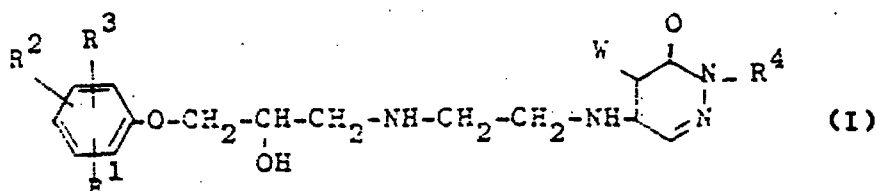


(68)

Pyridazines containing basic substituents, their preparation and their use

The present invention relates to pharmacologically valuable pyridazines, containing basic substituents, of the general formula I



wherein R^1 , R^2 and R^3 independently of one another denote hydrogen, halogen, hydroxyl, nitro, trifluoromethyl, alkyl, alkoxy-alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, phenyl, alkoxy, hydroxyalkoxy, alkoxy-alkoxy, alkenyloxy, alkynyloxy, cycloalkoxy, phenalkoxy, alkanoyl, acylamino and an $-NH-CO-R^9$ - radical, R^9 representing morpholino, piperidino or 1-pyrrolidinyl, or an optionally substituted ureido radical, and R^4 denotes hydrogen or lower alkyl, and W denotes hydrogen, chlorine or bromine and to the acid addition salts thereof.

The compounds of the general formula I have an asymmetric C atom in the alkanolamine side chain, and can therefore exist in racemic and optically active forms. Within the scope of the present invention, the compounds of the general formula I are also understood as meaning possible stereoisomers and optically active compounds, and mixtures thereof, particularly the racemate.

The substituents mentioned for R^1 , R^2 and R^3 have the following meanings, in particular, in addition to hydrogen, halogen, hydroxyl, nitro, trifluoromethyl and phenyl: alkyl having 1 to 8, preferably 1 to 4, C atoms, for example methyl, ethyl, propyl, isopropyl, n-butyl, isobutyl, tert.-butyl, sec.-butyl, n-pentyl, isopentyl, neopentyl, tert.-pentyl, n-hexyl, isohexyl, n-heptyl and n-octyl; alkenyl having up to 6, preferably 3 or 4, C atoms, for example vinyl, allyl, 1-propenyl, isopropenyl, methallyl, crotyl, 2-pentenyl and 2-hexenyl; alkynyl having up to 6, preferably 3 or 4, C atoms, for example propargyl; cycloalkyl having a ring size of from 5 to 8, preferably 5 or 6, C atoms, for example cyclopentyl and cyclohexyl; cycloalkenyl having a ring

size of from 5 to 8, preferably 5 or 6, C atoms, for example cyclopentenyl; alkoxy having 1 to 8 C atoms, for example methoxy, ethoxy, propoxy, butoxy, isopropoxy, isohexyloxy, n-heptyloxy, n-octyloxy, pentyloxy, isopropoxy (sic), isohexyloxy (sic), n-heptyloxy (sic), n-octyloxy (sic) and pentyloxy (sic); cycloalkoxy having a ring size of from 5 to 8 C atoms in the cycloalkyl part, preferably cyclopentyloxy and cyclohexyloxy; alkenyloxy having up to 6, preferably 3 or 4, C atoms, for example allyloxy, methallyloxy, crotyloxy and 2-hexenyloxy; alkinyloxy having up to 6, preferably 3 or 4, C atoms, for example propargyloxy; alkanoyl having 1 to 6 C atoms, for example formyl, acetyl, propionyl, butyryl, isobutyryl, valeryl, isovaleryl and pivaloyl; alkoxyalkoxy having a total of up to 8 C atoms, the alkoxyalkoxy radical being of the form $R^{60}-R^{50}-$, and R^5 representing an alkylene radical having 2 to 7 C atoms, R^6 representing an alkyl radical having 1 to 6 C atoms and it also being possible for the radicals R^5 and/or R^6 to be branched in the case of 3 and more C atoms. Examples of suitable alkoxyalkoxy radicals are: 2-methoxy-ethoxy, 2-ethoxy-ethoxy, 3-methoxy-n-propoxy, 2-methoxy-n-propoxy, 4-methoxy-n-butoxy, 3-ethoxy-n-propoxy, 2-ethoxy-n-propoxy, 4-ethoxy-n-butoxy, 3-ethoxy-n-butoxy, 2-ethoxy-n-butoxy, 2,2-dimethyl-2-ethoxy-ethoxy, 3-(n-propoxy)-n-propoxy, 2-(n-propoxy)-n-propoxy, 3-(iso-propoxy)-n-propoxy, 2-(iso-propoxy)-n-propoxy, 2-(n-propoxy)-ethoxy, 2-(iso-propoxy)-ethoxy, 4-(n-propoxy)-n-butoxy, 3-(n-propoxy)-n-butoxy, 2-(n-butoxy)-ethoxy, 2-(sec.-butoxy)-ethoxy, 2-(tert.-butoxy)-ethoxy, 3-(n-butoxy)-n-propoxy, 2-(n-butoxy)-n-propoxy, 3-(iso-butoxy)-n-propoxy, 3-(sec.-butoxy)-n-propoxy, 3-(tert.-butoxy)-n-propoxy, 4-(n-butoxy)-n-butoxy, 3-(n-butoxy)-n-butoxy, 2-(n-butoxy)-n-butoxy, 4-(iso-butoxy)-n-butoxy, 3-(iso-butoxy)-n-butoxy, 2-(sec.-butoxy)-n-butoxy, 2,2-dimethyl-2-(n-butoxy)-ethoxy, 2-(n-butoxy)-1-methyl-ethoxy, 2-(iso-butoxy)-2-methyl-ethoxy, 5-methoxy-n-pentyloxy, 4-methoxy-n-pentyloxy, 3-methoxy-n-pentyloxy, 5-ethoxy-n-pentyloxy, 4-ethoxy-n-pentyloxy, 3-ethoxy-n-pentyloxy, 5-(n-propoxy)-n-pentyloxy, 5-(iso-propoxy)-n-pentyloxy, 6-methoxy-n-hexyloxy, 5-methoxy-n-hexyloxy, 4-methoxy-n-hexyloxy, 6-ethoxy-n-hexyloxy, 3-ethoxy-n-hexyloxy and 7-methoxy-n-heptyloxy; alkoxyalkoyl (sic) having 2 to 6 C atoms, the alkoxyalkyl radical being of the form $R^{80}-R^7-$ and R^8 representing an alkyl radical and R^7 an alkylene radical, and it being also

possible for the radicals R^8 and/or R^7 to be branched if they contain more than 3 C atoms, for example: methoxy-methyl, ethoxy-methyl, n-propoxy-methyl, iso-propoxy-methyl, n-butoxy-methyl, n-pentyloxy-methyl, 2-methoxy-ethyl, 2-ethoxy-ethyl, 2-n-propoxy-ethyl, 2-iso-propoxy-ethyl, 2-n-butoxy-ethyl, 3-methoxy-n-propyl, 3-ethoxy-n-propyl, 3-n-propoxy-n-propyl, 2-methyloxy-2-methyl-ethyl, 2-ethoxy-1-methyl-ethyl, 2-n-propoxy-2-methyl-ethyl, 2-iso-propoxy-1-methyl-ethyl, 4-methoxy-n-butyl, 4-ethoxy-n-butyl and 5-methoxy-n-pentyl; hydroxyalkoxy having 2 to 6 C atoms, for example 2-hydroxy-ethoxy, 3-hydroxy-n-propoxy, 4-hydroxy-n-butoxy, 3-hydroxy-n-butoxy, 5-hydroxy-n-pentyloxy, 4-hydroxy-n-hexyloxy, 2-hydroxy-n-hexyloxy and 2-hydroxy-n-propoxy; phenalkyloxy, for example phen-ethyloxy, and particularly benzyloxy; ureido or a ureido radical which is substituted in the 3-position by alkyl having 1 to 6 C atoms, preferably 1 to 4 C atoms, alkenyl having 3 to 6 C atoms, or cycloalkyl having 5 or 6 C atoms, a disubstitution also being possible in the case of alkyl substitution and/or alkenyl substitution. Examples of suitable ureido radicals are ureido, 3-methyl-ureido, 3-ethylureido, 3-propylureido, 3-isopropylureido, 3-allyl-ureido, 3-cyclopentylureido, 3-cyclohexylureido, 3,3-dimethylureido and 3,3-diethylureido; fluorine, chlorine or bromine are examples of suitable halogens; and an $-NH-CO-R^9-$ radical, R^9 representing morpholino, piperidino or 1-pyrrolidinyl.

