respect to certain of their biological activities:

A=2 - (2,4 - Dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride,
B=2 - [2 - (2 - Methylsulfinyl - ethoxy) -

4 - methoxy - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride,

C=2 - (2 - Methoxy - 4 - methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride,

D=2 - (2 - Methoxy - 4 - methylsulfinyl - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride,

E=2 - (2 - Methoxy - 5 - methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

F=2 - (2 - Methoxy - 4 - methyl - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

G=2 - (2 - Ethoxy - 4 - methoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride,

H=2 - (2 - Ethoxy - 4 - methyl - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride,

I=2 - (2 - Methoxy - 4 - chloro - phenyl) - 1H - imidazo[4,5 - b] pyridine hydrochloride and

J=2 - [2 - (2 - Methylsulfinyl - ethoxy) - 4 - methylmercaptophenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride.

1. Positive inotropic activity in the isolated auricle of the guinea-pig:

Isolated auricles of guinea-pigs were put into an organ bath of 100 ml. The bath has been filled with a tyrode solution at a temperature of 30°C. The tyrode solution was infused with carbogen (95% of O₂ and 5% of CO₂). The spontaneous contractions of the auricles were registered isometrically with a Statham-Force-transducer on a Grasspolygraph. The auricles were charged with 1 g. After sufficient equilibrating time, the substances in question were added to the organ bath. The concentration of the substance in the bath was 1×10^{-5} g/ml in each case. 5 auricles were used for each solution.

The following Table gives the results:

TABLE I

Substance	Increase in the contraction amplitude in %	
A	57.0	
B	17.5	
C	10.3	
E	40.9	115
F	50.2	
G	33.9	
H	42.9	
I	21.4	
J	11.4	120

2. Circulation experiments on the narcotized cat:

Cat were narcotized with 30 mg/kg of pentobarbital-sodium i.v. A plastic catheter was introduced into the arteria femoralis and into the left ventricle of the heart a steel

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5 catheter was introduced from the arteria carotis. With Statham-pressure-transducers of the type P23 AA and P23 Dc, the arterial blood-pressure and the pressure in the left ventricle was registered continuously. From the ventricle-pressure-curve, the contractility parameters dp/dt_{max} and V_{CE} were continuously determined by means of an analogous computer. The heart frequency was

ascertained from the ventricle-pressure-curve using a tachograph. In addition, the EKG was registered in the II derivation.

All registrations were effected on a Brush-direct-writer. The substances were injected over a vena cannular into the vena femoralis. At least three cats were used for the test on each substance.

The following Table gives the results:

TABLE II

Substance	Dose mg/kg i.v.	Blood-pressure alteration in mm Hg	Heart activity	
			Alteration of the contraction force in %	Alteration of the heart frequency in %
A	0.5	- 5	+ 20	+ 4
	1.0	- 5	+ 41	+ 5
B	0.5	+ 10	+ 16	- 2
	1.0	+ 20	+ 29	- 9
C	0.5	+ 5	+ 22	+ 1
	1.0	+ 10	+ 36	+ 5
D	0.5	0	+ 34	+ 5
	1.0	- 5	+ 39	+ 5
E	0.5	+ 10	+ 14	0
	1.0	+ 15	+ 25	0
F	0.5	+ 10	+ 44	- 3
	1.0	+ 15	+ 53	0
G	0.5	0	+ 7	0
	1.0	+ 5	+ 29	- 5
H	0.5	+ 10	+ 15	0
	1.0	+ 15	+ 25	0
I	0.5	- 5	+ 17	+ 2
	1.0	- 5	+ 19	+ 2
J	0.5	+ 10	+ 14	0
	1.0	+ 15	+ 22	- 15

20 None of the compounds showed any toxic side effects using the doses applied.

25 According to yet a further feature of the present invention there are provided pharmaceutical compositions comprising as active ingredient at least one compound of formula I or isomer thereof of formula Ia or physiologically compatible acid addition salt thereof in association with a pharmaceutical carrier or excipient.

30 The compositions may for example be presented in a form suitable for oral, rectal

or parenteral administration. Thus for example compositions for oral administration may be solid or liquid and may take the form of tablets, coated tablets or drops, such compositions comprising carriers or excipients conventionally used in the pharmaceutical art.

For parenteral administration the carrier may be a parenterally acceptable liquid, such as sterile water or a parenterally acceptable oil, e.g. arachis oil, contained in ampoules. For rectal administration compositions may take

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the form of suppositories, the carrier comprising a suppository base.

Advantageously the compositions may be formulated as dosage units. Each dosage unit preferably contains from 35 to 200 mg, preferably from 50 to 100 mg, of active ingredient.

The following Examples serve to illustrate the preparation of compounds according to the invention and of pharmaceutical compositions containing the same.

Example 1

2 - (2,4 - Dimethoxyphenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

54.5 g of 2,3 - diaminopyridine and 91.1 g of 2,4 - dimethoxybenzoic acid were finely pulverized and added in small amounts to 1500 ml of phosphorus oxychloride whilst stirring. Afterwards, the mixture was refluxed for 2 hours, and the phosphorus oxychloride was distilled off in vacuo. The residue was triturated with 200 ml of 2N hydrochloric acid and the solid product obtained was suction filtered and recrystallized from water.

Yield: 121 g (85% of theory), m.p.: 238°C.

Example 2

2 - (2,4 - Dimethoxyphenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

360 mg of 2,4 - dimethoxybenzoic acid were dissolved in 2 ml of pyridine and a solution of 220 mg of 2,3 - diaminopyridine in 2 ml of pyridine was added, whereupon the corresponding salt precipitated out. Whilst stirring and ice-cooling, 0.38 ml of phosphorus oxychloride were added dropwise and the mixture was stirred for a further hour at 0°C and 1 hour at room temperature. Subsequently the excess of pyridine was removed in vacuo and the residue was dissolved by adding dilute hydrochloric acid. The mixture was neutralized with sodium hydroxide solution and extracted with ethyl acetate. The ethyl acetate layer was evaporated, the residue was treated with a small quantity of 2N hydrochloric acid, and the precipitate was suction filtered and recrystallized from water.

M.p.: 238 to 239°C.

Example 3

2 - (2,4 - Dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 2 from 2,3 - diaminopyridine, 2,4 - dimethoxybenzoic acid and thionyl chloride.

M.p.: 238 to 239°C.

Example 4

2 - (2,4 - Dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

900 mg of 2,4 - dimethoxy - benzoic acid were converted into the acid chloride

by heating in a mixture of 3 ml of benzene and 2 ml of thionyl chloride. Subsequently, the mixture was evaporated in vacuo and the residue obtained was taken up in 5 ml of benzene. This solution was dropped into a solution of 550 mg of 2,3 - diamino - pyridine in 5 ml of pyridine whilst stirring. Afterwards, the mixture was heated for a short time at 60°C, then cooled to room temperature, and 0.9 ml of phosphorus oxychloride were added dropwise. After the mixture had been stirred for a further 3 hours at room temperature, 2N hydrochloric acid was added. The mixture was then neutralized and extracted with ethyl acetate. The ethyl acetate layers were evaporated and a small quantity of 2N hydrochloric acid was added to the residue. The crystals which precipitated were suction filtered and recrystallized from water.

M.p.: 237 to 238°C.

Example 5

2 - (2,4 - Dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

a. 2 - Amino - 3 - (2,4 - dimethoxybenzoyl - amino) - pyridine hydrochloride

530 mg of 2,4 - dimethoxybenzoic acid were converted into the acid chloride analogously to Example 4 and this acid chloride was dissolved in 1 ml of benzene. The solution obtained was added dropwise to a mixture of 440 mg of 2,3 - diamino - pyridine, 3 ml of pyridine and 2 ml of triethylamine. After the whole mixture had been stirred for a further 2 hours at room temperature, water was added, the mixture was neutralized with concentrated hydrochloric acid and extracted with ethyl acetate. The ethyl acetate was removed, the residue was treated with dilute hydrochloric acid, the precipitated crystals were suction filtered and recrystallized from ethanol.

M.p.: 172 to 174°C.

b. 2 - (2,4 - Dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

155 mg of 2 - amino - 3 - (2,4 - dimethoxybenzoyl - amino) - pyridine hydrochloride were dissolved in 2 ml of pyridine. 0.2 ml of phosphorus oxychloride were dropped in whilst stirring at room temperature. After 2 hours the mixture was poured into water and worked up analogously to Example 4.

M.p.: 237 to 238°C.

Example 6

2 - (2,4 - Dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

155 mg of 2 - amino - 3 - (2,4 - dimethoxybenzoyl - amino) - pyridine hydrochloride were heated for 5 minutes at 200-210°C. The mixture was treated with a small quantity of 2N hydrochloric acid, and the precipitate was filtered and recrystallized from water.

M.p.: 237 to 238°C.

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Example 7

- 2 - (2,4 - Dimethoxy - phenyl) - 1H -
imidazo[4,5 - b]pyridine hydrochloride
155 mg of 2 - amino - 3 - (2,4 - dimethoxy-
benzoyl - amino) - pyridine hydrochloride
were refluxed for 30 minutes in 2 ml of gly-
col. The mixture was then diluted with water,
neutralized, extracted with ethyl acetate and
processed analogously to Example 4.
M.p.: 238 to 239°C.

Example 8

- 2 - (2,4 - Dimethoxy - phenyl) - 1H -
imidazo[4,5 - b]pyridine hydrochloride
5.45 g of 2,3 - diaminopyridine were added
in small amounts to 150 ml of phosphorus
oxychloride whilst stirring and 9.81 g of
methyl 2,4 - dimethoxybenzoate were also
added dropwise. The mixture was then heated
at 120°C. After two hours the excess of
phosphorus oxychloride was evaporated in
vacuo, the residue was digested with 2N
hydrochloric acid and the solid product ob-
tained was suction filtered and recrystallized
from water.

M.p.: 238 to 239°C.

Example 9

- 2 - (2,4 - Dimethoxy - phenyl) - 1H -
imidazo[4,5 - b]pyridine hydrochloride
0.5 ml of morpholine were added whilst
stirring to 470 mg of 2,4 - dimethoxybenzoyl
chloride in 6 ml of toluene. After 20 minutes
the toluene was evaporated, the residue was
treated with dilute hydrochloric acid and this
mixture was extracted with ethylacetate. After
washing the ethyl acetate layer with sodium
bicarbonate solution and evaporating off the
solvent, crude 2,4 - dimethoxybenzoylmorpho-
line was obtained as oil. This oil was dissolved
in 5 ml of pyridine, 250 mg of 2,3 - diamino-
pyridine was added and finally 1 ml of phos-
phorus oxychloride was added dropwise whilst
stirring and ice-cooling. After stirring for 5
hours at 0°C, ice-water was added, the mix-
ture was made alkaline with concentrated
ammonia, heated for a short time on the
steam bath and extracted with ethyl acetate.
The ethyl acetate was removed, and the resi-
due obtained was treated with 2N hydro-
chloric acid, suction filtered and recrystallized
from water.

M.p.: 238°C.

Example 10

- 2 - (2,4 - Dimethoxy - phenyl) - 1H -
imidazo[4,5 - b]pyridine hydrochloride
300 mg of 2,4 - dimethoxybenzoyl - (4 -
chloro - anilide) and 110 mg of 2,3 - diamino-
pyridine were mixed and added in small
amounts to 3 ml of phosphorus oxychloride
whilst stirring. Afterwards the mixture was
refluxed for 8 hours. Then the phosphorus
oxychloride was removed in vacuo, the residue
was triturated with 2N hydrochloric acid and

the solid product obtained was suction
filtered and recrystallized from water.

M.p.: 237 to 238°C.

Example 11

- 2 - (2,4 - Dimethoxy - phenyl) - 1H -
imidazo[4,5 - b]pyridine hydrochloride
600 mg of 2,4 - dimethoxybenzoyl - (4 -
chloro - anilide) in a mixture of 5 ml of
benzene and 2 ml of thionyl chloride were
refluxed for 3 hours. After the mixture had
been evaporated the crude 2,4 - dimethoxy -
N - (4 - chlorophenyl) - benzimidic acid
chloride was obtained as an oil. This oil was
dissolved in 9 ml of toluene and the solution
was added to a solution of 200 mg of 2,3 - di-
aminopyridine in 10 ml of isopropanol. The
mixture was heated for 10 minutes at 70°C.
The 2,4 - dimethoxy - benzoic acid N -
(4 - chlorophenyl) - N' - (2 - amino - 3 -
pyridyl) - amidine hydrochloride which
formed was not isolated but was dissolved
in 20 ml of glycol after removing the iso-
propanol in vacuo. The glycol solution was
refluxed for 10 minutes. Subsequently water
was added, the mixture was made alkaline
with concentrated ammonia, extracted with
ethyl acetate and worked up as described in
Example 4.

M.p.: 237 to 238°C.

Example 12

- 2 - (2,4 - Dimethoxy - phenyl) - 1H -
imidazo[4,5 - b]pyridine hydrochloride
100 mg of 2,3 - diaminopyridine, 200 mg
of 2,4 - dimethoxybenzonitrile and 400 mg
of p - toluenesulfonic acid monohydrate were
mixed together and heated for 3½ hours at
-60°C. The product was triturated with dilute
ammonia and ethyl acetate until the whole
product had dissolved. The aqueous layer
was extracted with ethyl acetate. After some
time, when the combined ethyl acetate layers
had been extracted with a small quantity
of 2N hydrochloric acid, the product crystal-
lized out from the aqueous phase.

M.p.: 237 to 238°C.

Example 13

- 2 - (3,4,5 - Trimethoxyphenyl) - 1H -
imidazo[4,5 - b]pyridine
3.4 g of p - toluenesulfonic acid mono-
hydrate and 15 ml of benzene were heated
at 120°C until all the benzene had evapor-
ated. Subsequently 1.1 g of 2,3 - diamino-
pyridine and 2 g of 3,4,5 - trimethoxybenzoyl
nitrile were added and the mixture was heated
for 2 hours at 150°C. After cooling, water
was added, the mixture was extracted with
ethyl acetate, the ethyl acetate layers were
washed with dilute sodium hydroxide solution,
evaporated and the residue was recrystallized
from isopropanol/petroleum ether.

M.p.: 226°C.

