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# PATENT SPECIFICATION

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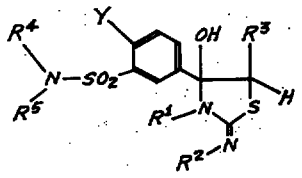
(19)

## (54) THIAZOLIDINE DERIVATIVES AND PROCESS FOR THEIR MANUFACTURE

(71) We, HOECHST AKTIENGESELLSCHAFT, a body corporate organised according to the laws of the Federal Republic of Germany, of 6230 Frankfurt/Main 80, Postfach 80 03 20, Federal Republic of 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 thiazolidine derivatives and a process for their manufacture.

The thiazolidine derivatives of the invention have the general formula I




(I)

in which

$R^1$ stands for an alkyl or alkenyl radical having up to 4 carbon atoms, a cycloalkyl radical having from 3 to 6 carbon atoms, or a dialkylamino group having a total of 7 carbon atoms, which may form together with the nitrogen atom of the amino group a saturated heterocyclic ring;

$R^2$ stands for an alkyl, alkenyl, or alkynyl radical having up to 8 carbon atoms which may be substituted by one or more alkoxy groups having from 1 to 4 carbon atoms; a cycloalkyl radical having from 3 to 8 carbon atoms; a phenylalkyl radical having 1 or 2 carbon atoms in the alkyl moiety, which may be substituted in the phenyl ring by one or more substituents, which may be the same or different, selected from halogen atoms, alkyl and alkoxy groups having up to 4 carbon atoms, and alkylenedioxy groups; or

$R^2$ stands for an alkyl group having 1 or 2 carbon atoms which is substituted by a cycloalkyl radical having from 3 to 6 carbon atoms or by a 5- or 6-membered saturated or unsaturated heterocyclic radical containing one or more heteroatoms selected from oxygen, nitrogen and sulfur atoms; or

$R^2$ stands for a dialkylamino group having a total of up to 7 carbon atoms, which may form together with the nitrogen atom of the amino group a saturated heterocyclic ring; or

$R^1$ and $R^2$ together stand for an alkylene group having from 2 to 4 carbon atoms;

$R^3$ stands for a hydrogen atom or an alkyl group having 1 or 2 carbon atoms;

$R^4$ and $R^5$ are identical or different, and each stands for a hydrogen atom; an alkyl or alkenyl radical having up to 6 carbon atoms, which may be substituted by one or more alkoxy groups having 1 to 4 carbon atoms; a cycloalkyl or cycloalkylalkyl group having a total of 3 to 9 carbon atoms; a phenyl group or a phenylalkyl group having 1 to 3 carbon atoms in the alkyl moiety, the phenyl ring optionally being substituted by one or more substituents, which may be the same or different, selected from halogen atoms, alkyl and alkoxy groups having up to 4 carbon atoms, and alkylenedioxy groups; or stands for an alkyl group having 1 or 2 carbon atoms which is substituted by a 5- or 6-membered unsaturated heterocyclic radical containing one or more hetero-atoms selected from oxygen, nitrogen and sulfur atoms; or

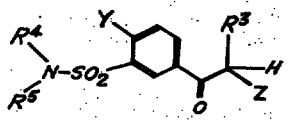
$R^4$ and $R^5$ together with the nitrogen atom form a saturated, optionally methyl-substituted, 5- or 6-membered heterocyclic ring, in which optionally a $-CH_2-$ group may be replaced by an oxygen atom; and

Y stands for a hydrogen or halogen atom or a methyl or trifluoromethyl group.

This invention also provides the acid addition salts of the compounds of formula I, especially the physiologically tolerable acid addition salts.

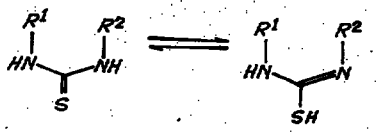
The invention also provides a process for the manufacture of a compound of the general formula I, which comprises

(a) reacting a compound of the general formula II



(II)

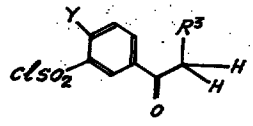
in which $R^3$, $R^4$, $R^5$ and Y are defined as above and Z stands for the radical of an activated ester of an inorganic or organic acid, with a thiourea of the general formula III, which can be represented by formulae IIIa and IIIb



(IIIa) (IIIb)

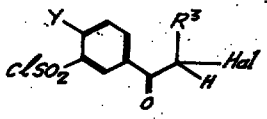
in which $R^1$ and $R^2$ are defined as above or

(b) treating a compound of the general formula IV



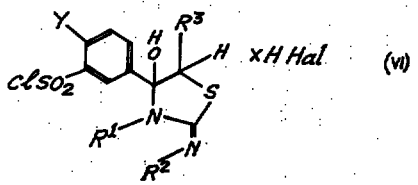
(IV)

in which $R^3$ and Y are defined as above, with a halogenating agent and reacting the $\alpha$-halogen ketone of the general formula V



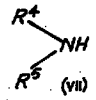
(V)

thus obtained in which $R^3$ and Y are defined as above and Hal stands for a chlorine or bromine atom, if desired without isolation or purification, with a thiourea of the formula III and reacting the thiazolidine derivative thus obtained of the general formula VI



(VI)

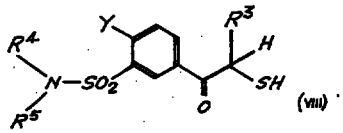
in which $R^1$, $R^2$ and $R^3$ are defined as above, with ammonia, a primary or secondary amine of the general formula VII



(VII)

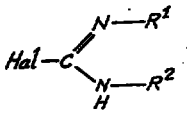
in which $R^4$ and $R^5$ are defined as above or

(c) reacting a compound of the general formula VIII



(VIII)

with a compound of the formula IX



(IX)

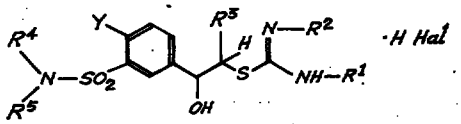
in which $R^1$, $R^2$, $R^3$ and Y are defined as above, Hal stands for a chlorine or bromine atom,

(d) reacting a compound of the formula VIII with a carbodiimide of formula X

$$R^1—N=C=N—R^2 \qquad (X)$$

in which $R^1$ and $R^2$ are defined as above

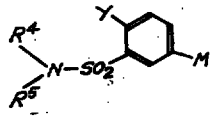
(e) treating a compound of the general formula XI



(XI)

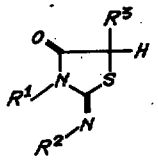
in which $R^1$, $R^2$, $R^3$, $R^4$ and $R^5$ and Y are defined as above and Hal stands for a chlorine or bromine atom with an oxidation agent or

(f) reacting a compound of the general formula XII



(XII)

in which $R^4$ and $R^5$ and Y are defined as above but $R^4$ and $R^5$ do not stand for hydrogen atoms and Y does not stand for a bromine or iodine atom and M stands for lithium or a MgBr-group, with a compound of the general formula XIII



(XIII)

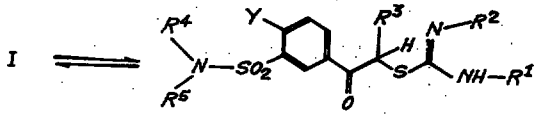
in which $R^1$, $R^2$ and $R^3$ are defined as above and hydrolizing the reaction product obtained

and, if desired, converting the compounds of the general formula I obtained according to any one of methods a) to f) in which $R^4$ and/or $R^5$ stands for a hydrogen atom, by alkylation into the corresponding compound in which $R^4$ and/or $R^5$ has one of

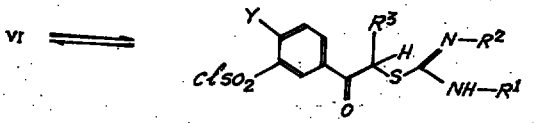
the other definitions given hereinbefore and/or converting the compound of the formula I, prepared according to any one of the methods indicated under a) to f), with an organic or inorganic acid into an acid addition salt thereof, or converting a salt of a compound of the general formula I with a base into the corresponding free basic compound of the formula I.

Suitable organic acids are, for example: formic acid, acetic acid, benzoic acid, succinic acid, fumaric acid, maleic acid, lactic acid, tartaric acid, citric acid, salicylic acid, oxyethanesulfonic acid, ethylenediamine- tetra-acetic acid, methanesulfonic acid, and *p*-toluenesulfonic acid.

Compounds I and VI can also be in their tautomeric forms, which are:



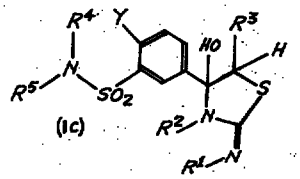
(Ia)



(VIa)

The compounds of the invention of the formula I can also be in their possible geometrical isomeric structures. The alkyl or alkenyl radicals in the substituents $R^1$ to $R^5$ can be not only straight-chained but also branched

The cyclic compounds of the formula I are in equilibrium with the positional isomeric compounds of the formula Ic and the acid addition salts thereof of the formula Ic



(Ic)

via the open-chained tautomeric form Ia, if the radicals $R^1$ and $R^2$ are different. Which of the two cyclic isomers I or Ic or the acid addition salts thereof is predominant depends especially on the different volume of the substituents $R^1$ or $R^2$ in such a way that the substituent having the smaller volume is preferably in the 3-position of the thiazolidine ring system. For the compounds of the invention, only one of the possible isomeric or tautomeric forms of a substance is indicated for the sake of simplicity in the following text.

Method a) is advantageously performed by reacting the compound II with the thiourea III in a molar ratio of 1:1 to 1:1.5. The use of a larger molar excess of the thiourea is possible but is generally without notable advantages. The reaction is advantageously carried out in an inert solvent or diluent, for example, in a polar organic solvent or diluent, for example, dimethyl formamide, dimethyl acetamide, dioxane, tetrahydrofuran, acetonitrile, nitromethane, or diethylene glycoldimethyl ether. However, especially advantageous solvents and diluents (called hereinafter "solvents") proved to be lower alkyl acetates, for example, methyl- and ethyl acetate; lower alcohols, especially methanol, ethanol, and isopropanol; and lower dialkyl ketones, for example acetone and methyl-ethyl-ketone, as well as mixtures of any two or more solvents, especially mixtures of the above solvents but also mixtures of the above solvents with less preferred solvents, for example methanol/benzene, ethanol/toluene, methanol/diethyl ether, ethanol/carbon tetrachloride, acetone/chloroform, with the more polar solvent advantageously being in excess. The reactants may be suspensed or dissolved in the respective solvent. In principle, the reactants may also be reacted without the use of a solvent or diluent, especially when the thiourea concerned melts at a low temperature. Due to the exothermic course of the reaction, however, side reactions may occur, so that this embodiment of the reaction has no advantages over the operational method in solvents. The reaction is moderately exothermic and may be carried out at a temperature of from 0° to 100°C, preferably from 10° to 70°C, and with special advantage from 20° to 55°C.

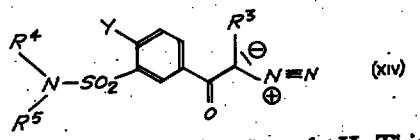
The reaction period largely depends on the reaction temperature and is generally in the range of 2 minutes at elevated temperatures to 60 hours at lower temperatures. In general, the reaction takes from 5 minutes to 40 hours in the favourable temperature range.

In many cases, the resulting compound I precipitates in the form of an acid addition salt in the course of the reaction if they are sparingly soluble. Optionally, the addition of a suitable precipitating agent at or towards the end of the reaction may increase the yield, the precipitating agent being, for example, a hydrocarbon, for example, benzene, toluene, cyclohexane, petroleum ether, ligroin, or carbon tetrachloride, especially an alkyl acetates of 1 to 4 carbon atoms in the alkyl portion, for example, ethyl acetate, butyl acetate or a diaikyl ether of 4—8 carbon atoms, for example diethyl ether, di-isopropyl ether or di-*n*-butyl ether. When the reacted compounds are in solution form, a salts of the compound I is advantageously precipitated, optionally after concentrating the reaction solution, with one of the precipitating agents mentioned above, or the solution is advantageously introduced, while filtering and stirring, into one of the precipitating agents mentioned above to eliminate inhomogeneous impurities. Since the yield of the reaction of a compound II with a thiourea III is practically quantitative when performed under optimal conditions, the crude products obtained of the compounds desired are mostly pure as per analysis.

The thioureas III used are mostly substances that are described in literature. They may be prepared in known manner by reacting an amine with an isothiocyanate, carbon disulfide or thiophosgene (cf. Houben-Weyl, "Methoden der organischen Chemie" vol. 9, page 884, 4th edition, Georg-Thieme-Verlag Stuttgart, 1955).

The compounds of the formula II contain as radical of an activated ester Z for example, Cl, Br, I, —O—CO—$C_6H_4$—$NO_2$, $CH_3$—$SO_2$—O—, $C_2H_5$—$SO_2$—O, $C_6H_5$—$SO_2$—O—, $CH_3C_6H_4$—$SO_2$—O—. They can be obtained according to various methods:

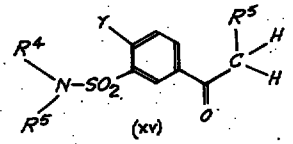
A diazo ketone of the general formula XIV



(XIV)

can be converted with an acid into a ketone of the formula II. This method, as well as a number of compounds II and XIV, are known in the literature (cf. Swiss Patent Specification No. 389 591 and Belgian Patent Specification No. 610 633) and the other compounds of the formulae II and XIV can be prepared and reacted accordingly.

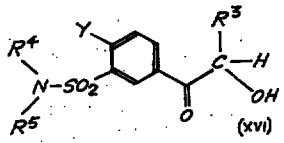
Since diazo alkanes are highly toxic, explosive and difficult to handle, the compounds of the formula II in which $R^3$, $R^4$, $R^5$ and Y are defined as above and Z stands for a chlorine or bromine atom are advantageously prepared by reacting a compound of the general formula XV



(XV)

with a suitable halogenating agent, for example elementary chlorine or bromine, sulfuryl chloride, monochlorourea, copper-II-bromide, bromodioxane, or N-bromosuccinimide, under conditions known in the literature. The easily accessible compounds XV in which Y stands for a chlorine atom, $R^3$ is a hydrogen atom or a methyl or ethyl group and $R^4$ and $R^5$ each stands for a hydrogen atom are known (E. Jucker, A. Lindenmann, E. Schenker, E. Flückinger and M. Taeschler, Arzneimittel-Forsch. *13*, 269 (1963)). The other compounds of the formula XV either may be prepared in an analogous manner or may be produced from the corresponding compound of the formula XV in which $R^4$ and $R^5$ each stands for a hydrogen atom, by means of an alkylation agent into other compounds of the formula XV.

A compound of the formula II may also be prepared by reacting an $\alpha$-hydroxyketone of the general formula XVI



(XVI)

known from Swiss Patent Specification No. 389 591 or correspondingly substituted compounds that can be prepared in an analogous manner, under known conditions with an organic or inorganic acid or an activated derivative thereof, for example, methanesulfonic acid chloride, ethane sulfonic acid chloride, benzenesulfonic acid chloride, *p*-toluenesulfonic acid chloride, thionyl bromide, phosphorous trichloride, phosphorous tribromide, phosphorous oxide chloride, or *p*-nitrobenzoyl chloride.

The hydroxyketones in which $R^4$ is H, $R^3$ and $R^5$ each represents a hydrogen atom or a lower alkyl group, Y is a hydrogen or halogen atom or a trifluoromethyl, lower alkyl or alkoxy group, are known in the literature (cf. Swiss Patent Specification No. 389 591).

According to the method described under b) a sulfochloride of the general formula IV is reacted with a halogenating agent, for example elementary chlorine, sulfuryl chloride, monochloro urea, bromodioxane, N-bromosuccinimide, especially, however, with elementary bromine preferably or with copper-II-bromide. Compound IV is halogenated with bromine by adding dropwise undilute or dilute bromine to a solution or suspension of the equimolar amount of compound IV in an inert solvent, for example a halogenated hydrocarbon, for example, chloroform or methylene chloride, in acetic acid, preferably, however, in a lower alkyl acetate, for example, methyl acetate, ethyl acetate, n-butyl acetate or in a mixture of these solvents, at 0° to 50°C, preferably at 10° to 35°C. Since halogenating reactions of the ketone are catalyzed by acids, the reaction solution is preferably inoculated either *a priori* with a catalytic amount of an acid, advantageously hydrobromic acid, or the protons required for reaction are produced after adding dropwise a small amount of bromine and subsequent heating the reaction mixture until the halogen has decolored, which can be done by briefly increasing the temperature range. Suitable diluents for the bromine to be added dropwise are the inert solvents mentioned or mixtures thereof. The compounds IV in which $R^3$ is defined as above and Y stands for a chlorine atom are known in the literature.

A compound IV may be brominated with copper-II-chloride according to the method described in J. Org. Chem. *29*, 3459, (1964) the ketone IV being boiled with 2 mols of powdered copper-II-bromide in water-free or alcohol-free ethyl acetate or a mixture of ethyl acetate and chloroform until the dark colour of the copper-II-bromide has disappeared and colorless copper-I-bromide has precipitated instead. The copper-I-bromide can subsequently be separated by filtration.

The chlorinating agent is especially sulfuryl chloride, which can be reacted with a solution or a suspension of the compound IV in a suitable solvent, preferably a halogenated hydrocarbon, for example chloroform or carbon tetrachloride. The reaction is carried out preferably at a temperature of from 10° to 100°C, advantageously from 20° to 80°C. The reaction generally takes 5 to 30 hours. Hydrolysis follows optionally after concentrating the reaction mixture with ice water, and the organic phases are worked up.

The solution or suspension obtained according to the corresponding methods are advantageously evaporated under reduced pressure and the compound V obtained as a residue may be purified by crystallization from an inert solvent, for example benzene, toluene, carbon tetrachloride, cyclohexane, or petroleum ether. However, it is more advantageous to react the compound V so obtained without further purification in a suitable inert solvent with an equimolar amount of the thiourea III to yield the compound of the general formula VI. When the halogenated ketone V is reacted with the thiourea III without prior isolation, the amount of the thiourea III to be used is calculated on the ketone IV. The use of 1.5 mols of thiourea can lead to higher yields of compounds VI whereas the use of greater excesses of compound III has no notable advantages. Suitable inert solvents are, for example, dimethyl formamide and dimethyl acetamide, dioxane, tetrahydrofuran, acetonitrile, nitromethane, and diethylene-glycol-dimethyl ether and others, especially suitable solvents being lower alkyl acetates, for example methyl, ethyl and n-butyl acetate, as well as lower dialkyl ketones, for example acetone and methyl-ethyl ketone, as well as mixtures of these solvents. The reaction is moderately exothermic and is generally effected at 0° to 60°C, preferably at 20° to 40°C. The reaction times are especially dependent on the reaction temperature used and are generally within the range of from 5 minutes to 40 hours.

The thiazolidine of the formula VI generally precipitates in the course of the reaction as a sparingly soluble substance and at the end of the reaction, optionally after concentration, the yield of compound VI can be improved by adding a suitable precipitating agent. Suitable precipitating agents are the solvents used in the operational method a) for the same purposes. When the reaction yields a solution, the compound of the formula VI is advantageously precipitated, optionally after concentration of the reaction mixture, with one of the precipitating agents mentioned or it is advantageously intro-

duced into the corresponding precipitating agent while filtering and stirring. The compounds of the formula VI prepared according to this method are generally distinguished by a high purity, however, should they need to be purified, they can be recrystallized from an inert, suitable solvent free from water and alcohol, if possible, for example acetone, methyl-ethyl ketone, acetonitrile, or nitromethane. However, reprecipitation is especially advantageous to avoid a heavy thermal charge of compounds VI. For this purpose, the crude product of the formula VI is dissolved in a pure and inert solvent, for example in dimethyl formamide, dimethyl acetamide, acetone, acetonitrile, or nitromethane at a temperature within the range of from 0° to 30°C, the solution is treated optionally with active charcoal and the compounds are precipitated after filtration with one of the precipitating agents mentioned.

The reaction of the halogen ketone V with the thiourea III to yield the thiazolidine VI is surprising inasmuch as, on the one hand, the thiourea III specifically reacts with the bromoketone radical in compound V without the chlorosulfonyl grouping being attacked and on the other hand, the sulfochloride moiety of compounds V and VI does not react with the hydroxy group of compounds VI despite the presence of the thiourea III, which reacts as a weak base.

Now, the sulfonic acid chloride so obtained of the general formula VI is reacted with ammonia or an amine of the formula VII to yield a compound of the formula I. For this reaction, an aqueous solution of ammonia or of the amine VII, or liquid ammonia or a pure amine can be used in excess, the excess amount of ammonia or amine acting as solvent. The reaction may also be effected in an organic solvent, for example dimethyl formamide, dimethyl acetamide, dimethyl sulfoxide, dioxane, tetrahydrofuran, or diethyleneglycol dimethyl ether. Alcohols of 1—4 carbon atoms, for example methanol, ethanol or isopropanol, are especially suitable. Theoretically, the conversion of the sulfochloride VI to the sulfonamide I requires 1 mol of ammonia or amine VII in the presence of 2 mols of an auxiliary base. For this reason, at least 3 mols of ammonia or amine VII, preferably 3 to 7 mols are preferably used per mol of sulfochloride VI, however, greater excesses of VII can be used. Only one or two mols of ammonia or amine VII need be used if an auxiliary base is present, about 1—6 mols equivalent of auxiliary base generally being used. Suitable auxiliary bases are inorganic and organic hydroxides, carbonates and hydrogen carbonates, and salt solutions of weak inorganic and organic acids, tertiary amines, for example triethyl amine, tri-*n*-butyl amine, methyl-dicyclohexyl amine, ethyl-dicyclohexyl amine being especially advantageous in all cases. When used in excess, the tertiary amine can also serve as a reactant without adding a solvent. The reaction is exothermic, so cooling is advantageous and working is preferably carried out at temperatures within the range of from −35° to +60°C, preferably from +10° to +35°C. The reaction time in general should last 30 minutes at least and the reaction can be interrupted after two days at the latest, longer reaction times not being more advantageous. A reaction time of 6 to 20 hours is preferred. The reaction products are worked up advantageously by diluting with water, optionally after distilling off the amine and concentrating the reaction mixture, the compounds I being precipitated as sparingly soluble substances. When in the compound I so prepared $R^4$ or $R^5$ is hydrogen, the pH should be adjusted to 7.5—8.5, if possible. Immediately after precipitating with water, the compound I generally separates in the form of viscous oil that crystallizes more or less rapidly when the substituents $R^1$ and $R^2$ have a small volume. Crystallization can be accelerated by treatment several times with a suitable solvent, for example water, ether, diisopropyl ether, carbon tetrachloride, petroleum ether, or n-butyl acetate.

After precipitation with water, the compound I can be extracted with a suitable solvent, preferably a lower alkyl acetate, for example methyl or ethyl acetate. After drying the extract over a suitable drying agent, for example sodium or magnesium sulfate, the compound I is preferably obtained by evaporating the solution under reduced pressure.

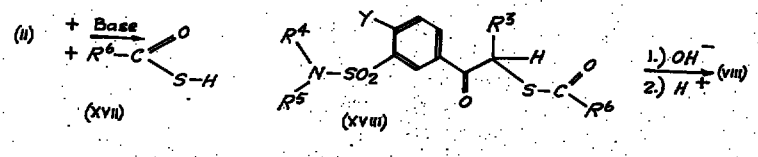
The compound I can also be converted to the corresponding acid addition product without further isolation and purification by treating with a protonic acid H—Z.

According to method c) a compound of the formula VIII is reacted in a solvent with a compound of the formula IX. Suitable solvents are alcohols having 1—4 carbon atoms and alkyl acetates with 1—4 carbon atoms in the alkyl part, for example, methyl and etyhl acetate.

The reaction is generally performed within a temperature range of from 0° to 60°C, preferably 15° to 35°C and with a reaction time of 5 to 60 hours. Especially suitable are compounds VIII that carry on the sulfamoyl group a hydrogen atom as $R^4$ and a voluminous organic radical $R^5$, for example cyclooctyl or tertiary butyl radical, or in which $R^4$ and $R^5$ each represent an organic radical.