In the case of the acylamino radical representing R^1 and/or R^2 and/or R^3 , the term acyl is understood as meaning the aryl-substituted, arylalkyl-substituted or alkyl-substituted carbonyl radical which has up to 11 C atoms and which is derived from an aromatic, aromatic-aliphatic or aliphatic carboxylic acid. Suitable acylamino radicals are, for example, acetamino, propionylamino, butyrylamino, benzoylamino, α - and β -naphthoylamino and phenyl-acetylamino, and acetamino and benzoylamino are preferred.

In addition to representing hydrogen, the substituent R^4 can represent, in particular, an alkyl radical having 1 to 4 C atoms, for example methyl, ethyl, n-propyl, isopropyl, n-butyl and isobutyl.

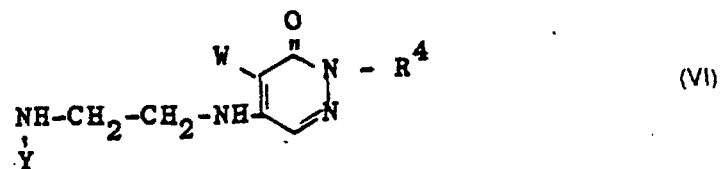
Normally, compounds of the general formula I, or the acid addition salts thereof, are preferred in which R^4 represents hydrogen, or only one of the substituents R^1 , R^2 or R^3 is

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For the preparation of the compounds of the general formula I, a compound of the general formula V



a halogen atom, particularly chlorine or bromine, is reacted with a compound of the general formula IV

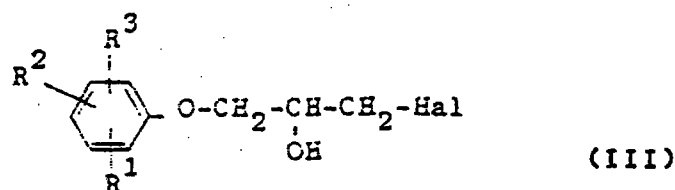
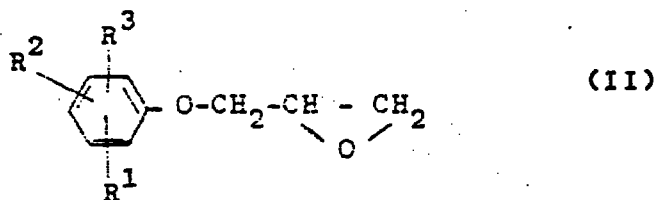


wherein Y represents hydrogen or a radical which can be split off hydrogenolytically, and an available radical which can be split off hydrogenolytically is then split off, by means of hydrogenolysis, from the compound obtained, and the resulting compound is reacted with an acid to give an acid addition salt, if appropriate.

Many radicals which can be split off hydrogenolytically have been known for a long time and proved particularly useful in the area of peptide synthesis. Very instructive papers and reviews have been published, particularly by R.A. Boissonnas and G. Preitner, Helvetica Chimica Acta Volume 36, page 875 (1953) and R.A. Boissonnas, Advances in Organic Chemistry Volume 3, page 159 et seq. (1963), with many references to the primary literature.

Examples of radicals which can be split off hydrogenolytically are, in particular, benzyl, carbobenzoxy or carbophenylloxy which are substituted in the phenyl nucleus by methyl, methoxy, chlorine or phenylazo, as well as carboallyloxy.

Instead of an individual compound of the general formula V, a mixture of a compound of the general formula II with a compound, which has the same substituents in the phenyl nucleus, of the general formula III



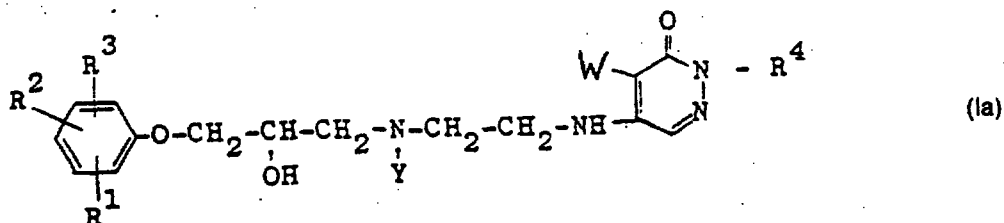
wherein, in formula III, Hal denotes a halogen atom, particularly chlorine or bromine, can also be employed. (73)

The reaction of the compounds of the general formulae IV and V is normally carried out in a suitable solvent or dispersing agent, in which the reactants are dissolved or suspended. Such solvents or dispersing agents are, for example, water, aromatic hydrocarbons, such as, for example, benzene, toluene and xylene; ketones, such as, for example, acetone and methyl ethyl ketone; halogenated hydrocarbons, such as, for example, chloroform, carbon tetrachloride, chlorobenzene and methylene chloride; ethers, such as, for example, tetrahydrofuran and dioxane; sulfoxides, such as, for example, dimethyl sulfoxide; and tertiary acid amides, such as, for example, dimethylformamide and N-methylpyrrolidone. Polar solvents, such as, for example, alcohols, are particularly used as the solvents. Suitable alcohols are, for example, methanol, ethanol, isopropanol, tert.-butanol, etc. Alcohols having 1 to 4 C atoms are preferred. The reaction is carried out at temperatures of from 20°C up to the reflux temperature of the solvent or dispersing agent used. The reaction frequently proceeds at temperatures of from 60 to 100°C. It can be advantageous to employ the starting compound of the general formula IV in up to 10-fold, or if appropriate even greater, molar excess and/or to add the reaction component of the general formulae II and III in dissolved or suspended form to the dissolved or suspended reaction component of the general formula IV. The molar ratio between the compounds of the general formula II or III and IV can therefore be 1:1 to 1:10 and, if appropriate, even more. In the presence of a compound of the general formula III, the reaction can also be carried out in the presence of acid-binding agents, such as potassium carbonate, sodium carbonate, triethylamine, etc. Without acid-binding agents, the hydrohalides are customarily obtained, in the case in which Y = hydrogen, the hydrohalides of the compounds of the general formula I.

The reaction of epoxides and halohydrins with compounds containing amino groups and the conditions under which this reaction is carried out advantageously are known per se. An illustrative summary is to be found in Houben-Weyl, 4th edition (1965), volume XI/1, pages 24-74 and 314-326.

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In the reaction of the compounds of the general formulae IV and V, in the case in which, in the general formula IV, Y represents a radical which can be split off hydrogenolytically, for example a benzyl or carbobenzoxy radical, compounds of the general formula Ia



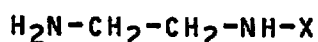
wherein Y represents a radical which can be split off hydrogenolytically, are first obtained. The hydrohalides of the compounds of the general formula Ia are obtained when compounds of the general formula III are used, and in the absence of acid-binding agents. The conversion of the compounds of the general formula Ia, or the hydrohalides thereof, into the compounds of the general formula I is effected by splitting off the radical Y hydrogenolytically, according to customary processes. In these processes, the compound of the general formula Ia, or the hydrohalides thereof, is dissolved or suspended in a suitable solvent, such as, for example, an alkanol, an ether or a hydrocarbon, such as ethanol, dioxane, toluene, xylene, etc., and is treated with hydrogen, in the presence of a suitable catalyst, such as, for example, palladium/charcoal, at temperatures from room temperature (20°C) up to the reflux temperature of the solvent used. After the catalyst has been filtered off under suction, the compound of the general formula I can be isolated. In most cases, the radical Y is already split off hydrogenolytically at room temperature (20°C).

The preparation of the starting compounds of the general formula IV can be effected by reacting compounds of the general formula VI



(75)

wherein W has the abovementioned meanings and T represents chlorine or bromine, with a compound of the general formula VII



(VII)

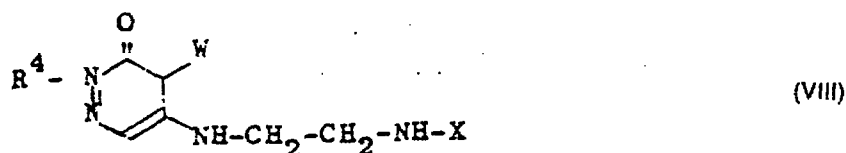
wherein X denotes a radical, which can be split off hydrolytically, of a protective group, or the radical Y (= hydrogen or a radical which can be split off hydrogenolytically). An example of a radical which can be split off hydrolytically is the acetyl radical or another acyl radical, that is to say a radical derived from an aliphatic, aromatic or araliphatic carboxylic acid by splitting off OH. As already mentioned, an example of a radical which can be split off hydrogenolytically is the benzyl radical or the carbo-benzoyl radical. The reaction of the compounds of the general formula VI with the compounds of the general formula VII is normally carried out in a suitable solvent or dispersing agent in which the reactants are dissolved or suspended, such as, for example, benzene, toluene, xylene, chloroform, methylene chloride, carbon tetrachloride, diethyl ether, dioxane, tetrahydrofuran, dimethyl-sulphoxide, acetone, methyl ethyl ketone, dimethylformamide, N-methylpyrrolidone, etc. The molar ratio between the compounds of the general formula VI and VII can be 1:1 to 1:10 and, if appropriate, even more. The reaction can be carried out at room temperature, or it can be accelerated or completed using heat, for example by heating the mixture to a temperature of from 80 to 110°C.