Example 14

2 - (3,4,5 - Trimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine

A mixture of 4.2 g of 3,4,5 - trimethoxybenzoic acid and 2.2 g of 2,3 - diaminopyridine was refluxed for 2 hours in 40 ml of phosphorus oxychloride. Subsequently the excess of phosphorus oxychloride was distilled off, water was added to the residue and the precipitated solid product was suction filtered. The product was dissolved in hot water, made alkaline with concentrated ammonia, and the precipitate was suction filtered and recrystallized from a small quantity of isopropanol.

M.p.: 225 to 226°C.

Example 15

2 - (2,5 - Dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine

a) 2,5 - Dimethoxy - thiobenzyl morpholide
A mixture of 10 g of 2,5 - dimethoxybenzaldehyde, 10 g of morpholine and 4 g of sulfur was heated at 130°C for 3½ hours and subsequently dissolved in 300 ml of hot ethanol. The product which precipitated out on cooling, was recrystallized from ethanol.

M.p.: 127°C.

b) S - Methyl - 2,5 - dimethoxy - thiobenzyl morpholide iodide

6 g of 2,5 - dimethoxy - thiobenzyl morpholide, 6.5 g of methyl iodide and 30 ml of acetone were refluxed for 8 hours. Subsequently the precipitated solid product was suction filtered and washed with ether. The product obtained was not purified further.

c) 2 - (2,5 - Dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine

2 g of S - methyl - 2,5 - dimethoxy - thiobenzyl morpholide iodide and 1.1 g of 2,3 - diaminopyridine were heated in 30 ml of glycol for 40 minutes at 130°C. Subsequently the mixture was poured on ice-water, suction filtered and recrystallized from ethanol/water.

M.p.: 235°C.

Example 16

2 - (4 - Hydroxy - phenyl) - 1H - imidazo[4,5 - b]pyridine

a) 4 - Hydroxy - thiobenzyl morpholide
Prepared analogously to Example 15a from 12.2 g of 4 - hydroxy - benzaldehyde, 16 g of morpholine and 3.2 g of sulfur.

M.p.: 205°C.

b) S - Methyl - 4 - hydroxy - thiobenzyl morpholide iodide

Prepared analogously to Example 15b from 14.4 g of 4 - hydroxy - thiobenzyl morpholide and 2.1 g of methyl iodide in 100 ml of acetone.

M.p.: 181°C.

c) 2 - (4 - Hydroxy - phenyl) - 1H - imidazo[4,5 - b]pyridine

1.84 g of S - methyl - 4 - hydroxy - thiobenzyl morpholide iodide were heated for 20 minutes at 130°C with 1.1 g of 2,3 - diaminopyridine in 30 ml of glycol. The product precipitated whilst cooling and was dissolved in sodium hydroxide solution and reprecipitated with an acid.

Analysis:

Calculated:

65.87% C 5.13% H 16.46% N

Found:

65.90% C 5.16% H 16.47% N

Example 17

2 - [4 - Methoxy - 2 - (3 - chloropropoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

a) 4 - Methoxy - 2 - (3 - chloro - propoxy) - benzoyl morpholide

21.9 g of 2 - hydroxy - 4 - methoxy - benzoyl morpholide were dissolved in 200 ml of dimethylformamide and 11.2 g of potassium tert. - butoxide were added. After the whole product had dissolved, 50 g of 1 - chloro - 3 - bromopropane were added and the mixture was heated for 2 hours at 130°C. Subsequently the mixture was evaporated in vacuo, the residue was dissolved in ethyl acetate, and the solution was washed with sodium hydroxide solution and water and evaporated.

b) 2 - [4 - Methoxy - 2 - (3 - chloropropoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

20 g of 4 - methoxy - 2 - (3 - chloro - propoxy) - benzoyl morpholide, 7 g of 2,3 - diamino - pyridine and 170 ml of phosphorus oxychloride were refluxed for 2 hours. After evaporation of the phosphorus oxychloride, the residue was mixed with water, neutralized with sodium hydroxide solution and extracted with ethyl acetate. The hydrochloride was precipitated with ethereal hydrochloric acid.

M.p.: 198°C (decomp).

Example 18

2 - [4 - Methoxy - 2 - (2 - chloroethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

a) 4 - Methoxy - 2 - (2 - hydroxy - ethoxy) - benzoyl morpholide

23.7 g of 2 - hydroxy - 4 - methoxy - benzoyl morpholide 33.6 g of potassium tert. - butoxide and 37.4 g of ethylene bromohydrin were heated in 100 ml of dimethylformamide for 6 hours at 120°C. After evaporation in vacuo, the residue was dissolved in chloroform and the solution was washed with sodium hydroxide solution and water and evaporated.

b) 2 - [4 - Methoxy - 2 - (2 - chloroethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

2.8 g of 4 - methoxy - 2 - (2 - hydroxy - ethoxy) - benzoyl morpholide, 1.1 g of 2,3 - diaminopyridine and 20 ml of phosphorus oxychloride were refluxed for 2 hours. After evaporation water was added, the mixture was neutralized, extracted with ethyl acetate and the hydrochloride was precipitated with ethereal hydrochloric acid from the organic layer.

M.p.: 110°C (decomp).

Example 19

2 - [4 - Methoxy - 2 - (3 - chloropropoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

a) 4 - Methoxy - 2 - (3 - chloropropoxy) - benzoyl anilide

2.5 g of 2 - hydroxy - 4 - methoxy - benzoyl anilide, 5 ml of 1 - chloro - 3 - bromopropane, 1.12 g of potassium tert. - butoxide and 20 ml of dimethylformamide were heated for 2 hours at 130°C. Subsequently the mixture was evaporated in vacuo, water was added and the mixture was suction filtered.

M.p.: 87 to 90°C.

b) 2 - [4 - Methoxy - 2 - (3 - chloropropoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 17b from 4 - methoxy - 2 - (3 - chloropropoxy) - benzoyl anilide and 2,3 - diamino - pyridine.

M.p.: 198°C.

Example 20

2 - [4 - Methoxy - 2 - (3 - morpholino - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine

0.5 g of 2 - [4 - methoxy - 2 - (3 - chloropropoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride were refluxed for 4½ hours in 5 ml of morpholine. Water was then added, the precipitate was suction filtered and recrystallized from water.

M.p.: 108—110°C.

Example 21

2 - [4 - Methoxy - 2 - (2 - (4 - phenyl - 1 - piperazinyl) - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine

Prepared from 1.7 g of 2 - [4 - methoxy - 2 - (2 - chloro - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine and 3.2 g of 1 - phenylpiperazine by boiling for 8 hours in ethanol.

M.p.: 164 to 165°C (from isopropanol).

Example 22

2 - [4 - Methoxy - 2 - (3 - dimethylamino - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

1.8 g of 2 - [4 - Methoxy - 2 - (3 -

chloropropoxy) - phenyl] - 1H - imidazo[4,5 - b] - pyridine hydrochloride and 20 ml of saturated dimethylamine solution in ethanol were heated for 8 hours in a closed vessel at 100°C. Subsequently the mixture was evaporated in vacuo and recrystallized from isopropanol.

M.p.: 209—210°C.

Example 23

2 - [4 - Methoxy - 2 - (3 - dimethylamino - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine dihydrochloride

1.64 g of 4 - methoxy - 2 - (3 - dimethylamino - propoxy) - thiobenzoyl morpholide were dissolved in a mixture of 17 ml of glacial acetic acid and 3 ml of acetic anhydride. 1 ml of dimethyl sulfate was added and the mixture was heated on the steam bath for 1 hour. Subsequently, the mixture was evaporated in vacuo. The crude 5 - methyl - 4 - methoxy - 2 - (3 - dimethylamino - propoxy) - thiobenzoyl morpholide methyl sulfate obtained was dissolved in 13 ml of glycol. 0.7 g of 2,3 - diaminopyridine was added and the mixture was heated for 2 hours at 160°C. Subsequently, the mixture was poured into 50 ml of water, 5 ml of concentrated ammonia were added and the mixture was extracted with ethyl acetate. The ethyl acetate layers were evaporated, the residue was dissolved in ethanol, ethereal hydrochloric acid was added and it was again evaporated. The residue crystallized after trituration with toluene and a small quantity of ethanol. The product was suction filtered and recrystallized from isopropanol.

M.p.: of the dihydrochloride hydrate: 228 to 245°C (decomp).

Example 24

2 - (2,4 - Dimethoxy - phenyl) - 3 - methyl - 3H - imidazo[4,5 - b]pyridine

800 mg of 2,4 - dimethoxybenzoyl methylamide were refluxed for 3 hours with 500 mg of 2 - chloro - 3 - aminopyridine in 10 ml of phosphorus oxychloride. Subsequently, the mixture was poured into water, neutralized with concentrated ammonia and extracted with ethyl acetate. After evaporation, the crude N - methyl - N' - (2 - chloro - 3 - pyridyl) - 2,4 - dimethoxy - benzamidine obtained was dissolved in 10 ml of 10% glycolic sodium hydroxide solution and heated for 4 hours at 180 to 190°C. The mixture was poured into water and extracted with ethyl acetate. The compound obtained was purified by column chromatography (silica gel, eluent CHCl₃: MeOH=19:1).

M.p. of the hydrochloride: 196 to 197°C.

Example 25

2 - (2,4 - Dimethoxy - phenyl) - 3 - (4 - chlorophenyl) - 1H - imidazo[4,5 - b]pyridine

3 g of 2,4 - dimethoxy - benzoyl (4 -

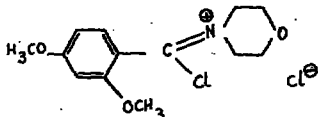
chloroanilide) and 1.3 g of 2 - chloro - 3 - aminopyridine were refluxed for 2 hours in 16 ml of phosphorus oxychloride. Subsequently the mixture was poured into water, neutralized with concentrated ammonia and extracted with ethyl acetate. The ethyl acetate layer was extracted with 3N hydrochloric acid. After neutralization of the aqueous layer, the mixture was again extracted with ethyl acetate. The solid product remaining after evaporation of the organic layer was crystallized from methanol.

M.p.: 176 to 178°C.

Example 26

2 - (2,4 - Dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

2.2 g of 2,3 - diaminopyridine, 6.8 g of imido chloride of 2,4 - dimethoxy - benzoyl morpholide having the formula



and 12 ml of triethylamine were heated for ½ hour at 120°C in 10 ml of diethyleneglycol dimethyl ether. After cooling, water was added, the reaction mixture was extracted with chloroform and the chloroform layer was extracted with 2N sodium hydroxide solution. The yellow hydrochloride which precipitated from the acidic solution was converted into the base with ammonia, and was purified by column chromatography. The hydrochloride was again precipitated from acetone with ethereal hydrochloric acid.

M.p.: 237 to 238°C.

Example 27

2 - (2,4 - Dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared from 1.1 g of 2,3 - diaminopyridine and 3.5 g of 2,4 - dimethoxybenzoyl anhydride by heating for 5 hours at 180°C. The further processing was carried out as in Example 26.

M.p.: 236 to 238°C.

Example 28

2 - (2 - Methoxyphenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

a) 2 - Methoxy - thiobenzoyl morpholide
34 g of 2 - methoxybenzaldehyde, 16 g of sulfur and 32.6 g of morpholine were heated for 3 hours at 120°C. The reaction mixture thus obtained was dissolved in ethanol, filtered, cooled and the precipitated yellow crystals were suction filtered.

Yield: 54.1 g (91% of theory), m.p.: 80 to 82°C.

b) 2 - Methoxy - thiobenzoyl morpholide methiodide 55

47.4 g of 2 - methoxy - benzyl thiomorpholide were refluxed for 1 hour in 150 ml of acetone with 25 ml of methyl iodide and the precipitated yellow crystals were suction filtered after cooling.

Yield: 64.4 g (85% of theory), m.p.: 162 to 164°C.

c) 2 - (2 - Methoxyphenyl) - 1H - imidazo[4,5 - b]pyridine 65

19 g of 2 - methoxy - thiobenzoyl morpholide methiodide and 8.7 g of 2,3 - diaminopyridine were heated for 3 hours at 120°C in 70 ml of glycol. After cooling, water was added, the mixture was made alkaline with ammonia and extracted with chloroform. The organic layer was washed with water and subsequently 2N hydrochloric acid was added. The precipitated product was suction filtered and the base was freed with ammonia, dissolved in chloroform and purified by passing it through a silica gel column. The colorless hydrochloride was obtained from acetone by addition of ethereal hydrochloric acid.

M.p.: 233 to 234°C.

Example 29

2 - (2 - Methoxyphenyl) - 3 - methyl - 3H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 28 from 2 - methyl - amino - 3 - amino - pyridine and 2 - methoxy - thiobenzoyl morpholide methiodide.

M.p.: 208—210°C.

Example 30

2 - [2 - (2 - Methoxy - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride 90

Prepared analogously to Example 28 from 2 - (2 - methoxy - ethoxy) - thiobenzoyl morpholide methiodide and 2,3 - diaminopyridine.

M.p.: 170 to 172°C.

Example 31

2 - (4 - Methoxyphenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride 100

Prepared analogously to Example 28 from 4 - methoxy - thiobenzoyl morpholide methiodide (m.p.: 142—144°C) and 2,3 - diaminopyridine.

M.p.: 243 to 245°C.

Example 32

2 - (3 - Methoxy - 4 - hydroxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride 110

Prepared analogously to Example 28 from 3 - methoxy - 4 - hydroxy - thiobenzoyl morpholide methiodide (m.p.: 178 to 180°C) and 2,3 - diaminopyridine.

M.p.: 251 to 254°C.

115

(77)

10

1,445,824

10

Example 33

2 - (2,3 - Dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

5 Prepared analogously to Example 28 from 2,3 - dimethoxy - thiobenzoyl morpholide methiodide (m.p.: 138 to 140°C) and 2,3 - diaminopyridine.

M.p.: 270—272°C.

Example 34

10 2 - (2 - hydroxy - 4 - methoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

15 Prepared analogously to Example 28 from 2 - hydroxy - 4 - methoxy - thiobenzoyl morpholide methiodide (m.p.: 180 to 181°C) and 2,3 - diaminopyridine.

M.p.: 190 to 192°C (decomp.).

M.p. of the free base: 292 to 293°C.