Method d) is generally performed by reacting the mercapto ketone of the formula VIII in an anhydrous, polar, inert solvent, for example dioxane, tetrahydrofuran, methyl acetate or ethyl acetate, with the carbodiimide of the formula X in the molar ratio of 1:1. The preferred meanings of $R^4$ and $R^5$ in the compound of the formula VIII are the same as in method c). The reaction may be performed in a range of temperature of from 0° to 40°C, preferably from 10° to 30°C and with a reaction time of 1 to 20 hours.

The compound of the formula VIII used in methods c) and d) can be obtained by any one of various methods, for example, by converting a compound of the formula II with a thiocarboxylic acid of the formula XVII

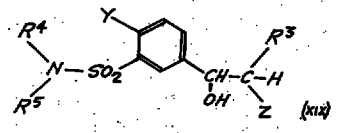


preferably with thioacetic acid ($R^6 = CH_3$) in the presence of an equivalent of a base, for example KOH, in an aqueous or alcoholic medium into a thioester of the general formula XVIII, that is then hydrolyzed in a slightly alkaline medium to give the compound of the formula VIII.

It is also possible to react a compound II with an alkali metal hydrogen sulfide in an inert solvent, for example sodium or potassium hydrogen sulfide in dimethyl formamide, at a temperature ranging from 0° to 40°C. Processes by which a compound VIII may be prepared are known.

According to method e) a compounds of the general formula XI is converted with a suitable oxidation agent, preferably with active manganese-IV-oxide, into a compound of the formula I or an acid addition salt thereof. The solvent preferably used is a halogenated hydrocarbon, for example methylene chloride, chloroform or tetrachlorethane, the reaction generally being performed at a temperature ranging from 0 to 40°C, preferably from 20 to 30°C, for 10 to 60 hours.

The compound of the formula XI may be obtained by converting a halogenoketone of the formula II in which Z preferably stands for a chlorine or bromine atom, for example according to "Arzneimittel-Forschung" 22, 2095, 1972 with a suitable reducting agent, preferably sodium boronhydride in methanol at a temperature within the range of from 0° to 25°C into a compound of the formula XIX

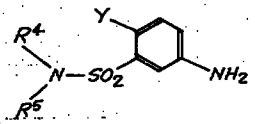


The compound of the formula XIX reacts as an alkyl halide with the thiourea of the formula III to give an isothiouronium salt of the formula XI.

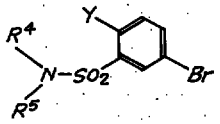
The reaction is preferably performed under the same conditions as described in method a).

In method f), a compound of the formula XII in which Y does not stand for a bromine or iodine atom and $R^4$ and $R^5$ are other than hydrogen atoms is reacted with a compound of the formula XIII, which compound is known. The compounds XII and XIII are advantageously reacted in the molar ratio 1:1 to 1:1.5 in an inert and anhydrous solvent usual for organometallic reactions, preferably ether or tetrahydrofuran, at a temperature within the range of from 0°C to 60°C, preferably from 15° to 35°C and with a reaction time of 1 to 30 hours. In this reaction, a solution of the compounds XIII may be added dropwise to a solution of the compound XII, however, it is especially advantageous to do it the opposite way i.e. a solution of 1 mol of the organometallic compound XII is added dropwise to a solution of 1 to 1.5 mols of the compound XIII in one of the solvents mentioned. After the reaction is complete, the reaction products are hydrolyzed in a manner usual for organometallic reactions, for example by introducing the reaction mixture at a temperature ranging from −5°C to +20°C into an aqueous, saturated ammonium chloride solution at a constant pH of from 6 to 8. The compounds of the formula I so obtained may be worked up in an analogous manner to that described under method b).

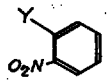
The compound of the formula XII used in method f) is for example, prepared by converting a compound of the formula XX



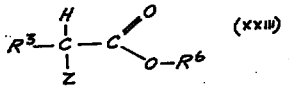
in known manner via diazotization by a Sandmeyer reaction or one of its variants, into a bromine derivative of the formula XXI



or by brominating a compound of the formula XXII



in the *m*-position to the nitro group, reducing the nitro group, diazotizing the amino group obtained, sulfochlorinating according to Meerwein and finally reacting with an amine of the formula VII. Finally, the compound of the formula XXI may be converted according to known methods in an inert, anhydrous solvent, for example tetrahydrofuran or diethyl ether, into the compound of the formula XXII. A great number of the compounds of the formula XIII used in method f) are known and is accessible by converting a thiourea of the formula III with an $\alpha$-halogenated carboxylic acid or an ester thereof of the general formula XXIII



(XXIII)

in which $R^3$ is defined as above, $R^6$ preferably stands for a hydrogen atom or a methyl or ethyl group and Z stands for a chlorine or bromine atom. (c.f. R. C. Elderfield, "Heterocyclic Compounds", vol. 5, page 616, John Wiley & Sons, Inc. 1957). The compounds of the formula XIII that have not yet been described may be prepared in the same manner.

The compound of the formula I may be reacted reversibly in a suitable solvent with an acid of the formula H—Z. The compounds I may be introduced into a pure acid at 0° to 40°C, when it is liquid or has a melting point hardly higher than 40°C and when it does not cause side reactions. However, it is advantageous to work in a solvent, for example in water or in an organic solvent, for example dioxane, tetrahydrofuran, ether, an alkyl acetate with 1—4 carbon atoms in the alkyl part, acetonitrile, nitromethane, acetone, or methyl-ethyl ketone, an alcohol having 1—4 carbon atoms being especially suitable. 1—1.5 mols of the acid H—Z is generally used per mol of compound I, however, greater amounts of acid may be used. Temperatures within the range of from 0° to 40°C, preferably from 10 to 25°C are advantageous. The reaction is moderately exothermic.

When working in aqueous solution the compound I is generally instantly dissolved after adding the acid of the formula H—Z and only in rare cases does the corresponding acid addition compound separate. The salt of the invention is advantageously isolated with the obtention of a solution by careful evaporation of water, preferably by lyophilizing. When working in an organic solvent the acid addition salt often precipitates after adding the coresponding acid H—Z as a sparingly soluble substance. When a solution is obtained, the acid addition compounds is generally precipitated, optionally after concentrating the reaction mixture, with a suitable precipitating agent, those agents being the solvents described in method I for the same purpose.

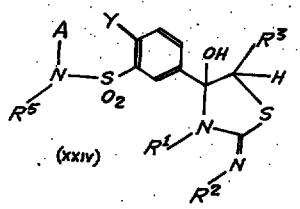
Even when highly pure, the acid addition product very often precipitates as a viscous oil or as an amorphous glasslike product. These amorphous products can be

crystallized in many cases, optionally by heating to 40 to 80°C, and treatment with an organic solvent. Solvents which promote crystallization are especially alkyl acetates of 1—4 carbon atoms in the alkyl part, for example methyl, ethyl, and n-butylacetate, and dialkyl ketones, for example, acetone and methylethyl ketone, di-($C_1$—$C_4$)-alkyl ethers, for example, diethyl ether, diisopropyl ether and di-n-butyl ether, acetonitrile, nitromethane and, in some cases, lower alcohols, for example, methanol, ethanol, isopropanol and *n*-butanol.

An acid addition product can be deprotonized in a suitable solvent by treatment with a base, for example, a solution of an inorganic hydroxide, for example, lithium, sodium, potassium, calcium or barium hydroxide, carbonate or hydrogen carbonate, for example, sodium carbonate, potassium carbonate, sodium or potassium hydrogen carbonate, ammonia or an amine, for example, triethyl amine, dicyclohexyl amine, piperidine, or methyl-di-cyclohexyl amine.

When working in an aqueous medium, the free basic compound I precipitates in a sparingly soluble form and can be separated and isolated by filtration or extraction with an organic solvent, preferably ethyl acetate. Especially suitable organic reaction media are alcohols of 1—4 carbon atoms, preferably methanol and ethanol, however, ethyl acetate, dietyhl ether, tetrahydrofuran, dioxane, diethylene glycol dimethyl ether, dimethyl formamide and others can also be used. There is spontaneous reaction to give the compound I. The reaction is generally performed at −35°C to 100°C, preferably 0° to 25°C. When an organic solvent miscible with water is used, the free base of the formula I may be precipitated by adding water, optionally after concentrating the reaction mixture. When the solvent used is not miscible with water, the reaction mixture is advantageously washed with water after reaction and the organic solvent is evaporated optionally after drying.

When at least 1 mol of a sufficiently strong base is allowed to act on a compound of the formula I, in which $R^4$ and/or $R^5$ each stands for hydrogen, a salt of the general formula XXIV are obtained



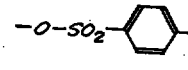
(XXIV)

accompanied by the deprotonization of the sulfonamide group, in which formula A is the cation of an alkali metal or alkaline earth metal and $R^1$, $R^2$, $R^3$, $R^4$ and $R^5$ as well as Y are defined as above. Such a base is, for example, a hydroxide of an alkali metal or alkaline earth metal, preferably NaOH or KOH, an alkali metal or alkaline earth metal alcoholate, preferably $NaOCH_3$ or $NaOC_2H_5$, NaH, or sodium methylsulfinyl methide. The solvent may be water or a polar organic solvent, for example, methanol, ethanol, isopropanol, *n*-butanol, dimethylformamide, dimethyl sulfoxide, diethylene glycol dimethylether, or acetonitrile.

The potassium salts of the formula XXIV have a particularly good solubility in water. By the addition of 1 mol of a suitable acid, the corresponding free compound of the formula I of the invention is recovered, favourable acids being especially ammonium salts.

This reversible acid-base reaction can be used for the purification of the compounds I. Moreover, the salts of the formula XXIV can be used in order to obtain compounds of the formula I which are correspondingly modified via alkylation reactions taking place at the sulfonamide group.

In the case of an alkylation reaction, working may be effected in water, preferably, however, in one of the polar organic solvents mentioned, and the reaction is generally carried out at a temperature within the range of from −20°C to +50°C, preferably +15°C to +35°C during a period of time of from 5 to 72 hours. The alkylation reaction may be performed with the usual alkylating agents of the general formula $R^4$—X, in which $R^4$ is defined as indicated above, and X stands, for example, for Br, I, Cl, —O—$SO_2$—$CH_3$, —O—$SO_2$—$OR^4$, or



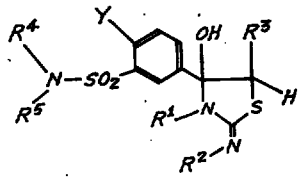
The most important compounds of the general formula I of the invention are those in which the substituents are defined as follows:

$R^1$ = methyl, ethyl, allyl,
$R^2$ = methyl, ethyl, allyl, methoxypropyl
$R^1$ and $R^2$ together = alkylene
$R^3$, $R^4$, $R^5$ = each hydrogen
Y = chlorine, bromine.

Further preferred compounds of the formula I of the invention are those in which the substituents are defined as follows:

$R^1$ = propyl, isopropyl
$R^2$ = propyl, butyl, cyclohexyl, cyclohexylmethyl, benzyl
$R^3$ and $R^4$ each = hydrogen
$R^5$ = hydrogen, lower alkyl, benzyl
Y = chlorine, bromine.

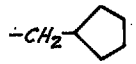
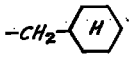
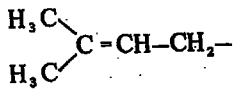
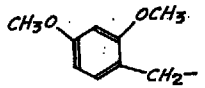
In the process of the invention, there may be used in addition to the 4-(3-sulfamoyl-phenyl)-1,3-thiazolidine-4-ols described in the Examples the compounds of the general formula

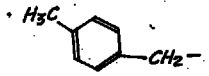
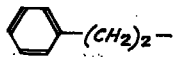
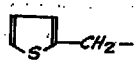
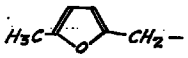
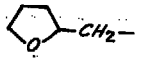
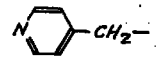
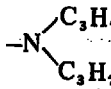


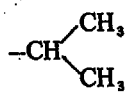
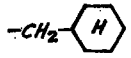
(I)

or the acid addition products thereof summarized in the following Table:

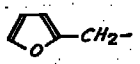
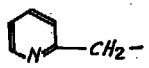
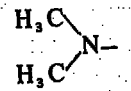
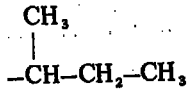
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3$ | $C_2H_5$ | H | H | H | Cl |
| $CH_3$ | $n\text{-}C_3H_7$ | H | H | H | Cl |
| $CH_3$ | $n\text{-}C_4H_9$ | H | H | H | Cl |
| $CH_3$ | $-C(CH_3)_2-CH_3$ | H | H | H | Cl |
| $CH_3$ | $-(CH_2)_4-CH_3$ | H | H | H | Cl |
| $CH_3$ | $-(CH_2)_5-CH_3$ | H | H | H | Cl |
| $CH_3$ |  | H | H | H | Cl |
| $CH_3$ |  | H | H | H | Cl |
| $CH_3$ |  | H | H | H | Cl |

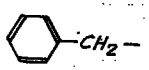
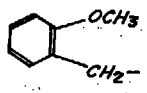
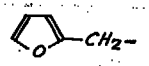
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3$ |  | H | H | H | Cl |
| $CH_3$ | | H | H | H | Cl |
| $CH_3$ |  | H | H | H | Cl |
| $-(CH_2)_4-$ | | H | H | H | Cl |
| $CH_3$ | $-(CH_2)_2-OCH_3$ | H | H | H | Cl |
| $CH_3$ | $-(CH_2)_7-CH_3$ | H | H | H | Cl |
| $CH_3$ | $-CH_2-CH=CH_2$ | H | H | H | Cl |
| $CH_3$ |  | H | H | H | Cl |
| $CH_3$ |  | H | H | H | Cl |

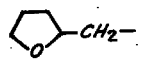
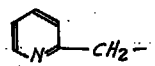
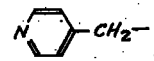
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3$ |  | H | H | H | Cl |
| $CH_3$ |  | H | H | H | Cl |
| $CH_3$ |  | H | H | H | Cl |
| $CH_3$ |  | H | H | H | Cl |
| $CH_3$ |  | H | H | H | Cl |
| $CH_3$ |  | H | H | H | Cl |
| $CH_3$ |  | H | H | H | Cl |

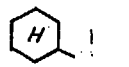
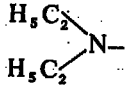
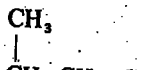
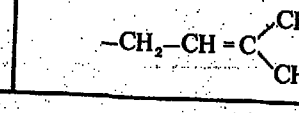
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $-CH_2-CH(CH_3)-$ | | H | H | H | Cl |
| $H_5C_2-$ | $-(CH_2)_2-CH_3$ | H | H | H | Cl |
| $H_5C_2-$ |  | H | H | H | Cl |
| $H_5C_2-$ | $-(CH_2)_3-CH_3$ | H | H | H | Cl |
| $H_5C_2-$ | $-CH_2-CH(CH_3)_2$ | H | H | H | Cl |
| $H_5C_2-$ | | H | H | H | Cl |
| $H_5C_2-$ | | H | H | H | Cl |
| $H_5C_2$ |  | H | H | H | Cl |
| $H_5C_2-$ | $-(CH_2)_2-O-C_2H_5$ | H | H | H | Cl |

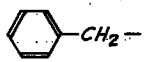
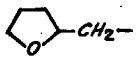
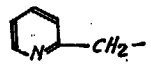
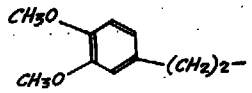
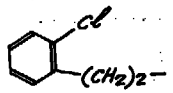
| R¹ | R² | R³ | R⁴ | R⁵ | Y |
|---|---|---|---|---|---|
| $H_5C_2-$ |  | H | H | H | Cl |
| $H_5C_2-$ | $H_2C=CH-CH_2-$ | H | H | H | Cl |
| $H_5C_2-$ | $H_3C-CH=CH-CH_2-$ | H | H | H | Cl |
| $H_5C_2-$ |  | H | H | H | Cl |
| $H_5C_2-$ |  | H | H | H | Cl |
| $H_5C_2-$ |  | H | H | H | Cl |
| $H_5C_2-$ |  | H | H | H | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $H_5C_2$ |  | H | H | H | Cl |
| $H_5C_2$– |  | H | H | H | Cl |
| $H_5C_2$– |  | H | H | H | Cl |
| $H_5C_2$– | $CH_3$–CO–NH– | H | H | H | Cl |
| $H_3C$–$(CH_2)_2$– | $H_3C$–$(CH_2)_3$– | H | H | H | Cl |
| $H_3C$–$(CH_2)_2$– | –$CH(CH_3)_2$ | H | H | H | Cl |
| $H_3C$–$(CH_2)_2$– | –$CH_2$–$CH(CH_3)_2$ | H | H | H | Cl |
| $CH_3$–$(CH_2)_2$– |  | H | H | H | Cl |

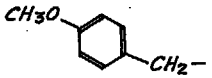
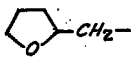
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-(CH_2)_2-$ | | H | H | H | Cl |
| $CH_3-(CH_2)_2-$ | | H | H | H | Cl |
| $CH_3-(CH_2)_2-$ | $H_3C-CH-CH_2-$ <br> $H_3CO$ | H | H | H | Cl |
| $CH_3-(CH_2)_2-$ | $CH_2-CH-CH_2-$ | H | H | H | Cl |
| $CH_3-(CH_2)_2-$ |  | H | H | H | Cl |
| $CH_3-(CH_2)_2-$ |  | H | H | H | Cl |
| $CH_3-(CH_2)_2-$ |  | H | H | H | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-(CH_2)_2-$ |  | H | H | H | Cl |
| $CH_3-(CH_2)_2-$ |  | H | H | H | Cl |
| $CH_3-(CH_2)_2-$ |  | H | H | H | Cl |
| $CH_3-(CH_2)_2-$ | $-N(CH_3)_2$ | H | H | H | Cl |
| $(CH_2)_3-CH_3$ | $-CH(CH_3)_3$ | H | H | H | Cl |
| $(CH_2)_5-CH_3$ | $-CH(CH_3)_2$ | H | H | H | H |
| $(CH_3)_2CH-CH_2$ | $-CH(CH_3)_2$ | H | H | H | Cl |
|  | $-CH(CH_3)_2$ | H | H | H | Cl |

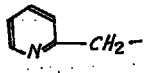
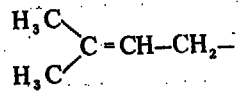
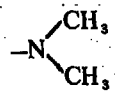
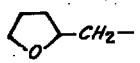
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
|  | $-CH(CH_3)_2$ | H | H | H | Cl |
|  | $-CH(CH_3)_2$ | H | H | H | Cl |
| $CH_3(CH_2)_3-$ |  | H | H | H | Cl |
| $CH_3(CH_2)_3-$ | $-CH_2-CH(CH_3)_2$ | H | H | H | Cl |
| $CH_3(CH_2)_3-$ | | H | H | H | Cl |
| $CH_3(CH_2)_3-$ | | H | H | H | Cl |
| $CH_3(CH_2)_3-$ | $-CH_2-CH=CH_2$ | H | H | H | Cl |
| $CH_3(CH_2)_3-$ |  | H | H | H | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3(CH_2)_3-$ | $-CH_2-CH_2-OCH_3$ | H | H | H | Cl |
| $CH_3-(CH_2)_3-$ |  | H | H | H | Cl |
| $CH_3-(CH_2)_3-$ |  | H | H | H | Cl |
| $CH_3-(CH_2)_3-$ |  | H | H | H | Cl |
| $CH_3-(CH_2)_3-$ | $-N(CH_3)_2$ | H | H | H | Cl |
| $CH_3-$ |  | H | H | H | Cl |
| $CH_3-$ |  | H | H | H | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $C_2H_5$ |  | H | H | H | Cl |
| $-CH_2-CH(CH_3)_2$ |  | H | H | H | Cl |
|  |  | H | H | H | Cl |
| $-CH_2-CH(CH_3)_2$ |  | H | H | H | Cl |
| $-CH_2-CH(CH_3)_2$ | $-(CH_2)_2-OCH_3$ | H | H | H | Cl |
| $-CH_2-CH(CH_3)_2$ | $-CH_2-CH=C(CH_3)_2$ | H | H | H | Cl |
|  | $-CH_2-CH=CH_2$ | H | H | H | Cl |

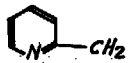
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $-CH_2-CH(CH_3)_2$ |  | H | H | H | Cl |
| $-CH_2-CH(CH_3)_2$ |  | H | H | H | Cl |
| $(CH_3)_2N-$ | $-CH_2-CH(CH_3)_2$ | H | H | H | Cl |
| $-(CH_2)_5CH_3$ | | H | H | H | Cl |
| | | H | H | H | Cl |
| | $-CH_2-CH=C(OH_3)_2$ | H | H | H | Cl |
| | | H | H | H | Cl |

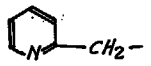
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_2=CH-CH_2-$ |  | H | H | H | Cl |
| $CH_2=\underset{\displaystyle CH_3}{\underset{\vert}{C}}-CH-$ |  | H | H | H | Cl |
| $CH_3O-(CH_2)_2-$ |  | H | H | H | Cl |
| $(H_3C)_2N-$ |  | H | H | H | Cl |
| $CH_3-(CH_2)_3\diagdown\ \diagup-(CH_2)_3-$<br>$CH_3-(CH_2)_3\diagup\ \diagdown-(CH_2)_3-$ |  | H | H | H | Cl |
| $CH_2=CH-CH_2-$ |  | H | H | H | Cl |

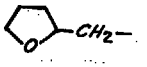
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $H_3C-CH=CH-CH_2$ |  | H | H | H | Cl |
|  |  | H | H | H | Cl |
| $CH_2=CH-CH_2-$ |  | H | H | H | Cl |
| $H_5C_2-$ | $H_5C_2-$ | $H_5C_2-$ | H | H | Cl |
| $CH_3-$ | $-CH(CH_3)_2$ | $-CH_3$ | H | H | Cl |
| $H_3C-$ | | $-C_2H_5$ | H | H | Cl |
| $(H_3C)_2CH-CH_2-$ | $CH_2=CH-CH_2-$ | $-C_2H_5$ | H | H | Cl |
| $H_5C_2-$ | | $-C_2H_5$ | H | H | Cl |