If, in the reaction a compound (sic) of the general formula VI with a compound of the general formula VII, X represents hydrogen, the compound of the general formula VII is advantageously employed in excess, in some cases even as the solvent. If, in the reaction of a compound of the general formula VI with a compound of the general formula VII, X represents a protective group which can be split off hydrolytically or hydrogenolytically, and if both reaction components are employed in equimolar quantities, the reaction is advantageously carried out in the presence of acid-binding agents, such as, for example, potassium carbonate, sodium carbonate, triethylamine, etc.

If, in the reaction of a compound of the general formula

V* with a compound of the general formula VII, X represents a protective group, a compound of the general formula VIII

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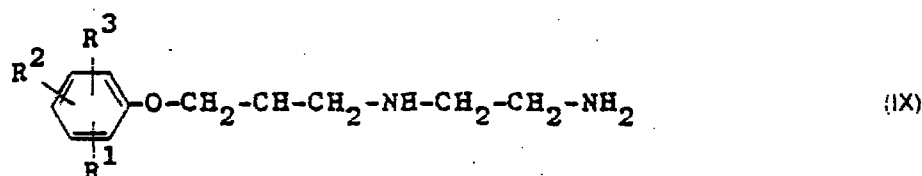


is then first formed, from which compound a compound of the general formula IV, in which Y represents H is obtained by splitting off the protective group X by means of the customary methods, for example by hydrolysis if X represents an acyl radical, or by hydrogenolysis if X represents a radical which can be split off hydrogenolytically.

For the preparation of the compounds of the general formula 1, pyridazines of the general formula VI



wherein R⁴, W and T have the abovementioned meanings, can also be reacted with a diamine of the general formula IX



and the compound obtained can be reacted with an acid to give an acid addition salt, if appropriate.

The reaction of a compound of the general formula VI with a compound of the general formula IX is normally carried out in a suitable solvent or dispersing agent in which the reactants are dissolved or suspended, such as, for example, benzene, toluene, xylene, chloroform, methylene chloride, carbon tetrachloride, chlorobenzene, dioxane, ether, tetrahydrofuran, water, dimethyl sulphoxide, dimethylformamide, N-methylpyrrolidone, etc.

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The reaction can be carried out at room temperature, or it can be accelerated or completed using heat, for example by heating the mixture to a temperature between 80 and 120°C. The molar ratio between the compounds of the general formulae VI and IX can be 1:1 to 1:10 and, if appropriate, even more. If equimolar quantities of the compounds of the general formulae VI and IX are employed, it is advisable to carry out the reaction in the presence of at least equimolar quantities of an acid-binding agent such as, for example, potassium carbonate, sodium carbonate, triethylamine, etc. Without acid-binding agents, the hydrohalides of the compounds of the general formula I are customarily obtained.

The reaction of halogenopyridazines with compounds containing amino groups and the advantageous reaction conditions are also likewise known *per se*. A general account and numerous literature references are to be found in R. Elderfield, *Heterocyclic Compounds* (1957), volume 6, page 130. Examples of other publications on this reaction are German Patent Specification 579,391 [CA 27, 4631 (1933)] and Meier, Ringier Druey, *Helv. Chim. Acta*, volume 37, pages 510 and 523 (1954).

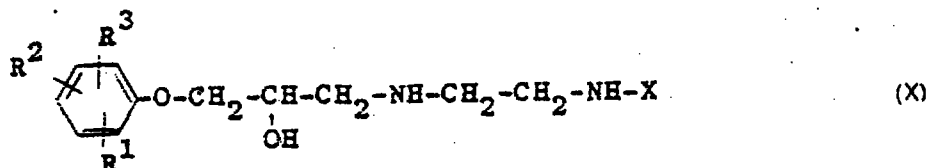
For the preparation of the starting diamines of the general formula IX, a compound of the general formula II or III, or a mixture of a compound of the general formula II with a compound, which has the same substituents in the phenyl nucleus, of the general formula III, can be reacted with a compound of the general formula VII (X denoting hydrogen or a protective group which can be split off hydrolytically, such as an acetyl radical or another acyl radical). This reaction is normally carried out in a suitable solvent or dispersing agent in which the reactants are dissolved or suspended. Such solvents or dispersing agents are, for example, water, aromatic hydrocarbons, such as, for example, benzene, toluene and xylene; ketones, such as, for example, acetone and methyl ethyl ketone; halogenated hydrocarbons, such as, for example, chloroform, carbon tetrachloride, chlorobenzene and methylene chloride; ethers, such as, for example, tetrahydrofuran and dioxane; sulphoxides, such as, for example, dimethyl sulphoxide; and tertiary acid amides, such as, for example, dimethylformamide and N-methylpyrrolidone. Polar solvents, such as, for example, alcohols, are particularly used as the solvents. Methanol, ethanol, isopropanol, tert.-buta-

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nol, etc. are examples of suitable alcohols.

The reaction is carried out at temperatures of from 20°C up to the reflux temperature of the solvent or dispersing agent used. The reaction frequently proceeds at temperatures of from 60 to 100°C. It can be advantageous to employ the starting compounds of the general formula VII in up to 10-fold, or if appropriate even greater, molar excess and/or to add the reaction component of the general formula (sic) II and III in dissolved or suspended form to be the dissolved or suspended reaction component of the general formula VII. The molar ratio between the compounds of the general formula II or III and VII can be 1:1 to 1:10 and, if appropriate, even more. In the presence of a compound of the general formula III, the reaction can also be carried out in the presence of acid-binding agents, such as potassium carbonate, sodium carbonate, etc. Without acid-binding agents, the hydrohalides of the compounds of the general formula IX are customarily obtained.

If, in the reaction of the compounds of the general formula II or III with a compound of the general formula VII, X represents a protective group, a compound of the general formula X



is then first formed, from which compound a compound of the general formula IX is obtained by splitting off the protective group X according to customary methods, for example by hydrolysis if X represents an acyl radical.

The abovementioned preparation processes are preferred for the compounds according to the invention in which W denotes chlorine or bromine.

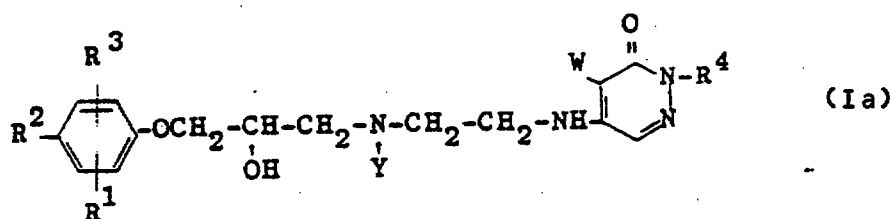
In principle, compounds, according to the invention, of the formula I in which W is hydrogen can be obtained by the preparation processes described above. Frequently, however, starting compounds of the formulae IV or VI in which W denotes hydrogen can only be obtained in a complicated manner by means of synthesis in several stages (cf. for example, Elderfield, Heterocyclic Compounds, volume 6, page 130 (1957)). It is therefore advantageous

to prepare compounds, according to the invention, of the formula I in which W denotes hydrogen from compounds, according to the invention, of the formula I in which W is chlorine or bromine by replacement by hydrogen of the halogen atom representing W. The selective replacement of a halogen atom representing W and bonded on the pyridazinone ring is carried out in a simple manner in a smooth reaction by hydrogenation. In general, in such a reaction, a solution or dispersion of the substance in a solvent or dispersing agent is treated with hydrogen in the presence of a hydrogenation catalyst, for example Raney nickel or a finely divided platinum metal on a suitable support, such as, for example, palladium on charcoal.