Example 35

20 2 - (2,4 - Dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

25 Prepared analogously to Example 28 from 2,4 - dimethoxy - thiobenzoyl morpholide methiodide (m.p.: 138 to 140°C (decomp.)) and 2,3 - diaminopyridine.

M.p.: 238°C (from methanol).

Example 36

30 2 - (2,4 - Dimethoxy - phenyl) - 6 - methyl - 1H - imidazo[4,5 - b]pyridine hydrochloride

35 Prepared analogously to Example 35 from 2,3 - diamino - 5 - methyl - pyridine and 2,4 - dimethoxy - thiobenzoyl morpholide methiodide.

M.p.: 260 to 261°C.

Example 37

40 2 - (2,4 - Dimethoxy - phenyl) - 7 - methyl - 1H - imidazo[4,5 - b]pyridine hydrochloride

45 Prepared analogously to Example 35 from 2,3 - diamino - 4 - methyl - pyridine and 2,4 - dimethoxy - thiobenzoyl morpholide methiodide.

M.p.: 230 to 231°C.

Example 38

50 2 - (2,4 - Dimethoxy - phenyl) - 5 - methyl - 1H - imidazo[4,5 - b]pyridine hydrochloride

55 Prepared analogously to Example 35 from 2,3 - diamino - 6 - methyl - pyridine and 2,4 - dimethoxy - thiobenzoyl morpholide methiodide.

M.p.: 245 to 246°C.

Example 39

2 - (2,4 - Dimethoxy - phenyl) - 6 - chloro - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 35 from 2,3 - diamino - 5 - chloro - pyridine and

2,4 - dimethoxy - thiobenzoyl morpholide methiodide.

M.p.: 253 to 255°C.

Example 40

2 - (2 - Ethoxy - 4 - methoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride.

65 Prepared analogously to Example 28 from 2 - ethoxy - 4 - methoxy - thiobenzoyl morpholide methiodide (m.p.: 152 to 154°C) and 2,3 - diamino - pyridine.

M.p.: 228 to 230°C.

Example 41

2 - (2 - Methoxy - 4 - ethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

75 Prepared analogously to Example 28 from 2 - methoxy - 4 - ethoxy - thiobenzoyl morpholide methiodide and 2,3 - diamino - pyridine.

M.p.: 224 to 225°C (from methanol).

Example 42

2 - (2 - Diethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

85 Prepared analogously to Example 28 from 2,4 - diethoxy - thiobenzoyl morpholide methiodide and 2,3 - diaminopyridine.

M.p.: 224 to 226°C.

Example 43

2 - [2 - (2 - Hydroxy - ethoxy) - 4 - methoxy - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

90 Prepared analogously to Example 28 from 2 - (2 - hydroxy - ethoxy) - 4 - methoxy - thiobenzoyl morpholide methiodide and 2,3 - diaminopyridine.

M.p.: 237 to 239°C.

Example 44

2 - [2 - (3 - Hydroxy - propoxy) - 4 - methoxy - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

100 Prepared analogously to Example 28 from 2 - (3 - hydroxy - propoxy) - 4 - methoxy - thiobenzoyl morpholide methiodide and 2,3 - diaminopyridine.

M.p.: 170°C (whilst sintering)

Example 45

2 - [2 - (2 - Methoxy - ethoxy) - 4 - methoxy - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

110 Prepared analogously to Example 28 from 2 - (2 - methoxy - ethoxy) - 4 - methoxy - thiobenzoyl morpholide methiodide and 2,3 - diaminopyridine.

M.p.: 191 to 193°C.

(78)

Example 46

2 - [2 - Methoxy - 4 - (2 - methylmercapto - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

a) 4 - (2 - Methylmercapto - ethoxy) - 2 - hydroxy - benzaldehyde

12 g of 2,4 - dihydroxy - benzaldehyde and 9.6 g of potassium tert.butoxide were dissolved in 50 ml of ethylene glycol monomethyl ether, 9.6 g of methylmercaptoethyl chloride were added and the reaction mixture was stirred for 8 hours at 80°C (bath temperature). After removing the solvent, the residue was dissolved in dilute sodium hydroxide solution, the mixture was extracted twice with chloroform, the aqueous alkaline solution was separated, acidified and extracted with chloroform. The organic phase was dried and evaporated. The residue was purified by column chromatography (silica gel). The oil thus obtained was processed directly.

b) 4 - (2 - Methylmercapto - ethoxy) - 2 - methoxy - benzaldehyde

9.7 g of 4 - (2 - methylmercapto - ethoxy) - 2 - hydroxy - benzaldehyde were dissolved in ethanol together with 6.7 g of potassium tert. - butoxide 4.3 ml of dimethyl sulfate were added and the mixture was refluxed for 3 hours. A further 1 ml of dimethyl sulfate was then added and the mixture was heated for 1 hour more. After the ethanol had been distilled off the residue was dissolved in water/chloroform and 2N sodium hydroxide solution was added. The chloroform layer was separated, washed with water, dried and evaporated.

M.p.: 99 to 100°C (from cyclohexane).

c) 4 - (2 - Methylmercapto - ethoxy) - 2 - methoxy - thiobenzoyl morpholide

Prepared analogously to Example 28a from 4 - (2 - methylmercapto - ethoxy) - 2 - methoxy benzaldehyde.

M.p.: 131 to 132°C (from ethanol).

d) 2 - [2 - Methoxy - 4 - (2 - methylmercapto - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

5.4 g of 4 - (2 - methylmercapto - ethoxy) - 2 - methoxy - thiobenzoyl morpholide were refluxed for 1½ hours together with 1.2 ml of methyl iodide in 50 ml of acetone. After cooling, the solvent was removed and the syrupy methiodide obtained was heated with 3.6 of 2,3 - diamino - pyridine in 20 ml of glycol for 1½ hours at 120°C. The mixture was diluted with water and extracted with chloroform. Subsequently, 2N hydrochloric acid was added to the organic layer and the yellow precipitate was suction filtered.

M.p.: 197 to 199°C (from methanol).

Example 47

2 - [2 - Methoxy - 4 - (2 - ethylmercapto - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 46 from 4 - (2 - ethylmercapto - ethoxy) - 2 - methoxy - thiobenzoyl morpholide and 2,3 - diaminopyridine. The purification of the final product was effected by chromatography over silica gel and the precipitation of the hydrochloride was effected by dissolving the base in acetone and adding an excess of ethereal hydrochloric acid.

M.p.: 195 to 196°C.

Example 48

2 - [2 - Methoxy - 4 - (3 - methylmercapto - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 46 from 4 - (3 - methylmercapto - propoxy) - 2 - methoxy - thiobenzoyl morpholide and 2,3 - diaminopyridine.

M.p.: 189 to 191°C (decomp.).

Example 49

2 - [2 - Methoxy - 4 - (3 - ethylmercapto - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 46 from 4 - (3 - ethylmercapto - propoxy) - 2 - methoxy - thiobenzoyl morpholide and 2,3 - diaminopyridine.

M.p.: 183 to 185°C decomp).

Example 50

2 - [2 - (2 - Methylmercapto - ethoxy) - 4 - methoxy - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 46 from 2 - (2 - methylmercapto - ethoxy) - 4 - methoxy - thiobenzoyl morpholide and 2,3 - diamino - pyridine.

M.p.: 204 to 206°C (decomp.).

Example 51

2 - [2 - (2 - Ethylmercapto - ethoxy) - 4 - methoxy - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 46 from 2 - (2 - ethylmercapto - ethoxy) - 4 - methoxy - thiobenzoyl morpholide and 2,3 - diaminopyridine.

M.p.: 193 to 195°C.

Example 52

2 - [2 - (3 - Methylmercapto - propoxy - 4 - methoxy - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 46 from 2 - (3 - methylmercapto - propoxy) - 4 - methoxy - benzoyl morpholide and 2,3 - diaminopyridine.

M.p.: 191 to 193°C.



Example 53

2 - [2 - (3 - Ethylmercapto - propoxy - 4 - methoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

5 Prepared analogously to Example 46 from 2 - (3 - ethylmercapto - propoxy) - 4 - methoxy - thiobenzoyl morpholide and 2,3 - diamino pyridine.
M.p.: 187 to 189°C.

Example 54

10 2 - (2,3,4 - Trimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

15 Prepared analogously to Example 28 from 2,3,4 - trimethoxy - thiobenzoyl morpholide methiodide (m.p.: 147 to 150°C) and 2,3 - diaminopyridine.
M.p.: 231 to 233°C (decomp.).

Example 55

20 2 - (2 - Methoxy - 3,4 - methylenedioxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

25 Prepared analogously to Example 28 from 2 - methoxy - 3,4 - methylenedioxy - thiobenzoyl morpholide methiodide (m.p.: 109 to 111°C and 2,3 - diaminopyridine.
M.p.: 266 to 268°C.

Example 56

30 2 - (2,4 - Dimethoxy - 3 - hydroxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

35 Prepared analogously to Example 28 from 2,4 - dimethoxy - 3 - hydroxy - thiobenzoyl morpholide methiodide and 2,3 - diaminopyridine.
M.p.: 115 to 118°C.

Example 57

40 2 - (2 - Methoxy - 4 - chloro - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 28 from 2 - methoxy - 4 - chloro - thiobenzoyl morpholide methiodide and 2,3 - diaminopyridine.
M.p.: 302 to 305°C.

Example 58

45 2 - (2 - Methoxy - 4 - methyl - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

50 Prepared analogously to Example 28 from 2 - methoxy - 4 - methyl - thiobenzoyl morpholide and 2,3 - diaminopyridine.
M.p.: 256°C (decomp.).

Example 59

55 2 - (2 - Ethoxy - 4 - methyl - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

60 Prepared analogously to Example 28 from 2 - ethoxy - 4 - methyl - thiobenzoyl morpholide methiodide (m.p.: 142 to 144°C) and 2,3 - diaminopyridine.
M.p.: 224 to 225°C (decomp.).

Example 60

2 - (2 - Methoxy - 4 - methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

65 Prepared analogously to Example 25 from 2 - methoxy - 4 - methylmercapto - benzoyl morpholide (m.p.: 124 to 129°C) and 2,3 - diamino - pyridine.
M.p.: 232 to 234°C.

Example 61

70 2 - (2 - Methoxy - 5 - methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

75 Prepared analogously to Example 25 from 2 - methoxy - 5 - methylmercapto - benzoyl morpholide (m.p.: 106 to 108°C) and 2,3 - diamino - pyridine.
M.p.: 247 to 248°C.

Example 62

80 2 - (2 - Methoxy - 4 - ethylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

85 Prepared analogously to Example 25 from 2 - methoxy - 4 - ethylmercapto - benzoyl morpholide and 2,3 - diaminopyridine.
M.p.: 215 to 217°C.

Example 63

90 2 - (2 - Methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 28 from 2 - methyl - mercapto - thiobenzoyl morpholide methiodide and 2,3 - diaminopyridine.
M.p.: 185 to 187°C.

Example 64

95 2 - (2,4 - Bismethylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

100 Prepared analogously to Example 28 from 2,4 - bismethylmercapto - thiobenzoyl morpholide methiodide and 2,3 - diaminopyridine.
M.p.: 249 to 250°C.

Example 65

105 2 - [2 - (2 - Methylmercapto - ethoxy) - 4 - methylmercapto - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 28 from 2 - (2 - methylmercapto - ethoxy) - 4 - methylmercapto - thiobenzoyl morpholide methiodide and 2,3 - diaminopyridine.
M.p.: 180 to 182°C.

Example 66

110 2 - [2 - (2 - Diethylamino - ethoxy) - 4 - methyl - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride.

Prepared analogously to Example 28 from 2 - (2 - diethylamino - ethoxy) - 4 - methyl - thiobenzoyl morpholide methiodide hydrochloride and 2,3 - diaminopyridine.
M.p.: 221 to 223°C.

Example 67

2 - (2 - Allyloxy - 4 - methoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

5 16.5 g of 2 - allyloxy - 4 - methoxy - benzoyl morpholide and 7.1 g of 2,3 - diaminopyridine were powdered and intimately mixed and 30 ml of phosphorus oxychloride were added dropwise whilst stirring. Subsequently, the reaction mixture was refluxed for 3 hours, the excess of phosphorus oxychloride was removed and the residue was decomposed with ice-water. The solution, which had been made alkaline with ammonia, was extracted with chloroform. The organic solution was extracted with 2N hydrochloric acid and the aqueous phase was made alkaline with ammonia and extracted with chloroform. The chloroform solution was dried, treated with charcoal/tonsil, filtered and evaporated. The residue was dissolved in acetone and the light yellow colored hydrochloride was precipitated with ethereal hydrochloric acid.

M.p.: 189 to 191°C.

Example 68

2 - (2,4,5 - Trimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

a) 2 - (2,4,5 - Trimethoxy - phenyl) - 1,3 - dithiolanium - iodide

30 50 g of 1,2,4 - trimethoxybenzene and 150 g of 2 - methylmercapto - 1,3 - dithiolanium - methyl sulfate were stirred in 600 ml of glacial acetic acid for 4 hours at 70°C bath temperature. Subsequently, the solvent was removed, the residue was dissolved in a mixture of chloroform and water and an excess of potassium iodide solution was added to the aqueous layer, whereby the product precipitated as orange-colored crystals.

40 b) 2 - (2,4,5 - Trimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride
3.8 g of 2 - (2,4,5 - trimethoxy - phenyl) - 1,3 - dithiolanium - iodide and 2.2 g of 2,3 - diaminopyridine were heated for 10 minutes in 40 ml of glycol at 200°C. After cooling the mixture was extracted with ether and then with chloroform. The chloroform layer was extracted with 2N hydrochloric acid and the precipitated yellow hydrochloride was suction filtered and recrystallized from glycol.

M.p.: 278 to 280°C.

Example 69

2 - (2,4,6 - Trimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

a) 2 - (2,4,6 - Trimethoxy - phenyl) - 1,3 - dithiolanium - iodide

55 33.6 g of phloroglucinol - trimethyl ether and 105 g of 2 - methylmercapto - 1,3 - dithiolanium - methyl sulfate were held at 75°C for 6 hours in 200 ml of glacial acetic acid and the crystals which precipitated after

standing overnight were suction filtered, dissolved in water and the iodide thereof was precipitated with potassium iodide solution.
M.p.: 152 to 154°C.

b) 2 - (2,4,6 - Trimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

4 g of 2 - (2,4,6 - trimethoxy - phenyl) - 1,3 - dithiolanium - iodide, 2.2 g of 2,3 - diaminopyridine and 5 g of lead acetate were heated for 10 minutes in 75 ml of glycol. Subsequently the precipitated lead salt was filtered off, the filtrate was diluted with water and the precipitated product was suction filtered. After dissolving in methanolic hydrochloric acid, the product was purified by passage through a silica gel column (eluent: chloroform:methanol=9:1).