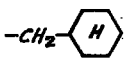
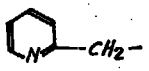
| R¹ | R² | R³ | R⁴ | R⁵ | Y |
|---|---|---|---|---|---|
| $H_3C-$ |  | $-CH_3$ | H | H | Cl |
| $H_3C-$ | $-(CH_2)_5-CH_3$ | $-CH_3$ | H | H | Cl |
| $CH_2=CH-CH_2-$ | $CH_2=CH-CH_2-$ | $-C_2H_5$ | H | H | Cl |
| $H_3C-$ |  | $-C_2H_5$ | H | H | Cl |
| $H_3C-$ |  | $-CH_3$ | H | H | Cl |
| $CH_3-$ | $-CH(CH_3)_2$ | $C_2H_5-$ | H | H | Cl |
| $CH_3-$ | $-CH_2-CH(CH_3)_2$ | $-CH_3$ | H | H | Cl |
| $-N(CH_3)_2$ | $-N(CH_3)_2$ | $-C_2H_5$ | H | H | Cl |
| | $-(CH_2)_2-$ | $-C_2H_5$ | H | H | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $-(CH_2)_4-$ | | $-CH_3$ | H | H | Cl |
| $-CH_2-C(CH_3)_2-$ | | $-CH_3$ | H | H | Cl |
| $CH_3-$ | $CH_3-$ | H | $-CH_3$ | H | Cl |
| $CH_3-$ | $CH_3-$ | $C_2H_5$ | $-CH_3$ | H | Cl |
| $CH_3-$ | $-CH(CH_3)_2$ | H | $-CH_3$ | H | Cl |
| $CH_3$ | $-(CH_2)_5CH_3$ | H | $-CH_3$ | H | Cl |
| $CH_3$ | $-CH_2-CH=CH_2$ | H | $-(CH_2)_3-CH_3$ | H | Cl |
| $CH_3$ | $CH_3$ | H | $-(CH_2)_5-CH_3$ | H | Cl |
| $CH_2=CH-CH_2-$ | | $-CH_3$ | $-C_2H_5$ | H | Cl |
| $CH_3-$ | | $-C_2H_5$ | $-CH_2-CH(CH_3)_2$ | H | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ |  | H | $-(CH_2)_3-CH_3$ | H | Cl |
| $CH_3-$ | $H_3C$, $CH_3O$ $CH-CH_2-$ | H | $-(CH_2)_3-CH_3$ | H | Cl |
| $CH_3-$ | $N(CH_3)_2$ | H | $-(CH_2)_3-CH_3$ | H | Cl |
| $-N(CH_3)_2$ | $-N(CH_3)_2$ | $-C_2H_5$ | $-CH(CH_3)_2$ | H | Cl |
| $-(CH_2)_2-$ | | H | $CH_3-$ | H | Cl |
| $-(CH_2)_3-$ | | H | $-CH(CH_3)_2$ | H | Cl |
| $-(CH_2)_3-$ | | Et | $-(CH_2)_3CH_3$ | H | Cl |
| $CH_3-$ | $CH_3-$ | $CH_3$ | $H_3C-CH(OCH_3)-CH_2-$ | H | Cl |
| $CH_3-$ | $(H_3C)_2CH-$ | H | $H_3C-CH(OCH_3)-CH_2-$ | H | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3$– | $-CH_2-CH(CH_3)_2$ | H | $H_5C_2O-(CH_2)_2$– | H | Cl |
| $CH_3$– |  | H | $H_3CO-(CH_2)_2$– | H | Cl |
| $H_5C_2$– | $H_3C-CH(O-CH_3)-CH_2$– | $H_5C_2$– | $H_3CO-(CH_2)_2$– | H | Cl |
| $H_2C=CH-CH_2$– | $-N(CH_3)_2$ | H | $H_3C-O-(CH_2)_3$– | H | Cl |
| $CH_3$– | | H | $H_3C-CH(OCH_3)-CH_2$ | H | Cl |
| $CH_3$– | | H | $H_5C_2-O-(CH_2)_2$ | H | Cl |
| $-(CH_2)_2-$ | | H | $H_3CO-(CH_2)_2$– | H | Cl |
| $H_3C$– | $-CH(CH_3)_2$ | H | | H | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $H_3C-$ | $-CH_2-CH=CH_2$ | H | | H | Cl |
| $-(CH_2)_3-$ | | H | | H | Cl |
| $H_3C$ | $-CH_2-CH(CH_3)_2$ | H | | H | Cl |
| $H_3C-$ | | H | | H | Cl |
| $H_3C-$ | | H | | H | Cl |
| $H_3C-$ |  | $CH_3$ | | H | Cl |
| $H_3C-$ | $CH_3-CH(OCH_3)-CH_2-$ | H | | H | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $H_3C-$ | $-N(CH_3)_2$ | H | | H | Cl |
| $H_3C-$ | | H | | H | Cl |
| $H_5C_2-$ | $H_5C_2-$ | H | | H | Cl |
| $CH_3-$ |  | H | | H | Cl |
| $C_2H_5$ | $C_2H_5-$ | H | $CH_2=CH-CH_2-$ | H | Cl |
| $CH_3-$ | $-CH(CH_3)_2$ | H | $CH_2=CH-CH_2-$ | H | Cl |
| $CH_3-$ |  | H | $CH_2=CH-CH_2$ | H | Cl |



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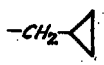
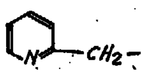
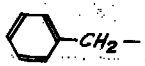
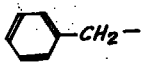
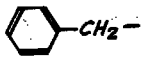
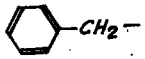
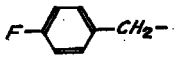
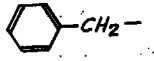
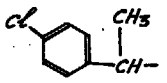
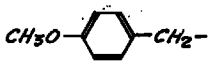
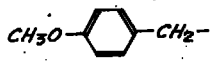
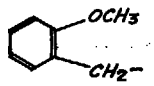
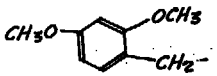
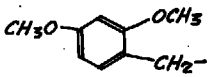
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $H_5C_2-$ | $CH_3$, $CH_3O$ $\rangle CH-CH_2-$ | $-C_2H_5$ | $CH_2=CH-CH_2-$ | H | Cl |
| $CH_3-$ | $-N(CH_3)_2$ | H | $CH_2=CH-CH(CH_3)-$ | H | Cl |
| $H_5C_2-$ |  | H | $CH_2=CH-CH_2-$ | H | Cl |
| $CH_3-$ | | H | $CH_2=CH-CH_2-$ | H | Cl |
| $CH_3-(CH_2)_3-$ | $CH_3(CH_2)_3-$ | H | $CH_2=CH-CH_2-$ | H | Cl |
| $CH_3-$ | $-CH_3$ | H | $(H_3C)_2C=CH-CH_2-$ | H | Cl |
| $CH_3-$ |  | H | $(H_3C)_2C=CH-CH_2-$ | H | Cl |
| $CH_3-$ |  | H | $H_2C=CH-CH_2-$ | H | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3$– |  | H | $H_2C=CH-CH_2$– | H | Cl |
| $CH_3$– | | H | $H_2C=CH-CH_2$– | H | Cl |
| $CH_3$– | $-CH(CH_3)_2$ | H |  | H | Cl |
| $C_2H_5$– | $-C_2H_5$ | H |  | H | Cl |
| $CH_3$– | $-CH_2-CH(CH_3)_2$ | $C_2H_5$– |  | H | Cl |
| $CH_3$– | $-CH(CH_3)_2$ | H |  | H | Cl |
| $CH_3$– | | H |  | H | Cl |

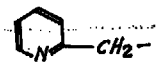
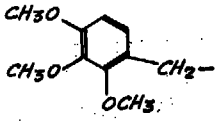
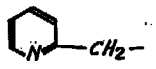
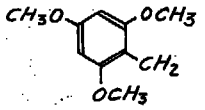
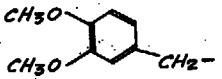
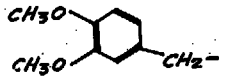
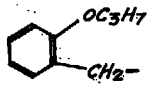
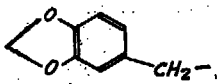
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3$– | $-CH(CH_3)_2$ | H |  | H | Cl |
| $CH_3$– | $-CH(CH_3)_2$ | H |  | H | Cl |
| $C_2H_5$– | $C_2H_5$– | H |  | H | Cl |
| $H_5C_2$– | $-CH_2-CH=CH_2$ | H |  | H | Cl |
| $CH_3$– | $-CH(CH_3)_2$ | H |  | H | Cl |
| $H_5C_2$– | $H_5C_2$– | H |  | H | Cl |

| R¹ | R² | R³ | R⁴ | R⁵ | Y |
|---|---|---|---|---|---|
| $CH_3$– | $-CH(CH_3)_2$ | H |  | H | Cl |
| $CH_3$– | $-CH_2-CH=CH_2$ | H |  | H | Cl |
| $CH_3$– | $-CH_2-CH=CH_2$ | H |  | H | Cl |
| $H_5C_2$– |  | H |  | H | Cl |
| $H_3C$– | $-N(CH_3)_2$ | H |  | H | Cl |
| $H_3C$– |  | H |  | H | Cl |

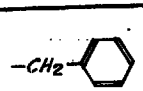
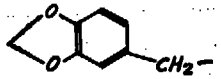
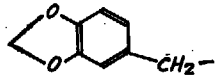
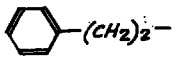
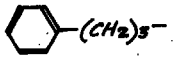
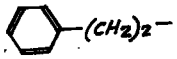
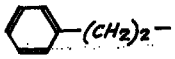
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $H_3C-$ |  | H |  | H | Cl |
| $H_3C-$ | $-CH(CH_3)_2$ | H |  | H | Cl |
| $C_2H_5-$ |  | H |  | H | Cl |
| $H_3C-$ | $-N(CH_3)_2$ | $CH_3$ |  | H | Cl |
| $-(CH_2)_3-$ | | H |  | H | Cl |
| $H_3C-$ | $-CH(CH_3)_2$ | H |  | H | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $H_3C-$ | $-CH_2-CH(CH_3)_2$ | H |  | H | Cl |
| $H_5C_2-$ | $-CH_2-CH=CH_2$ | H |  | H | Cl |
| $CH_3-$ | $-CH_2-CH(CH_3)_2$ | H |  | H | Cl |
| $-(CH_2)_2-$ | | H |  | H | Cl |
| $CH_3-$ | $-CH(CH_3)_2$ | H |  | H | Cl |
| $C_2H_5-$ | $C_2H_5-$ | $C_2H_5$ |  | H | Cl |

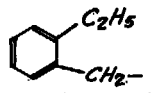
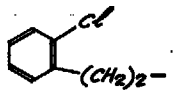
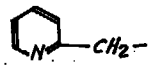
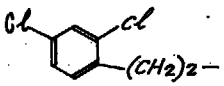
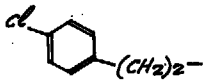
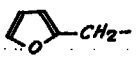
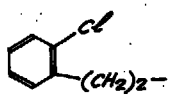
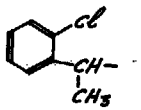
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ |  | H |  | H | Cl |
| $-CH_2-CH=CH_2$ | $-CH_2-CH=CH_2$ | H |  | H | Cl |
| $CH_3-$ |  | H |  | H | Cl |
| $C_2H_5$ |  | H |  | H | Cl |
| $CH_3-$ | $N(CH_3)_2$ | H |  | H | Cl |

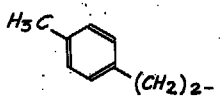
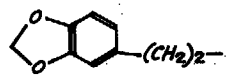
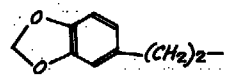
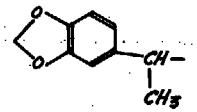
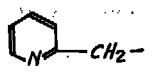
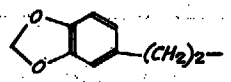
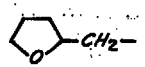
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ |  | H |  | H | Cl |
| $CH_3-$ |  | H |  | H | Cl |
| $-(CH_2)_3-$ | | H |  | H | Cl |
| $CH_3-$ | | H |  | H | Cl |
| $C_2H_5-$ | $C_2H_5-$ | H |  | H | Cl |
| $CH_3-$ | $-CH_2-CH(CH_3)_2$ | H |  | H | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ |  | H |  | H | Cl |
| $H_5C_2-$ | $-CH_2-CH=CH_2$ | H |  | H | Cl |
| $H_5C_2-$ |  | H |  | H | Cl |
| $CH_3-$ |  | H |  | H | Cl |
| $CH_3-$ | $-N(CH_3)_2$ | H |  | H | Cl |
| $CH_3-$ |  | H |  | H | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $H_5C_2-$ |  | H |  | H | Cl |
| $-(CH_2)_3-$ | | H |  | H | Cl |
| $CH_3-$ | $-CH(CH_3)_2$ | H |  | H | Cl |
| $CH_3-$ | $-CH(CH_3)_2$ | $C_2H_5$ |  | H | Cl |
| $C_2H_5-$ | $-CH_2-CH(CH_3)_2$ | H |  | H | Cl |
| $CH_3-$ | | $CH_3$ |  | H | Cl |

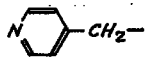
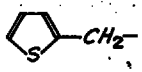
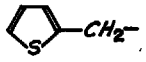
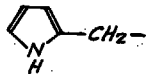
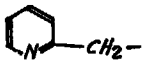
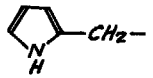
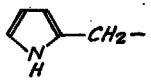
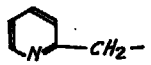
| R¹ | R² | R³ | R⁴ | R⁵ | Y |
|---|---|---|---|---|---|
| $CH_3-$ | $-N(C_2H_5)_2$ | H |  | H | Cl |
| $CH_2=CH-CH_2-$ | $CH_2=CH-CH_2-$ | H |  | H | Cl |
| $CH_3-$ | $-CH(CH_3)_2$ | H |  | H | Cl |
| $C_2H_5-$ | $C_2H_5$ | H |  | H | Cl |
| $CH_3-$ |  | H |  | H | Cl |
| $CH_3-$ | $-CH_2-CH(CH_3)-O-CH_3$ | H |  | H | Cl |

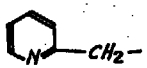
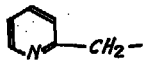
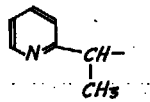
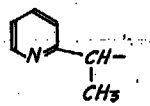
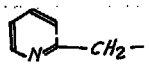
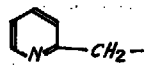
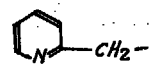
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $C_2H_5-$ | $C_2H_5-$ | H |  | H | Cl |
| $CH_3-$ | $-CH(CH_3)_2$ | $CH_3-$ |  | H | Cl |
| $CH_3-$ |  | H |  | H | Cl |
| $C_2H_5-$ | $CH_2=CH-CH_2-$ | H |  | H | Cl |
| $CH_3-$ |  | H |  | H | Cl |
| $C_2H_5-$ | $C_2H_5-$ | H |  | H | Cl |

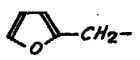
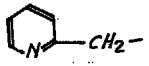
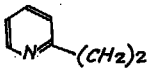
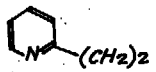
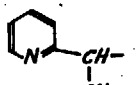
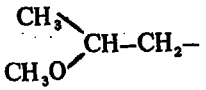
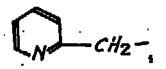
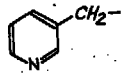
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ | $-CH(CH_3)_2$ | $CH_3-$ |  | H | Cl |
| $C_2H_5-$ | $C_2H_5-$ | $C_2H_5$ |  | H | Cl |
| $CH_3-$ | $CH(CH_3)_2$ | H |  | H | Cl |
| $C_2H_5-$ | $-CH_2-CH=CH_2$ | H |  | H | Cl |
| $CH_3-$ |  | H |  | H | Cl |
| $C_2H_5-$ | $C_2H_5$ | $C_2H_5$ |  | H | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3$– | $-CH(CH_3)_2$ | H |  | H | Cl |
| $C_2H_5$– | $-\underset{\displaystyle CH_3}{\underset{\vert}{CH}}-CH_2-CH_3$ | H |  | H | Cl |
| $CH_3$– | $CH_3$ | H |  | H | Cl |
| $CH_3$– | $-N(CH_3)_2$ | H |  | H | Cl |
| $CH_3$– | $CH_2=CH-CH_2-$ | H |  | H | Cl |
| $C_2H_5$– |  | H |  | H | Cl |

| R¹ | R² | R³ | R⁴ | R⁵ | Y |
|---|---|---|---|---|---|
| $CH_3$ |  | H |  | H | Cl |
| $CH_3$ | $CH_3$ | H |  | H | Cl |
| $CH_3$ | $-CH(CH_3)_2$ | $CH_3$ |  | H | Cl |
| $C_2H_5-$ | $-CH_2-CH(CH_3)_2$ | H |  | H | Cl |
| $CH_3-$ |  | H |  | H | Cl |
| $CH_3-$ |  | H |  | H | Cl |

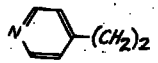
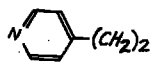
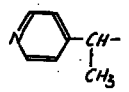
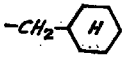
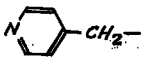
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $C_2H_5$– |  | H |  | H | Cl |
| $CH_2$=CH–$CH_2$– | –$N(C_2H_5)_2$ | H |  | H | Cl |
| $CH_3$– | –$CH(CH_3)_2$ | H |  | H | Cl |
| $CH_3$– |  | H |  | H | Cl |
| $CH_2$=CH–$CH_2$– | –$N(CH_3)_2$ | H |  | H | Cl |
| $CH_3$– | $CH_3$– | H |  | H | Cl |

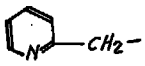
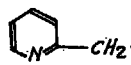
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $C_2H_5-$ | $C_2H_5-$ | $C_2H_5-$ |  | H | Cl |
| $CH_3-$ | $-CH_2-CH(CH_3)_2$ | H |  | H | Cl |
| $C_2H_5-$ | $-CH(CH_3)_2$ | H |  | H | Cl |
| $CH_3-$ | $-N(CH_3)_2$ | H |  | H | Cl |
| $CH_3-$ |  | H |  | H | Cl |
| $CH_2=CH-CH_2-$ | $CH_2=CH-CH_2-$ | $CH_3-$ |  | H | Cl |

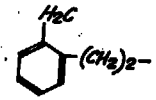
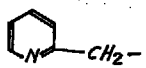
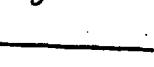
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $C_2H_5-$ |  | H |  | H | Cl |
| $CH_3-$ | $-CH(CH_3)_2$ | H |  | H | Cl |
| $C_2H_5-$ | $-N(CH_3)_2$ | H |  | H | Cl |
| $CH_3-$ | $CH_3-$ | H |  | H | Cl |
| $C_2H_5-$ |  | H |  | H | Cl |
| $CH_3-$ | $CH_3-$ | H |  | H | Cl |

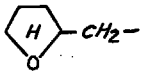
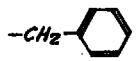
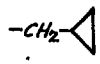
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $C_2H_5$ | $C_2H_5$ | H |  | H | Cl |
| $CH_3$– | $-CH(CH_3)_2$ | H |  | H | Cl |
| $CH_3$– |  | $C_2H_5$ |  | H | Cl |
| $C_2H_5$– | $CH_2=CH-CH_2$– | $CH_3$ |  | H | Cl |
| $C_2H_5$– |  | H |  | H | Cl |
| $CH_3-(CH_2)_3$– | $CH_3-(CH_2)_3$– | H |  | H | Cl |

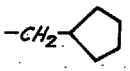
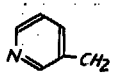
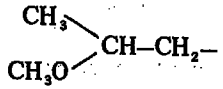
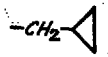
| R¹ | R² | R³ | R⁴ | R⁵ | Y |
|---|---|---|---|---|---|
| | –(CH₂)₃– | CH₃ |  | H | Cl |
| C₂H₅– |  | H |  | H | Cl |
| CH₃– | | (CH₃)₂C=CH–CH₂ |  | H | Cl |
| CH₃– | | –CH(CH₃)₂ |  | H | Cl |
| C₂H₅– | | C₂H₅– |  | H | Cl |
| CH₃– | |  |  | H | Cl |

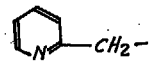
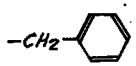
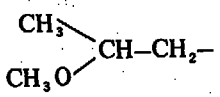
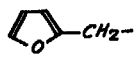
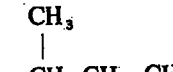
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $-(CH_2)_3-$ | | H |  | H | Cl |
| $C_2H_5-$ | $-N(CH_3)_2$ | H |  | H | Cl |
| $CH_3-CH_2-CH_2-$ |  | H |  | H | Cl |
| $C_2H_5-$ |  | H |  | H | Cl |
| $CH_3-$ | $-CH(CH_3)_2$ | H | $-(CH_2)_4-$ | | Cl |
| $C_2H_5-$ | $CH_2=CH-CH_2-$ | H | $-(CH_2)_4-$ | | Cl |
| $CH_3-$ | $CH_3-$ | H | $-(CH_2)_4-$ | | Cl |
| $CH_3-$ | $-CH(CH_3)_2$ | H | $-(CH_2)_5-$ | | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $C_2H_5-$ | $-N(CH_3)_2$ | H | $-(CH_2)_5-$ | | Cl |
| $C_2H_5$ |  | H | $-(CH_2)_5-$ | | Cl |
| $CH_3-$ | $CH_3-$ | $C_2H_5$ | $-(CH_2)_4-$ | | Cl |
| $-(CH_2)_3-$ | | H | $-(CH_2)_5-$ | | Cl |
| $CH_3-$ | $-CH_2-CH(CH_3)_2$ | H | $-(CH_2)-O-(CH_2)_2-$ | | Cl |
| $CH_3-$ | $C_2H_5-$ | $C_2H_5-$ | $-(CH_2)_2-O-(CH_2)_2-$ | | Cl |
| $C_2H_5-$ | | H | $-(CH_2)_2-O-(CH_2)_2-$ | | Cl |
| $CH_2=CH-CH_2-$ | $-N(CH_3)_2$ | H | $-(CH_2)_2-O-(CH_2)_2-$ | | Cl |
| $C_2H_5-$ |  | H | $-(CH_2)_2-O-(CH_2)_2-$ | | Cl |