Lower alkanols having 1-4 C atoms, water or water/alkanol mixtures have proved to be particularly advantageous as the solvent or dispersing agent. In order to absorb the hydrogen halide resulting from the hydrogenation, the reaction is carried out in the presence of a base, such as, for example, a tertiary amine, MgO, an alkali metal acetate or an alkali metal hydroxide.

The accomplishment of such replacement reactions by hydrogenation has already been investigated and described in detail, cf. for example, Houben-Weyl, 4th edition (1965), volume V/4, pages 773 et seq. and volume IV ac, pages 364 et seq.

Instead of the compounds according to the invention of the formula I in which W is chlorine or bromine it is also possible to use compounds of the formula



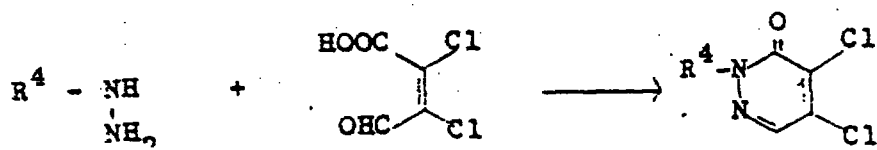
wherein W is chlorine or bromine and Y is a radical which can be split off hydrogenolytically, and R¹, R², R³ and R⁴ have the abovementioned meanings, according to the invention, of the

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formula I in which W is hydrogen. When these compounds are hydrogenated in the abovementioned manner, which is known per se, both the halogen atom represented by W and the radical Y which can be split off hydrogenolytically can be replaced by hydrogen in one and the same reaction step.

As stated above, compounds of the formula Ia are obtained when compounds of the formula V are reacted with compounds of the formula IV in which Y is a radical which can be split off hydrogenolytically.

The starting compounds of the general formula VI are either known or can be prepared in a known manner. Accordingly, starting compounds in which W and T are chlorine or bromine can readily be prepared from the hydrazine derivatives of the general formula XI by reacting the latter with mucochloric acid, mucobromic acid or the appropriate chlorine/bromine compound (cf. Katritzky, Boulton, *Advances in Heterocyclic Chemistry* (1968), volume 9, pages 235-236). The course of the reaction may be demonstrated using mucochloric acid as an example:



Starting compounds of the formula VI in which W denotes hydrogen can be prepared, for example, in accordance with the reaction scheme in R. Elderfield, *Heterocyclic Compounds* (1957), volume 6, page 130, starting from 4,5-dibromopyridazin-3-one.

The compounds of the general formulae II and III can be prepared according to known methods, for example by the reaction of the appropriate phenol with epichlorohydrin.

Optically active forms of the alkylenediamines of the general formula I can be obtained by separation of the corresponding racemic alkylenediamines of the general formula I by means

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of customary methods, for example by reacting the racemate of a compound of the general formula I with an optically active acid, subsequently carrying out, from a suitable diluent or solvent, such as, for example, ethanol, a fractional crystallisation of the diastereomeric salt mixture thus obtained, and finally liberating the optically active alkylenediamine from the salt, using a base. Optically active compounds of the general formula I can also be obtained by employing optically active starting compounds III or IX. These optically active starting compounds are obtained from the optically inactive compounds III or IX in a known manner, by resolving the racemate.

The compounds according to the invention, of the general formula I, and the acid addition salts thereof, have valuable pharmaceutical properties. In particular, they have a very pronounced β -adrenalytic (sic) action which is also cardioselective, that is to say the compounds have a higher degree of specificity in the blocking of cardiac β -receptors than of peripheral β -receptors, for example β -receptors in the bronchial muscle. In addition, some of them have strong α -lytic, antiarrhythmic and hypotensive actions. They are therefore suitable, for example, for the treatment or prophylaxis of cardiac complaints and cardiac diseases, such as angina pectoris and cardiac arrhythmias, and also for treating hypertension, without the lungs being affected in the case of sensitive patients.

The compounds according to the invention of the general formula I are, surprisingly, significantly superior, in their pharmaceutical action, to the known compounds, of similar structure, of DE-A (German Auslegeschrift) 2,819,629.

The pyridazine according to the invention can therefore be administered to humans, on their own, as mixtures with one another or in pharmaceutical preparations which contain, as the active constituent, an effective dose of at least one pyridazine according to the invention or one acid addition salt thereof, in addition to customary pharmaceutically acceptable excipients and additives.

Examples of suitable excipients are water, vegetable oils, starch, gelatine, lactose, magnesium stearate, waxes, vaselines, etc. Wetting agents, disintegrating agents, preservatives, etc.

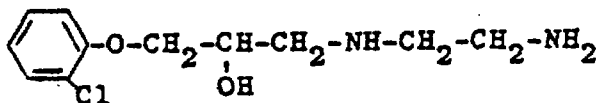
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can be used, for example, as additives.

The pharmaceutical preparations can be present, for example, in the form of tablets, capsules, aqueous or oleaginous solutions or suspensions, emulsions, injectable aqueous or oleaginous solutions or suspensions, or dispersible powders or aerosol mixtures. In addition to the compounds of the general formula I, the pharmaceutical preparations can also contain one, or more, other pharmaceutically active substances, for example tranquillizers, such as, for example, Luminal, meprobamate and chlorpromazines, and benzodiazepine sedatives, such as, for example, diazepam or chlor-diazepoxide; vasodilators, such as, for example, glycerol tri-nitrate, pentaerythritol tetranitrate and carbochromen; diuretics, such as, for example, chlorothiazide; heart-tonicising agents, such as, for example, preparations of digitalis; hypotensive agents, such as, for example, Rauwolfia alkaloids and guanethidine; broncho-dilators and sympathomimetic agents, such as, for example, iso-prenaline, osciprenaline (sic) adrenaline and ephedrine; α -adren-ergic blocking agents, such as, for example, phentolamine; cardiac membrane stabilising agents (antiarrhythmics), such as, for example, quinidine, and catecholamines, such as noradrenaline.

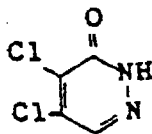
The examples which follow illustrate in more detail the preparation of the compounds of the general formula I:

Example 1

4.9 g of N-[3-(o-chlorophenoxy)-2-hydroxy (sic)]-ethylene-diamine



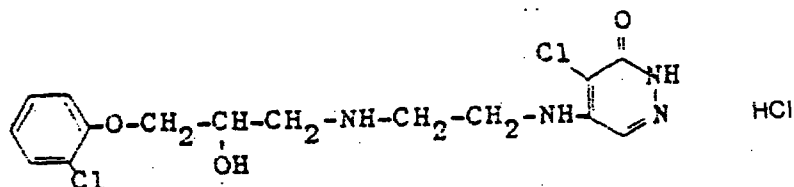
are dissolved in 50 ml of ethanol. A solution of 3.3 g of 4,5-dichloropyridazin-3-one



in 50 ml of ethanol is added to the above solution, and the mixture

is then heated under reflux for 12 hours. The mixture is then concentrated in vacuo, the residue is digested with a little ethyl acetate and decanted off from the ethyl acetate, and the residue is finally recrystallised from ethanol.

The N-[3-(o-chlorophenoxy)-2-hydroxy-propyl]-N'-[4-chloro-3-oxo-pyridaz-5-yl]-ethylenediamine hydrochloride



is thus obtained.

Melting point: 219°C

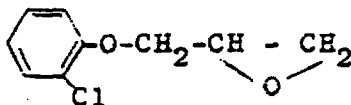
Analysis: (C₁₅H₁₉Cl₃N₄O₃)

	C	H	Cl	N	O
calculated:	44.0	4.6	26.0	13.7	11.7
found:	44.4	4.8	27.7	13.5	12.2

Yield: 78% of theory.

The N-[3-(o-chlorophenoxy)-2-hydroxypropyl]-ethylenediamine used as the starting material can be prepared as follows:

120 g of ethylenediamine are dissolved in 150 ml of ethanol. A solution of 20 g of o-chlorophenyl glycidyl ether



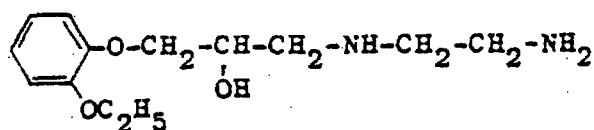
in 40 ml of ethanol is added to the above solution, and the mixture is heated under reflux for 20 hours. Excess ethylenediamine and ethanol are then distilled off in vacuo, and the residue is then distilled in vacuo.