M.p.: 241 to 244°C (from ethanol).

Example 70

2 - (2 - Dihydroxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 69 from 3 - hydroxy - 4 - [1',3' - dithiacyclopentylidene - (2')] - cyclohexadiene - (2,5) - one - (1) and 2,3 - diaminopyridine.

M.p.: 298 to 301°C.

Example 71

2 - (4 - Dimethylamino - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 69 from 2(4 - dimethylamino - phenyl) - 1,3 - dithiolanium - iodide and 2,3 - diaminopyridine in n-propanol.

M.p.: 337 to 339°C

Example 72

2 - (2 - Methoxy - 4 - dimethylamino - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

a) 2 - (2 - Methoxy - 4 - dimethylamino - phenyl) - 1,3 - dithiolanium - iodide
22.6 g of 3 - dimethylamino - anisole, 43.2 g of 2 - methylmercapto - 1,3 - dithiolanium - methyl sulfate, 150 ml of glacial acetic acid and 22.5 ml of pyridine were refluxed for ½ hour. After cooling, the mixture was poured into an aqueous potassium iodide solution, the precipitated product was suction filtered and dried.

M.p.: 189 to 195°C (from dimethylformamide).

b) 2 - (2 - Methoxy - 4 - dimethylamino - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 42 from 2 - (2 - methoxy - 4 - dimethylamino - phenyl) - 1,3 - dithiolanium - iodide and 2,3 - diaminopyridine.

M.p.: 258 to 260°C (from methanol)

8

Example 73

2 - (2 - Methylsulfinyl - phenyl) - 1H -
imidazo[4,5 - b]pyridine hydrochloride
1.35 g of 2 - (2 - methylmercapto -
5 phenyl) - 1H - imidazo[4,5 - b]pyridine
were dissolved in 20 ml of glacial acetic
acid and 0.64 g of 30% hydrogen peroxide
dissolved in 5 ml of glacial acetic acid were
10 added dropwise. After standing overnight, the
mixture was diluted with water, neutralized
with sodium bicarbonate and the precipitated
product was suction filtered and dried. By
addition of ethereal hydrochloric acid to a
methanolic solution of the product the color-
15 less hydrochloride was obtained.
M.p.: 205 to 210°C.

Example 74

2 - (2 - Methylsulfonyl - phenyl) - 1H -
imidazo[4,5 - b]pyridine hydrochloride
20 450 mg of 2 - (2 - methylmercapto -
phenyl) - 1H - imidazo[4,5 - b]pyridine
hydrochloride and 370 mg of 30% hydrogen
peroxide were heated for 3 hours at 70°C
in 20 ml of glacial acetic acid. After evapora-
25 tion and trituration with petroleum ether,
the desired product crystallized.
M.p.: 259 to 262°C (from isopropanol).

Example 75

2 - [2 - (2 - Methylsulfinyl - ethoxy) -
30 phenyl] - 1H - imidazo[4,5 - b]pyridine
hydrochloride
a) 2 - [2 - (2 - Methylmercapto - ethoxy) -
phenyl] - 1H - imidazo[4,5 - b]pyridine
hydrochloride
35 Prepared analogously to Example 28 from
2 - (2 - methylmercapto - ethoxy) - thio-
benzoyl morpholide methiodide and 2,3 -
diaminopyridine.
M.p.: 138 to 140°C.
40 b) 2 - [2 - (2 - Methylsulfinyl - ethoxy) -
phenyl] - 1H - imidazo[4,5 - b]pyridine
hydrochloride
4.3 g of 2 - [2 - (2 - methylmercapto -
45 ethoxy) - phenyl] - 1H - imidazo[4,5 - b]-
pyridine hydrochloride and 1.5 g of 30%
hydrogen peroxide were stirred for 2 hours
at room temperature in 100 ml of glacial
acetic acid. After standing overnight, the
50 mixture was diluted with water, neutralized
with bicarbonate and extracted with chloro-
form. The chloroform layer was evaporated,
the residue was dissolved in acetone and
the hydrochloride was precipitated with
methanolic hydrochloric acid.
55 M.p.: 163 to 165°C.

Example 76

2 - [2 - (2 - Methylsulfinyl - ethoxy) - 4 -
methoxy - phenyl] - 1H - imidazo-
[4,5 - b]pyridine hydrochloride
60 Prepared analogously to Example 75b from
2 - [2 - (2 - methylmercapto - ethoxy) - 4 -

methoxy - phenyl] - 1H - imidazo[4,5 - b]-
pyridine hydrochloride.
M.p.: 231 to 232°C.

Example 77

2 - [2 - (2 - Ethylsulfinyl - ethoxy) - 4 -
methoxy - phenyl] - 1H - imidazo[4,5 -
b]pyridine
Prepared analogously to Example 75b from
2 - [2 - (2 - ethylmercapto - ethoxy) - 4 -
70 methoxy - phenyl] - 1H - imidazo[4,5 - b]-
pyridine hydrochloride.
M.p.: 188 to 189°C.

Example 78

2 - [2 - (2 - Methylsulfinyl - propoxy) - 4 -
methoxy - phenyl] - 1H - imidazo-
[4,5 - b]pyridine
Prepared analogously to Example 75b from
2 - [2 - [2 - (3 - methylmercapto - propoxy) -
4 - methoxy - phenyl] - 1H - imidazo]4,5 -
80 b]pyridine hydrochloride.
M.p.: 132 to 133°C.

Example 79

2 - [2 - (3 - Ethylsulfinyl - propoxy) - 4 -
methoxy - phenyl] - 1H - imidazo-
[4,5 - b]pyridine
Prepared analogously to Example 75b from
2 - [2 - (3 - ethylmercapto - propoxy) -
4 - methoxy - phenyl] - 1H - imidazo-
[4,5 - b]pyridine hydrochloride.
90 M.p.: 126 to 127°C.

Example 80

2 - (2 - Methoxy - 4 - methylsulfinyl -
phenyl) - 1H - imidazo[4,5 - b]pyridine
hydrochloride
95 6.6 g of 2 - (2 - methoxy - 4 - methyl-
mercapto - phenyl) - 1H - imidazo[4,5 - b]-
pyridine were dissolved in 100 ml of chloro-
form and a solution of 2.96 g of 3 - chloro-
perbenzoic acid in 600 ml of chloroform was
100 dropped in at -15 to -20°C during 5 hours.
Subsequently, the mixture was extracted with
a dilute sodium carbonate solution and the
chloroform layer was dried and evaporated.
The residue was purified over a silica gel
column (eluent: chloroform/methanol=9:1).
105 By addition of ethereal hydrochloric acid to a
methanolic solution of the base the yellow
hydrochloride was obtained.
M.p.: 154 to 155°C.
110

Example 81

2 - (2 - Methoxy - 4 - methylsulfonyl -
phenyl) - 1H - imidazo[4,5 - b]pyridine
hydrochloride
Prepared analogously to Example 74 from
2 - (2 - methoxy - 4 - methylmercapto -
phenyl) - 1H - imidazo[4,5 - b]pyridine
hydrochloride.
115 M.p.: 240 to 242°C.

82

Example 82

2 - (2 - Methoxy - 4 - ethylsulfinyl - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

- 5 Prepared analogously to Example 80 from 2 - (2 - methoxy - 4 - ethylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine.
M.p.: 121 to 123°C.

Example 83

10 2 - [2 - (2 - Methylsulfinyl - ethoxy) - 4 - methylmercapto - phenyl] - 1H - imidazo[4,5 - b]pyridine

- 15 Prepared analogously to Example 80 from 2 - [2 - methylmercapto - ethoxy) - 4 - methylmercapto - phenyl] - 1H - imidazo[4,5 - b]pyridine and an equimolar quantity of 3 - chloroperbenzoic acid.
M.p.: 191 to 192°C (from acetone).

Example 84

20 2 - [2 - (2 - Methylsulfinyl - ethoxy - 4 - methylsulfinyl - phenyl] - 1H - imidazo[4,5 - b]pyridine

- 25 Prepared analogously to Example 80 from 2 - [2 - (2 - methylsulfinyl - ethoxy) - 4 - methylmercapto - phenyl] - 1H - imidazo[4,5 - b]pyridine and an equimolar quantity of 3 - chloro - perbenzoic acid
M.p.: 190 to 191°C.

Example 85

30 2 - [2 - (2 - Methylsulfinyl - ethoxy) - 4 - methyl - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

- 35 Prepared analogously to Example 75b from 2 - [2 - (2 - methylmercapto - ethoxy) - 4 - methyl - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride.
M.p.: 191 to 192°C (from acetone/ether).

Example 86

40 2 - [2 - (2 - Methylsulfinyl - ethoxy) - 4 - chlorophenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

- 45 Prepared analogously to Example 75b from 2 - [2 - (2 - methylmercapto - ethoxy) - 4 - chloro - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride.
M.p.: 221 to 222°C (from acetone/ether).

Example 87

50 2 - [2 - Methoxy - 4 - (2 - methylsulfinyl - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine

- 55 Prepared analogously to Example 75b from 2 - [2 - methoxy - 4 - (2 - methylmercapto - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride.
M.p.: 204 to 205°C.

Example 88

2 - [2 - Methoxy - 4 - (2 - ethylsulfinyl - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine

- 60 Prepared analogously to Example 75b from 2 - [2 - methoxy - 4 - (2 - ethyl - mercapto - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride.
M.p.: 217 to 219°C.

Example 89

65 2 - [2 - Methoxy - 4 - (3 - methylsulfinyl - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine

- 70 Prepared analogously to Example 75b from 2 - [2 - methoxy - 4 - (3 - methylmercapto - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride.
M.p.: 179 to 180°C.

Example 90

75 2 - [2 - Methoxy - 4 - (3 - ethylsulfinyl - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

- 80 Prepared analogously to Example 75b from 2 - [2 - methoxy - 4 - (3 - ethylmercapto - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride.
M.p.: 167 to 168°C.

Example 91

85 2 - (2 - Methoxy - 5 - methylsulfinyl - phenyl) - 1H - imidazo[4,5 - b]pyridine

- 90 Prepared analogously to Example 80 from 2 - (2 - methoxy - 5 - methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride.
M.p.: 211 to 212°C.

Example 92

2 - (2 - Methoxy - 5 - methylsulfonyl - phenyl) - 1H - imidazo[4,5 - b]pyridine

- 95 Prepared analogously to Example 74 from 2 - (2 - methoxy - 5 - methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride.
M.p.: 240 to 241°C.

Example 93

100 2 - (2,4 - Dimethoxy - phenyl - 1H - imidazo[4,5 - b]pyridine - oxide - (4)

- 105 1 g of 2 - (2,4 - dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine and 1.35 g of 3 - chloroperbenzoic acid were stirred for 15 hours at 60°C in 15 ml of glacial acetic acid. Subsequently, the mixture was recrystallized from 2N acetic acid by addition of charcoal. The further purification was effected by boiling with acetone.
M.p.: 266 to 267°C.

Example 94

2 - (2,4 - Dimethoxy - phenyl) - 3 - methyl - 3H - imidazo[4,5 - b]pyridine hydrochloride

- 115 3.6 g of methyl iodide were added drop-

wise to a solution of 3.5 g of 2 - (2,4 - dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride and 27 g of potassium tert. - butoxide in 40 ml of dimethylformamide. The mixture was stirred for 2 hours at room temperature and then evaporated. The residue was dissolved in chloroform/water, the organic layer was separated, dried and evaporated. The product was purified by column chromatography and subsequently precipitated from the solution in acetone with ethereal hydrochloric acid.
M.p.: 196 to 197°C.

Example 95
2 - (2 - Hydroxy - phenyl) - 3 - methyl - 3H - imidazo[4,5 - b]pyridine hydrochloride
Prepared analogously to Example 94 from 2 - (2 - hydroxy - phenyl) - 1H - imidazo[4,5 - b]pyridine and methyl iodide.
M.p.: 215 to 216°C.

Example 96
2 - (2 - Hydroxy - 4 - methoxy - phenyl) - 3 - (3 - hydroxypropyl) - 2H - imidazo[4,5 - b]pyridine hydrochloride
Prepared analogously to Example 94 from 2 - (2 - hydroxy - 4 - methoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine and 3 - bromo - propanol.
M.p.: 154 to 155°C.

Example 97
2 - (2,4 - Dimethoxy - phenyl) - 3 - benzyl - 3H - imidazo[4,5 - b]pyridine hydrochloride
Prepared analogously to Example 94 from 2 - (2,4 - dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine and benzyl bromide.
M.p.: 148 to 150°C.

Example 98
2 - (2,4 - Dimethoxy - phenyl) - 3 - (2 - diethylaminoethyl) - 3H - imidazo[4,5 - b]pyridine dihydrochloride
Prepared analogously to Example 94 from 2 - (2,4 - dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine and 2 - diethylamino - ethyl chloride at 80°C.
M.p.: 185°C.

Example 99
2 - (2,4 - Dimethoxy - phenyl) - 3 - (3 - dimethylaminopropyl) - 3H - imidazo[4,5 - b]pyridine dihydrochloride
Prepared analogously to Example 94 from 2 - (2,4 - dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine and 3 - dimethylaminopropyl bromide at 70°C.
M.p.: 190 to 192°C (decomp.).

Example 100
2 - (2 - Methoxy - 4 - benzyloxy - phenyl) - 1H - imidazo[4,5 - b]pyridine
Prepared analogously to Example 10 from

2 - methoxy - 4 - benzyloxy - benzoyl morpholide and 2,3 - diamino - pyridine.
M.p. of the hydrochloride: 218 to 219°C (decomp.).

Example 101
2 - (2,4 - Dimethoxy - phenyl) - 3 - butyl - 3H - imidazo[4,5 - b]pyridine
Prepared analogously to Example 10 from 2,4 - dimethoxy - benzoyl morpholide and 3 - amino - 2 - butylamino - pyridine.
M.p. of the hydrochloride: 218 to 219°C.