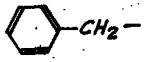
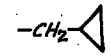
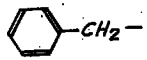
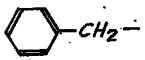
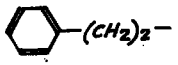
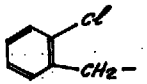
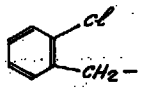
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ |  | H | $-(CH_2)_2-O-(CH_2)_2-$ | | Cl |
| $CH_3$ | $CH_3$ | H |  | | Cl |
| $CH_3-$ | $-CH(CH_3)_2$ | $C_2H_5-$ | $CH_3-$ | $CH_3-$ | Cl |
| $CH_3-$ | $CH_3-$ | $CH_3-$ | $CH_3-$ | $CH_3-$ | Cl |
| $CH_3-$ | $-CH(CH_3)_2$ | H | $CH_3-$ | $CH_3-$ | Cl |
| $CH_3-$ | $-CH_2-CH(CH_3)_2$ | H | $CH_3-$ | $CH_3-$ | Cl |
| $C_2H_5-$ |  | H | $CH_3-$ | $CH_3-$ | Cl |
| $C_2H_5-$ |  | H | $CH_3-$ | $CH_3-$ | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ | $CH_2=CH-CH_2-$ | H | $CH_3-$ | $CH_3-$ | Cl |
| $C_2H_5-$ | | H | $CH_3-$ | $CH_3-$ | Cl |
| $CH_3-$ |  | H | $CH_3-$ | $CH_3-$ | Cl |
| $CH_3-$ |  | H | $CH_3-$ | $CH_3-$ | Cl |
| $C_2H_5-$ | $-N(C_2H_5)_2$ | H | $CH_3$ | $CH_3-$ | Cl |
| $CH_3-$ | $-N(CH_3)_2$ | H | $CH_3-$ | $CH_3-$ | Cl |
| $CH_3-$ | | H | $CH_3-$ | $CH_3-$ | Cl |
| $C_2H_5-$ |  | H | $CH_3-$ | $CH_3-$ | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ |  | H | $CH_3-$ | $CH_3-$ | Cl |
| $C_2H_5-$ |  | H | $CH_3-$ | $CH_3-$ | Cl |
| $CH_3-$ | $CH_3O-(CH_2)_2-$ | H | $CH_3-$ | $CH_3-$ | Cl |
| $C_2H_5-$ |  | H | $CH_3-$ | $CH_3-$ | Cl |
| $-(CH_2)_3CH_3$ |  | H | $C_2H_5-$ | $C_2H_5-$ | Cl |
| $C_2H_5-$ | | H | $C_2H_5-$ | $C_2H_5-$ | Cl |
| $C_2H_5-$ | $CH_2=CH-CH_2-$ | H | $CH_3-$ | $C_2H_5-$ | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ |  | H | $CH_3-$ | $C_2H_5-$ | Cl |
| $CH_3-$ |  | H | $CH_3-$ | $-(CH_2)_3-CH_3$ | Cl |
| $CH_3$ | $-CH(CH_3)_2$ | $CH_3$ | $CH_3-$ | $-(CH_2)_3-CH_3$ | Cl |
| $CH_2=CH-CH_2-$ | $-N(CH_3)_2$ | H | $CH_3-$ | $-(CH_2)_3-CH_3$ | Cl |
| $CH_3-$ |  | H | $CH_3-$ | $-CH(CH_3)_2$ | Cl |
| $CH_3-$ |  | H | $CH_3-$ | $-CH(CH_3)_3$ | Cl |
| $CH_3-$ |  | H | $C_2H_5-$ | $-CH_2-CH(CH_3)_3$ | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| |  | $-CH_3$ | $C_2H_5-$ | $-CH_2-CH(CH_3)_2$ | Cl |
| $-CH_3$ | $-CH(CH_3)_2$ | H | $-(CH_2)_3-CH_3$ | $-(CH_2)_3-CH_3$ | Cl |
| $CH_3-$ | $CH_2=CH-CH_2-$ | H | $-(CH_2)_3-CH_3$ | $-(CH_2)_3-CH_3$ | Cl |
| $CH_3-$ | $-N(CH_3)_2$ | H | $-(CH_2)_3-CH_3$ | $-(CH_2)_3-CH_3$ | Cl |
| $CH_3-$ | $CH_3-$ | H | $CH_3O-(CH_2)_2-$ | $-CH_3$ | Cl |
| $CH_3-$ | $-CH(CH_3)_2$ | H | | $CH_3$ | Cl |
| $CH_3-$ | $CH_2=CH-CH_2-$ | H | | $CH_3$ | Cl |
| $CH_3-$ | | H | | $CH_3$ | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $C_2H_5-$ | $C_2H_5$ | H | $CH_2=CH-CH_2-$ | $CH_3$ | Cl |
| $CH_3-$ | $-CH(CH_3)_2$ | H |  | $CH_3$ | Cl |
| $CH_3-$ |  | H |  | $CH_3$ | Cl |
| $-(CH_2)_3-CH_3$ | $-N(CH_3)_2$ | H |  | $(CH_2)_2CH_3$ | Cl |
| $C_2H_5-$ | $C_2H_5$ | H |  | $CH_3$ | Cl |
| $CH_3-$ | $CH_2=CH-CH_2-$ | H |  | $CH_3$ | Cl |
| $CH_3$ | $CH(CH_3)_2$ | H |  | $CH_3$ | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $-(CH_2)_3-CH_3$ |  | H |  | $CH_3$ | Cl |
| $CH_3-$ |  | H |  | $CH_3$ | Cl |
| | $-(CH_2)_2-$ | H |  | $CH_3$ | Cl |
| $C_2H_5-$ |  | H |  | $-CH_2-CH_3$ | Cl |
| $CH_3$ | $-CH_2-CH(CH_3)_2$ | H |  | $CH_3$ | Cl |
| $CH_2=CH-CH_2-$ |  | H |  | $CH_3$ | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3$– |  | H |  | $(CH_2)_3CH_3$ | Cl |
| $C_2H_5$– | $C_2H_5$ | H |  | $CH_3$ | Cl |
| $C_2H_5$– | $C_2H_5$– | H |  | –$CH_3$ | Cl |
| $CH_3$ | $CH_2$=CH–$CH_2$– | H |  | –$CH_3$ | Cl |
| $CH_3$– |  | H |  | –$(CH_2)_3CH_3$ | Cl |
| $CH_3$– | –$CH(CH_3)_2$ | H |  | $CH_3$ | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $C_2H_5-$ |  | H |  | $CH_3$ | Cl |
| $CH_3-$ | $CH_2=CH-CH_2-$ | $CH_3$ |  | $CH_3$ | Cl |
| $CH_3-$ |  | H |  | $CH_3$ | Cl |
| $CH_3-$ | $-N(CH_3)_2$ | H |  | $(CH_2)_2CH_3$ | Cl |
| $C_2H_5-$ |  | H |  | $(CH_2)_3CH_3$ | Cl |
| $CH_3-$ | $CH_3-$ | H | H | H | F |
| $C_2H_5-$ | $C_2H_5-$ | H | H | H | F |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ | $-CH(CH_3)_3$ | H | H | H | F |
| $C_2H_5-$ | $C_2H_5-$ | $C_2H_5$ | H | H | F |
| $CH_3-$ | $CH_2=CH-CH_2-$ | H | H | H | F |
| $-CH_2-CH_2-CH_3$ |  | H | H | H | F |
| $C_2H_5-$ |  | $CH_3$ | H | H | F |
| $CH_3-$ | $-N(CH_3)_2$ | H | H | H | F |
| $C_2H_5-$ |  | H | H | H | F |
| $CH_3-$ |  | H | H | H | F |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $C_2H_5$– |  | H | H | H | F |
| $CH_3$– | $-CH(CH_3)_2$ | H |  | H | F |
| $C_2H_5$– | $C_2H_5$– | $C_2H_5$ | $CH_3$ | H | F |
| $CH_3$– |  | H | $C_4H_9$– | H | F |
| $CH_3$– | $CH_2=CH-CH_2$– | H | $CH_3$– | $CH_3$– | F |
| $CH_3$– |  | H | $CH_3$– | $CH_3$– | F |
| $CH_3$– | $-CH(CH_3)_2$ | $C_2H_5$ | $CH_3$– | $CH_3$– | F |
| $CH_3$– | $CH_3$<br>\|<br>$-CH-CH_2-CH_3$ | H |  | $CH_3$– | F |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $C_2H_5$– | $CH_3$–CH(–$CH_2$–)–$CH_3O$ | H |  | $CH_3$– | F |
| $CH_3$– | $-N(CH_3)_2$ | H |  | $CH_2$–$CH_3$– | F |
| $C_2H_5$– | $C_2H_5$ | H |  | $CH_3$– | F |
| $CH_3$– | $-CH(CH_3)_3$ | H |  | $CH_3$– | F |
| –$CH_3$– | –$CH_3$– | H | H | H | Br |
| $CH_3$– | $CH_3$– | $-C_2H_5$ | H | H | Br |
| –$CH_3$ | $-CH(CH_3)_2$ | $-CH_3$ | H | H | Br |
| –$CH_3$ | $-CH(CH_3)_2$ | H | H | H | Br |

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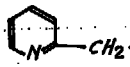
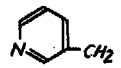
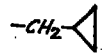
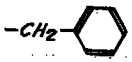
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $-C_2H_5$ | $-CH_2-CH(CH_3)_2$ | H | H | H | Br |
| $CH_3-$ |  | H | H | H | Br |
| $C_2H_5-$ |  | H | H | H | Br |
| $C_2H_5-$ | $CH_2=CH-CH_2-$ | H | H | H | Br |
| $C_2H_5-$ | $-N(CH_3)_2$ | H | H | H | Br |
| $C_2H_5-$ |  | H | H | H | Br |
| $CH_3-$ |  | H | H | H | Br |
| $CH_3-$ | $-CH(CH_3)_2$ | H | $CH_3-$ | H | Br |

| R¹ | R² | R³ | R⁴ | R⁵ | Y |
|---|---|---|---|---|---|
| $CH_3-(CH_2)_3-$ | $-CH_3-(CH_2)_3-$ | H | $CH_3-$ | H | Br |
| $CH_3-$ | $CH_2=CH-CH_2-$ | H | $CH_3-(CH_2)_4-$ | H | Br |
| $C_2H_5-$ |  | H | $CH_3-(CH_2)_4-$ | H | Br |
| $CH_3-$ |  | $CH_3$ | $C_2H_5-$ | H | Br |
| $CH_3-$ |  | H | $CH_3-(CH_2)_3-$ | H | Br |
| $C_2H_5$ | $C_2H_5$ | H | $(CH_3)_2CH-$ | H | Br |
| $CH_3-$ | $-CH(CH_3)_2$ | H |  | H | Br |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ |  | H |  | H | Br |
| $CH_3-$ | $-CH(CH_3)_2$ | H |  | H | Br |
| $C_2H_5-$ | $C_2H_5-$ | H |  | H | Br |
| $CH_3-$ | $-CH(CH_3)_2$ | H |  | $CH_3-$ | Br |
| $CH_3-$ | $-CH_2-CH(CH_3)_2$ | H | $CH_3-$ | $CH_3-$ | Br |
| $CH_2=CH-CH_2-$ |  | H | $CH_3-$ | $CH_3-$ | Br |

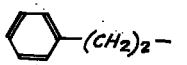
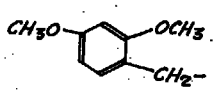
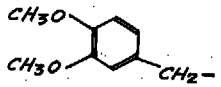
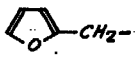
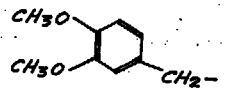
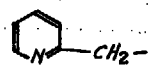
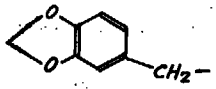
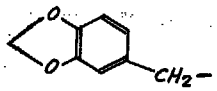
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3$– |  | H | $CH_3$– | $CH_3$– | Br |
| $CH_3$– | $CH_3$– | H | H | H | $CF_3$ |
| $CH_3$– | $CH_3$– | $C_2H_5$– | H | H | $CF_3$ |
| $CH_3$– | $-CH(CH_3)_2$ | H | H | H | $CF_3$ |
| $-C_2H_5$ | $-C_2H_5$ | H | H | H | $CF_3$ |
| $CH_3$– | $CH_3$–$(CH_2)_4$– | H | H | H | $CF_3$ |
| | | $CH_3$– | H | H | $CF_3$ |
| $C_2H_5$– | | H | H | H | $CF_3$ |
| $CH_3$– | | H | H | H | $CF_3$ |

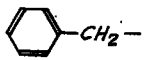
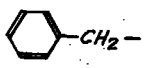
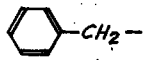
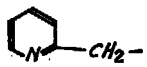
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-CH_2-CH_2-$ |  | H | H | H | $CF_3$ |
| | $-(CH_2)_3-$ | H | H | H | $CF_3$ |
| $CH_3-$ | $CH_2=CH-CH_2-$ | H | H | H | $CF_3$ |
| $C_2H_5-$ | $-N(CH_3)_2$ | H | H | H | $CF_3$ |
| $CH_3-$ |  | H | H | H | $CF_3$ |
| $CH_3-$ |  | H | H | H | $CF_3$ |
| $C_2H_5-$ |  | $CH_3$ | H | H | $CF_3$ |
| $CH_3-$ |  | H | H | H | $CF_3$ |

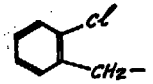
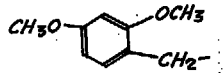
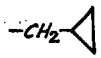
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $-(CH_2)_2-CH_3$ | $-(CH_2)_2-CH_3$ | H | H | H | $CF_3$ |
| $C_2H_5-$ |  | $C_2H_5$ | H | H | $CF_3$ |
| $CH_3-$ | $CH_3$ | $C_2H_5$ | $-CH_3$ | H | $CF_3$ |
| $CH_3-$ | $-CH(CH_3)_2$ | H | $-(CH_2)_3-CH_3$ | H | $CF_3$ |
| $C_2H_5-$ | $C_2H_5-$ | H | $-C_2H_5$ | H | $CF_3$ |
| $CH_3(CH_2)_3-$ | $CH_3-(CH_2)_3-$ | H | $-CH_2-CH_2-CH_3$ | H | $CF_3$ |
| $CH_3$ | | H | $-CH_3$ | H | $CF_3$ |
| $C_2H_5-$ |  | H | $-(CH_2)_3-CH_3$ | H | $CF_3$ |
| $CH_3-$ |  | H | $-CH(CH_3)_2$ | H | $CF_3$ |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ |  | H | $-CH(CH_3)_2$ | H | $CF_3$ |
| $C_2H_5-$ | $CH_2=CH-CH_2-$ | H | $-C_2H_5$ | H | $CF_3$ |
| $CH_3-$ | $-N(CH_3)_2$ | H | $-C_2H_5$ | H | $CF_3$ |
| $CH_3-$ | $-CH(CH_3)_2$ | H |  | H | $CF_3$ |
| $C_2H_5-$ | $C_2H_5-$ | $C_2H_5-$ |  | H | $CF_3$ |
| $CH_3$ |  | H |  | $CH_3$ | $CF_3$ |
| $CH_3-$ | $CH_3-$ | H | $-(CH_2)_3-CH_3$ |  | $CF_3$ |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ | $CH_2=CH-CH_2-$ | H |  | H | $CF_3$ |
| $CH_3-$ | $-CH_2-CH(CH_3)_2$ | H |  | H | $CF_3$ |
| | $-(CH_2)_5-$ | $CH_3-$ |  | $C_2H_5$ | $CF_3$ |
| $CH_3-$ | | H |  | H | $CF_3$ |
| $CH_3-$ | | H |  | H | $CF_3$ |
| $C_2H_5-$ | $CH_2=CH-CH_2-$ | H |  | H | $CF_3$ |

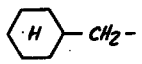
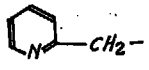
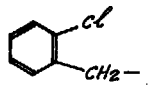
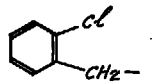
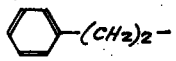
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $C_2H_5-$ | $-C_2H_5$ | H |  | H | $CF_3$ |
| $CH_3-$ | $-CH_2-CH(CH_3)_2$ | H |  | H | $CF_3$ |
| $C_2H_5-$ | | H |  | H | $CF_3$ |
| $C_2H_5-$ |  | H |  | H | $CF_3$ |
| $C_2H_5-$ |  | H |  | H | $CF_3$ |
| $CH_3-$ | $-CH(CH_3)_2$ | H |  | H | $CF_3$ |

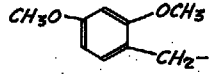
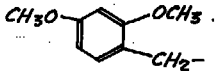
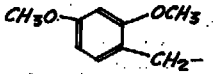
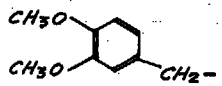
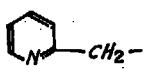
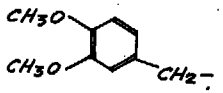
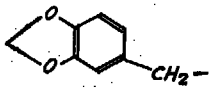
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^9$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ | $-CH_3$ | H |  | $-CH_3$ | $CF_3$ |
| $C_2H_5-$ | $-C_2H_5$ | H |  | $-(CH_2)_3CH_3$ | $CF_3$ |
| $CH_3-$ | $CH_3$<br>$-CH-CH_2-CH_3$ | H |  | $-CH(CH_3)_2$ | $CF_3$ |
| $C_2H_5-$ | $-C_2H_5$ | H | $CH_3-$ | $-CH_3$ | $CF_3$ |
| $CH_3-$ | $-CH_2-CH(CH_3)_2$ | H | $CH_3-$ | $-CH_3$ | $CF_3$ |
| $CH_3-$ | | H | $CH_3-$ | $-CH_3$ | $CF_3$ |
| $CH_3-$ |  | $CH_3-$ | $CH_3-$ | $-CH_3$ | $CF_3$ |

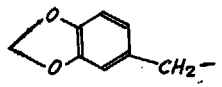
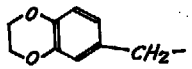
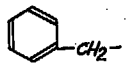
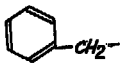
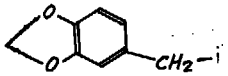
| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $-(CH_2)_2-$ | | H | $CH_3-$ | $-CH_3$ | $CF_3$ |
| $CH_3-$ | $CH_3-$ | H |  | H | $CF_3$ |
| $CH_3$ | $CH_3-$ | H |  | H | $CF_3$ |
| $CH_3-$ | $-CH_3$ | H | H | H | $CH_3$ |
| $CH_3-$ | $-CH_3$ | $C_2H_5-$ | H | H | $CH_3$ |
| $CH_3-$ | $CH_3-(CH_2)_5-$ | H | H | H | $CH_3$ |
| $C_2H_5-$ |  | H | H | H | $CH_3$ |
| $CH_3-$ | | H | H | H | $CH_3$ |

| R¹ | R² | R³ | R⁴ | R⁵ | Y |
|---|---|---|---|---|---|
| $C_2H_5$– | $CH_2=CH-CH_2$– | H | H | H | $CH_3$ |
| | –$(CH_2)_3$– | H | H | H | $CH_3$ |
| $C_2H_5$– |  | H | H | H | $CH_3$ |
| $CH_3$– |  | H | H | H | $CH_3$ |
| $C_2H_5$– |  | $CH_3$– | H | H | $CH_3$ |
| $CH_3$– |  | H | H | H | $CH_3$ |
| $C_2H_5$– | –$N(CH_3)_2$ | $C_2H_5$– | H | H | $CH_3$ |
| $CH_3$– |  | H | H | H | $CH_3$ |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ |  | $CH_3-$ | H | H | $CH_3$ |
| $CH_3-$ | $CH_3-$ | $C_2H_5-$ | $-C_2H_5$ | H | $CH_3$ |
| $CH_3-$ | $-CH(CH_3)_2$ | H | $-(CH_2)_3-CH_3$ | H | $CH_3$ |
| $C_2H_5-$ | $-HC(CH_3)-CH_2-CH_3$ | H | $-CH_2-CH_2-CH_3$ | H | $CH_3$ |
| $CH_3-$ |  | H | $-(CH_2)_3CH_3$ | H | $CH_3$ |
| $CH_3-$ | $-CH(CH_3)_2$ | H | $-CH_2-CH(CH_3)_2$ | H | $CH_3$ |
| $C_2H_5-$ | $-CH_2-CH(CH_3)_2$ | H |  | H | $CH_3$ |
| $CH_3-$ | $CH_2=CH-CH_2-$ | $CH_3-$ |  | H | $CH_3$ |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ | $-CH(CH_3)_2$ | H |  | H | $CH_3$ |
| $C_2H_5-$ |  | H | | H | $CH_3$ |
| $C_2H_5-$ | $CH_2=CH-CH_2-$ | H |  | H | $CH_3$ |
| $C_2H_5-$ | | H |  | H | $CH_3$ |
| $CH_3-$ | $CH_3$<br>$-CH-CH_2-CH_3$ | H | | H | $CH_3$ |
| $CH_3-$ | $-N(CH_3)_2$ | H |  | H | $CH_3$ |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ | $CH_3-$ | $CH_3-$ |  | H | $CH_3$ |
| $CH_3-$ | $-CH_2-CH(CH_3)_2$ | H |  | H | $CH_3$ |
| $C_2H_5-$ | $CH_2=CH-CH_2-$ | H |  | H | $CH_3$ |
| $C_2H_5-$ | | H |  | H | $CH_3$ |
| $CH_2=CH-CH_2-$ |  | H |  | H | $CH_3$ |
| $C_2H_5-$ | $C_2H_5-$ | $CH_3-$ |  | H | $CH_3$ |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3-$ | $-CH(CH_3)_2$ | H |  | H | $CH_3$ |
| $C_2H_5-$ | $-CH_2-CH=CH_2$ | H |  | H | $CH_3$ |
| $C_2H_5$ | $-CH(CH_3)_2$ | H |  | $CH_3-$ | $CH_3$ |
| $CH_3-$ | $CH_2=CH_2-CH_2-$ | H |  | $-CH_3$ | $CH_3$ |
| $CH_3-$ | $-CH(CH_3)_2$ | H |  | $-(CH_2)_3-CH_3$ | $CH_3$ |
| $CH_3-$ | $CH_3-$ | H | $CH_3-$ | $CH_3-$ | $CH_3$ |
| $C_2H_5-$ | $-CH_2-CH(CH_3)_2$ | H | $CH_3-$ | $CH_3-$ | $CH_3$ |
| $C_2H_5-$ | $C_2H_5-$ | $CH_3-$ | $CH_3-$ | $CH_3-$ | $CH_3$ |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3$ | $(CH_2)_2OCH_3$ | H | H | H | Cl |
| $C_2H_5$ | $(CH_2)_2OCH_3$ | H | H | H | Cl |
| $CH_3$ | $(CH_2)_2OCH_3$ | H | n-$C_3H_7$– | H | Cl |
| $CH_3$ | $(CH_2)_2OCH_3$ | H | H | H | Br |
| $CH_3$ | $(CH_2)_3OCH_3$ | H | H | H | Cl |
| $CH_3$ | $(CH_2)_2OC_2H_5$ | H | H | H | Cl |
| n-$C_3H_7$ | $(CH_2)_2OC_2H_5$ | H | H | H | Cl |
| $C_2H_5$ | $CH_2$–CH(–$OCH_3$)–$CH_3$ | H | H | H | Cl |
| $C_2H_5$ | $CH_2$–CH(–O–$C_2H_5$)–$CH_3$ | H | H | H | Cl |
| $CH_3$ | $CH_2$–CH(–$OCH_3$)–$C_2H_5$ | H | H | H | Cl |

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y |
|---|---|---|---|---|---|
| $CH_3$ | $CH_2-CH(OCH_3)-C_2H_5$ | H | $n\text{-}C_5H_7$ | H | Cl |
| $C_2H_5$ | $CH_2-CH(O-C_2H_5)-C_2H_5$ | H | H | H | Cl |
| $CH_3$ | $CH_2-CH(O-C_2H_5)-C_2H_5$ | H | $CH_2-C_6H_5$ | H | Cl |
| $CH_3$ | $CH_2-CH(O-C_2H_5)-C_2H_5$ | H | H | H | Br |

The products of the invention are valuable medicaments and are distinguished by a very good diuretic and saluretic activity.

4-Aryl-1,3-thiazolidine-4-ol-derivatives having an anorectic, diuretic activity stimulating the CNS are known from German Offenlegungsschrift No. 1,938,674 and U.S. Patent No. 3,671,534, these compounds have no sulfonamide groups on the aromatic nucleus and their diuretic action depends to a high degree on a specific substitution of the thiazolidine ring. It was surprising that the compounds of the present invention have a high salidiuretic activity independent of that specific ring substitution by the introduction of a sulfonamide group in 3-position of the benzene nucleus, which are distinctly superior in quality and quantity to these known thiazolidine derivatives. Moreover, the less desirable anorectic and CNS-stimulating action is largely suppressed.

The salidiuretic activity of the compounds of the invention was determined on the rat in a dosage unit of 50 mg/kg *per os*. It is superior to the salidiuretic activity of known commercial products of the thiazide group, for example, hydrochlorothiazide and that of chlorothalidone. Moreover, the compounds of the invention are distinguished by

a long-lasting activity which is about the same as that of chlorothalidone. For this reason, the products of the invention are especially suitable for the treatment of hypertonic states in human beings, in which case they can be combined, as is generally usual, nowadays, optionally with an antihypertonic agent.

The present invention accordingly provides a pharmaceutical preparation which comprises a compound of the general formula I or a physiologically tolerable acid addition salt thereof, in admixture or conjunction with a pharmaceutically suitable carrier. The preparations are preferably in unit dosage form, for example, tablets, effervescent tablets, dragées, capsules, suppositories, and ampoules for parenteral administration for example, intravenous, subcutaneous and intramuscular, and the active substance is preferably one of the physiologically tolerable acid addition salts. The amount of active substance per dosage unit is generally from 5 to 500 mg, preferably from 10 to 100 mg. The pharmaceutical preparation may also comprise one or more further active substances, especially for the treatment of high blood pressure in human beings, for example, an antihypertensive agent, for example, reserpin, hydralazin, guanethidin, L-methyldopa or clonidin; a potassium retaining compound, for example, an aldosterone antagonist, for example spironolactone or a pseudoaldosterone antagonist, for example, triamterene or amiloride, and/or a $K^+$-substitution substance.

The following Examples illustrate the invention, the melting and decomposition points are not corrected. The IR-spectra were taken in KBr, the indicated IR-spectroscopic data are taken from routine spectra and are also not corrected.

## EXAMPLE 1.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide

a) 4.7 g of 4′-chloro-3′-sulfamoylacetophenone were suspended in 50 ml of ethyl acetate and to that suspension, some drops of a solution of 3.2 g of bromine were added until the mixture was distinctly brown. The suspension was heated to about 60—70°C unti the color changed (addition of a drop of 48% hydrobromic acid possible), cooled and the residual amount of the bromine solution was added dropwise at room temperature, while stirring. fter distilling off the solvent, 2-bromo-4′-chloro-3′-sulfamoylacetophenone was obtained which melted at 169°C (from n-butanol).

b) The residue was dissolved in 70 ml of acetone without further isolating the 2-bromo-4′-chloro-3′-sulfamoylacetophenone to which solution 2.1 g of 1,3-dimethylthiourea were added. Shortly thereafter, the oily 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide was separated and crystallized upon heating the reaction mixture to 40°C, forming colorless crystals that melted at 218—219°C (decomposition).