N-[3-(o-chlorophenoxy)-2-hydroxy-propyl]-ethylenediamine is thus obtained as an oil which can be distilled at a boiling point of 190°C/0.4 mm. The 4,5-dichloro-pyridazin-3-one used as the starting material can be prepared in a known manner by the reaction of mucochloric acid with hydrazine (for example according to K. Dury, Angew. Chemie 77, page 282 (1965)).

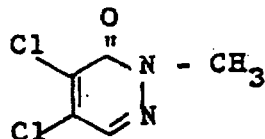
(84)

Example 2

5.1 g of N-[3-(o-ethoxyphenoxy)-2-hydroxy-propyl]-ethylene-diamine

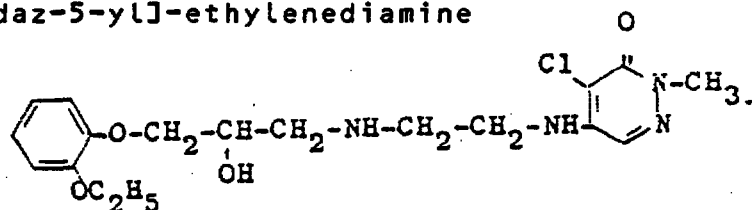


are dissolved in 50 ml of toluene, and 3 g of potassium carbonate are added to the solution. A solution of 3.6 g of 2-methyl-4,5-dichloro-pyridazin-3-one



in 50 ml of toluene is then added to the above solution at room temperature, whilst stirring, and the mixture is then heated under reflux for 17 hours, whilst stirring. The mixture is then allowed to cool to room temperature, the inorganic residue is filtered off under suction and the filtrate is concentrated in vacuo. The residual oil, which solidifies after a short time, is recrystallised from ethyl acetate.

N-[3-(o-ethoxyphenoxy)-2-hydroxy-propyl]-N'-2-methyl-3-oxo-[4-chloro-pyridaz-5-yl]-ethylenediamine



is thus obtained.

Melting point: 120°C.

Analysis: (C₁₈H₂₅ClN₄O₄)

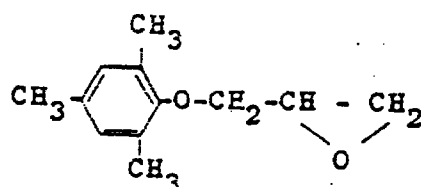
	C	H	Cl	N	O
calculated:	54.5	6.3	9.0	14.1	16.1
found:	54.7	6.3	9.1	13.8	16.4

Yield: 84% of theory.

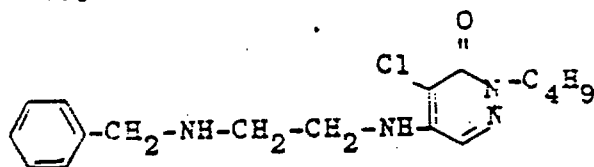
The starting materials can be prepared analogously to the processes described in Example 1.

Example 3

3.8 g of 2',4',6'-trimethyl-phenyl glycidyl ether



together with 7 g of N-benzyl-N'-[2-butyl-3-oxo-4-chloro-pyridaz-5-yl]-ethylenediamine.

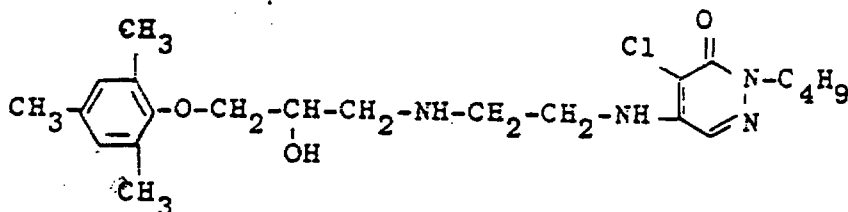


are heated under reflux in 80 ml of ethanol for 1 hour. The mixture is then cooled and the solution is concentrated in vacuo.

The residue is dissolved, without purification, in 120 ml of dioxane, and is then hydrogenated at room temperature with H_2 , in the presence of Pd/charcoal.

The mixture was (sic) then filtered under suction, the filtrate is concentrated in vacuo and the residue is recrystallised from ethanol.

N-[3-(2',4',6'-trimethylphenoxy)-2-hydroxy-propyl]-N-[2-butyl-3-oxo-4-chloro-pyridaz-5-yl]-ethylenediamine (sic)



is thus obtained.

Melting point: 137°C.

Analysis: $(C_{22}H_{33}ClN_4O_3)$

	C	H	Cl	N	O
calculated:	60.5	7.6	8.1	12.8	11.0
found:	60.2	7.4	8.3	12.7	11.3

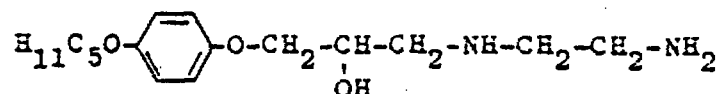
Yield: 68% of theory.

The N-benzyl-N'-[2-butyl-3-oxo-4-chloro-pyridaz-5-yl]-ethylenediamine used as the starting material can be obtained analogously to Example 2 by the reaction of 2-butyl-4,5-dichloro-pyridazin-3-one with benzylethylenediamine in boiling toluene, in the presence of 1 mol of potassium carbonate.

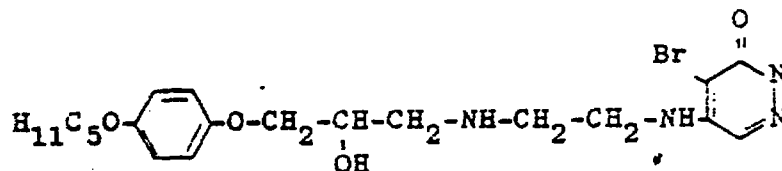
(26)

Example 4

5.85 g of N-[3-(p-pentyloxyphenoxy)-2-hydroxypropyl]-ethylene-diamine of the formula



and 5.0 g of 4,5-dibromopyridazin-3-one in 60 ml of ethanol are boiled under reflux for 10 hours. The resulting solution is then filtered and concentrated, leaving a viscous oil as residue. This oily residue is triturated with 100 ml of water and 5-10 ml of ethyl acetate, and its pH is adjusted to a value of 9.0 with aqueous 2N sodium carbonate solution. This mixture is stirred until the oil has crystallised completely, and the resulting solid product is filtered off with suction. The residue (5.4 g, corresponding to 58% of theory) is recrystallised from ethanol. 4.2 g of N-[3-(p-pentyloxyphenoxy)-2-hydroxypropyl]-N'-[3-oxy-4-bromopyridaz-5-yl]-ethylenediamine (sic) of the formula



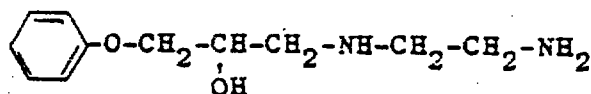
having a melting point of 173-175°C are obtained.

Analysis: C₂₀H₂₉BrN₄O₄

	C	H	N	O	Br
calculated:	51.14	6.2	11.9	13.6	17.0
found:	51.0	6.3	11.5	13.9	16.8

Example 5

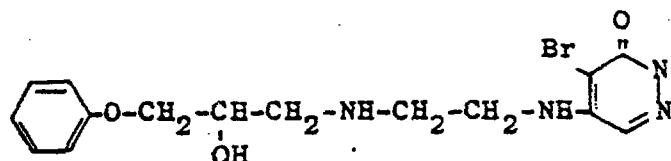
4.13 g of N-(3-phenoxy-2-hydroxypropyl)-ethylenediamine of the formula



and 5.0 g of 4,5-dibromopyrazin-3-one in 80 ml of anhydrous ethanol are boiled under reflux for 30 hours. The resulting solution is

filtered and the filtrate is evaporated. This leaves a semi-solid residue, which is triturated with 100 ml of water and 10 ml of ethyl acetate. The pH of the mixture is then adjusted to a value of 9.0 by adding aqueous 2N sodium carbonate solution, whereupon the reaction product gradually solidifies.

The solid product is filtered off with suction and recrystallised from ethanol. This gives N-(3-phenoxy-2-hydroxypropyl)-N'-[3-oxo-4-bromopyridaz-5-yl]-ethylenediamine of the formula



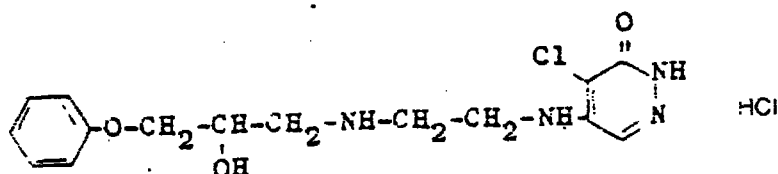
of melting point 165°C in a yield of 3.9 g, corresponding to 52% of theory.