Example 102
2 - (2 - Methoxy - 4 - hydroxy - phenyl) - 1H - imidazo[4,5 - b]pyridine
Prepared analogously to Example 10 from 2 - methoxy - 4 - hydroxy - benzoyl morpholide and 2,3 - diamino - pyridine.
M.p. of the hydrochloride: 230 to 231°C.

Example 103
2 - (2 - Ethoxy - 4 - ethylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine
Prepared analogously to Example 10 from 2 - ethoxy - 4 - ethyl - mercapto - benzoyl morpholide and 2,3 - diamino - pyridine.
M.p. of the hydrochloride: 198 to 199°C (decomp.).

Example 104
2[4 - Methoxy - 2 - (3 - (4 - methyl - 1 - piperazinyl) - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine
Prepared analogously to Example 21 from 2 - [3 - methoxy - 2 - (3 - chloro - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine and 1 - methylpiperazine.
M.p. of the trihydrochloride: 248°C (decomp.).

Example 105
2 - [4 - Methoxy - 2 - (2 - thiomorpholino - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine
Prepared analogously to Example 21 from 2 - [4 - methoxy - 2 - (2 - chloro - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine and thiomorpholine.
M.p.: 158 to 160°C.

Example 106
2 - (2 - Fluoro - 4 - methoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine
Prepared analogously to Example 1 from 2 - fluoro - 4 - methoxy - benzoic acid and 2,3 - diamino - pyridine.
M.p. of the hydrochloride: 237 to 238°C (decomp.).

Example 107
2 - (4 - Fluoro - 2 - methoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine
Prepared analogously to Example 1 from 4 - fluoro - 2 - methoxy - benzoic acid and 2,3 - diamino - pyridine.
M.p. of the hydrochloride: 235 to 236°C (decomp.).

Example 108

2 - (2,4 - Dimethyl - phenyl) - 1H - imidazo-
[4,5 - b]pyridine

Prepared analogously to Example 1 from
2,4 - dimethyl - benzoic acid and 2,3 -
diamino - pyridine.

M.p. of hydrochloride: 185°C.

Example 109

2 - (2 - Hydroxy - 4 - methoxy - phenyl) -
3 - phenyl - 3H - imidazo[4,5 - b]-
pyridine

4.9 g of 2 - hydroxy - 4 - methoxy - benz-
anilide and 2.6 g of 2 - chloro - 3 - amino -
pyridine were refluxed for 1½ hours in 50
ml of phosphorus oxychloride. After distilling
off the excess of phosphorus oxychloride the
residue was boiled for 45 minutes with 2N
hydrochloric acid, neutralized with ammonia
and the precipitated product was recrystal-
lized from isopropanol.

M.p.: 201°C.

Example 110

2 - (2 - Hydroxy - 4 - methoxy - phenyl) -
3 - (2 - methoxy - phenyl) - 3H -
imidazo[4,5 - b]pyridine

Prepared analogously to Example 109 from
N - (2 - methoxy - phenyl) - 2 - hydroxy -
4 - methoxy - benzamide and 2 - chloro -
3 - amino - pyridine.

M.p.: 197°C.

Example 111

2 - (2 - Hydroxy - 4 - methoxy - phenyl) -
3 - (4 - methoxy - phenyl) - 3H -
imidazo[4,5 - b]pyridine

Prepared analogously to Example 109 from
N - (4 - methoxy - phenyl) - 2 - hydroxy -
4 - methoxy - benzamide and 2 - chloro -
3 - amino - pyridine.

M.p.: 175°C.

Example 112

2 - (2 - Hydroxy - 4 - methoxy - phenyl) -
3 - (2 - phenethyl) - 3H - imidazo[4,5 -
b]pyridine

Prepared analogously to Example 109 from
N - (2 - phenylethyl) - 2 - hydroxy - 4 -
methoxy - benzamide and 2 - chloro - 3 -
amino - pyridine.

M.p.: 155°C.

Example 113

2 - (2,4 - Dimethoxy - phenyl) - 3 -
phenyl - 3H - imidazo[4,5 - b]pyridine

Prepared from N - phenyl - N' - (2 -
chloro - 3 - pyridyl) - 2,4 - dimethoxy -
benzamidine by heating for 5 minutes with
sodium hydride in dimethylformamide at
120°C.

M.p.: 138°C (from cyclohexane/isopro-
panol=9/1).

Example 114

2 - (2,4 - Dimethoxy - phenyl) - 3 - (2 -
methoxy - phenyl) - 3H - imidazo-
[4,5 - b]pyridine

Prepared analogously to Example 113 from
N - (2 - methoxy - phenyl) - N' - (2 -
chloro - 3 - pyridyl) - 2,4 - dimethoxy -
benzamidine.

M.p.: 156°C.

Example 115

2 - (2,4 - Dimethoxy - phenyl) - 3 - (4 -
methoxy - phenyl) - 3H - imidazo-
[4,5 - b]pyridine

Prepared analogously to Example 113 from
N - (4 - methoxy - phenyl) - N' - (2 -
chloro - 3 - pyridyl) - 2,4 - dimethoxy -
benzamidine.

M.p.: 163°C.

Example 116

2 - (2,4 - Dimethoxy - phenyl) - 3 - (3,4 -
dimethoxy - phenyl) - 3H - imidazo-
[4,5 - b]pyridine

Prepared analogously to Example 113 from
N - (3,4 - dimethoxy - phenyl) - N' -
(2 - chloro - 3 - pyridyl) - 2,4 - dimethoxy -
benzamidine.

M.p.: 190°C.

Example 117

2 - (3,4 - Dimethoxy - phenyl) - 3 - (4 -
methoxy - phenyl) - 3H - imidazo-
[4,5 - b]pyridine

Prepared from N - (4 - methoxy - phenyl) -
N' - (2 - chloro - 3 - pyridyl) - 2,4 -
dimethoxy - benzamidine analogously to
Example 113 or by boiling in chlorobenzene.

M.p.: 181°C.

Example 118

2 - (2,4 - Dimethoxy - phenyl) - 3 - (3 -
morpholino - 1 - propyl) - 3H - imidazo -
4,5 - b]pyridine

Prepared analogously to Example 113 from
N - (3 - morpholino - 1 - propyl) - N' -
(2 - chloro - 3 - pyridyl) - 2,4 - dimethoxy -
benzamidine.

M.p.: 207°C.

Example 119

2 - (2,6 - Dimethoxyphenyl) - 1H - imidazo-
[4,5 - b]pyridine hydrochloride

9.1 g of 2,6 - dimethoxy - benzoic acid
and 5.5 g of 2,3 - diaminopyridine were re-
fluxed for 3 hours in 100 ml of phosphorus
oxychloride. Subsequently the excess of phos-
phorus oxychloride was distilled off and the
residue was carefully decomposed with ice-
water. The obtained solution was filtered,
neutralized with potassium carbonate and
made alkaline with concentrated ammonia.
The suspension which formed was extracted
three times with chloroform. The chloroform
layer was dried over magnesium sulfate,

filtered and the solvent was removed. The remaining residue was dissolved in 50 ml of methanolic hydrochloric acid, subsequently 100 ml of isopropanol were added and the product was kept in the deep freezer overnight. The precipitate was suction filtered and washed with ether.

M.p.: 250 to 254°C.

Example 120

2 - (2 - Propoxy - 4 - methyl - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 119 from 2 - propoxy - 4 - methyl - benzoyl morpholide.

M.p.: 221 to 223°C. (decomp.).

Example 121

2 - (2 - Butoxy - 4 - methyl - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 119 from 2 - butoxy - 4 - methyl - benzoyl morpholide.

M.p.: 212 to 213°C (decomp.).

Example 122

2 - (4 - Methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 119 from 4 - methyl - mercaptobenzoic acid.

M.p.: 230 to 232°C.

Example 123

2 - [2 - (2 - Methylmercapto - ethoxy) - 5 - methylmercapto - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

50 g of S - methyl - [2 - (2 - methylmercapto - ethoxy) - 5 - methylmercapto] - thiobenzoyl morpholide iodide (obtained by reaction of [2 - (2 - methylmercapto - ethoxy) - 5 - methylmercapto] - thiobenzoyl morpholide with methyl iodide in methanol) and 15 g of 2,3 - diaminopyridine were heated for 3 hours at 130°C in 150 ml of glycol. After cooling, the mixture was diluted with water and 30 ml of concentrated ammonia were added. Subsequently, the mixture was extracted with chloroform, the organic layer was washed with water and 2N hydrochloric acid was added. The precipitate was suction filtered and recrystallized from methanol.

M.p.: 190 to 191°C.

Example 124

2 - (2 - Methoxy - 4 - propylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 119 from 2 - methoxy - 4 - propylmercapto - benzoyl morpholide.

M.p.: 203 to 204°C (decomp.).

Example 125

2 - (2 - Ethoxy - 4 - propylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 119 from 2 - ethoxy - 4 - propylmercapto - benzoyl morpholide.

M.p.: 182 to 183°C.

Example 126

2 - (2 - Methoxy - 4 - butylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 119 from 2 - methoxy - 4 - butylmercapto - benzoyl morpholide.

M.p.: 203 to 204°C.

Example 127

2 - (2 - Ethoxy - 4 - butylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 119 from 2 - ethoxy - 4 - butylmercaptobenzoyl morpholide.

M.p.: 207 to 208°C.

Example 128

2 - (4 - Methylsulfinyl - phenyl) - 1H - imidazo[4,5 - b]pyridine

5.9 g of 2 - (4 - methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride were dissolved in 100 ml of glacial acetic acid and 2.4 g of 30% hydrogen peroxide were added at 10°C. Subsequently the mixture was stirred for 3 hours, and then left to stand overnight in the refrigerator and for 10 hours at laboratory temperature. The mixture was made alkaline with ammonia and was extracted several times with chloroform. The starting material was separated by column chromatography. The residue was suspended in acetone and the crystals which formed were suction filtered.

M.p.: 240 to 242°C.

Example 129

2 - (2 - Ethoxy - 5 - methylsulfinyl - phenyl) - 1H - imidazo[4,5 - b]pyridine

Prepared analogously to Example 128 from 2 - (2 - ethoxy - 5 - methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine.

M.p.: 197 to 198°C.

Example 130

2 - [2 - (2 - Methylsulfinyl - ethoxy) - 5 - methylmercapto - phenyl] - 1H - imidazo[4,5 - b]pyridine

Prepared analogously to Example 128 from 2 - [2 - (2 - methylmercapto - ethoxy) - 5 - methylmercapto - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride.

M.p.: 189 to 190°C.

Example 131

2 - (2 - Ethoxy - 4 - ethylsulfinyl - phenyl) - 1H - imidazo[4,5 - b]pyridine

Prepared analogously to Example 128 from

2 - (2 - Ethoxy - 4 - propylsulfinyl - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride.

M.p.: 166 to 167°C.

Example 132

2 - (2 - Methoxy - 4 - propylsulfinyl - phenyl) - 1H - imidazo[4,5 - b]pyridine

Prepared analogously to Example 128 from

2 - (2 - methoxy - 4 - propylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride.

M.p.: 182 to 183°C.

Example 133

2 - (2 - Ethoxy - 4 - propylsulfinyl - phenyl) - 1H - imidazo[4,5 - b]pyridine

Prepared analogously to Example 128 from

2 - (2 - ethoxy - 4 - propylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride.

M.p.: 182 to 183°C (decomp.).

Example 134

2 - (2 - Ethoxy - 4 - butylsulfinyl - phenyl) - 1H - imidazo[4,5 - b]pyridine

Prepared analogously to Example 128 from

2 - (2 - ethoxy - 4 - butylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride.

M.p.: 185 to 186°C.

Example 135

2 - (4 - Methylsulfonyl - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

6.95 g of 2 - (4 - methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride were dissolved in 100 ml of glacial acetic acid, 8.5 g of 30% hydrogen peroxide were added and the mixture was left standing for 4 days at room temperature. After purification by passage through a silica gel column, the residue was dissolved in acetone and the hydrochloride was precipitated with methanolic hydrochloric acid.

M.p.: 286°C.

Example 136

2 - (2 - Ethoxy 4 - ethylsulfonyl - phenyl) - 1H - imidazo[4,5 - b]pyridine

400 mg of 2 - (2 - ethoxy - 4 - ethylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride were dissolved in 30 ml of glacial acetic acid together with 0.5 ml of 30% hydrogen peroxide. The mixture was allowed to stand overnight and was then heated for 1 hour at 90°C. After cooling, the mixture was diluted with water, neutralized with bicarbonate, extracted with chloroform and the organic layer was evaporated after drying. The residue was purified by column chromatography.

M.p.: 207 to 208°C (from acetone).

Example 137

2 - (2 - Methoxy - 4 - propylsulfonyl - phenyl) - 1H - imidazo[4,5 - b]pyridine

Prepared analogously to Example 136 from

2 - (2 - methoxy - 4 - propylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine

M.p.: 219 to 220°C.

Example 138

2 - (2 - Ethoxy - 4 - butylsulfonyl - phenyl) - 1H - imidazo[4,5 - b]pyridine

Prepared analogously to Example 136 from

2 - (2 - ethoxy - 4 - butylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine.

M.p.: 156 to 157°C.

Example 139

2 - [2 - Methoxy - 4 - (2 - dimethylamino - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine dihydrochloride

a) 2 - [2 - Methoxy - 4 - (2 - chloroethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

14 g of 2 - methoxy - 4 - (2 - hydroxy - ethoxy) - benzoyl morpholide were refluxed for 1½ hours with 7.1 g of 2,3 - diamino - pyridine in 100 ml of phosphorus oxychloride. Subsequently the mixture was decomposed with ice-water. The gradually crystallizing precipitate was suction filtered and washed with acetone.

M.p.: 266 to 268°C (decomp.).

b) 2 g of 2 - [2 - methoxy - 4 - (2 - chloroethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride were heated in a closed vessel for 12 hours at 120°C with 5 g of dimethylamine in 100 ml of ethanol. After evaporation, the residue was purified by column chromatography. The hydrochloride was precipitated from acetone with methanolic hydrochloric acid and subsequently recrystallized from methanol.