## EXAMPLE 2.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol

a) *4 - (4 - Chloro - 3 - chlorosulfonylphenyl - 3 - methyl - 2 - methylimino-1,3 - thiazolidine - 4 - ol - hydrobromide* 5.1 g of 4′ - chloro - 3′ - chlorosulfonylacetophenone were reacted in the manner described in Example 1a) with 3.2 g bromine in ethyl acetate to yield the 2-bromo-4′-chloro-3′-chlorosulfonylacetophenone (melting point: 111°C from chloroform, $\tilde{\nu}$ C=O 1700 $cm^{-1}$) which was reacted without further isolation, as described in Example 1b) with 2.1 g of 1,3-dimethylthiourea in 50 ml of acetone. The mixture was stirred for 30 minutes at 30—35°C, cooled to 10°C and the 4 - (4 - chloro - 3 - chlorosulfonylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thazolidine - 4 - ol - hydrobromide was filtered. Colorless crystals melting at 162°C (decomposition).

b) 4.4 g of 4 - (4 - chloro - 3 - chlorosulfonylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were introduced portionwise, while stirring, into 30 ml of a 8% methanolic ammonia solution. The mixture was allowed to dwell over night at room temperature, the precipitate of (4 - (4 - chloro - 3-sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol) was filtered and washed several times with water. Colorless crystals were obtained which melted at 188°C (decomposition) $\tilde{\nu}$ C=N 1620 $cm^{-1}$.

c) 10 g of powdered 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2-methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were dissolved in 500 ml of water at 50°C, while stirring, 100 ml of saturated sodium bicarbonate solution were added and the solution was thoroughly stirred for 2 hours at 5—10°C, 4 - (4 - chloro-3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol was

filtered off and washed several times with water. Melting point: 187—188°C (decomposition).

EXAMPLE 3.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride

a) 20 g of 4'-chloro-3'-sulfamoyl-diazoacetophenone were introduced, portionwise, while cooling and stirring, into a mixture of 200 ml of diethyleneglycol dimethyl ether. 2,4'-dichloro-3'-sulfamoylacetophenone was precipitated (melting point: 179°C) with 1 liter of ice water.

5.3 g of 2,4'-dichloro-3'-sulfamoylacetophenone were suspensed in 35 ml of methanol to which 2.1 g of 1,3-dimethylthiourea was added. The mixture was stirred for 30 minutes at 40°C, cooled to 5°C and 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3-methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride was filtered off.

b) 3 g of 4'-chloro-3'-sulfamoyl-2-hydroxyacetophenone were boiled under reflux for 2 hours in 30 ml of thionylchloride and the thionyl chloride was distilled off. The residue was treated with 20 ml of 80% methanol while cooling (heavy reaction), the solvent was expelled under reduced pressure and the residue was reacted without isolating the 2,4'-dichloro-3'-sulfamoylacetophenone in 20 ml of acetone with 1.7 g of 1,3-dimethylthiourea, as has been described in Example 3a).

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride precipitated and was filtered off.

c) 10 g of 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol were suspensed in 50 ml of ethanol to which suspension a 15% ethanolic hydrochloric acid solution was rapidly added dropwise, while stirring and cooling with ice, until the test paper showed a heavy acid reaction. The reaction temperature should not be exceeded. After shortly clearing the mixture, 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride precipitated. Stirring was continued for 10 minutes, 30 ml of ethyl acetate were added, the mixture was stirred for another 10 minutes at room temperature and the crystals were filtered off. They were colorless and melted at 210°C (decomposition).

EXAMPLE 4.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - p -toluenesulfonate

1 g of p-toluene sulfonic acid was added to a suspension of 1.5 g of 4 - (4 - chloro-3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol in 10 ml of ethanol. The clear solution was poured into 60 ml of diisipropyl ether and the oil so obtained was crystalilzed by treating with diethyl ether. Colorless crystals were obtained which were decomposed from 94°C onwards.

EXAMPLE 5.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - methansulfonate

1.5 g of 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino-1,3 - thiazolidine - 4 - ol were reacted in 10 ml of ethanol with 0.5 g of methanesulfonic acid and the colorless crystals were filtered off after stirring for 3 hours. Melting point: 168°C (decomposition).

EXAMPLE 6.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - amidosulfonate

4.5 g of 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino-1,3 - thiazolidine - 4 - ol were reacted with 1.5 g of ground amidosulfonic acid in 70 ml of ethanol. After 1 hour at 50°C and subsequent stirring for 10 hours at room temperature the desired salt precipitated in the form of colorless crystals which melted at 171°C.

EXAMPLE 7.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - formiate

According to the method of Example 5 there was obtained from 1.5 g of 4 - (4-chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol and 0.25 g of formic acid the desired formate in the form of colorless crystals which melted at 154°C (decomposition).

EXAMPLE 8.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - lactate

To 1.5 g of 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol 0.7 g of lactic acid were added in 10 ml of ethanol, the mixture was stirred for 3 hours at room temperature and precipitated with diisopropyl ether. After decanting of the solvent the oil was dissolved in water and lyophilized. The result was a colorless, amorphous solid substance that was decomposed from 120°C onwards, $\tilde{\nu}$ C=N 1630 $cm^{-1}$.

EXAMPLE 9.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - maleinate

1.5 g of 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino-1,3 - thiazolidine - 4 - ol were stirred in 10 ml of ethanol with 0.7 of maleic acid for 1 hour at room temperature, the salt desired was precipitated with 50 ml of diisopropyl ether and crystallized under fresh diisopropyl ether/ethyl acetate to yield colorless crystals which melted at 167°C (decomposition).

EXAMPLE 10.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - citrate

1.5 g of 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino-13 - thiazolidine - 4 - ol were reacted in the manner described in example 8 with 1 g of ground citric acid and worked up. Colorless amorphous solid substance, decomposition from 130°C on, $\tilde{\nu}$ C=N 1620 $cm^{-1}$.

EXAMPLE 11.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - salicylate

1.5 g of 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino-1,3 - thiazolidine - 4 - ol were reacted with 0.7 g of salizylic acid in the manner described in Example 8 and worked up. Colorless, amorphous solid substance: decomposition from 131°C, $\tilde{\nu}$ C=N 1630 $cm^{-1}$.

EXAMPLE 12.

3 - Ethyl - 2 - ethylimino - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 1,3 - thiazolidine-4 - ol - hydrobromide

To 6.2 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone 2.2 g or ground 1,3-diethyl-thiourea were added in 40 ml of methanol, the mixture was stirred for 10 minutes at 40°C and for 3 hours at room temperature and the salt was precipitated by adding diethyl ether. After decanting the solvent, the oily product was crystallized with diisopropyl ether heated to 30—40°C. Colorless crystals melting at 203°C (decomposition).

EXAMPLE 13.

3 - Ethyl - 2 - ethylimino - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 1,3 - thiazolidine-4 - ol - hydrochloride

a) 5.2 g of 2,4'-dichloro-3'-sulfamoylacetophenone were reacted in the manner described in Example 12, the end product was precipitated with diethyl ether and crystallized with etyhl acetate. Reprecipitation from 1 part of methanol (active charcoal) and 3 parts of ethyl acetate led to colorless crystals which melted at 177°C (decomposition).

b) 17 g of 3 - ethyl - 2 - ethylimino - 4 - (4 - chloro - 3 - sulfamoylphenyl)-1,3 - thiazolidine - 4 - ol - hydrobromide were suspensed in 100 ml of methanol and shortly heated to boiling after the addition of 10 ml of triethyl amine. The solvent was distilled off under reduced pressure, 150 ml of water were added to the residue and the mixture was extracted with 200 ml of ethyl acetate. After drying the organic phase over sodium sulfate the solvent was distilled off under reduced pressure. The residue was dissolved in 100 ml of acetone, the solution was acidified with 15% ethanolic HCl and the oily precipitate of the end product was crystallized with acetone heated to 40°C. Melting point: 177°C (decomposition).

EXAMPLE 14.

3 - Ethyl - 2 - ethylimino - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 5 - methyl - 1,3-thiabolidine - 4 - ol - hydrobromide

4.6 g of 4'-chloro-3'-sulfamoyl-propiophenone were reacted according to the prescription given in Example 1a) with 1 ml of bromine and the solvent was distilled off under reduced pressure. The oily residue of the 2-bromo-4'-chloro-3'-sulfamoyl-propiophenone was dissolved without further purification in 50 ml of ethanol, stirred for 2 hours at room temperature after adding 2.6 g of 1,3-diethylthio urea and allowed to dwell over night. The end product was precipitated with ether, the solvent was decanted, the oily residue was dissolved in water and lyophilized. Colorless, amorphous solid body: decomposition from 140°C on, $\tilde{\nu}$ C=N 1610 cm$^{-1}$.

EXAMPLE 15.

5 - Ethyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3-thiazolidine - 4 - ol -hydrobromide

a) 6.1 g of 4'-chloro-3'-sulfamoyl-butyrophenone were reacted according to the prescription given in Example 1a) with 3.85 g of bromine in 100 ml of ethyl acetate, the solvent was decanted under reduced pressure and the oily residue of the 2-bromo-4'-chloro-3'-sulfamoyl-butyrophenone was crystallized with a small amount of diisopropyl ether. Melting point: 59°C.

b) 5.6 g of 2-bromo-4'-chloro-3'-sulfamoyl-butyrophenone and 1.7 g of 1,3-dimethylthio urea were heated in 50 ml of methanol for 10 minutes to 40°C and stirred for another 2 hours at room temperature. Precipitation followed by adding diisopropyl ether and the oily end product was crystallized with diethyl ether. Colorless solid body: decomposition from 98°C on, $\tilde{\nu}$ C=N 1620 cm$^{-1}$.

EXAMPLE 16.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - propyl - 2 - propylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride

5.3 g of 2,4'-dichloro-3'-sulfamoylacetophenone and 3.2 g of ground 1,3-dipropyl-thio urea were heated in 45 ml of methanol for 5 minutes to 50°C and stirred for another 30 minutes at room temperature. After pouring the reaction mixture into 120 ml of diethyl ether the end product was obtained as a viscous mass which crystallized under mild heating rapidly with ether. Colorless solid body: melting point: 175°C (decomposition).

EXAMPLE 17.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 2 - isopropylamino - 3 - methyl - 1,3 - thiazolidine - 4 - ol - hydrobromide

6.1 g of 2-bromo-4'-chloro-3' - sulfamoylacetophenone were heated with 2.4 g of 1-methyl-3-isopropylthiourea in 50 ml of acetone for 10 minutes to 40°C, the separating oil was triturated to form crystals and the crystalline suspension was stirred for 1 hour at room temperature. Colorless solid body: melting point: 195°C (decomposition).

EXAMPLE 18.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 2 - isopropylamino - 3 - methyl - 1,3 - thiazolidine - 4 - ol

7 g of ground 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - isopropylimino - 3-methyl - 1,3 - thiazolidine - 4 - ol - hydrobromide were dissolved in 80 ml of 40°C hot water and stirred for 30 minutes at 40°C after adding it to a mixture of 60 ml of saturated sodium bicarbonate solution and 100 ml of water. After cooling to room temperature, the mixture was extracted with 200 ml of diethyl ether, the organic phase was dried over sodium sulfate and the solvent was distilled off under reduced pressure. The residue was dissolved in 40 ml of diisopropyl ether and the end product was precipitated by pouring it into 200 ml of stirred petroleum ether. Colorless solid body: decomposition beginning at 110°C, $\tilde{\nu}$ C=N 1610 cm$^{-1}$.

EXAMPLE 19.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 2 - isopropylimino - 3 - methyl - 1,3 - thiazolidine - 4 - ol - hydrochloride

A solution of 6 g of 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - isopropylimino - 3 - methyl - 1,3 - thiazolidine - 4 - ol in 30 ml of ethyl acetate was made acid by adding, dropwise, 15% ethanolic hydrochloric acid. The solution was triturated to crystallize, allowed to stand over night at 0°C and the crystals were filtered off. Colorless solid body: melting point: 186°C (decomposition).

EXAMPLE 20.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - isopropyl - 2 - isopropylimino - 1,3-thiazolidine - 4 - ol - hydrochloride

5.2 g of 2,4'-dichloro-3-sulfamoylacetophenone were reacted with 3.2 g of 1,3-diisopropylthio urea and worked up in the manner prescribed in Example 12. Colorless solid body: melting point: 191°C (decomposition).

EXAMPLE 21.

3 - n - Butyl - 2 - n - butylimino - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 1,3 - thiazolidine - 4 - ol - hydrobromide

6.2 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone were reacted with 3.8 g of 1,3-di-n-butylthiourea according to the prescription given in Example 12 and the end product was precipitated with diisopropyl ether. Colorless amorphous solid body: decomposition beginning at 100°C, $\tilde{\nu}$ C=N 1615 cm$^{-1}$.

EXAMPLE 22.

3 - n - Butyl - 2 - n - butylimino - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 1,3 - thiazolidine - 4 - ol - hydrochloride

5.2 g of 2,4'-dichloro-3'-sulfamoylacetophenone were reacted with 3.8 g of 1,3-di-n-butylthiourea according to the prescription given in Example 12 and the end product was precipitated with diisopropyl ether. Colorless crystalline solid body: melting point: 164°C (decomposition).

EXAMPLE 23.

3 - Ethyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - isopropylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride

6.2 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 2.92 g of 1-ethyl-3-isopropylthiourea were heated in 40 ml of acetone for 15 minutes to 40°C, the mixture was stirred for another 30 minutes at room temperature and the crystals were filtered. Colorless crystalline solid body: melting point: 188°C (decomposition).

EXAMPLE 24.

3 - Ethyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - isopropylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride

5.5 g of 3 - ethyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - isopropylimino-1,3 - thiazolidine - 4 - ol - hydrochloride were dissolved in 30 ml of hot water and added to a stirred mixture of 50 ml of ethyl acetate and 20 ml of saturated aqueous sodium bicarbonate solution. The organic phase was separated, dried over sodium sulfate and the solvent was distilled off under reduced pressure. The oily 3 - ethyl - 4-(4 - chloro - 3 - sulfamoylphenyl) - 2 - isopropylimino - 1,3 - thiazolidine - 4 - ol was dissolved in 15 ml of ethanol, 15% ethanolic hydrochloric acid were added dropwise while cooling and the end product was precipitated by adding diisopropyl ether. Colorless crystalline solid body: melting point: 175°C (decomposition).

EXAMPLE 25.

3 - sec. - Butyl - 2 - sec. - butylimino - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 1,3-thiazolidine - 4 - ol -hydrochloride

5.3 g of 2,4'-dichloro-3'-sulfamoylacetophenone and 3.8 g of 1,3-di-sec.-butylthiourea were reacted in the manner described in Example 16, the reaction mixture was introduced into a solution of 40 ml of diethyl ether and 120 ml of ethyl acetate and the colorless, crystalline end product was filtered off after stirring for 4 hours at room temperature. Melting point: 186°C (decomposition).

EXAMPLE 26.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - isobutyl - 2 - isobutylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride

5.3 g of 2,4'-dichloro-3'-sulfamoylacetophenone and 3.8 g of 1,3-diisobutylthiourea were reacted according to the prescription made in Example 16 and worked up as described in Example 25. Colorless, crystalline end product: melting point: 176°C (decomposition).

EXAMPLE 27.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 2 - isobutylimino - 3 - methyl - 1,3 - thiazolidine - 4 - ol - hydrobromide

6.2 g of 4'-chloro-3'-sulfamoyl-2-bromoacetophenone and 3.0 g of 1-isobutyl-3-methylthiourea were reacted according to the prescription made in Example 23 and the

colorless end product was precipitated with 200 ml of diethyl ether. Decomposition beginning at 122°C, $\tilde{\nu}$ C=N 1620 $cm^{-1}$.

EXAMPLE 28.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 2 - isobutylimino - 3 - methyl - 1,3 - thiazolidine - 4 - ol

8 g of 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - isobutylimino - 3 - methyl-1,3 - thiazolidine - 4 - ol - hydrobromide were dissolved in 30 ml of water and the end product was precipitated by pouring it into 20 ml of a saturated and stirred sodium carbonate solution. Colorless, amorphous solid body, $\tilde{\nu}$ C=N 1615 $cm^{-1}$.

EXAMPLE 29.

2 - sec. - Butylimino - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 1,3-thiazolidine - 4 - ol - hydrobromide

4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 2.19 g of 1-sec.-butyl-3-methylthiourea were reacted according to the prescription given in Example 23 and the crystals were filtered off. Melting point: 163°C (decomposition).

EXAMPLE 30.

2 - sec. - Butylimino - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 1,3 - thiazolidine - 4 - ol

6 g of 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - sec. - butylimino - 3 - methyl-1,3 - thiazolidine - 4 - ol-hydrobromide were reacted according to the prescription given in Example 28. Colorless solid body: decomposition beginning at 99°C, $\tilde{\nu}$ C=N 1610 $cm^{-1}$.

EXAMPLE 31.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - n - hexyl - 2 - n - hexylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride

5.2 g of 2,4'-dichloro-3'-sulfamoylacetophenone and 4.8 g of 1,3-di-n-hexyl-thiourea were reacted according to the prescription given in Example 12, the end product was precipitated with diethyl ether and the remaining oil was treated with cyclohexane. Colorless, amorphous solid body: decomposition beginning at 75°C, $\tilde{\nu}$ C=N 1615 $cm^{-1}$.

EXAMPLE 32.

3 - Allyl - 2 - allylimino - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 1,3 - thiazolidine-4 - ol - hydrochloride

5.2 g of 2,4'-dichloro-3'-sulfamoylacetophenone and 2.5 g of 1,3-diallyl-thiourea were reacted according to the prescription given in Example 12, the end product was precipitated with diisopropyl ether and the oil obtained was crystallized with diethyl ether/ethyl acetate (1:1). Colorless solid body: melting point: 158°C (decomposition).

EXAMPLE 33.

3 - Allyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - isopropylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide

6.2 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 3.16 g of 1-allyl-3-isopropylthiourea were reacted according to the prescription given in Example 23 and the colorless crystalline end product was filtered off. Melting point: 180°C (decomposition).

EXAMPLE 34.

3 - Allyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - cyclopropylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide

6.2 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 3.1 g of 1-allyl-3-cyclopropylthiourea were reacted and worked up according to the prescription given in Example 12. Colorless, amorphous solid body: decomposition beginning at 90°C, $\tilde{\nu}$ C=N 1600 $cm^{-1}$.

EXAMPLE 35.

3 - Allyl - 4 - (4 - chloro - 3 -sulfamoylphenyl) - 2 - cyclopropylamino - 1,3 - thiazolidine - 4 - ol

6.2 g of 3 - allyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - cyclopropylimino-1,3 - thiazolidine - 4 - ol - hydrobromide were reacted according to the prescription given in Example 28. Colorless, crystalline solid body: melting point: 140°C (decomposition).

EXAMPLE 36.

4 - (4 - Chloro - 3 - sulfamoyl - phenyl) - 2 - cyclopropylimino - 3 - methyl - 1,3-thiazolidine - 4 - ol - hydrobromide

4.15 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone were reacted with 1.95 g of 1-cyclopropyl-3-methylthiourea according to the prescription given in Example 23 and the oily precipitate was crystallized with diisopropyl ether. Colorless, crystalline solid body: melting point: 204°C (decomposition).

EXAMPLE 37.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 2 - cyclopentylmethylimino - 3 - methyl - 1,3-thiazolidine - 4 - ol - hydrobromide

4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone were reacted with 2.6 g of 1-cyclopentylmethyl-3-methylthiourea according to the prescription given in Example 23 and the colorless crystalline final product was filtered off. Melting point: 189°C (decomposition).

EXAMPLE 38.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 2 - cyclopentylmethylimino - 3 - methyl - 1,3-thiazolidine - 4 - ol

6 g of 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - cyclopentylmethylimino - 3-methyl - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted according to the prescription given in Example 2c) with sodium bicarbonate. Colorless solid body: decomposition beginning at 115°C $\tilde{\nu}$ C=N 1615 $cm^{-1}$.

EXAMPLE 39.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 2 - cyclohexylimino - 3 - methyl - 1,3 - thiazolidine - 4 - ol - hydrobromide

4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone were reacted with 2.6 g of 1-cyclohexyl-3-methylthiourea in the manner described in Example 23 and the colorless crystalline end product was filtered off. Melting point: 178°C (decomposition).

EXAMPLE 40.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 2 - cyclohexylimino - 3 - methyl - 1,3 - thiazolidine - 4 - ol

6 g of 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - cyclohexylimino - 3 - methyl-1,3 - thiazolidine - 4 - ol - hydrobromide were reacted according to the prescription made in Example 28. Colorless solid body: decomposition beginning at 106°C, $\tilde{\nu}$ C=N 1610 $cm^{-1}$.

EXAMPLE 41.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - cyclopropyl - 2 - cyclopropylimino - 1,3-thiazolidine - 4 - ol - hydrochloride

5.2 g of 2,4'-dichloro-3'-sulfamoylacetophenone and 3.1 g of 1,3-dicyclopropylthiourea were reacted according to the prescription given in Example 12 and the colorless crystalline precipitate of the end product was filtered off.

EXAMPLE 42.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - cyclohexyl - 2 - cyclohexylimino - 1,3-thiazolidine - 4 - ol - hydrochloride

5.2 g of 2,4'-dichloro-3'-sulfamoylacetophenone and 4.8 g of 1,3-dicyclohexylthiourea were reacted according to the prescription made in Example 12, the end product was precipitated with 200 ml of diethyl ether and the oil was crystallized after decanting the solvent with diethyl ether. Colorless, crystalline solid body: melting point: 177°C (from acrylonitrile).

EXAMPLE 43.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - cyclooctyl - 2 - cyclooctylimino - 1,3-thiazolidine - 4 - ol - hydrochloride

5.2 g of 2,4'-dichloro-3'-sulfamoylacetophenone and 5.8 g of 1,3-dicyclooctylthiourea were reacted according to the prescription made in Example 12 and worked up according to the prescription of Example 42. Colorless solid body, decomposition beginning at 118°C, $\tilde{\nu}$ C=N 1600 $cm^{-1}$.

EXAMPLE 44.

3 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - hydroxy - 2,3,5,6 - tetrahydroimidazo-[2,1-b] - thiazole - hydrobromide

6.2 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 2 g of ground 2-imidazolidine-thione were reacted according to the prescription given in Example 12 and the

crystalline precipitate was filtered off. Colorless solid body: decomposition beginning at 100°C, $\tilde{\nu}$ C=N 1590 cm$^{-1}$.

EXAMPLE 45.

3 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - hydroxy - 2,3,6,7 - tetrahydro - 5H - thiazolo[3,2-a]pyrimidine - hydrobromide

6.2 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 2.4 g of ground 3,4,5,6-tetrahydro-2-pyrimidine-thiol were reacted according to the prescription given in Example 12, the reaction mixture was poured into 400 ml of ethyl acetate and the oily precipitate of the end product was crystallized by heating to 50—60°C. Colorless, crystalline solid body: melting point: 330—333°C (water separation at 210—220°C).

EXAMPLE 46.

3 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - hydroxy - 2,3,6,7 - tetrahydro - 5H - thiazolo[3,2-a]pyrimidine - hydrochloride

5.2 g of 2,4'-dichloro-3'-sulfamoylacetophenone and 2.4 g of ground 3,4,5,6-tetrahydro-2-pyrimidine-thiol were reacted in the manner described in Example 12, the reaction mixture was precipitated with 200 ml of diethyl ether, the solvent was decanted and the oily end product was crystallized under warm ethyl acetate. Colorless crystalline solid body, melting point: 180°C (decomposition).

EXAMPLE 47.

3 - (4 - Chloro - 3 - sulfamoylphenyl) - 6,6 - dimethyl - 3 - hydroxy - 2,3,5,6 - tetrahydro - imidazo[2,1-b]thiazole - hydrobromide

3.1 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 1.3 g of 4,4-dimethyl-2-imidazolidine-thione were reacted as described in Example 12 in 15 ml of methanol, the reaction mixture was precipitated with 70 ml of diethyl ether and the oily precipitate was crystallized with ethyl acetate at 40 to 50°C. Colorless, crystalline solid body: melting point: 164°C (decomposition).

EXAMPLE 48.

From 4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 2.7 g of 1-ethyl-3 - (2 - furylmethyl) - thiourea the 3 - ethyl - 4 - (4 - chloro - 3 - sulfamoylphenyl)-2 - (2 - furylmethylimino) - 1,3 - thiazolidine - 4 - ol - hydrobromide, which was converted in an analogous manner to Example 2c) with aqueous $NaHCO_3$ solution into the 3 - ethyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - (2 - furylmethylimino)-1,3 - thiazolidine - 4 - ol, decomposition beginning at 115°C).

EXAMPLE 49.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 2 - (2 - chlorobenzylimino) - 3 - methyl - 1,3-thiazolidine - 4 - ol - hydrobromide

4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 3.1 g of 1-(2-chlorobenzyl)-3-methylthiourea were reacted according to Example 23 and the crystalline end product was filtered off. Colorless crystalline solid body: melting point: 182°C (decomposition).