Analysis: C₁₅H₁₉BrN₄O₃

	C	H	N	O	Br
calculated:	47.0	5.0	14.6	12.5	20.9
found:	46.8	4.7	14.6	12.9	20.8

Example 6

3.0 g of N-(3-phenoxy-2-hydroxypropyl)-N'-[4-chloro-3-oxopyridaz-5-yl]-ethylenediamine hydroxychloride (sic) of the formula



are dissolved in 100 ml of 5% strength by weight sodium hydroxide solution, and 0.3 g of 10% strength palladium/charcoal is added to the solution. Hydrogenation is then carried out at room temperature in a shaken vessel attached to a balloon containing an atmospheric pressure of hydrogen until no further consumption of hydrogen takes place, and the mixture is then allowed to stand overnight at room temperature.

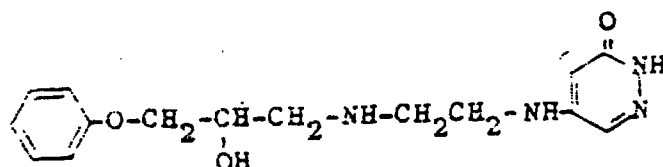
The reaction mixture thus obtained is filtered, the filter

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residue R₁ consisting essentially of the catalyst is kept and the filtrate is evaporated to dryness. The residue from evaporation is kneaded thoroughly with 50 ml of water, and the resulting suspension is filtered with suction. This gives filter residue R₂.

Filter residue R₁ is shaken thoroughly with 50 ml of ethanol, with warming, and the catalyst is filtered off from the suspension. The alcohol filtrate is evaporated, the residue from evaporation is combined with filter residue R₂, and both are recrystallised together from water. 2.0 g (approximately 82% of theory) are obtained.

N-(3-phenoxy-2-hydroxypropyl)-N'-[3-oxopyridaz-5-yl]-ethylenediamine of the formula



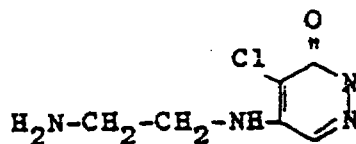
Melting point 151-153°C

Analysis: C₁₅H₂₀N₄O₃

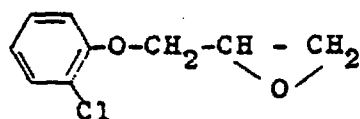
	C	H	N	O
calculated:	59.18	6.63	18.41	15.78
found:	59.1	6.2	18.4	16.0

sample 7

f N-[4-chloro-3-oxopyridaz-5-yl]-ethylenediamine of the formula



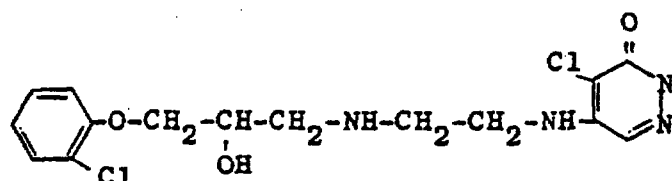
and 1.95 g of o-chlorophenyl glycidyl ether of the formula



in 20 ml of anhydrous ethanol are stirred, first for 24 hours at

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room temperature and then for a further 40 hours at the boil under a reflux condenser. The mixture is then cooled and the precipitate which has separated out is filtered off with suction. The filter residue is recrystallised again from ethanol. This gives 3.1 g (approximately 78.3% of theory) of N-[3-(o-chlorophenoxy)-2-hydroxypropyl]-N'-[4-chloro-3-oxopyridaz-5-yl]-ethylenediamine of the formula



having a melting point of 170-172°C.

Analysis: $C_{15}H_{18}Cl_2N_4O_3$

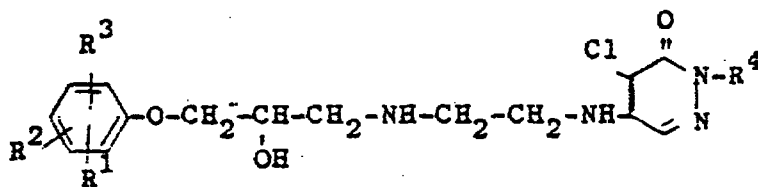
	C	H	Cl	N	O
calculated:	48.24	4.86	19.02	15.01	12.86
found:	48.3	4.8	19.2	15.5	12.6

The N-[4-chloro-3-oxopyridaz-5-yl]-ethylenediamine employed in the above example was prepared as follows:

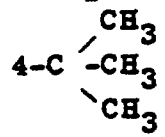
11 g of 4,5-dichloropyridazin-3-one were added to a solution of 400 g of ethylenediamine in 100 ml of absolute ethanol, and the mixture was heated at 120°C for 12 hours in an autoclave.

After cooling the resulting solution was evaporated to dryness, and the residue was recrystallised from ethanol/water. Yield: 9 g (approximately 71.6% of theory).

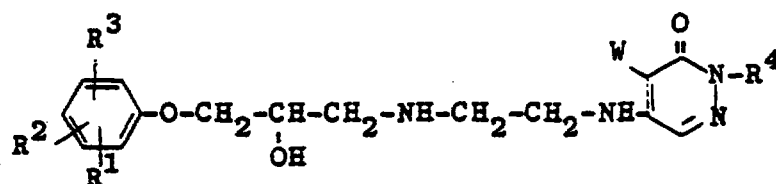
The compounds mentioned in the Table below were prepared according to Examples 1-7:



R ¹	R ²	R ³	R ⁴	Melting point
4-OC ₄ H ₉	H	H	-CH ₃	92°C
2-OC ₂ H ₅	H	H	H	185°C
				Hydro-chloride

R ¹	R ²	R ³	R ⁴	Melting point
2-OC ₂ H ₅	H	H	-C ₂ H ₅	83°C
4-OCH ₃	H	H	H	213°C Hydrochloride
4-OC ₅ H ₁₁	H	H	H	223°C Hydrochloride
2-CH ₃	H	H	H	228°C Hydrochloride
H	H	H	H	198°C Hydrochloride
4-OC ₄ H ₉	H	H	H	210°C Hydrochloride
3-OCH ₃	H	H	H	213°C Hydrochloride
3-OCH ₃	4-OCH ₃	5-OCH ₃	-CH ₃	69°C
2-OCH ₃	3-OCH ₃	4-OCH ₃	-C ₃ H ₇	199°C Hydrochloride
2- 	H	H	H	224°C Hydrochloride
2-OCH ₂ -CH-CH ₂	H	H	-CH ₃	111°C
2- 	H	H	-C ₂ H ₅	109°C
2-OCH ₃	6-OCH ₃	H	H	218°C Hydrochloride
4-NH-CO-CH ₃	H	H	-C ₃ H ₇	197°C Hydrochloride
2-O-CH ₂ -C≡CH	H	H	-CH ₃	121°C
4-NH-CO-NH ₂	H	H	H	113°C
2- 	H	H	H	68°C
4-NH-CO-N 	H	H	-C ₂ H ₅	219°C Hydrochloride
4-CH ₂ -O-CH ₃	H	H	H	117°C
4-C 	H	H	-C ₄ H ₉	71°C
2-CO-CH ₃	H	H	H	193°C Hydrochloride
2-CH ₂ -OC ₂ H ₅	H	H	-CH ₃	211°C Hydrochloride
4-NH-CO-NH-C ₂ H ₅	H	H	H	217°C Hydrochloride

R ¹	R ²	R ³	R ⁴	Melting point
4-NH-CO-NH- 	H	H	H	119°C
4-NH-CO-NH-CH ₂ -CH=CH ₂	H	H	-C ₃ H ₇	231°C Hydrochloride
2-Cl	6-Cl	H	-C ₃ H ₇	101°C
2-CH ₃	4-CH ₃	H	-CH ₃	74°C
2-CH ₃	6-CH ₃	H	H	198°C Hydrochloride
H-OC ₂ H ₄ -OC ₂ H ₅	H	H	-C ₂ H ₅	206°C Hydrochloride
4-OCH ₂ -CH ₂ -OH	H	H	-CH ₃	89°C
4-C ₂ H ₅	H	H	-C ₂ H ₅	102°C
2-OCH ₃	4-CH ₂ -CH=CH ₂	H	-CH ₃	107°C
3-CF ₃	H	H	H	216°C Hydrochloride
4-OH	H	H	-C ₂ H ₅	122°C
2-Cl	4-Cl	H	H	199°C Hydrochloride
4-O-CH ₂ - 	H	H	-C ₂ H ₅	204°C Hydrochloride
4-NO ₂	H	H	H	57°C
2-Cl	4-Cl	H	-CH ₃	87°C
4-Br	H	H	-C ₂ H ₅	223°C Hydrochloride
2-H	H	H	H	196°C Hydrochloride
2-CH ₃	4-NO ₂	H	H	112°C
3-CH ₂	4-Cl	H	-C ₄ H ₉	208°C Hydrochloride
2-CH ₂ -C=CH	H	H	-C ₂ H ₅	74°C
2-CH ₂	3-CH ₃	5-CH ₃	-C ₃ H ₇	121°C