M.p.: >250°C.

Example 140

2 - [2 - methoxy - 4 - (3 - dimethylamino - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine dihydrochloride

Prepared analogously to Example 139 from

2 - [2 - methoxy - 4 - (3 - chloropropoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride.

M.p.: 238 to 242°C.

Example 141

2 - [2 - Methoxy - 4 - (3 - diethylamino - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine dihydrochloride

Prepared analogously to Example 139 from

2 - [2 - methoxy - 4 - (3 - chloropropoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride.

M.p.: 222 to 224°C.

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Example 142

2 - [2 - Methoxy - 4 - (3 - piperidino - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine dihydrochloride

5 Prepared analogously to Example 140 from 2 - [2 - methoxy - 4 - (3 - chloropropoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride.

M.p.: 225 to 226°C (decomp.).

Example 143

10 2 - [2 - Methoxy - 4 - (3 - (4 - phenyl - piperazin - 1 - yl) - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine dihydrochloride

15 Prepared analogously to Example 140 from 2 - [2 - methoxy - 4 - (3 - chloro - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride.

M.p.: 197 to 200°C.

Example 144

20 2 - [2 - Methoxy - 4 - (3 - (4 - 2 - methoxy - phenyl) - piperazin - 1 - yl) - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine trihydrochloride hydrate

25 Prepared analogously to Example 140 from 2 - [2 - methoxy - 4 - (3 - chloro - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride.

M.p.: Sintering from 180°C.

Example 145

30 2 - (2,6 - Dichlorophenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

35 Prepared analogously to Example 119 from 2,6 - dichlorobenzoic acid. Purification by column chromatography.

M.p.: 262 to 264°C (decomp.).

Example 146

40 2 - (2 - Methoxy - 4 - morpholino - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

a) 2 - (2 - Methoxy - 4 - morpholino - phenyl) - 1,3 - dithiolanium - iodide
10.5 g of 3 - morpholino - anisole and 15.7 g of 2 - methylmercapto - 1,3 - dithiolanium - methyl sulfate were boiled in a mixture of 60 ml of glacial acetic acid and 8.3 ml of pyridine for 1 hour. After cooling, the mixture was poured into a saturated potassium iodide solution. The red precipitate was suction filtered and washed with water. The product was used without further purification.

b) 22 g of 2 - (2 - methoxy - 4 - morpholino - phenyl) - 1,3 - dithiolanium iodide, 10.9 g of 2,3 - diaminopyridine and 60 ml of glycol were heated for 2 hours at 130°C. After cooling, water was added and the mixture was extracted with chloroform. After evaporation, the residue was purified by column chromatography and the hydro-

chloride was precipitated from acetone with ether/hydrochloric acid.

M.p.: 207 to 209°C (decomp.).

Example 147

2 - [2 - Methoxy - 4 - (4 - methyl - piperazin - 1 - yl) - phenyl] - 1H - imidazo[4,5 - b]pyridine dihydrochloride

Prepared analogously to Example 146 from 3 - (4 - methyl - piperazin - 1 - yl) - anisole.

M.p.: 279 to 282°C.

Example 148

2 - [2 - Methoxy - 4 - (4 - ethyl - piperazin - 1 - yl) - phenyl] - 1H - imidazo[4,5 - b]pyridine dihydrochloride

Prepared analogously to Example 147 from 3 - (4 - ethyl - piperazin - 1 - yl) - anisole.

M.p.: 218 to 222°C.

Example 149

2 - [2 - Methoxy - 4 - (4 - propyl - piperazin - 1 - yl) - phenyl] - 1H - imidazo[4,5 - b]pyridine dihydrochloride

Prepared analogously to Example 146 from 3 - (4 - propyl - piperazin - 1 - yl) - anisole.

M.p.: 256 to 258°C.

Example 150

2 - [2 - Ethoxy - 4 - (4 - methyl - piperazin - 1 - yl) - phenyl] - 1H - imidazo[4,5 - b]pyridine dihydrochloride

Prepared analogously to Example 146 from 3 - (4 - methyl - piperazin - 1 - yl) - 1 - ethoxybenzene.

M.p.: 269 to 271°C.

Example 151

2 - (2 - Ethoxy - 4 - (4 - ethyl - piperazin - 1 - yl) - phenyl) - 1H - imidazo[4,5 - b]pyridine dihydrochloride

Prepared analogously to Example 146 from 3 - (4 - ethyl - piperazin - 1 - yl) - 1 - ethoxybenzene.

M.p.: 257 to 259°C.

Example 152

2 - [2 - Methoxy - 4 - (4 - phenyl - piperazin - 1 - yl) - phenyl] - 1H - imidazo[4,5 - b]pyridine dihydrochloride

Prepared analogously to Example 146 from 3 - (4 - phenyl - piperazin - 1 - yl) - anisole.

M.p.: 217 to 219°C.

Example 153

2 - [4 - Methoxy - 2 - (2 - morpholino - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine

Prepared from 6.3 g of 2 - [4 - methoxy - 2 - (2 - chloro - ethoxy) - phenyl] - 1H -

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imidazo[4,5 - b]pyridine by refluxing for 3 hours in 60 ml of morpholine, distilling off the excess of morpholine in vacuo and recrystallizing the residue from isopropanol.

M.p.: 188 to 190°C.

Example 154

2 - [4 - Methoxy - 2 - (3 - (4 - phenyl - piperazin - 1 - yl) - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine

10 10 g of 2 - [4 - methoxy - 2 - (3 - chloropropoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine, 10.2 g of 1 - phenyl - piperazine and 5 g of potassium carbonate were refluxed for 8 hours in 100 ml of ethanol. After distilling off the ethanol in vacuo, the mixture was recrystallized from ethanol/water 3:1.

M.p.: 162 to 163°C.

Example 155

20 2 - [4 - Methoxy - 2 - (3 - (2 - phenyl - ethylamino) - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine dihydrochloride

Prepared by heating 1.77 g of 2 - [4 - methoxy - 2 - (3 - chloropropoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine in 10 ml of 2 - phenyl - ethylamine for 1½ hours at 180°C. The free base was converted into the dihydrochloride with methanolic hydrochloric acid. Recrystallization from isopropanol.

M.p.: 238°C.

Example 156

35 2 - [4 - methoxy - 2 - (3 - (N - methyl - N - 2 - phenylethyl - amino) - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine dihydrochloride

Prepared from 3.2 of 2 - [4 - methoxy - 2 - (3 - chloropropoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine and 2.7 g of N - methyl - 2 - phenyl - ethylamine by heating for 6 hours in ethanol at 120°C in a closed vessel. The dihydrochloride was precipitated with ethereal hydrochloric acid from an ethyl acetate solution of the base, purified by column chromatography and recrystallized from isopropanol.

M.p.: 212 to 215°C.

Example 157

50 2 - [4 - Methoxy - 2 - (3 - (N - methyl - N - (2 - (3,4 - dimethoxyphenyl) - ethyl) - amino) - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine dihydrochloride

Prepared from 5.0 g of 2 - [4 - methoxy - 2 - (3 - chloro - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine and 8.5 g of N - [2 - (3,4 - dimethoxy - phenyl) - ethyl] - methylamine by refluxing for 12 hours in ethylene glycol monomethyl ether. Precipitation of the dihydrochloride from ethyl acetate with ethereal hydrochloric acid.

M.p.: 169°C.

Example 158

2 - [4 - Methoxy - 2 - (3 - thiomorpholino - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine

Prepared analogously to Example 157 from 2 - [4 - methoxy - 2 - (3 - chloropropoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine and thiomorpholine by heating for 30 hours. Purification was by precipitation of the maleate from ethyl acetate solution. The free base was obtained from the maleate with 2N ammonia.

M.p.: 111°C.

Example 159

2 - [4 - Methoxy - 2 - (2 - (4 - methyl - piperazin - 1 - yl) - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine

Prepared from 3.0 g of 2 - [4 - methoxy - 2 - (2 - chloro - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine and 2.0 g of N - methylpiperazine by refluxing for 40 hours in ethanol. After purification by column chromatography over silica gel, the product was recrystallized from water.

M.p.: 136 to 137°C.

Example 160

2 - [4 - Methoxy - 2 - (3 - (4 - (2 - phenyl - ethyl) - piperazin - 1 - yl) - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine trihydrochloride

Prepared analogously to Example 156 from 2 - [4 - methoxy - 2 - (3 - chloro - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine and 1 - (2 - phenyl - ethyl) - piperazine.

M.p.: 236 to 238°C.

Example 161

2 - [4 - Methoxy - 2 - (3 - methylamino - propoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine hydrochloride

Prepared analogously to Example 156 from 2 - [4 - methoxy - 2 - (3 - chloropropoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine and methylamine.

M.p.: 215°C.

Example 162

2 - [4 - Methoxy - 2 - (2 - dimethylamino - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine dihydrochloride

Prepared analogously to Example 156 from 2 - [4 - methoxy - 2 - (2 - chloro - ethoxy) - phenyl] - 1H - imidazo[4,5 - b]pyridine and dimethylamine.

M.p.: 240 to 242°C.

Example 163

2 - (2 - Methylamino - phenyl) - 1H - imidazo[4,5 - b]pyridine

1.77 g of N - methyl - isatoic anhydride and 1.09 g of 2,3 - diaminopyridine were melted and heated for 10 minutes at 180°C. Recrystallization from ethyl acetate.

M.p.: 262 to 263°C.

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Example 164

- 2 - (2,4 - Dimethoxy - phenyl) - 3 - (2 - phenyl - ethyl) - 3H - imidazo[4,5 - b] - pyridine
- 5 0.17 g of 2 - (2 - hydroxy - 4 - methoxy - phenyl) - 3 - (2 - phenyl - ethyl) - 3H - imidazo[4,5 - b]pyridine were dissolved in 7 ml of dimethylformamide. The mixture was stirred for 5 minutes with 0.02 g of sodium hydride (80% suspension in oil) and reacted with 0.07 g of methyl iodide under ice-cooling. After 4 hours, water was added to the reaction mixture. The precipitated product was dissolved in ethyl acetate, and the organic layer was washed with 2N sodium hydroxide solution and water and evaporated. Recrystallization from ethanol/water. M.p.: 157°C.

Example 165

- 20 2 - (2,4 - Dimethoxy - phenyl) - 3 - [2 - (3,4 - dimethoxy - phenyl) - ethyl] - 3H - imidazo[4,5 - b]pyridine hydrochloride
- 25 Prepared analogously to Example 119 from 3 - amino - 2 - [2 - (3,4 - dimethoxy - phenyl) - ethylamino]pyridine and 2,4 - dimethoxy - benzoic acid. The hydrochloride was precipitated from ether. M.p.: 195°C.

Example 166

- 30 2 - (2 - Fluoro - 5 - methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine
- 35 Prepared analogously to Example 119 from 2,3 - diaminopyridine and 2 - fluoro - 5 - methylmercapto - benzoic acid. M.p.: 195°C.

Example 167

- 40 2 - (2 - Fluoro - 5 - methylsulfinyl - phenyl) - 1H - imidazo[4,5 - b]pyridine
- 45 Prepared from 2 - (2 - fluoro - 5 - methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine by oxidation with hydrogen peroxide in glacial acetic acid at room temperature. The purification was effected by column chromatography on silica gel with chloroform-methanol 19:1 as eluent. M.p.: 190 to 192°C.

Example 168

- 50 2 - (2 - Fluoro - 5 - methylsulfonyl - phenyl) - 1H - imidazo[4,5 - b]pyridine
- 55 Prepared from 2 - (2 - fluoro - 5 - methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine according to Example 167, but at 40°C. M.p.: 242°C.

Example 169

- 2 - (3,4 - Dimethoxyphenyl) - 3 - (3 - morpholino - propyl) - 3H - imidazo[4,5 - b]pyridine dihydrochloride

- a) N' - (2 - Chloro - 3 - pyridyl) - N - (3 - morpholinopropyl) - 3,4 - dimethoxy - benzamidine 60

4.9 g of N - (3 - morpholinopropyl) - 3,4 - dimethoxy - benzamide and 2.04 g of 2 - chloro - 3 - aminopyridine were refluxed for 2 hours in 85 ml of phosphorus oxychloride, the mixture was poured into water. The solution was made alkaline and extracted with ethyl acetate. After evaporation of the residue, the product remained as viscous oil. 65 70

- b) 2 - (3,4 - Dimethoxyphenyl) - 3 - (3 - morpholino - propyl) - 3H - imidazo[4,5 - b]pyridine dihydrochloride
- 5.2 g of N - (2 - chloro - 3 - pyridyl) - N' - (3 - morpholino - propyl) - 3,4 - dimethoxy - benzamidine and 1.5 g of sodium hydride (80% suspension in oil) were heated in 100 ml of dimethylformamide for 2 hours at 120°C. The dihydrochloride was precipitated from ether with hydrochloric acid and recrystallized from ethanol/cyclohexane. M.p.: 180°C. 75 80

Example 170

- 2 - (4 - Methoxy - phenyl) - 3 - (3 - morpholino - propyl) - 3H - imidazo[4,5 - b]pyridine dihydrochloride 85
- Prepared analogously to Example 169 from N' - (2 - chloro - 3 - pyridyl) - N - (3 - morpholino - propyl) - 5 - methoxy - benzamidine. M.p.: 218°C. 90

Example 171

- 2 - (4 - Methoxy - phenyl) - 3 - [3,4 - phenyl - piperazin - 1 - yl] - propyl] - 3H - imidazo[4,5 - b]pyridine dihydrochloride hydrate 95
- Prepared analogously to Example 169 from N' - (2 - chloro - 3 - pyridyl) - N - [3 - (4 - phenyl - piperazin - 1 - yl) - propyl] - methoxy - benzamidine. Mp: 100°C 100

Example 172

- 2 - (4 - Methoxy - phenyl) - 3(2 - morpholino - ethyl) - 3H - imidazo[4,5 - b]pyridine hydrochloride 105
- Prepared analogously to Example 169 from N' - (2 - chloro - 3 - pyridyl) - N - (2 - morpholino - ethyl) - 4 - methoxy - benzamidine Mp: 149°C 110

Example 173

- 2 - (4 - Methoxy - phenyl) - 3 - [3 - (4 - methyl - piperazin - 1 - yl) - propyl] - 3H - imidazo[4,5 - b]pyridine trihydrochloride 115
- Prepared analogously to Example 169 from N' - (2 - chloro - 3 - pyridyl) - N - [3 - (4 -

methyl - piperazin - 1 - yl) - propyl] - 4 - methoxy - benzamidine.
M.p.: 257°C.