EXAMPLE 50.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 2 - (2 - chlorobenzylimino) - 3 - methyl - 1,3-thiazolidine - 4 - ol

6 g of 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - (2 - chlorobenzylimino) - 3-methyl - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted according to the prescription given in Example 2c). Colorless solid body: decomposition beginning at 114°C, $\tilde{\nu}$ C=N 1615 cm$^{-1}$.

EXAMPLE 51.

2 - Benzylimino - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 1,3 - thiazolidine - 4 - ol

4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 2.7 g of 1-benzyl-3-methylthiourea were reacted as prescribed in Example 23 and the reaction mixture was introduced into 200 ml of diethyl ether while stirring. The hygroscopic crystals of the 2 - benzylimino - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 1,3 - thiazolidine - 4 - ol - hydrobromide were rapidly filtered off, dissolved in 70 ml of water and converted into the end product according to the prescription of Example 28. Colorless solid body: decomposition beginning at 110°C, $\tilde{\nu}$ C=N 1610 cm$^{-1}$.

EXAMPLE 52.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - (3,4- methylenedioxybenzyl)-1,3 - thiazolidine - 4 - ol - hydrobromide

4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 3.36 g of 1-methyl-3-(3,4-methylenedioxybenzyl)-thiourea were reacted according to the prescription of Example 23 and the crystalline end product was filtered off. Melting point: 145°C (decomposition).

EXAMPLE 53.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - dimethylamino - 4 - hydroxy - 1,3 - thiazolidine - 2 - N,N - dimethylhydrazone - hydrochloride

5.2 g of 2,4'-dichloro-3'-sulfamoylacetophenone and 3.2 g of 1,1,5,5-tetramethyl-thiocarbohydrazide were reacted as prescribed in Example 12 and the reaction mixture was poured into diethyl ether. After decanting the solvent, the oily end product was crystallized under diisopropyl ether. Colorless crystals: melting point 117°C (decomposition).

EXAMPLE 54.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - cyclohexyl - 4 - hydroxy - 1,3 - thiazolidine - 2 - N,N - dimethylhydrazone

4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 3 g of 4-cyclohexyl-1,1-dimethylthiosemicarbazide were reacted according to the prescription of Example 23, the 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - cyclohexyl - 4 - hydroxy - 1,3-thiazolidine - 2 - N,N - dimethylhydrazone - hydrobromide was precipitated with 200 ml of diethyl ether, the hygroscopic crystals were rapidly filtered aff ond dissolved in 30 ml of warm water. The end product was obtained according to the prescription of Example 2c) by treating with saturated sodium carbonate solution. Colorless crystalline solid body: melting point 119°C (decomposition).

EXAMPLE 55.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - dimethylamino - 2 - isopropylimino - 1,3-thiazolidine - 4 - ol - hydrobromide

4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 2.4 g of 1,1-dimethyl-4-isopropylthiosemicarbazide were reacted according to the prescription of Example 23 and the crystalline end product was filtered off. Colorless crystals: melting point: 189°C (decomposition).

EXAMPLE 56.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 4 - hydroxy - 3 - methyl - 1,3 - thiazolidine-2 - N,N - dimethylhydrazone - hydrobromide

4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 2 g of 1,1,4-trimethyl-thiosemicarbazide were reacted according to the prescription of Example 23 and the crystalline end product was filtered off. Colorless crystals: melting point: 145°C (decomposition).

EXAMPLE 57.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 2 - (2 - furylmethylimino) - 3 - methyl-1,3 - thiazolidine - 4 - ol - hydrobromide

4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 2.55 g of 1-(2-furyl-methyl)-3-methylthiourea were reacted according to the prescription of Example 23 and the end product was precipitated by adding 100 ml of diethyl ether. Colorless crystalline solid body: melting point: 168°C (decomposition).

EXAMPLE 58.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - (2 - methoxypropylimino)-1,3 - thiazolidine - 4 - ol - hydrobromide

4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 2.19 g of 1-methyl-3-(2-methoxypropyl)-thiourea were reacted as prescribed in Example 23 and the crystalline end product was filtered off. Colorless solid crystals: melting point: 167°C (decomposition).

EXAMPLE 59.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - (2 - methoxypropylimino)-1,3 - thiazolidine - 4 - ol

5 g of 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - (2 - methoxypropylimino) - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted as prescribed

in Example 18 and the end product was extracted with 150 ml of ethyl acetate. After drying the organic phase over sodium sulfate, the solvent was distilled off under reduced pressure, the solid residue was additioned with 40 ml of diisopropyl ether and the colorless crystals were filtered off. Melting point: 149°C (decomposition).

EXAMPLE 60.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - (2 - pyridylmethylimino)-1,3 - thiazolidine - 4 - ol - hydrochloride

5.2 g of 2,4'-dichloro-3'-sulfamoylacetophenone and 3.5 g of 1-methyl-3-(2-pyridylmethyl)-thiourea were reacted as prescribed in Example 12 and the end product was precipitated with 400 ml of ethyl acetate while stirring. Colorless crystals, melting point 152°C (decomposition $\tilde{\nu}$ C=N 1620 $cm^{-1}$.

EXAMPLE 61.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - (3 - pyridylmethylimino)-1,3 - thiazolidine - 4 - ol

4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 2.7 g of 1-methyl-3-(3-pyridylmethyl)-thiourea were reacted as prescribed in Example 23, whereupon the 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - (3 - pyridylmethylimino)-1,3 - thiazolidine - 4 - ol - hydrobromide precipitated in the form of colorless hygroscopic crystals. The substance was rapidly filtered off, introduced into 30 ml of saturated sodium bicarbonate solution while stirring and the end product was crystallized by trituration. Fair yellow crystals melting at 184°C (decomposition).

EXAMPLE 62.

3 - Allyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - (3 - pyridylmethylimino) - 1,3-thiazolidine - 4 - ol - hydrobromide

4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 3 g of 1-allyl-3-(3-pyridylmethyl)-thiourea were reacted as prescribed in Example 23 and the end product was filtered off. Colorless solid body, decomposition beginning at 82°C $\tilde{\nu}$ C=N 1605 $cm^{-1}$.

EXAMPLE 63.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - cyclohexyl - 2 - (3 - pyridylmethylimino)-1,3 - thiazolidine - 4 - ol - hydrobromide

4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 3.7 g of 1-cyclohexyl-3-(3-pyridylmethyl)-thiourea were reacted as prescribed in Example 23. The end product precipitated first as oil and crystallized after stirring for several hours at room temperature. Colorless crystals, melting point 140°C, decomposition beginning at 165°C, $\tilde{\nu}$ C=N 1600 $cm^{-1}$.

EXAMPLE 64.

4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - cyclohexyl - 2 - (2 - pyridylmethylimino)-1,3 - thiazolidine - 4 - ol - hydrobromide

4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 3.75 g of 1-cyclohexyl-3-(2-pyridylmethyl)-thiourea were reacted according to the prescription given in Example 23 and the crystals were filtered off. Colorless solid body, melting point: 249°C (decomposition).

EXAMPLE 65.

3 - Ethyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - (2 - pyridylmethylimino)-1,3 - thiazolidine - 4 - ol

4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and 3 g of 1-ethyl-3-(2-pyridylmethyl)-thiourea were reacted according to the prescription given in Example 23 and 150 ml of diethyl ether were added to the reaction mixture. The hygroscopic 3 - ethyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - (2 - pyridylmethylimino) - 1,3-thiazolidine - 4 - ol - hydrobromide which had separated as crystals was rapidly filtered off, dissolved in 50 ml of water and converted into the end product as described in Example 28. Colorless solid body, decomposition beginning at 135°C, $\tilde{\nu}$ C=N 1615 $cm^{-1}$.

## EXAMPLE 66.

3 - Ethyl - 2 - ethylimino - 4 - (4 - bromo - 3 - sulfamoylphenyl) - 1,3 - thiazolidine-4 - ol - hydrochloride

a) 4-Bromo-3-sulfamoylbenzoyl chloride

10 g of 4-bromo-3-sulfamoylbenzoic acid were heated under reflux in a mixture of 80 ml of thionyl chloride and 50 ml of dioxane unit HCl had completely developed. Then, the reaction mixture was concentrated under reduced pressure to 40 ml, 200 ml of petroleum ether were added and the crystals were filtered off. Melting point: 138°C (decomposition).

b) 4'-Bromo-3'-sulfamoyl-2-chloroacetophenone

The operational method described hereinafter has to be carried out under the precautions generally to be taken when working with N-nitroso-N-methyl urea and diazomethane.

26 g of freshly prepared N-nitroso-N-methyl urea were introduced portionwise at 0 to −5°C into a stirred two-phase mixture of 200 ml of diethyl ether (or diisopropyl ether) and 80 ml of 40% aqueous potassium hydroxide solution, the ice-cold etheral diazomethane solution was separated in the separating funnel and dried over a small amount of solid potassium hydroxide at −10°C during 3 hours. The dry solution of the diazomethane in diethyl ether (or diisopropyl ether) was cooled to −5°C to −10°C in a 500 ml three-neck flask provided with stirrer, inner thermometer and KOH drying tube. A suspension of 16.8 g of 4-bromo-3-sulfamoylbenzoyl chloride was added in small portions into 40 ml of anhydrous ethyl acetate, the temperature of the reaction mixture not being allowed to exceed +5°C. After the addition of 4-bromo-3-sulfamoylbenzoyl chloride stirring was continued for another 10 minutes at +5°C and the fair yellow crystalline precipitate of 4'-bromo-3'-sulfamoyl-diazoacetophenone was filtered off. The 4'-bromo-3'-sulfamoyl-diazoacetophenone so obtained was introduced without further purification in small portions into a stirred mixture cooled to 0°C of 30 ml of diethylene glycol dimethyl ether and 20 ml of concentrated HCl (37%). After nitrogen development had finished, stirring was continued for another 10 minutes at 0°C, 150 ml of water were added and after dwelling for 1 hour at 0°C the crystalline precipitate of 4'-bromo-3'-sulfamoyl-2-chloroacetophenone was filtered off. Colorless crystals, melting point: 152°C.

c) 3 - Ethyl - 2 - ethylimino - 4 - (4 - bromo - 3 - sulfamoylphenyl) - 1,3 - thiazolidine - 4 - ol - hydrochloride

4.6 g of 4'-bromo-3'-sulfamoyl-2-chloroacetophenone and 1.8 g of ground 1,3-diethylthiourea were reacted and worked up according to the prescription given in Example 12. Colorless solid body, decomposition beginning at 103°C, C=N 1615 $cm^{-1}$.

## EXAMPLE 67.

3 - Ethyl - 2 - ethylimino - 4 - (4 - methyl - 3 - sulfamoylphenyl) - 1,3 - thiazolidine-4 - ol - hydrochloride

a) 4-Methyl-3-sulfamoylbenzoyl chloride

10 g of 4-methyl-3-sulfamoylbenzoic acid were boiled under reflux for 8 hours in 50 ml of thionyl chloride and the reaction mixture was allowed to stand over night at 0°C. The crystals were collected on a sinter glass frit and washed with petroleum ether and diisopropyl ether. Melting point: 180°C (decomposition).

b) 4'-Methyl-3'-sulfamoyl-diazoacetophenone

12 g of 4-methyl-3-sulfamoylbenzoyl chloride were reacted as prescribed in Example 66b) with diazomethane in diethyl ether and the substance precipitating as fair yellow precipitate was filtered off. Melting point: 176°C (decomposition).

c) 4'-Methyl-3'-sulfamoyl-2-chloroacetophenone

10 g of 4'-methyl-3'-sulfamoyl-diazoacetophenone were reacted as prescribed in Example 66b) in diethylene glycol dimethyl ether with 37% HCl and worked up. Colorless crystals, melting point: 166°C (from isopropanol).

d) 3 - Ethyl - 2 - ethylimino - 4 - (4 - methyl - 3 - sulfamoylphenyl) - 1,3 - thiazolidine - 4 - ol - hydrochloride

5 g of 2-chloro-4'-methyl-3'-sulfamoylacetophenone and 2.7 g of 1,3-diethylthiourea were reacted as prescribed in Example 12. After addition of 200 ml of diisopropyl

ether the solvent was decanted and the oily end product was crystallized under ethyl acetate heated to 40 to 50°C. Colorless solid body, melting point: 160°C (decomposition).

EXAMPLE 68.

3 - Hydroxy - 3 - (4 - methyl - 3 - sulfamoylphenyl) - 2,3,6,7 - tetrahydro - 5H-thiazolo[3,2-a]pyrimidine - hydrochloride

5 g of 2-chloro-4'-methyl-3'-sulfamoylacetophenone and 2.35 g of ground 3,4,5,6-tetrahydro-2-pyrimidine-thiol were reacted as prescribed in Example 12 and worked up as prescribed in Example 67d). Colorless crystals, melting point: 190°C (decomposition).

EXAMPLE 69.

3 - Isopropyl - 2 - isopropylimino - 4 - (4 - methyl - 3 - sulfamoylphenyl) - 1,3-thiazolidine - 4 - ol - hydrochloride

5 g of 2-chloro-4'-methyl-3'-sulfamoylacetophenone and 3.2 g of 1,3-diisopropyl thiourea were reacted as prescribed in Example 12 and worked up according to Example 67d). Colorless crystals, melting point: 152°C (decomposition).

EXAMPLE 70.

3 - Ethyl - 2 - ethylimino - 4 - (4 - isopropyl - 3 - sulfamoylphenyl) - 1,3 - thiazolidine - 4 - ol - hydrochloride

a) 4-Isopropyl-3-sulfamoylbenzoic acid

10.3 g of 4-isopropyl benzoic acid were heated to 100°C during 20 minutes in 30.5 ml of chlorosulfonic acid. The temperature was raised to 120°C and maintained at that level until the HCl development had finished. Then, the reaction mixture was cooled to 10°C and poured dropwise onto 200 g of ice while stirring. The crystalline precipitate of 3-chloro-sulfonyl-4-isopropyl benzoic acid was filtered, washed with water several times and the still moist product was introduced in 80 ml of 25% aqueous ammonia solution, the temperature being maintained below 25°C. After dwelling over night, the reaction mixture was heated to 80°C for 2 hours, the hot mixture was stirred for 15 minutes after the addition of a teaspoonfull of active charcoal and the charcoal was filtered off. The filtrate was adjusted to pH 1 with concentrated HCl, the crystalline 4-isopropyl-3-sulfamoylbenzoic acid was filtered off and washed with water several times. Colorless crystals, melting point: 245°C (from water/ethanol).

b) 4-Isopropyl-3-sulfamoylbenzoylchloride

5 g of 4-isopropyl-3-sulfamoylbenzoic acid were boiled under reflux in 50 ml of thionylchloride until completely dissolved and the reaction mixture was then concentrated to 25 ml under reduced pressure. After allowing to dwell over night at 0°C, the crystals were filtered off over a sinter glass frit and washed with petroleum ether. Colorless body, melting point: 177°C.

c) 2-Chloro-4'-isopropyl-3'-sulfamoylacetophenone

13.5 g of 4-isopropyl-3-sulfamoylbenzoyl chloride were reacted as prescribed in Example 66b) with diazomethane in ether, the 4'-isopropyl-3'-sulfamoyldiazoacetophenone remaining in solution without precipitating as crystals. The solution so obtained was allowed to flow into a mixture of 200 ml of diethylene glycol-dimethyl ether and 100 ml of concentrated hydrochloric acid while stirring and cooling with ice, whereafter the solvent was largely distilled off under reduced pressure. To the oily residue, 500 ml of water were added and the solution was extracted with 200 ml of ethyl acetate. Drying followed over sodium sulfate and the solvent was distilled off under reduced pressure. The oily residue crystallized in the course of 1 to 3 days and was then triturated under a small amount of xylene and filtered off. Melting point: 141°C.

d) 3 - Ethyl - 2 - ethylimino - 4 - (4 - isopropyl - 3 - sulfamoylphenyl) - 1,3 - thiazolidine - 4 - ol - hydrochloride

5.5 g of 2-chloro-4'-isopropyl-3'-sulfamoylacetophenone and 2.2 g of 1,3-diethyl-thio urea were reacted and worked up as prescribed in Example 12. Colorless solid body, decomposition beginning at 96°C, $\nu$ C=N 1610 $cm^{-1}$.

EXAMPLE 71.

3 - Methyl - 2 - methylimino - 4 - (3 - sulfamoylphenyl) - 1,3 - thiazolidine - 4 - ol-hydrochloride

a) 3-Sulfamoylbenzoyl chloride

10 g of ground 3-sulfamoylbenzoic acid were reacted as prescribed in Example 70b), the thionyl chloride was distilled off and the residue was crystallized under a mixture of petroleum ether and diethyl ether (1:1). Melting point: 123°C.

b) 3'-Sulfamoyl-diazoacetophenone

11 g of 3-sulfamoylbenzoyl chloride were reacted as prescribed in Example 66b) with diazomethane in diethyl ether and the crystals were filtered off. Melting point: 142°C.

c) 2-Chloro-3'-sulfamoylacetophenone

9.5 g of 3'-sulfamoyl-diazoacetophenone were reacted as prescribed in Example 66b) with 37% HCl in diethylene glycol dimethyl ether and worked up. Colorless crystals, melting point: 118°C (from a small amount of ethanol).

d) 3 - Methyl - 2 - methylimino - 4 - (3 - sulfamoylphenyl) - 1,3 - thiazolidine - 4-ol - hydrochloride

3.5 g of 2-chloro-3'-sulfamoylacetophenone and 1.56 g of ground 1,3-dimethyl-thiourea were reacted as prescribed in Example 12 and the end product was precipitated with a mixture of 1 part of diethyl ether and 2 parts of ethyl acetate. Colorless crystals, melting point: 184°C.

EXAMPLE 72.

3 - Ethyl - 2 - ethylimino - 4 - (3 - sulfamoylphenyl) - 1,3 - thiazolidine - 4 - ol-hydrochloride

3.5 g of 2-chloro-3'-sulfamoylacetophenone and 2.1 g of ground 1,3-diethylthiourea were reacted as prescribed in Example 12. 150 ml of diisopropyl ether were added, the solvent was decanted and the amorphous end product was crystallized under ethyl acetate. Colorless solid body, decomposition beginning at 80°C, $\tilde{\nu}$ C=N 1615 $cm^{-1}$.

EXAMPLE 73.

3 - Ethyl - 2 - ethylimino - 4 - (4 - chloro - 3 - methylsulfamoylphenyl) - 1,3 - thiazolidine - 4 - ol - hydrochloride

a) 4'-chloro-3'-methylsulfamoyl-diazoacetophenone

14 g of 4-chloro-3-sulfamoylbenzoylchloride were reacted as prescribed in Example 66b) with diazomethane in diethyl ether and the crystallized precipitate was filtered. Fair yellow crystals, melting point: 174°C (decomposition).

b) 2,4'-Dichloro-3'-methylsulfamoylacetophenone

12 g of 4'-chloro-3'-methylsulfamoyl-diazoacetophenone were reacted as prescribed in Example 66b) with concentrated HCl in diethyleneglycol dimethyl ether and worked up. Colorless crystals, melting point: 153°C.

c) 3 - Ethyl - 2 - ethylimino - 4 - (4 - chloro - 3 - methylsulfamoylphenyl) - 1,3-thiazolidine - 4 - ol - hydrochloride

5.6 g of 2,4'-dichloro-3'-methylsulfamoylacetophenone and 2.7 g of 1,3-diethyl-thiourea were reacted as prescribed in Example 12. After the addition of 100 ml of diisopropyl ether and a dwelling period of 1 hour at 0°C, the solvent was decanted and the oily end product was crystallized under boiling diethyl ether. Colorless solid body, melting point: 168°C (decomposition).

EXAMPLE 74.

3 - Ethyl - 2 - ethylimino - 4 - (3 - n - butylsulfamoyl - 4 - chlorophenyl) - 1,3 - thiazolidine - 4 - ol - hydrochloride

a) 3-n-Butylsulfamoyl-4-chlorobenzoylchloride

29.4 g of 3-n-butylsulfamoyl-4-chlorobenzoic acid were boiled under reflux in 140 ml of thionyl chloride until complete dissolution and until HCl had finished to develop (about 2 hours), the thionyl chloride was distilled off under reduced pressure and the residue was crystallized under diisopropyl ether. Colorless crystals, melting point: 110°C.

b) 3'-n-Butylsulfamoyl-2,4'-dichloroacetophenone
17 g of 3-n-butylsulfamoyl-4-chlorobenzoyl chloride were reacted as prescribed in Example 66b) with diazomethane in diethyl ether, the 3'-butylsulfamoyl-4'-chlorodiazoacetophenone remaining in solution without being separated. To the total of the reaction mixture, concentrated HCl in diethylene glycol dimethyl ether was added as prescribed in Example 70c). The diethyl ether was distilled off under reduced pressure, the remaining solution was poured into 600 ml of water and the colorless crystals were filtered off. Melting point: 89°C.

c) 3 - Ethyl - 2 - ethylimino - 4 - (3 - n - butylsulfamoyl - 4 - chlorophenyl) - 1,3-thiazolidine - 4 - ol - hydrochloride
6.4 g of 3'-n-butylsulfamoyl-2,4'-dichloroacetophenone and 2.7 g of ground 1,3-diethylthiourea were reacted as prescribed in Example 12. With the addition of 200 ml of diisopropyl ether, the oily end product was precipitated and the solvent was decanted. The amorphous residue was dissolved in 100 ml of water and liophylized. Colorless solid body, decomposition beginning at 130°C, $\tilde{\nu}$ C=N 1620 $cm^{-1}$.

## EXAMPLE 75.

4 - (3 - tert. - Butylsulfamoyl - 4 - chlorophenyl) - 3 - methyl - 2 - methylimino - 1,3-thiazolidine - 4 - ol - hydrochloride

a) 3-tert.-Butylsulfamoyl-4-chlorobenzoic acid
To a mixture of 36.5 g (0.5 mol) of tert.-butylamine and 250 ml of ethanol were added 25.5 g (0.1 mol) of 4-chloro-3-chlorosulfonylbenzoic acid in small portions while stirring and cooling, the reaction temperature being maintained at about 30°C. After a dwelling time over night at room temperature, the solvent was distilled off, the residue was dissolved in about 200 ml of water, the pH was adjusted to 1 with concentrated HCl and the crystals were filtered off. Melting point: 250°C.
When reacting and working up correspondingly, there were obtained from 0.1 mol of 4-chloro-3-chlorosulfonylbenzoic acid and
a) 0.5 mol of n-butyl amine
3-n-butylsulfamoyl-4-chlorobenzoic acid, melting point: 134°C (from ethanol/water)
b) 0.5 mol of cyclohexyl amine
4-chloro-3-cyclohexylsulfamoyl-benzoic acid, melting point: 179—180°C
c) 0.12 mol of o-chlorobenzyl amine and 0.4 mol of triethyl amine
4-chloro-3-o-chlorobenzylsulfamoylbenzoic acid, melting point: 195—197°C
d) 0.12 mol of $\beta$-phenylethyl amine and 0.4 mol of triethyl amine
4-chloro-3-$\beta$-phenethylsulfamoylbenzoic acid, melting point: 123°C (from toluene and active charcoal)
e) 75 ml of 40% aqueous dimethyl amine solution
4-chloro-3-dimethylsulfamoylbenzoic acid, melting point: 242°C
f) 0.5 mol of diethyl amine
4-chloro-3-diethylsulfamoylbenzoic acid, melting point: 162°C
g) 0.5 mol of dipropyl amine
4-chloro-3-dipropylsulfamoylbenzoic acid, melting point: 145°C
h) 0.5 mol of di-n-butyl amine
4-chloro-3-di-n-butylsulfamoylbenzoic acid, melting point: 73—75°C (from methylcyclohexane)
i) 0.4 mol of cyclohexyl-N-methyl amine
4-chloro-3-N-cyclohexyl-N-methylsulfamoylbenzoic acid, melting point: 157°C
j) 0.5 mol of piperidine
4-chloro-3-N-piperidinosulfonylbenzoic acid, melting point: 213°C
k) 0.4 mol of morpholine
4-chloro-3-N-morpholinosulfonylbenzoic acid, melting point: 187°C (from ethanol/water).

b) 3-tert.-Butylsulfamoyl-4-chlorobenzoylchloride
29 g of tert.-butylsulfamoyl-4-chlorobenzoic acid were reacted as prescribed in Example 74a) and the residue was crystallized under petroleum ether after distilling off thionyl chloride. Colorless crystals, melting point: 97°C.

c) 3'-tert.-Butylsulfamoyl-2,4'-dichloroacetophenone
16 g of 3-tert.-butylsulfamoyl-4-chlorobenzoyl chloride were reacted as prescribed in Example 66b) with a solution of diazomethane in diisopropyl ether, sparingly soluble 3'-tert.-butylsulfamoyl-4'-chlorodiazoacetophenone being separated. The crystals were

filtered and converted as prescribed in Example 66b) with concentrated HCl in diethyleneglycol dimethyl ether to yield 3'-tert.-butyl-2,4'-dichloroacetophenone. Colorless crystals, melting point: 159°C.

d) 4 - (3 - tert. - Butylsulfamoyl - 4 - chlorophenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride

4.8 g of 3'-tert.-butylsulfamoyl-2,4'-dichloroacetophenone and 1.5 g of 1,3-dimethylthiourea were reacted as prescribed in Example 23 and the end product was filtered off with the addition of 30 ml of ethyl acetate. Colorless crystals, melting point: 288°C (decomposition).