R ¹	R ²	R ³	R ⁴	W	Melting point
4-OC ₄ H ₉	H	H	H	Br	221°C Hydrochloride
2-O-CH ₂ -CH=CH ₂	H	H	H	Br	166°C Hydrochloride

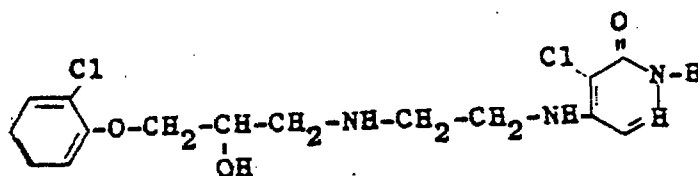
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R ¹	R ²	R ³	R ⁴	R ⁵	Melting point
4-NH-CO-N ₂ O	H	H	H	Br	208°C Hydrochloride
2-O-CH ₂ -C≡CH	H	H	H	Br	188°C Hydrochloride
2-CH ₃	4-CH ₃	H	CH ₃	Br	87°C
2-Cl	H	H	H	Br	159°C
3-OCH ₃	H	H	H	Br	162°C
2-OC ₂ H ₅	H	H	H	Br	200°C Hydrochloride
2-Cl	H	H	H	H	143°C
3-CH ₃ O	H	H	H	H	149°C
2-OC ₂ H ₅	4-Cl	H	H	H	168°C
2-O-CH ₂ -CH-CH ₂	4-OCH ₃	H	H	H	154°C

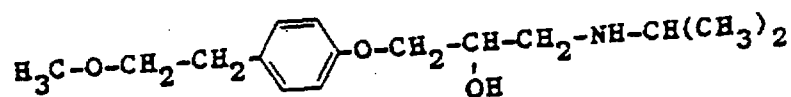
The substantial technical superiority of the compounds according to the invention compared with a typical representative of known commercial products having the same direction of action and similar chemical structure, namely metoprolol, can be seen from the following comparative pharmacological data.

The structures of the compounds compared are:

1. According to the invention



2. Metoprolol:



1. Action on the circulation of narcotised dogs.

1.1 -Receptor blockade

On dogs anaesthetised with pentobarbital, the compound accor-

ding to the invention inhibits the increase, due to isoprenaline, in contractility and heart rate at an ED₅₀ of 0.003 mg/kg, administered intravenously, whereas the corresponding figure for metoprolol is 0.14 mg/kg. for metoprolol is 0.14 mg/kg (sic). The compound according to the invention is, accordingly, approximately 40 times more effective on the heart than metoprolol (and 11 times more powerful than propranolol).

The comparison of the inhibition of the cardiac β -receptors with that of the blood vessels, ED₅₀(heart):ED₅₀(vessel), which can be regarded as a criterion of cardioselectivity, gave a ratio of 1:76 for the compound according to the invention and a ratio of 1:18 for metoprolol. Accordingly, the compound according to the invention has a markedly more cardioselective action.

1.2. Haemodynamics

The haemodynamic profile of action of the compound according to the invention on dogs anaesthetised with pentobarbital is characterised by a pronounced fall in the blood pressure (-35 mm Hg at 0.05 mg/kg, administered intravenously, metoprolol -5 mm Hg), in the left ventricular end-diastolic pressure (LVEDP -2 mm Hg, metoprolol +2mm Hg) and in the total peripheral resistance (TPR -1,191 dyn. sec. cm⁻⁵, metoprolol -135 dyn. sec. cm⁻⁵) without being accompanied by a reduction in the contractility of the heart, which is present in a pronounced manner with metoprolol, particularly at fairly high doses.

A reduction in the contractility and cardiac output is prevented, in the case of the compound according to the invention, by a moderate intrinsic sympathomimetic activity (ISA), which is about 1/3 of that of pindolol.

The compound according to the invention thus has a more advantageous haemodynamic profile of action than metoprolol, since, on the one hand, it reduces the afterload on the heart via a reduction in the TPR and, on the other hand, also reduces the preload on the heart, without having a negative inotropic action.

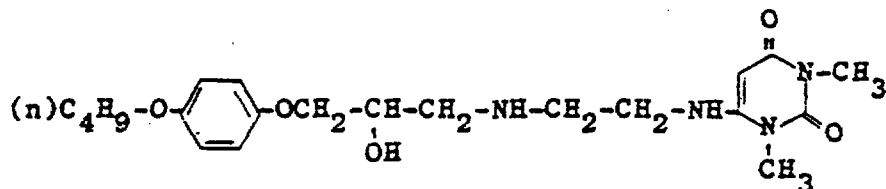
2. Action on conscious, renal-hypertensive dogs

In a dose of 3.0 mg/kg, administered orally, metoprolol has virtually no acute hypotensive action on conscious, renal-hypertensive dogs (Δ BD_s - 6 mm Hg, Δ BD_d - 3 mm Hg), whereas the compound according to the invention, even in a dose of 0.2 mg/kg

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administered orally, reduces the systolic blood pressure by -28 mm Hg and the diastolic blood pressure by -15 mm Hg.

The data of pharmacological action which can be seen in the following Table are obtained for further compounds according to the invention and for a structurally comparable compound, known from DE-A (German Auslegeschrift) 2,819,629, of the formula



by testing in an analogous manner:

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R ¹	R ²	R ³	R ⁴	X	β_1 -Blockade ED ₅₀ mg/kg	Cardio- selectivity $\frac{ED_{50} \text{ Heart}}{ED_{50} \text{ Vessel}}$	LVEDP Dose mg/kg/ Δ p [mbar]	TPR Dose / $\left[\frac{\text{dyn cm}}{\text{sec}^5} \right]$
2-Cl	H	H	H	Cl	0.05 i.d. 0.003 i.d.	$\frac{1}{76}$	0.05 i.v. -2.7	0.05 -1191
2-OC ₄ H ₉	H	H	H	Cl	0.008 i.v.	$\frac{1}{30}$	0.05 i.v. -1.3	0.05 - 530
2-OC ₄ H ₉	H	H	-CH ₃	Cl	0.007 i.v.	$\frac{1}{30}$	0.05 i.v. - 2	0.05 - 620
2-Cl	H	H	H	Br	0.0008 i.v. 0.0023 i.v.	$\frac{1}{81}$ $\frac{1}{127}$		
2-OC ₂ H ₅	H	H	H	Br	0.0049 i.v.	$\frac{1}{20}$		
H	H	H	H	Br	0.0009 i.v.	$\frac{1}{743}$	0.05 -5.33	
H	H	H	H	H	0.009 i.v.	$\frac{1}{4}$		
Metoprolol					0.3 i.d. 0.14 i.v.	$\frac{1}{18}$	+2.7	0.05 - 135
Compound known from DE-A 2,819,629					0.0096 i.v.		4.0 i.v. 0	0.05 0

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R ¹	R ²	R ³	R ⁴	X	Blood pressure				ISA	Inhibition of k-strophanthin arrhythmias
					Dose mg/kg		ΔP_s	ΔP_d [mbar]		
2-Cl	H	H	H	Cl	0,2	p.o.	-37	-20	$\frac{1}{3}$	+
2-OC ₄ H ₉	H	H	H	Cl	1	p.o.	-53	-40		+
2-OC ₄ H ₉	H	H	-CH ₃	Cl	0.1	p.o.	-33.3	-26.7		+
2-Cl	H	H	H	Br	0,01	i.v.	-20	-20	$\frac{1}{3}$ $\frac{1}{3}$ -	
2-OC ₂ H ₅	H	H	H	Br	0,001	i.v.	-40	-6.7		
H	H	H	H	Br	0,5	i.v.	-100	-66.7		
					0.025	i.v.	-40	-33.3		
					0.064	i.v.	-53.3	-40		
H	H	H	H	H	0,04	i.v.	-33.3	-20		
					0,01	i.v.	-26.7	-20		
					0.004	i.v.	-33.3	-26.7		
Metoprolol					3.0		0	0	0	0
Compound known from DE-A 2,819,629					4,0	i.v.	0	0	0	0

Explanatory notes:

i.v. = intravenous i.d. = intraduodenal

p.o. = per os, oral ED = effective dose

The figures of intrinsic sympathomimetic activity (ISA) indicated in the above Table are quoted relative to pindolol, which is taken as the standard.