Example 174

5 2 - (4 - Methoxy - phenyl) - 3 - [2 - (4 - methyl - piperazin - 1 - yl) - ethyl] - 3H - imidazo[4,5 - b]pyridine trihydrochloride

10 Prepared analogously to Example 169 from N' - (2 - chloro - 3 - pyridyl) - N - [2 - (4 - methyl - piperazin - 1 - yl) - ethyl] - 4 - methoxy - benzamidine.
M.p.: 225°C.

Example 175

15 2 - (4 - Methoxy - phenyl) - 3 - (3 - dimethylamino - propyl) - 3H - imidazo[4,5 - b]pyridine dihydrochloride

20 Prepared analogously to Example 169 from N' - (2 - chloro - 3 - pyridyl) - N - (3 - dimethylamino - propyl) - 4 - methoxy - benzamidine.
M.p.: 229°C.

Example 176

25 2 - (4 - Methoxy - phenyl) - 3 - (3 - piperidino - propyl) - 3H - imidazo[4,5 - b]pyridine dihydrochloride

30 Prepared analogously to Example 169 from N' - (2 - chloro - 3 - pyridyl) - N - (3 - piperidino - propyl) - 4 - methoxy - benzamidine.
M.p.: 196°C.

Example 177

35 2 - (4 - Methoxy - phenyl) - 3 - (4 - morpholino - butyl) - 3H - imidazo[4,5 - b]pyridine dihydrochloride hydrate

Prepared analogously to Example 169 from N' - (2 - chloro - 3 - pyridyl) - N - (4 - morpholino - butyl) - 4 - methoxy - benzamidine.
M.p.: 136°C.

Example 178

40 2 - (2 - Fluoro - 4 - methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

45 Prepared analogously to Example 119 from 2 - fluoro - 4 - methyl - mercapto benzoic acid and 2,3 - diaminopyridine.
M.p.: 257°C.

Example 179

50 2 - (2 - Fluoro - 4 - methylsulfinyl - phenyl) - 1H - imidazo[4,5 - b]pyridine

55 Prepared analogously to Example 167 from 2 - (2 - fluoro - 4 - methyl - mercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine. Crystallization by trituration in petroleum ether.
M.p.: 219°C.

Example 180

2 - (4 - Methylmercapto - phenyl) - 3 - (3 - morpholino - propyl) - 3H - imidazo[4,5 - b]pyridine

60 Prepared analogously to Example 169 from N' - (2 - chloro - 3 - pyridyl) - N - (3 - morpholino - propyl) - 4 - methyl - mercapto - benzamidine. Recrystallized from ether/cyclohexane.
M.p.: 110°C.

Example 181

2 - [2 - Propoxy - 4 - (4 - methyl - piperazin - 1 - yl) - phenyl] - 1H - imidazo[4,5 - b]pyridine dihydrochloride

70 Prepared analogously to Example 146 from 3 - (4 - methyl - piperazin - 1 - yl) - 1 - propoxy benzene.
M.p.: 237 to 238°C.

Example 182

75 Tablets containing 100 mg of 2 - (2,4 - dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride

Composition:

1 tablet contains:

Active ingredient	100.0 mg	
lactose	50.0 mg	
polyvinyl pyrrolidone	5.0 mg	
carboxymethylcellulose	19.0 mg	
magnesium stearate	1.0 mg	
	175.0 mg	85

moist screening: 1.5 mm
Drying: in the circulating air drier at 50°C.
Dry screening: 1 mm

90 The dry granulate was admixed with the remaining auxiliary products and pressed into tablets.

Weight of tablet: 175 mg
Punch 2 mm ϕ 95

Example 183

Coated tablets containing 50 mg of 2 - (2,4 - dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine hydrochloride
1 coated tablet core contains:

Active ingredient	50.0 mg	
corn starch, dried	20.0 mg	
soluble starch	2.0 mg	
carboxymethylcellulose	7.0 mg	
magnesium stearate	1.0 mg	
	80.0 mg	105

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1,445,824

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The active ingredient and corn starch were homogeneously moistened with the aqueous solution of the soluble starch.

- 5 Moist screening: 1.0 mm
Dry screening: 1.0 mm
Drying: at 50°C in the circulating air drier

- 10 The granulate and the remaining auxiliary products were mixed and pressed to form coated tablet cores.

Weight of core: 80 mg
Punch: 6 mm, arched (5 mm)

- 15 The finished cores were covered with a coat consisting essentially of sugar and talcum in conventional manner. The finished coated tablets were polished with beeswax.

Weight of coated tablet: 120 mg

Example 184

- 20 Suppositories containing 75 mg of 2 - (2,4 - dimethoxy - phenyl) - 1H - imidazo - [4,5 - b]pyridine hydrochloride

1 suppository contains:

- 25 Active ingredient 75.0 mg
suppository mass (e.g.
"Witepsol" H 19 and
"Witepsol" W 45) 1,625.0 mg
1,700.0 mg

("Witepsol" is a registered TradeMark).

Method of preparation:

- 30 The suppository mass was melted. At 38°C the pulverized active ingredient was homogeneously dispersed in the melt. The suppository mass was cooled to 35°C and poured into pre-cooled moulds.

- 35 Weight of suppository: 1.7 g

Example 185

Ampoules containing 50 mg of 2 - (2,4 - dimethoxy - phenyl) - 1H - imidazo - [4,5 - b]pyridine hydrochloride

- 40 1 ampoule contains
Active ingredient 50.0 mg
sorbitol 250.0 mg
distilled water ad 5.0 ml

Method of preparation:

- 45 The active ingredient and the sorbitol were dissolved in distilled water. The solution was made up to the given volume and filtered sterile.

- 50 Filling: into ampoules of 5 ml capacity
Sterilisation 20 minutes at 120°C.

Example 186

Drop solution containing 25 mg of 2 - (2,4 - dimethoxy - phenyl) - 1H - imidazo - [4,5 - b]pyridine hydrochloride per 5 ml

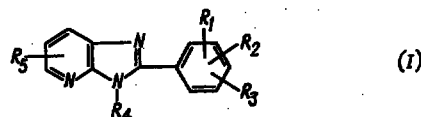
- | | | |
|----------------------------------|-------------|----|
| Active ingredient | 5.0 g | 55 |
| methyl <i>p</i> -hydroxybenzoate | 0.035 g | |
| propyl <i>p</i> -hydroxybenzoate | 0.015 g | |
| aniseed oil | 0.05 g | |
| menthol | 0.06 g | |
| sodium saccharine | 1.0 g | 60 |
| glycerine | 10.0 g | |
| ethanol | 40.0 g | |
| distilled water | ad 100.0 ml | |

Method of preparation:

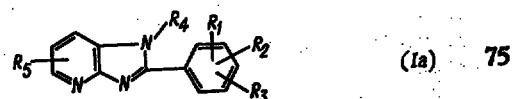
The benzoic acid esters were dissolved in ethanol and subsequently the aniseed oil and the menthol were added. Active ingredient, glycerine and sodium saccharine were dissolved in water and added. The solution was filtered pure.

WHAT WE CLAIM IS:—

1. Compounds of general formula



and isomers thereof of general formula



[wherein R₁, R₂ and R₃, which may be the same or different, each represents a hydrogen or halogen atom; a hydroxy, alkyl, allyloxy, benzyloxy, alkylthio, alkylsulfinyl or alkylsulfonyl group; an amino group optionally substituted by one or two alkyl groups; a morpholino or a piperazino group optionally substituted in the 4-position by a phenyl group or an alkyl group containing from 1 to 3 carbon atoms; or an alkoxy group containing from 1 to 4 carbon atoms, optionally substituted by a halogen atom or by a hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, dialkylamino, piperidino, morpholino, thiomorpholino, thiomorpholino - S - oxide, thiomorpholino - S,S - dioxide, 4 - alkylpiperazino, 3 - phenylpiperazino, 4 - dimethoxyphenylpiperazino, 4 - phenylethylpiperazino, phenylethylamino, N - methyl - phenylethylamino or N - methyl - dimethoxy - phenylethylamino group with the proviso that if any two of the groups R₁, R₂ and R₃ represent hydrogen atoms then the other group is other than a hydrogen or halogen atom or a methyl or unsubstituted amino group; or two of the groups

100

The active ingredient and corn starch were homogeneously moistened with the aqueous solution of the soluble starch.

- 5 Moist screening: 1.0 mm
Dry screening: 1.0 mm
Drying: at 50°C in the circulating air drier

- 10 The granulate and the remaining auxiliary products were mixed and pressed to form coated tablet cores.

Weight of core: 80 mg
Punch: 6 mm, arched (5 mm)

- 15 The finished cores were covered with a coat consisting essentially of sugar and talcum in conventional manner. The finished coated tablets were polished with beeswax.

Weight of coated tablet: 120 mg

- 20 Example 184
Suppositories containing 75 mg of 2 - (2,4 - dimethoxy - phenyl) - 1H - imidazo - [4,5 - b]pyridine hydrochloride
1 suppository contains:
Active ingredient 75.0 mg
suppository mass (e.g.
25 "Witepsol" H 19 and
"Witepsol" W 45) 1,625.0 mg
1,700.0 mg

("Witepsol" is a registered TradeMark).

- 30 Method of preparation:
The suppository mass was melted. At 38°C the pulverized active ingredient was homogeneously dispersed in the melt. The suppository mass was cooled to 35°C and poured into pre-cooled moulds.

- 35 Weight of suppository: 1.7 g

- 40 Example 185
Ampoules containing 50 mg of 2 - (2,4 - dimethoxy - phenyl) - 1H - imidazo - [4,5 - b]pyridine hydrochloride
1 ampoule contains
Active ingredient 50.0 mg
sorbitol 250.0 mg
distilled water ad 5.0 ml

- 45 Method of preparation:
The active ingredient and the sorbitol were dissolved in distilled water. The solution was made up to the given volume and filtered sterile.

- 50 Filling: into ampoules of 5 ml capacity
Sterilisation 20 minutes at 120°C.

Example 186

Drop solution containing 25 mg of 2 - (2,4 - dimethoxy - phenyl) - 1H - imidazo - [4,5 - b]pyridine hydrochloride per 5 ml

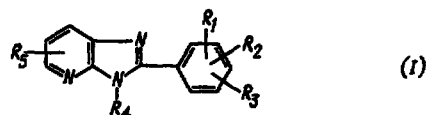
Active ingredient	5.0 g	55
methyl p-hydroxybenzoate	0.035 g	
propyl p-hydroxybenzoate	0.015 g	
aniseed oil	0.05 g	
menthol	0.06 g	
sodium saccharine	1.0 g	60
glycerine	10.0 g	
ethanol	40.0 g	
distilled water	ad 100.0 ml	

Method of preparation:

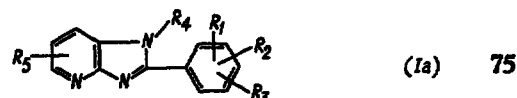
The benzoic acid esters were dissolved in ethanol and subsequently the aniseed oil and the menthol were added. Active ingredient, glycerine and sodium saccharine were dissolved in water and added. The solution was filtered pure.

WHAT WE CLAIM IS:—

1. Compounds of general formula



and isomers thereof of general formula



[wherein R₁, R₂ and R₃, which may be the same or different, each represents a hydrogen or halogen atom; a hydroxy, alkyl, allyloxy, benzyloxy, alkylthio, alkylsulfinyl or alkylsulfonyl group; an amino group optionally substituted by one or two alkyl groups; a morpholino or a piperazino group optionally substituted in the 4-position by a phenyl group or an alkyl group containing from 1 to 3 carbon atoms; or an alkoxy group containing from 1 to 4 carbon atoms, optionally substituted by a halogen atom or by a hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, dialkylamino, piperidino, morpholino, thiomorpholino, thiomorpholino - S - oxide, thiomorpholino - S,S - dioxide, 4 - alkylpiperazino, 3 - phenylpiperazino, 4 - dimethoxyphenylpiperazino, 4 - phenylethylpiperazino, phenylethylamino, N - methyl - phenylethylamino or N - methyl - dimethoxy - phenylethylamino group with the proviso that if any two of the groups R₁, R₂ and R₃ represent hydrogen atoms then the other group is other than a hydrogen or halogen atom or a methyl or unsubstituted amino group; or two of the groups



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R_1 to R_3 together represent a methylenedioxy group and the remaining R_1 , R_2 or R_3 group is as hereinbefore defined; each of the above mentioned alkyl groups containing from 1 to 4 carbon atoms;

R_4 represents a hydrogen atom; an alkyl group optionally substituted by a hydroxy, dialkylamino, phenyl, dimethoxyphenyl, piperidino, morpholino, 4 - methylpiperazino or 4 - phenylpiperazino group, each of the above mentioned alkyl groups containing from 1 to 4 carbon atoms, or a phenyl group optionally substituted by one or more halogen atoms or methoxy groups, with the proviso that when R_4 represents a hydrogen atom at least one of the groups R_1 to R_3 is other than hydrogen;

and R_5 represents a hydrogen atom, a halogen atom or an alkyl group containing from 1 to 3 carbon atoms and the corresponding imidazo[4,5 - b]pyridine - N - oxides and isomers thereof an acid addition salts thereof

2. Compounds of general formula Ia wherein R_1 , R_2 , R_3 and R_5 are as defined in claim 1 and R_4 represents a hydrogen atom.

3. Compounds of general formula I wherein R_1 to R_5 are as defined in claim 1.

4. Compounds of general formula I and isomers thereof of general formula Ia [wherein R_1 , R_4 and R_5 represent hydrogen atoms and R_2 and R_3 , which may be the same or different, each represents a halogen atom, or a methyl, methoxy, ethoxy, alkylthio, alkylsulfinyl, dialkylaminoalkoxy, morpholinoalkoxy, thiomorpholinoalkoxy, 4 - methylpiperazinoalkoxy, 4 - phenylpiperazinoalkoxy or alkylsulfinylalkoxy group (wherein each alkyl group contains from 1 to 3 carbon atoms and each alkoxy group contains 2 or 3 carbon atoms)] and physiologically compatible acid addition salts thereof.