## EXAMPLE 76.

4 - (4 - Chloro - 3 - cyclopentylmethylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol

8.8 g of 4 - (4 - chloro - 3 - chlorosulfonylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were introduced portionswise at 20°C in a stirred mixture of 4 g of cyclopentylmethyl amine, 8 g of triethyl amine and 100 ml of ethanol and the reaction mixture was allowed to stand over night. The solvent was distilled off under reduced pressure and the amorphous end product was crystallized under 80 ml of water. Colorless solid body, decomposition beginning at 80°C, $\tilde{\nu}$ C=N 1620 $cm^{-1}$.

## EXAMPLE 77.

4 - (4 - Chloro - 3 - $\beta$ - dimethylaminoethylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol

6 g of 4 - (4 - chloro - 3 - chlorosulfonylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted as prescribed in Example 76 with 1.8 g of $\beta$-dimethyl-aminoethyl amine and 6 g of triethyl amine in 100 ml of ethanol and worked up. The amorphous residue was treated with water and saturated sodium carbonate solution. Colorless solid body, decomposition beginning at 115°C, $\tilde{\nu}$ C=N 1620 $cm^{-1}$.

## EXAMPLE 78.

4 - [4 - Chloro - 3 - (2 - methoxypropylsulfamoyl )- phenyl] - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol

6.5 g of 4 - (4 - chloro - 3 - chlorosulfonylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted as prescribed in Example 76 with 5 g of 2-methoxypropyl amine in 100 ml of ethanol and worked up. Colorless crystalline solid substance, melting point: 148°C (acetonitrile/active charcoal).

## EXAMPLE 79.

4 - (3 - Allylsulfamoyl - 4 - chlorophenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol

8.7 g of 4 - (4 - chloro - 3 - chlorosulfonylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted as prescribed in Example 76 with 1.5 g of allyl amine and 4 g of triethyl amine in 50 ml of ethanol and worked up. The water was decanted and the amorphous end product was crystallized under diethyl ether. Colorless solid body, melting point: 146°C (decomposition).

## EXAMPLE 80.

4 - (4 - Chloro - 3 - cyclopropylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol

6.6 g of 4 - (4 - chloro - 3 - chlorosulfonylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted as prescribed in Example 76 with 1.5 g of cyclopropyl amine and 4 g of triethyl amine in 50 ml of ethanol and worked up. Fair yellow crystals, melting point: 180°C (decomposition).

## EXAMPLE 81.

4 - (4 - Chloro - 3 - cyclohexylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride

a) 4-Chloro-3-cyclohexylsulfamoylbenzoylchloride

30 g of 4-chloro-3-cyclohexylsulfamoylbenzoic acid were reacted as prescribed in Example 74a) with thionyl chloride and worked up analogously after HCl had finished to develop. Colorless crystals, melting point 119°C (from diisopropyl ether).

b) 2,4'-Dichloro-3'-cyclohexylsulfamoylacetophenone

17 g of 4-chloro-3-cyclohexylsulfamoylbenzoyl chloride were reacted as prescribed in Example 66b) with a solution of diazomethane in diisopropyl ether, the sparingly soluble 4'-chloro-3'-cyclohexylsulfamoyl-diazoacetophenone being separated. The crystals were filtered and converted according to Example 66b) with concentrated HCl in diethyleneglycol dimethyl ether to yield the 2,4'-dichloro-3'-cyclohexylsulfamoylacetophenone. Colorless crystals, melting point: 117°C.

c) 4 - (4 - Chloro - 3 - cyclohexylsulfamoylphenyl) - 3 - methyl - 2 - methyl - imino-1,3 - thiazolidine - 4 - ol - hydrochloride

5 g of 2,4'-dichloro-3'-cyclohexylsulfamoylacetophenone were reacted as prescribed in Example 23 with 1.7 g of 1,3-dimethylthiourea. To the reaction mixture were added 30 ml of ethyl acetate and the end product was filtered off. Colorless crystals, melting point: 261°C (decomposition).

## EXAMPLE 82.

4 - (4 - Chloro - 3 - cyclooctylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3-thiazolidine - 4 - ol - hydrochloride

a) 4-Chloro-3-cyclooctylsulfamoylbenzoyl chloride

25.5 g of 4-chloro-3-chlorosulfonylbenzoic acid were reacted as prescribed in Example 75a) with 45 g of cyclooctyl amine and worked up. The crystallized 4-chloro-3-cyclooctylsulfamoylbenzoic acid so obtained was dried and reacted without further purification in thionyl chloride as prescribed in Example 74a). Colorless crystals, melting point: 134°C.

b) 2,4'-Dichloro-3'-cyclooctylsulfamoylacetophenone

18 g of 4-chloro-3-cyclooctylsulfamoylbenzoyl chloride were reacted as prescribed in Example 66b) with a solution of diazomethane in diisopropyl ether, the 4'-chloro-3'-cyclooctylsulfamoyl-diazoacetophenone remaining in solution without being separated. The total of the reaction mixture was reacted with concentrated HCl in diethyleneglycol dimethyl ether as prescribed in Example 70c), worked up analogously, whereupon 2,4'-dichloro-3'-cyclooctylsulfamoylacetophenone was obtained as colorless to fair yellow visquous oil.

c) 4 - (4 - Chloro - 3 - cyclooctylsulfamoylphenyl) - 3 - methyl - 2 - methylimino-1,3 - thiazolidine - 4 - ol - hydrochloride

5.2 g of 2,4'-dichloro-3'-cyclooctylsulfamoylacetophenone and 1.8 g of 1,3-dimethylthiourea were reacted as prescribed in Example 23. To the reaction mixture were added 30 ml of ethyl acetate and the end product was filtered off. Colorless crystals, melting point: 192°C (decomposition).

## EXAMPLE 83.

4 - (4 - Chloro - 3 - phenylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride

a) 4'-Chloro-3'-phenylsulfamoylacetophenone

12.6 g of 4'-chloro-3'-chlorosulfonylacetophenone were introduced, while stirring, in a mixture of 5.6 g of aniline, 7.5 g of triethyl amine and 100 ml of dioxane. The mixture was allowed to dwell over night at 20°C, it was heated to 60°C during 30 minutes while stirring and the separated triethylamine-hydrochloride was separated. The filtrate was concentrated under reduced pressure and the residue was crystallized under water. Colorless crystals (from isopropanol/active charcoal), melting point: 142°C.

b) 2-Bromo-4'-chloro-3'-phenylsulfamoylacetophenone

8.8 g of copper-II-bromide in form of a fine powder were heated to boiling temperature in 75 ml of ethyl acetate and to the thoroughly stirred suspension was added a solution of 6.3 g of 4'-chloro-3'-phenylsulfamoylacetophenone in 75 ml of chloroform. The mixture was boiled at the reflux cooler while continuing thorough stirring until the black copper-II-bromide had disappeared and had turned into the colorless copper-I-bromide (about 6 hours). The colorless CuBr was filtered off and the solvent was evaporated under reduced pressure. Colorless crystals (from isopropanol/active charcoal), melting point: 154°C.

c) 4 - (4 - Chloro - 3 - phenylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3-thiazolidine - 4 - ol - hydrobromide

5.2 g of 2-bromo-4'-chloro-3'-phenylsulfamoylacetophenone and 1.5 g of 1,3-dimethylthiourea were reacted as prescribed in Example 23 and the precipitated end product was filtered off. Colorless crystals, melting point: 82°C (decomposition).

## EXAMPLE 84.

4 - (3 - Benzhydrylsulfamoyl - 4 - chlorophenyl) - 3 - methyl - 2 - methylimino - 1,3-thiazolidine - 4 - ol

6.5 g of 4 - (4 - chloro - 3 - chlorosulfonylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted as prescribed in Example 76 with 2.7 g of benzhydrylamine and 4 g of triethyl amine and worked up. Colorless solid body, decomposition beginning at 103°C, $\tilde{\nu}$ C=N 1620 $cm^{-1}$.

## EXAMPLE 85.

4 - (4 - Chloro - 3 - β - phenethylsulfamoylphenyl) - 3 - methyl - 2 - methylimino-1,3 - thiazolidine - 4 - ol - hydrochloride

a) 4-Chloro-3-β-phenethylsulfamoylbenzoyl chloride

30 g of 4-chloro-3-β-phenethylsulfamoylbenzoic acid were reacted as prescribed in Example 74a) in 200 ml of thionyl chloride and worked up. Melting point: 112°C.

b) 4'-Chloro-3'-β-phenethylsulfamoyl-diazoacetophenone

18 g of 4-chloro-3-β-phenethylsulfamoylbenzoyl chloride were reacted as prescribed in Example 66b) with diazomethane in diethyl ether and the crystalline precipitate was filtered off. Melting point: 128°C (decomposition).

c) 2,4'-Dichloro-3'-β-phenethylsulfamoylacetophenone

15 g of 4'-chloro-3'-β-phenethylsulfamoyl-diazoacetophenone were reacted as prescribed in Example 66b) with 50 ml of concentrated HCl in 100 ml of diethyleneglycol dimethyl ether and worked up. Colorless crystals, melting point: 127°C.

d) 4 - (4 - Chloro - 3 - β - phenethylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride

5.5 g of 2,4'-dichloro-3'-β-phenethylsulfamoyl-acetophenone were reacted as prescribed in Example 23 with 1.5 g of 1,3-dimethylthiourea and the crystals were filtered. Melting point: 155°C.

## EXAMPLE 86.

4 - (4 - Chloro - 3 - o - chlorobenzylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide

a) 4'-Chloro-3'-o-chlorobenzylsulfamoylacetophenone

25.5 g of 4'-chloro-3'-chlorosulfonylacetophenone were reacted with 16 g of o-chloro-benzyl amine and 25.5 g of triethyl amine and worked up. Colorless crystals from isopropanol (active charcoal), melting point: 102°C.

b) 4 - (4 - Chloro - 3 - o - chlorobenzylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide

7.2 g of 4'-chloro-3'-o-chlorobenzylsulfamoylacetophenone were reacted as prescribed in Example 1a) with 3.2 g of bromine and the solvent was distilled off. The 2-bromo-4'- without further purification according to Example 23 with 2.3 g of 1,3-dimethylthiourea and worked up. Colorless crystals, melting point: 165°C (decomposition).

## EXAMPLE 87.

4 - (4 - Chloro - 3 - o - chlorobenzylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol

a) 8.2 g of 4 - (4 - chloro - 3 - o - chlorobenzylsulfamoylphenyl) - 3 - methyl-2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were treated in the manner described in Example 2c) with aqueous sodium bicarbonate and the end product was filtered. Colorless crystals, melting point: 169°C.

b) 6.6 g of 4 - (4 - chloro - 3 - chlorosulfonyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted as prescribed in Example 76 with 2.5 g of o-chlorobenzyl amine and 4 g of triethyl amine and worked

up. The viscous residue contained in water was crystallized under a small amount of ethanol. Colorless crystals, melting point: 168—169°C.

EXAMPLE 88.

4 - (4 - Chloro - 3 - o - chlorobenzylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride

8 g of 4 - (4 - chloro - 3 - o - chlorobenzylsulfamoylphenyl) - 3 - methyl - 2-methylimino - 1,3 - thiazolidine - 4 - ol were reacted as prescribed in Example 3c) with ethanolic HCl solution and the end product was precipitated by adding ethyl acetate. Colorless crystals, melting point: 170°C (decomposition).

EXAMPLE 89.

3 - Ethyl - 2 - ethylimino - 4 - (4 - chloro - 3 - o - chlorobenzylsulfamoylphenyl)-1,3 - thiazolidine - 4 - ol - hydrochloride

30 g of 4-chloro-3-o-chlorobenzylsulfamoylbenzoic acid were reacted as prescribed in Example 74a) and the residue was crystallized after distilling off thionyl chloride under petroleum ether. Coloriess crystals, melting point: 125—127°C.

b) 2,4'-Dichloro-3'-o-chlorobenzylsulfamoylacetophenone

19 g of 4-chloro-3-o-chlorobenzylsulfamoylbenzoyl chloride were reacted as prescribed in Example 66b) with diazomethane in diethyl ether, the 4'-chloro-3'-o-chlorobenzylsulfamoyl-diazoacetophenone remaining in solution without being separated. To the total of the reaction mixture, there was added, according to Example 70c) concentrated HCl in diethylene glycol dimethyl ether and the mixture was worked up. The oily residue crystallized in the course of 1—3 days. It was triturated under diisopropyl ether and the crystals were filtered off. Melting point: 94°C.

c) 3 - Ethyl - 2 - ethylimino - 4 - (4 - chloro - 3 - o - chlorobenzylsulfamoyl - phenyl-1,3 - thiazolidine - 4 - ol - hydrochloride

7.8 g of 2,4'-dichloro-3'-o-chlorobenzylsulfamoylacetophenone and 2.5 g of 1,3-diethylthiourea were reacted as prescribed in Example 12 and worked up. Colorless crystals, decomposition beginning at 94°C, $\tilde{\nu}$ C=N 1615 $cm^{-1}$.

EXAMPLE 90.

4 - (4 - Chloro - 3 - o - chlorobenzylsulfamoylphenyl) - 3 - propyl - 2 - propylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide

7.2 g of 4'-chloro-3'-o-chlorobenzylsulfamoyl-acetophenone were reacted with 3.2 g of bromine according to Example 1a), the solvent was distilled off, the 2-bromo-4'-chloro-3'-o-chlorobenzylsulfamoyl acetophenone so obtained was reacted without further purification according to Example 23 with 3 g of 1,3-dipropylthiourea and the end product was filtered off. Colorless crystals, melting point: 193—194°C (decomposition).

EXAMPLE 91.

4 - (4 - Chloro - 3 - o - chlorobenzylsulfamoylphenyl) - 3 - propyl - 2 - propylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride

9 g of 4 - (4 - chloro - 3 - o - chlorobenzylsulfamoylphenyl) - 3 - propyl - 2-propylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted with 4 g of triethyl amine in 250 ml of methanol, the reaction mixture was stirred for 1 hour at room temperature and the solvent was distilled off under reduced pressure. The residue was introduced into 100 ml of water and 4 - (4 - chloro - 3 - o - chlorobenzylsulfamoylphenyl) - 3 - propyl - 2 - propyl - imino - 1,3 - thiazolidine - 4 - ol were extracted with 100 ml of ethyl acetate. The organic phase was dried over sodium sulfate, the solvent was distilled off under reduced pressure and the residue was dissolved in 30 ml of ethanol. After acidifying with 15% ethanolic hydrochloric acid, the end product was precipitated with diethyl ether. Colorless crystals, melting point: 167°C.

EXAMPLE 92.

4 - [4 - Chloro - 3 - (2,4 - dimethoxybenzylsulfamoyl) - phenyl] - 3 - methyl - 2-methylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride

8.8 g of 4 - (4 - chloro - 3 - chlorosulfonylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted as prescribed in Example 76 with 5 g of triethyl amine and 3.5 g of 2,4-dimethoxybenzyl amine and worked up. After treating with water, the amorphous 4 - [4 - chloro - 3 - (2,4-dimethoxybenzylsulfamoyl) - phenyl] - 3 - methyl - 2 - methylimino - 1,3 - thiazol-

idine - 4 - ol was extracted with 70 ml of ethyl acetate, dried over sodium sulfate and the solvent was acidified with ethanolic hydrochloric acid (15%). The amorphous precipitated end product was crystallized under isopropanol. Melting point: 163°C (decomposition).

EXAMPLE 93.

4 - [4 - Chloro - 3 - (3,4 - methylenedioxybenzylsulfamoyl) - phenyl] - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol

6.5 g of 4 - (4 - chloro - 3 - chlorosulfonylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted as prescribed in Example 76 with 2.4 g of 3,4-methylenedioxybenzyl amine and 3.5 g of triethyl amine and worked up. Colorless crystals from isopropanol, melting point: 131—132°C (decomposition).

EXAMPLE 94.

4 - [4 - Chloro - 3 - (2 - furylmethylsulfamoyl) - phenyl] - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol

6.5 g of 4 - (4 - chloro - 3 - chlorosulfonylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted as prescribed in Example 76 with 1.5 g of 2-furylmethyl amine and 3.5 g of triethyl amine and worked up. Melting point: 154°C (decomposition).

EXAMPLE 95.

4 - [4 - Chloro - 3 - (2 - picolylsulfamoyl) - phenyl] - 3 - methyl - 2 - methylimino-1,3 - thiazolidine - 4 - ol

8.8 g of 4 - (4 - chloro - 3 - chlorosulfonylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted with 3.0 g of 2-picolyl amine and 5 g of triethyl amine as prescribed in Example 76 and the end product precipitating as crystals was filtered off. Melting point: 166°C (decomposition).

EXAMPLE 96.

4 - [4 - Chloro - 3 - (3 - picolylsulfamoyl) - phenyl] - 3 - methyl - 2 - methylimino-1,3 - thiazolidine - 4 - ol

8.8 g of 4 - (4 - chloro - 3 - chlorosulfonylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted with 3.0 g of 3-picolyl amine and 5 g of triethyl amine according to Example 76, the solvent was distilled off under reduced pressure and the residue was taken up in 70 ml of water. Three extractions followed with 60 ml of ethyl acetate, the organic phase was dried over sodium sulfate and the solvent was evaporated under reduced pressure. The residue crystallized under diisopropyl ether. Melting point: 152—153°C.

EXAMPLE 97.

4 - (4 - Chloro - 3 - dimethylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3-thiazolidine - 4 - ol - hydrobromide

a) 4'-Chloro-3'-dimethylsulfamoylacetophenone

To a stirred mixture of 10 ml of 40% dimethyl amine solution and 60 ml of methanol, there were added, portionswise, 5.1 g of 4'-chloro-3'-chlorosulfonylacetophenone, so that the reaction temperature did not exceed 30°C. The reaction mixture was stirred for 3 hours at room temperature and 15 minutes at 60°C. After cooling, the reaction mixture was poured into 200 ml of water and the crystals were filtered off. Melting point: 108°C.

b) 2-Bromo-4'-chloro-3'-dimethylsulfamoylacetophenone

7.9 g of 4'-chloro-3'-dimethylsulfamoylacetophenone were reacted according to Example 1a) with 4.8 g of bromine and worked up. Colorless crystals from isopropanol, melting point: 98°C.

c) 4 - (4 - Chloro - 3 - dimethylsulfamoylphenyl) - 3 - methyl - 2 - methylimino-1,3 - thiazolidine - 4 - ol - hydrobromide

c1) 6.8 g of 2-bromo-4'-chloro-3'-dimethylsulfamoylacetophenone and 2.2 g of 1,3-dimethylthiourea were reacted as prescribed in Example 23 and the end product was precipitated by adding 20 ml of ethyl acetate. Colorless crystals, melting point: 161°C.

c2) To a solution of 6.4 g of 2-bromo-4'-chloro-3'-dimethylsulfamoylacetophenone in 28 ml of methanol were added dropwise, at a reaction temperature of 5°C, a

solution of 0.6 g of sodium borohydride in 5 ml of methanol and the solution was then stirred for 1 hour at room temperature. The reaction mixture was acidified while cooling (+5°C) with 2 N HCl and the solvent was distilled off under reduced pressure. After adding 70 ml of water, extraction followed with 200 ml of diethyl ether, the organic phase was dried over sodium sulfate the solvent was distilled off and 2-bromo-1-(4-chloro-3-dimethylsulfamoylphenyl)-ethanol was obtained as fair yellow to colorless oil.

c3) 6.4 g of 2-bromo-1-(4-chloro-3-dimethylsulfamoylphenyl)-ethanol were reacted as prescribed in Example 23 with 2.1 g of 1,3-dimethylthiourea and 2-(4-chloro-3-dimethylsulfamoylphenyl)-2-hydroxyethyl-N,N-dimethylisothiouronium-bromide was precipitated with 200 ml of diisopropyl ether. The highly hygroscopic crystals ($\tilde{\nu}$ C=N 1620 $cm^{-1}$ in chloroform) were rapidly filtered off and stored in the exsiccator.

c4) 4.5 g of 2-(4-chloro-3-dimethylsulfamoylphenyl)-2-hydroxyethyl-N,N-dimethylisothiuronium-bromide were dissolved in 200 ml of methylene chloride and after adding 40 g of active manganese dioxide, stirred at room temperature for 30 hours. The organic precipitate was filtered off and the solvent was distilled off under reduced pressure. The amorphous residue of the 4-(4-chloro-3-dimethylsulfamoylphenyl)-3-methyl-2-methylimino-1,3-thiazolidine-4-ol-hydrobromide was crystallized under ethyl acetate heated to 40°C.

## EXAMPLE 98.

4-(4-Chloro-3-dimethylsulfamoylphenyl)-3-methyl-2-methylimino-1,3-thiazolidine-4-ol

9.4 g of 4-(4-chloro-3-dimethylsulfamoylphenyl)-3-methyl-2-methylimino-1,3-thiazolidine-4-ol-hydrobromide were reacted according to Example 2c) and the amorphous precipitate of the end product was crystallized under boiling diisopropyl ether. Colorless crystals from ethyl butyrate, melting point: 157—158°C.

## EXAMPLE 99.

4-(4-Chloro-3-dimethylsulfamoylphenyl)-3-methyl-2-methylimino-1,3-thiazolidine-4-ol-hydrochloride

a) 12 g of 4-(4-chloro-3-dimethylsulfamoylphenyl)-3-methyl-2-methylimino-1,3-thiazolidine-4-ol were reacted as prescribed in Example 3c) and worked up. Colorless crystals, melting point: 169°C (decomposition).

b) 5.2 g of 4-chloro-3-dimethylsulfamoylacetophenone were stirred in a mixture of 100 ml of anhydrous carbon tetrachloride and 2.6 g of sulfuryl chloride with the exclusion of air humidity for 2 hours at room temperature and then boiled for 6 hours under reflux. The solvent was distilled off, the residue was decomposed under ice water and 2,4'-dichloro-3'-dimethylsulfamoylacetophenone was extracted with 100 ml of ethyl acetate. After drying the organic phase over sodium sulfate, the solvent was distilled off, the residue was reacted with 2.0 g of 1,3-dimethylthiourea according to Example 23 and crystalline 4-(4-chloro-3-dimethylsulfamoylphenyl)-3-methyl-2-methylimino-1,3-thiazolidine-4-ol-hydrochloride was filtered off.