The pharmacological figures show that the compounds according to the invention are distinguished, compared with the most comparable known compound, by a particularly balanced spectrum of action. As well as the effectiveness in respect of β_1 -blockade, which is improved by at least 100% compared with the compounds known from DE-A (German Auslegeschrift) 2,819,629, it is the favourable, acute hypotensive action and, in particular, the very balanced intrinsic sympathomimetic activity (ISA), which, on the one hand, prevents a reduction in the contractility, but, on the other hand, does not at this point result in an undesirable increase in the heart rate, which make the use of the compounds according to the invention appear particularly advantageous.

A further advantage of the compounds according to the invention, particularly compared with those known from DE-A (German Auslegeschrift) 2,819,629, is their improved tissue tolerance. As a result of this, local symptoms of irritation are largely prevented, for example in the case of intravenous administration.

By virtue of the advantageous combination of effects mentioned, the compounds according to the invention are particularly suitable for the therapy and prophylaxis of myocardial infarction.

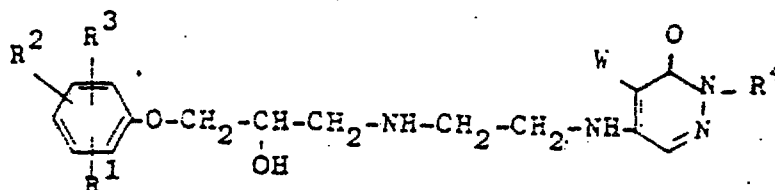
The daily dose for adults is in this case within the range of 5-30 ml as an individual dose or distributed over 2-3 individual doses.

Administration is preferably effected perorally or intravenously.



Claims

1. Pyridazines, containing basic substituents, of the general formula I:



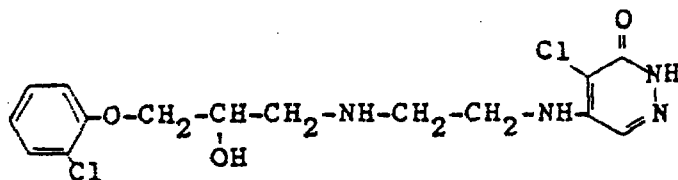
wherein R^1 , R^2 and R^3 independently of one another denote hydrogen, fluorine, chlorine, bromine, hydroxyl, nitro, trifluoromethyl, alkyl having 1 to 8 C atoms, alkoxyalkyl having 2 to 6 C atoms, alkenyl having up to 6 C atoms, alkynyl having up to 6 C atoms, cycloalkyl having a ring size of from 5 to 8 C atoms, cycloalkenyl having a ring size of from 5 to 8 C atoms, phenyl, alkoxy having 1 to 8 C atoms, hydroxyalkoxy having 2 to 6 C atoms, alkoxy-alkoxy having a total of up to 8 C atoms, alkenyloxy having up to 6 C atoms, alkynyloxy having up to 6 C atoms, cycloalkoxy having a ring size of from 5 to 8 C atoms, benzyloxy, phenethyloxy, alkanoyl having 1 to 6 C atoms, acylamino having up to 11 C atoms in the acyl radical, an $-NH-CO-R^9$ radical, R^9 representing morpholino, piperidino or 1-pyrrolidinyl, ureido, ureido which is monosubstituted in the 3-position by cycloalkyl having 5 or 6 C atoms, ureido which is monosubstituted or disubstituted in the 3-position by alkyl having 1 to 6 C atoms and/or alkenyl having 3 to 6 C atoms, R^4 denotes hydrogen or alkyl having 1 to 4 C atoms and W denotes hydrogen, chlorine or bromine and acid addition salts thereof.

2. Compounds of Claim 1, characterised in that only one of the substituents R^1 , R^2 or R^3 is not hydrogen.

3. Compounds of Claims 1 to 2, characterised in that R^4 is hydrogen.

4. Compounds of Claims 1 to 3, characterised in that one of the substituents R^1 , R^2 and R^3 denotes halogen and the other two denote hydrogen.

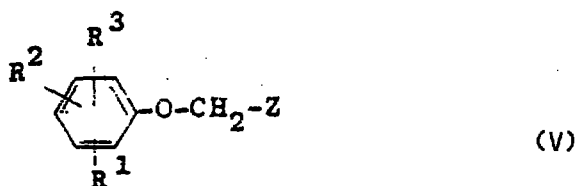
5. The compound of the formula



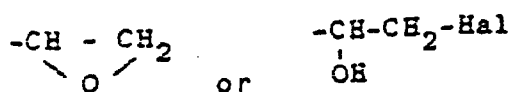
and pharmaceutically acceptable acid addition salts thereof.

6. Process for the preparation of pyridazines, containing basic substituents, of the general formula I according to Claim 1, characterised in that

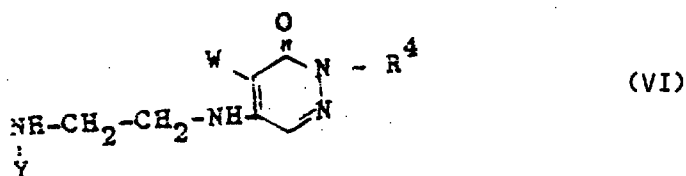
a) a compound of the general formula V



wherein Z represents



and Hal denotes halogen, is reacted with a compound of the general formula IV

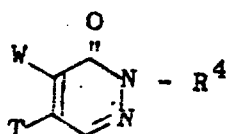


wherein R¹, R², R³, R⁴ and W have the abovementioned meanings and Y is hydrogen or a radical capable of being hydrogenolytically split off, and a radical Y which can be split off hydrogenolytically is split off by hydrogenolysis from the compound obtained, and the compound obtained is, if appropriate, reacted with an acid to give an acid addition salt, or

b) a compound of the general formula VI

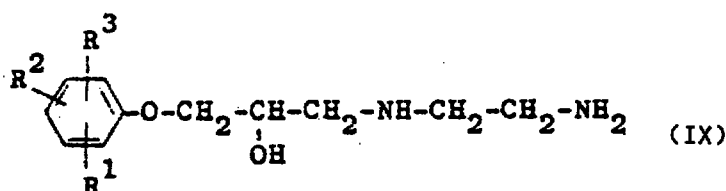


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(VI)

wherein R^4 and W have the abovementioned meanings and T is chlorine or bromine, is reacted with a compound of the general formula IX

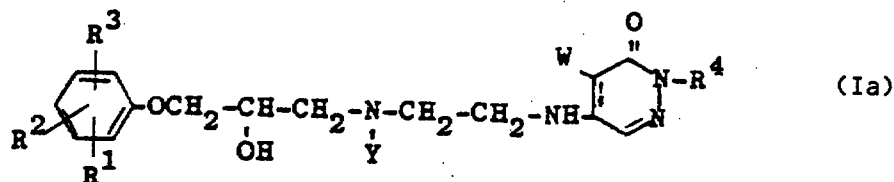


(IX)

wherein R^1 , R^2 and R^3 have the abovementioned meanings, and the compound obtained is, if appropriate, reacted with an acid to give an acid addition salt.

7. Process of Claim 6, characterised in that W is chlorine or bromine.

8. Process for the preparation of pyridazines, containing basic substituents, of the general formula I wherein W is hydrogen and R^1 , R^2 , R^3 and R^4 have the meanings indicated in Claim 1, characterised in that a pyridazine, containing basic substituents, of the general formula Ia



(Ia)

wherein R^1 , R^2 , R^3 and R^4 have the meanings indicated in Claim 1 and W is chlorine or bromine and Y is hydrogen or a radical which can be split off hydrogenolytically, is hydrogenated with hydrogen in a manner known per se in a solvent or dispersing agent and in the presence of a hydrogenation catalyst.



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9. Process of Claim 8, characterised in that a compound of formula Ia in which Y is hydrogen is employed.
10. Pharmaceutical preparation containing an effective dose of a pyridazine, containing basic substituents, of the general formula I or an acid addition salt thereof, prepared according to one of Claims 3 to 9, in addition to pharmaceutically permissible excipients and additives.
11. Pharmaceutical preparation of Claim 10, additionally containing one or several other pharmaceutically effective substances.