5. 2 - (2,4 - Dimethoxy - phenyl) - 1H - imidazo[4,5 - b]pyridine and physiologically compatible acid addition salts thereof.

6. 2 - (2 - Methoxy - 4 - methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine and physiologically compatible acid addition salts thereof.

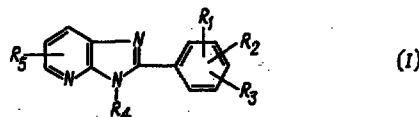
7. 2 - (2 - Methoxy - 4 - methylsulfinyl - phenyl) - 1H - imidazo[4,5 - b]pyridine and physiologically compatible acid addition salts thereof.

8. 2 - (2 - Methoxy - 4 - methyl - phenyl) - 1H - imidazo[4,5 - b]pyridine and physiologically compatible acid addition salts thereof.

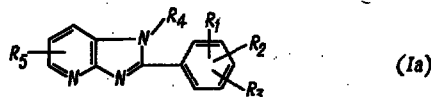
9. 2 - (2 - Methoxy - 5 - methylmercapto - phenyl) - 1H - imidazo[4,5 - b]pyridine and physiologically compatible acid addition salts thereof.

10. 2 - (2 - Ethoxy - 4 - methyl - phenyl) - 1H - imidazo[4,5 - b]pyridine and physiologically compatible acid addition salts thereof.

11. Compounds of general formula



and isomers thereof of general formula

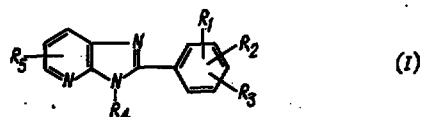


[wherein R_1 , R_2 and R_3 , which may be the same or different, each represents a hydrogen or halogen atom; a hydroxy, allyloxy, benzyloxy, alkylthio, alkylsulfinyl or alkylsulfonyl group; an amino group optionally substituted by one or two alkyl groups; or an alkoxy group containing from 1 to 4 carbon atoms optionally substituted by a halogen atom or by a hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, dialkylamino, morpholino, thiomorpholino, N - methylpiperazino or N - phenylpiperazino group with the proviso that if any two of the groups R_1 , R_2 and R_3 represent hydrogen atoms then the other group is other than a hydrogen or halogen atom or a methyl or unsubstituted amino group; or two of the groups R_1 to R_3 together represent a methylenedioxy group and the remaining R_1 , R_2 or R_3 group is as defined above; each of the above mentioned alkyl groups containing from 1 to 4 carbon atoms;

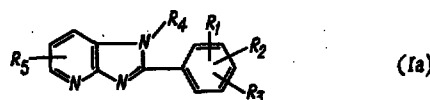
R_4 represents a hydrogen atom; an alkyl group optionally substituted by a hydroxyl, dialkylamino, phenyl or morpholino group, whereby each of the above mentioned alkyl group contains from 1 to 4 carbons; or a phenyl group optionally substituted by a halogen atom or a methoxy group; with the proviso that when R_4 represents a hydrogen atom at least one of the groups R_1 to R_3 is other than hydrogen;

and R_5 represents a hydrogen or halogen atom or an alkyl group containing from 1 to 3 carbon atoms and physiologically compatible acid addition salts thereof.

12. Compounds of general formula



and isomers thereof of general formula





[wherein R_1 , R_2 and R_3 , which may be the same or different each represents a hydrogen, fluorine or chlorine atom, a methyl or methyl-amino group, a morpholino or piperazino group optionally substituted in the 4-position by a phenyl group or by an alkyl group containing from 1 to 3 carbon atoms, or an alkoxy group containing from 2 to 4 carbon atoms substituted by a dimethylamino, diethylamino, piperidino, morpholino, thiomorpholino, phenylethylamino, N-methylphenylethylamino or N-methyldimethoxyphenylethylamino group or by a piperazino group substituted in the 4-position by a methyl, phenyl, dimethoxyphenyl or phenylethyl group with the proviso that if any two of the groups R_1 , R_2 and R_3 represents hydrogen atoms then the other group is other than a hydrogen or halogen atom or a methyl group;

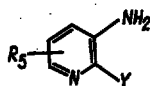
R_4 represents a hydrogen atom, an alkyl group containing from 2 to 4 carbon atoms substituted by a phenyl, dimethoxyphenyl, piperidino, morpholino, N-methylpiperazino or N-phenylpiperazino group; with the proviso that when R_4 represents a hydrogen atom at least one of the groups R_1 to R_3 is other than hydrogen; and R_5 represents a hydrogen atom] and physiologically compatible acid addition salts thereof.

13. Compounds as claimed in claim 1 other than those claimed in claims 5 to 10 as herein specifically described.

14. Compounds as claimed in claim 11 other than those claimed in claims 5 to 10 as herein specifically described.

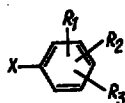
15. Compounds as claimed in claim 12 as herein specifically described.

16. A process for the preparation of compounds of general formula I and isomers thereof of general formula Ia as defined in claim 1 which comprises reacting a compound of formula



(II)

[wherein R_5 is as defined in claim 1 and Y represents a group of formula R_4NH- (wherein R_4 is as defined in claim 1)] with a compound of formula

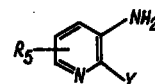


(III)

(wherein R_1 to R_3 are as defined in claim 1 and X represents a carboxyl, thiocarboxyl or dithiocarboxyl group) or a functional derivative thereof.

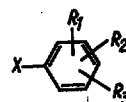
17. A process as claimed in claim 16 wherein the functional derivative is an acid halide, anhydride, ester or orthoester.

18. A process for the preparation of compounds of general formula I and isomers thereof of general formula Ia as defined in claim 1 which comprises reacting a compound of formula



(II)

(wherein R_5 is as defined in claim 1 and Y represents a halogen atom) with a compound of formula



(III)

[wherein R_1 to R_3 are as defined in claim 11 and X represents an appropriate $-NR_4-$ containing group (wherein R_4 is as defined in claim 1) which is derived from a carboxyl, thiocarboxyl or dithiocarboxyl group).

19. A process as claimed in claim 18 wherein the said $-NR_4-$ containing group is a nitrile, amide, imido ester, imido thioester, imido halide or amidine group.

20. A process as claimed in any of claims 16 to 19 wherein the reaction is effected in the presence of a solvent.

21. A process as claimed in any of claims 16 to 20 wherein the reaction is effected at temperatures from -20 to 250°C .

22. A process as claimed in either claim 16 or claim 18 wherein a compound of formula III wherein X represents a carboxyl or an amide group is reacted with a compound of formula II as defined in claim 16 or claim 18 respectively in the presence of phosphorous oxychloride or thionyl chloride and in the presence of pyridine or triethylamine at temperatures from -20 to 120°C .

23. A process as claimed in claim 18 wherein a compound of formula III wherein X represents a nitrile group is reacted with a compound of formula II as defined in claim 18 in the presence of a catalytic quantity of p-toluenesulfonic acid and at temperatures from 120 to 180°C .

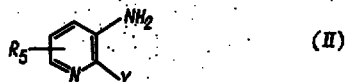
24. A process as claimed in claim 18 wherein a compound of formula III wherein X represents a thioamide group is reacted with a compound of formula II as defined in claim 18 at temperatures from 100 to 150°C .

25. A process as claimed in claim 18 wherein a compound of formula II wherein Y represents a chlorine atom is reacted with a compound of formula III as defined in claim 18 at temperatures from 100 to 200°C .

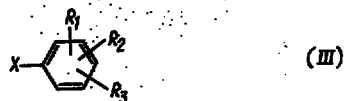


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26. A process for the preparation of compounds of general formula I and isomers thereof of general formula Ia as defined in claim 11 which comprises reacting a compound of formula

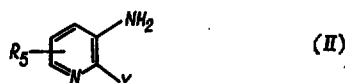


[wherein R_5 is as defined in claim 11 and Y represents a group of formula R_4NH- (wherein R_4 is as defined in claim 11)] with a compound of formula

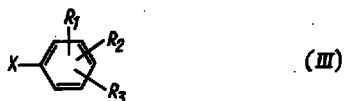


(wherein R_1 to R_3 are as defined in claim 11 and X represents a carboxyl, thiocarboxyl or dithiocarboxyl group) or with a functional derivative thereof.

27. A process for the preparation of compounds of general formula I and isomers thereof of general formula Ia as defined in claim 12 which comprises reacting a compound of formula

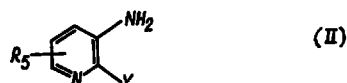


[wherein R_5 represents a hydrogen atom and Y represents a group of formula R_4NH- (wherein R_4 is as defined in claim 12)] with a compound of formula

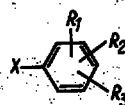


(wherein R_1 to R_3 are as defined in claim 12 and X represents a carboxy, thiocarboxy or dithiocarboxy group) or with a functional derivative thereof.

28. A process for the preparation of compounds of general formula I and isomers thereof of general formula Ia as defined in claim 11 which comprises reacting a compound of formula

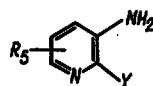


(wherein R_5 is as defined in claim 11 and Y represents a halogen atom) with a compound of formula

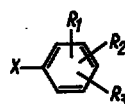


[wherein R_1 to R_3 are as defined in claim 11 and X represents an appropriate $-NR_4-$ containing group (wherein R_4 is as defined in claim 11) which is derived from a carboxyl, thiocarboxyl or dithiocarboxyl group].

29. A process for the preparation of compounds of general formula I and isomers thereof of general formula Ia as defined in claim 12 which comprises reacting a compound of formula



(wherein R_5 represents a hydrogen atom and Y represents a halogen atom) with a compound of formula



[wherein R_1 to R_3 are as defined in claim 12 and X represents an appropriate $-NR_4-$ containing group (wherein R_4 is as defined in claim 1) which is derived from a carboxyl, thiocarboxyl or dithiocarboxyl group].

30. A process as claimed in any of claims 16 to 25 wherein a compound of formula I or Ia containing a reactive halogen atom thereby obtained is subsequently converted into the corresponding amino compound by reaction with an amine.

31. A process as claimed in any of claims 16 to 25 and 30 wherein a compound of formula I or Ia containing a reacting hydrogen atom thereby obtained is subsequently alkylated by reaction with an alkylating agent in the presence of a base.

32. A process as claimed in any of claims 16 to 25, 30 and 31 wherein a compound of formula I or Ia thereby obtained is subsequently converted into the corresponding N - oxide, S - oxide or S,S - dioxide compound by means of an oxidising agent.

33. A process as claimed in any of claims 16 to 25 and 30 to 32 wherein a compound of formula I or Ia thereby obtained is subsequently converted into an acid addition salt thereof.

34. A process as claimed in claim 33 wherein the compound of formula I or Ia is converted into a physiologically compatible acid addition salt thereof.

35. A process as claimed in any of claims 30 to 34 wherein the compound of formula I or Ia is as defined in claim 11.



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36. A process as claimed in any of claims 30 to 34 wherein the compound of formula I or Ia is as defined in claim 12.
- 5 37. A process for the preparation of compounds of general formula I and isomers thereof of general formula Ia and the corresponding imidazo[4,5 - b]pyridine - N - oxides and isomers thereof as defined in claim 1 substantially as herein described.
- 10 38. A process for the preparation of compounds of general formula I and isomers thereof of general formula Ia as defined in claim 11 substantially as herein described.
- 15 39. A process for the preparation of compounds of general formula I and isomers thereof of general formula Ia as defined in claim 12 substantially as herein described.
- 20 40. A process for the preparation of compounds of general formula I and isomers thereof of general formula Ia and the corresponding imidazo[4,5 - b]pyridine - N - oxides and isomers thereof as defined in claim 1 substantially as herein described with reference to Examples 1 to 181.
- 25 41. A process for the preparation of compounds of general formula I and isomers thereof of general formula Ia as defined in claim 11 substantially as herein described with reference to Examples 1 to 118.
- 30 42. A process for the preparation of compounds of general formula I and isomers thereof of general formula Ia as defined in claim 12 substantially as herein described with reference to Examples 119 to 181.
- 35 43. Compounds of general formula I and isomers thereof of general formula Ia and the corresponding imidazo[4,5 - b]pyridine - N - oxides and isomers thereof as defined in claim 1 and acid addition salts thereof whenever prepared by a process as claimed in any of claims 16 to 25, 30 to 34, 37 and 40.
- 40 44. Compounds of general formula I and isomers thereof of general formula Ia as defined in claim 11 and physiologically compatible acid addition salts thereof whenever prepared by a process as claimed in any of claims 26, 28, 35, 38 and 41.
- 45 45. Compounds of general formula I and isomers thereof of general formula Ia as defined in claim 12 and physiologically compatible acid addition salts thereof whenever prepared by a process as claimed in any of claims 27, 29, 36, 39 and 42.
- 50 46. Pharmaceutical compositions comprising active ingredient as least one compound of formula I or isomer thereof of formula Ia or physiologically compatible acid addition salt thereof as claimed in claim 1 in association with a pharmaceutical carrier or excipient.
- 55 47. Compositions as claimed in claim 46 in a form suitable for oral, rectal or parenteral administration.
- 60 48. Compositions as claimed in claim 47 in the form of tablets, coated tablets, suppositories, ampoules or drops.
- 65 49. Compositions as claimed in any of claims 46 to 48 in the form of dosage units.
- 70 50. Compositions as claimed in claim 49 wherein each dosage unit contains from 35 to 200 mg of active ingredient.
- 75 51. Compositions as claimed in claim 50 wherein each dosage unit contains from 50 to 100 mg of active ingredient.
- 80 52. Compositions as claimed in claim 46 containing as active ingredient a compound as claimed in claim 11.
- 85 53. Compositions as claimed in claim 46 containing as active ingredient a compound as claimed in claim 12.
54. Compositions as claimed in claim 46 substantially as herein described.
55. Compositions as claimed in claim 46 substantially as herein described with reference to Examples 182 to 186.

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London, W.C.2.

ERRATUM

SPECIFICATION No. 1,445,824

Page 1, line 1, (71), *after We delete [DR]*
insert DR

THE PATENT OFFICE
31st January, 1977

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