## EXAMPLE 100.

4-(4-Chloro-3-dimethylsulfamoylphenyl)-3-methyl-2-methylimino-1,3-thiazolidine-4-ol-methylsulfonate

a) 4-Chloro-3-dimethylsulfamoylbenzoyl chloride

26.4 g of 4-chloro-3-dimethylsulfamoylbenzoic acid were reacted and worked up as prescribed in Example 74a). Melting point: 103—105°C.

b) 4'-Chloro-3'-dimethylsulfamoyl-diazoacetophenone

14.1 g of 4-chloro-3-dimethylsulfamoylbenzoyl-chloride were reacted as prescribed in Example 66b) with diazomethane in diethyl ether and the crystalline product was filtered off. Melting point: 136—137°C (decomposition).

c) Methanesulfonic acid-(4'-chloro-3'-dimethylsulfamoylacetophenone-2-yl)-ester

5 g of 4'-chloro-3'-dimethylsulfamoyl-diazoacetophenone were introduced portionwise into 20 ml of ice-cold and stirred methanesulfonic acid and stirred for 30 minutes at room temperature. 100 ml of water were added and the crystals were filtered off. Melting point: 116°C.

d) 4 - (4 - Chloro - 3 - dimethylsulfamoylphenyl) - 3 - methyl - 2 - methylimino-1,3 - thiazolidine - 4 - ol - methylsulfonate

2 g of methanesulfonic acid - (4' - chloro - 3' - dimethylsulfamoylacetophenone-2 - yl) - ester and 0.7 g of 1,3-dimethylthiourea were reacted as prescribed in Example 23 and the crystalline end product was filtered off. Melting point: 166°C (decomposition).

## EXAMPLE 101.

3 - Ethyl - 2 - ethylimino - 4 - (4 - chloro - 3 - dimethylsulfamoylphenyl) - 1,3 - thiazolidine - 4 - ol - hydrobromide

6.8 g of 2-bromo-4'-chloro-3'-dimethylsulfamoylacetophenone and 2.7 g of 1,3-diethylthiourea were reacted as prescribed in Example 23. The solvent was decanted and the oily precipitate of the end product was crystallized under fresh acetone. Colorless solid body, decomposition beginning at 154°C, $\tilde{\nu}$ C=N 1610 $cm^{-1}$.

## EXAMPLE 102.

3 - Ethyl - 2 - ethylimino - 4 - (4 - chloro - 3 - dimethylsulfamoylphenyl) - 1,3 - thiazolidine - 4 - ol - hydrochloride

10 g of 3 - ethyl - 2 - ethylimino - 4 - (4 - chloro - 3 - dimethylsulfamoylphenyl) - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted according to Example 2c) and the yellow precipitate of 3 - ethyl - 2 - ethylimino - 4 - (4-chloro - 3 - dimethylsulfamoylphenyl) - 1,3 - thiazolidine - 4 - ol was rapidly filtered off. The compound so obtained was treated according to Example 3c) with ethanolic hydrochloric acid and the end product was precipitated by adding diisopropyl ether. The solvent was decanted, 200 ml of water were added to the amorphous residue and the aqueous solution was lyophilized. Colorless amorphous solid body, decomposition beginning at 134°C, $\tilde{\nu}$ C=N 1615 $cm^{-1}$.

## EXAMPLE 103.

4 - (4 - Chloro - 3 - dimethylsulfamoylphenyl) - 3 - propyl - 2 - propylimino - 1,3-thiazolidine - 4 - ol - hydrochloride

6.8 g of 2-bromo-4'-chloro-3'-dimethylsulfamoylacetophenone were reacted according to Example 23 with 3.3 g of 1,3-dipropylthiourea. After adding 200 ml of diethyl ether, 4 - (4 - chloro - 3 - dimethylsulfamoylphenyl) - 3 - propyl - 2 - propylimino-1,3 - thiazolidine - 4 - ol - hydrobromide was separated as an oil. The solvent was decanted, the product was dissolved in 30 ml of water and extracted with 100 ml of ethyl acetate. After drying over sodium sulfate, the solvent was distilled off under reduced pressure, the amorphous residue was dissolved in 30 ml of ethanol and acidified with ethanolic hydrochloric acid. The solvent was distilled off, the residue was dissolved in 40 ml of water and the end product was obtained by lyophilization. Colorless amorphous solid body, decomposition beginning at 128°C, $\tilde{\nu}$ C=N 1615 $cm^{-1}$.

## EXAMPLE 104.

4 - (4 - Chloro - 3 - dimethylsulfamoylphenyl) - 3 - cyclohexyl - 2 - cyclohexylimino-1,3 - thiazolidine - 4 - ol

a) 4'-Chloro-3'-dimethylsulfamoylacetophenone-2-thiol

1.34 g of thioacetic acid were dissolved under nitrogen atmosphere in 15 ml of ethanol and made exactly neutral by adding a 40% aqueous potassium hydroxide solution. Then, 4.8 g of 2-bromo-4'-chloro-3'-dimethylsulfamoylacetophenone were added to the solution and stirring followed for 30 minutes at room temperature. The reaction mixture was poured into 100 ml of water and crystalline 2-acetylthio-4'-chloro-3'-dimethylsulfamoylacetophenone was filtered off. Melting point: 71°C. The compound so obtained was introduced into 35 ml of a 5% aqueous sodium hydroxide solution and the solution was stirred under nitrogen atmosphere for 45 minutes at room temperature. The solution was adjusted to pH 1 with 2 N hydrochloric acid and the end product was filtered off. Fair yellow crystals from ethanol, melting point: 93—95°C.

b) 4 - (4 - Chloro - 3 - dimethylsulfamoylphenyl) - 3 - cyclohexyl - 2 - cyclohexylimino - 1,3 - thiazolidine - 4 - ol

To a solution of 2.9 g of 4'-chloro-3'-dimethyl-sulfamoylphenylacetophenone-2-thiol in 30 ml of anhydrous tetrahydrofurane were added dropwise, with the exclusion of air humidity a solution of 2 g of dicyclohexylcarbodiimide in 20 ml of anhydrous tetrahydrofurane, the reaction temperature being maintained between 10 and 15°C. The reaction mixture was stirred for 20 hours at room temperature, the solvent was

distilled off under reduced pressure and the residue was crystallized under 40 ml of water. Colorless solid body, decomposition beginning at 89°C, $\tilde{\nu}$ C=N 1625 $cm^{-1}$.

EXAMPLE 105.

4 - (4 - Chloro - 3 - dimethylsulfamoylphenyl) - 3 - cyclohexyl - 2 - cyclohexylimino-1,3 - thiazolidine - 4 - ol - hydrobromide

2.5 g of 4 - (4 - chloro - 3 - dimethylsulfamoylphenyl) - 3 - cyclohexyl - 2-cyclohexylimino - 1,3 - thiazolidine - 4 - ol were dissolved in 10 ml of methanol and adjusted to pH 3 by adding dropwise 48% hydrobromic acid. The solvent was distilled off under reduced pressure and the amorphous end product was crystallized under dietyhl ether. Colorless crystals, melting point: 131°C (decomposition).

EXAMPLE 106.

3 - (4 - Chloro - 3 - dimethylsulfamoylphenyl) - 3 - hydroxy - 2,3,5,6 - tetra - hydro-imidazo[2,1-b]thiazol - hydrobromide

To 3 g of 2-bromo-1-imidazoline in 50 ml isopropanol were added 5.9 g of 4'-chloro-3'-dimethylsulfamoylacetophenone-2-thiol and the mixture was stirred for 10 hours at room temperature and a further 2 hours at 35°C. After cooling the end product was precipitated with 100 ml of diethyl ether and the solvent was decanted. The residue was stirred for 4 hours in 30 ml of acetone at room temperature and the crystalline precipitate was filtered off. Melting point: 155°C (decomposition).

EXAMPLE 107.

3 - (4 - Chloro - 3 - dimethylsulfamoylphenyl) - 3 - hydroxy - 2,3,5,6 - tetra - hydro-imidazo[2,1-b]thiazole

7.3 g of 3 - (4 - chloro - 3 - dimethylsulfamoylphenyl) - 3 - hydroxy - 2,3,5,6-tetrahydro - imidazo[2,1-b]thiazol - hydrobromide were dissolved in 100 ml of water at 35—40°C. After adding a solution of 6 g of sodium bicarbonate in 200 ml of water, the mixture was stirred for 15 minutes at room temperature and the end product was filtered off. Colorless crystals, melting point: 154°C (decomposition).

EXAMPLE 108.

4 - (4 - Chloro - 3 - diethylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3-thiazolidine - 4 - ol - hydrochloride

a) 4'-Chloro-3'-diethylsulfamoyl-diazoacetophenone

39 g of 4-chloro-3-diethylsulfamoylbenzoic acid were boiled under reflux in 200 ml of thionyl chloride until the development of HCl had finished and the thionyl chloride was then distilled off under reduced pressure. 4-chloro-3-diethylsulfamoylbenzoyl chloride was obtained as fair yellow oil.

16 g of the 4-chloro-3-diethylsulfamoylbenzoyl-chloride so obtained were reacted as prescribed in Example 66b) with diazomethane in diisopropyl ether and crystalline 4'-chloro-3'-diethylsulfamoyl-diazoacetophenone was filtered off. Fair yellow crystals, melting point: 120°C (decomposition).

b) 3'-Diethylsulfamoyl-2,4'-dichloroacetophenone

12 g of 4'-chloro-3'-diethylsulfamoyl-diazoacetophenone were reacted as prescribed in Example 66b) with concentrated HCl in diethyleneglycol dimethyl ether and worked up. Colorless crystals, melting point: 63—65°C.

c) 4 - (4 - Chloro - 3 - diethylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3-thiazolidine - 4 - ol - hydrochloride

4.8 g of 3'-diethylsulfamoyl-2,4'-dichloroacetophenone and 1.5 g of 1,3-dimethyl-thiourea were reacted as prescribed in Example 23 and the crystalline end product was filtered off. Melting point: 165°C (decomposition).

EXAMPLE 109.

4 - (4 - Chloro - 3 - dipropylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3-thiazolidine - 4 - ol - hydrochloride

a) 2,4'-Dichloro-3'-dipropylsulfamoylacetophenone

43 g of 4-chloro-3-dipropylsulfamoylbenzoic acid were reacted as prescribed in Example 108a) with thionyl chloride and worked up.

17 g of the 4-chloro-3-dipropylsulfamoylbenzoyl chloride so obtained as an oil were reacted according to Example 66b) with diazomethane in diisopropyl ether, the

4'-chloro-3'-dipropylsulfamoyl-diazoacetophenone remaining in solution without crystallizing out. The etheral solution was treated according to Example 70c) with hydrochloric acid and worked up accordingly, 2,4'-dichloro-3'-dipropylsulfamoylacetophenone being obtained as colorless crystalline product. (Melting point: 76°C).

b) 4 - (4 - Chloro - 3 - dipropylsulfamoylphenyl) - 3 - methyl - 2 - methylimino-1,3 - thiazolidine - 4 - ol - hydrochloride

4.8 g of 2,4'-dichloro-3'-dipropylsulfamoylacetophenone and 1.5 g of 1,3-dimethylthiourea were reacted as prescribed in Example 23 and worked up. Colorless crystals, melting point: 166°C (decomposition).

## EXAMPLE 110.

3 - Ethyl - 2 - ethylimino - 4 - (3 - di - n - butylsulfamoyl - 4 - chlorophenyl) - 1,3-thiazolidine - 4 - ol -hydrochloride

a) 3'-Di-n-butylsulfamoyl-2,4'-dichloroacetophenone

15 g of 3-di-n-butylsulfamoyl-4-chlorobenzoic acid were treated as prescribed in Example 108a) with thionyl chloride and reacted.

18 g of the 3-di-n-butylsulfamoyl-4-chlorobenzoyl-chloride so obtained as an oil were reacted as prescribed in Example 70c) in diethyl ether with diazomethane and then with concentrated HCl in diethyleneglycol dimethyl ether and worked up, 3'-di-n-butylsulfamoyl-2,4'-dichloroacetophenone being obtained in the form of colorless crystals having a melting point of 71°C.

b) 3 - Ethyl - 2 - ethylimino - 4 - (3 - di - n - butylsulfamoyl - 4 - chloro - phenyl)-1,3 - thiazolidine - 4 - ol - hydrochloride

7.0 g of 3'-di-n-butylsulfamoyl-2,4'-dichloro-acetophenone were reacted according to Example 12 with 2.7 g of 1,3-diethylthiourea and worked up. Colorless solid body, decomposition beginning at 139°C, $\tilde{\nu}$ C=N 1615 $cm^{-1}$.

## EXAMPLE 111.

4 - (4 - Chloro - 3 - N - cyclohexyl - N - methylsulfamoylphenyl) - 3 - methyl - 2-methylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride

a) 2,4'-Dichloro-3'-N-cyclohexyl-N-methylsulfamoylacetophenone

16 g of 4-chloro-3-N-cyclohexyl-N-methylsulfamoylbenzoic acid were reacted and worked up as prescribed in Example 108a).

18 g of the 4-chloro-3-N-cyclohexyl-N-methylsulfamoylbenzoyl chloride so obtained as an oil were reacted as prescribed in Example 66b) with diazomethane in diisopropyl ether and 4'-chloro-3'-N-cyclohexyl-N-methylsulfamoyl-diazoacetophenone (melting at 118°C) were converted according to Example 66b) into 2,4'-dichloro-3'-N-cyclohexyl-N-methylsulfamoylacetophenone. Colorless crystals, melting point: 84—86°C.

b) 4 - (4 - Chloro - 3 - N - cyclohexyl - N - methylsulfamoylphenyl) - 3 - methyl-2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride

5.4 g of 2,4'-dichloro-3'-N-cyclohexyl-N-methylsulfamoylacetophenone and 1.6 g of 1,3-dimethylthiourea were reacted as prescribed in Example 23 and worked up. Colorless crystals, melting point: 164°C (decomposition).

## EXAMPLE 112.

3 - Ethyl - 2 - ethylimino - 4 - (4 - chloro - 3 - N - piperidinosulfonylphenyl) - 1,3-thiazolidine - 4 - ol - hydrochloride

a) 2,4'-Dichloro-3'-N-piperidinosulfonylacetophenone

15 g of 4-chloro-3-N-piperidinosulfonylbenzoic acid were converted as prescribed in Example 108a) into 4-chloro-3-N-piperidinosulfonylbenzoyl chloride which was then reacted according to Example 66b) to yield 2,4'-dichloro-3'-N-piperidinosulfonylacetophenone. Colorless crystals, melting point: 134°C.

b) 3 - Ethyl - 2 - ethylimino - 4 - (4 - chloro - 3 - N - piperidinosulfonylphenyl)-1,3 - thiazolidine - 4 - ol - hydrochloride

5.1 g of 2,4'-dichloro-3'-N-piperidinosulfonylacetophenone and 2.0 g of 1,3-diethylthiourea were reacted and worked up as prescribed in Example 12. Colorless solid body, decomposition beginning at 110°C. $\tilde{\nu}$ C=N 1615 $cm^{-1}$.

## EXAMPLE 113.

3 - Ethyl - 2 - ethylimino - 4 - (4 - chloro - 3 - N - morpholinosulfonylphenyl) - 1,3-thiazolidine - 4 - ol - hydrochloride

a) 4-Chloro-3-N-morpholinosulfonylbenzoyl chloride

30.6 g of 4-chloro-3-N-morpholinosulfonylbenzoic acid were reacted and worked up as prescribed in Example 74a). Colorless crystals, melting point: 120—122°C.

b) 2,4'-Dichloro-3'-N-morpholinosulfonylacetophenone

17 g of 4-chloro-3-N-morpholinosulfonylbenzoyl chloride were reacted as prescribed in Example 66b) with 4'-chloro-3'-N-morpholinosulfonyl-diazoacetophenone (fair yellow crystals, melting point: 186°C (decomposition) to yield 2,4'-dichloro-3'-N-morpholinosulfonylacetophenone. Colorless crystals, melting point: 130°C.

c) 3 - Ethyl - 2 - ethylimino - 4 - (4 - chloro - 3 - N - morpholinosulfonyl - phenyl)-1,3 - thiazolidine - 4 - ol - hydrochloride

6.8 g of 2,4'-dichloro-3'-N-morpholinosulfonylacetophenone and 2.6 g of diethylthiourea were reacted as prescribed in Example 12, the end product was precipitated with diisopropyl ether and the solvent was decanted. The amorphous residue was dissolved in 100 ml of water and lyophilized. Colorless solid body, decomposition beginning at 139°C, $\tilde{\nu}$ C=N 1615 $cm^{-1}$.

## EXAMPLE 114.

4 - (4 - Chloro - 3 - N - methyl - N - phenylsulfamoylphenyl) - 3 - methyl - 2-methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide

a) 4'-Chloro-3'-N-methyl-N-phenylsulfamoylacetophenone

6 g of 4'-chloro-3'-chlorosulfonylacetophenone were reacted and worked up as prescribed in Example 83a). Colorless crystals, melting point: 80—81°C.

b) 2-Bromo-4'-chloro-3'-N-methyl-N-phenylsulfamoylacetophenone

9.6 g of 4'-chloro-3'-N-methyl-N-phenylsulfamoylacetophenone in 150 ml of chloroform were reacted as prescribed in Example 83b) with 14 g of powdered copper-II-bromide in 150 ml of ethyl acetate and worked up. Colorless crystals from n-butanol/active charcoal, melting point: 144—145°C.

c) 4 - (4 - Chloro - 3 - N - methyl - N - phenylsulfamoylphenyl) - 3 - methyl - 2-methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide

4 g of 2-bromo-4'-chloro-3'-N-methyl-N-phenyl-sulfamoylacetophenone were reacted as prescribed in Example 23 with 1.1 g of 1,3-dimethylthiourea and the end product was precipitated with diisopropyl ether. Colorless solid body, decomposition beginning at 98°C, $\tilde{\nu}$ C=N 1630 $cm^{-1}$.

## EXAMPLE 115.

4 - (3 - N - Benzyl - N - methylsulfamoyl - 4 - chlorophenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride

a) 3'-N-Benzyl-N-methylsulfamoyl-2,4'-dichloroacetophenone

25.5 g of 4-chloro-3-chlorosulfonylbenzoic acid were introduced in a stirred mixture of 60 ml of pyridine and 12.2 g of N-methyl-N-benzyl amine in such a way that the reaction temperature did not exceed 35°C. The mixture was stirred for 20 hours at room temperature and the solvent was distilled off. The residue was taken up in 200 ml of water, adjusted to pH 1 with 2 N HCl and the precipitate was extracted with 200 ml of ethyl acetate. After drying the organic phase over sodium sulfate, the solvent was distilled off, the amorphous residue of the 3-N-benzyl-N-methylsulfamoyl-4-chlorobenzoic acid was reacted according to Example 108a) with thionyl chloride and worked up analogously. The 3-N-benzyl-N-methylsulfamoyl-4-chlorobenzoyl chloride obtained as an oil was reacted as prescribed in Example 66b) with diazomethane in diisopropyl ether and the crystallized precipitate of 3'-N-benzyl-N-methyl-sulfamoyl-4'-chlorodiazoacetophenone (melting point 122°C with decomposition) was converted as prescribed in Example 66b) into 3'-N-benzyl-N-methylsulfamoyl-2,4'-dichloroacetophenone. Colorless crystals, melting point: 124°C.

b) 4 - (3 - N - Benzyl - N - methylsulfamoyl - 4 - chlorophenyl) - 3 - methyl - 2-methylimino - 1,3 - thiazolidine - 4 - ol - hydrochloride

5.3 g of 3'-N-benzyl-N-methylsulfamoyl-2,4'-dichloroacetophenone were reacted as prescribed in Example 23 with 1,3-dimethylthiourea and the crystallized end product was filtered off. Colorless crystals, melting point: 160°C (decomposition).

EXAMPLE 116.

4 - [4 - Chloro - 3 - N - (2 - hydroxy - 1 - methyl - 2 - phenylethyl) - N - methylsulfamoyl - phenyl]-3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol

4.3 g of 4 - (4 - chloro - 3 - chlorosulfonylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted as prescribed in Example 76 with 4.3 g of ephedrine and 4.1 g of triethyl amine and worked up. Colorless solid body, decomposition beginning at 134°C, $\tilde{\nu}$ C=N 1620 $cm^{-1}$.

EXAMPLE 117.

4 - [4 - Chloro - 3 - N - (2 - furylmethyl) - N - methylsulfamoylphenyl] - 3 - methyl-2 - methylimino - 1,3 - thiazolidine - 4 - ol

4.4 g of 4 - (4 - chloro - 3 - chlorosulfonylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide were reacted analogously to Example 76 with 1.6 g of 2-furylmethyl-N-methylamine and 4 g of triethyl amine and worked up. Colorless solid body, decomposition beginning at 158°C. $\tilde{\nu}$ C=N 1625 $cm^{-1}$.

EXAMPLE 118.

3 - (4 - Chloro - 3 - dimethylsulfamoylphenyl) - 3 - hydroxy - 2,3,4,5,6 - tetrahydroimidazo[2,1-b]thiazole - hydrobromide

a) 5-Bromo-2-chloroaniline

90 g of 5-bromo-2-chloronitrobenzene were hydrogenated in 500 ml of methanol at room temperature and under normal pressure with Raney-Nickel as catalyst and hydrogen. Colorless crystals, melting point: 47°C.

b) 5-Bromo-2-chlorobenzenedimethylsulfonic acid amide

13.6 g of 5-bromo-2-chloroaniline were diazosized in 50 ml of concentrated hydrochloric acid at 0—5°C with 4.7 g of sodium nitrite in 10 ml of water. The solution obtained was added to a solution of 6.6 g of sodium bisulfite and 1.5 g of copper-II-chloride in 40 ml of water, the solution was stirred for 30 minutes, diluted with 100 ml of water and the crystalline 5-bromo-2-chlorobenzenesulfonic acid chloride was filtered off; it was introduced without further purification into a mixture of 70 ml of ethanol and 50 ml of aqueous concentrated dimethylamine solution. After standing overnight it was diluted with water and the colorless crystals were suction-filtered. Melting point: 87°C (from diisopropyl ether).

c) 3 - (4 - Chloro - 3 - dimethylsulfamoylphenyl) - 3 - hydroxy - 2,3,5,6 - tetrahydroimidazo[2,1-b]thiazole - hydrobromide

To a thoroughly stirred solution of 0.05 mol of butyllithium in 150 ml of absolute tetrahydrofurane, 14.9 g of 5-bromo-2-chlorobenzenedimethylsulfonic acid amide in 100 ml of absolute tetrahydrofurane were added slowly at −45°C with the exclusion of oxygen and air humidity and the solution was further stirred for 20 minutes at −40°C. To the so-obtained solution of 4-chloro-3-dimethylsulfamoyl-phenyllithium, a solution of 7 g of 5,6-dihydroimidazo[2,1-b]thiazole-3-(2H)-one in 200 ml of absolute tetrahydrofurane were added dropwise in the course of 60 minutes, the solution was stirred overnight at room temperature and the reaction mixture was treated under ice-cooling with 25 ml of saturated ammonium chloride solution. The precipitate was filtered off, the filtrate was dried over magnesium sulfate, and treated with dry hydrogen bromide. Colorless crystals, melting point: 153—155°C (decomposition).

In an analogous manner as described under Example 23, there were obtained in the following Examples:

EXAMPLE 119.

from 4.9 g of 2-bromo-4'-chloro-3'-methylsulfamoylacetophenone and
1.8 g of 1-isopropyl-3-methyl thiourea
4 - (4 - chloro - 3 - methylsulfamoylphenyl) - 2 - isopropylimino - 3 - methyl - 1,3-thiazolidine - 4 - ol hydrobromide, melting point: 244°C (decomposition).

EXAMPLE 120.

from 5.1 g of 2-bromo-4'-chloro-3'-dimethylsulfamoylacetophenone and
1.8 g of 1-isopropyl-3-methylthiourea
4 - (4 - chloro - 3 - dimethylsulfamoylphenyl) - 2 - isopropylimino - 3 - methyl - 1,3-thiazolidine - 4 - ol - hydrobromide, melting point: 242°C (decomposition).

EXAMPLE 121.

from 6 g of 2-bromo-3'-benzylsulfamoyl-4'-chloroacetophenone and
2 g of 1,3-diethylthiourea and following precipitation with diisopropyl ether,
3 - ethyl - 2 - ethylimino - 4 - (3 - benzyl - sulfamoyl - 4 - chlorophenyl) - 1,3 - thiazolidine - 4 - ol-hydrobromide, melting point: 114°C (decomposition).

EXAMPLE 122.

from 6.3 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and
3.2 g of 1-ethyl-3-isobutylthiourea
3 - ethyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - isobutylimino - 1,3 - thiazolidine 4 - ol - hydrobromide, melting point: 187°C (decomposition), which was converted with sodium bicarbonate solution as described in Example 28 into 3 - ethyl - 4-(4 - chloro - 3 - sulfamoylphenyl) - 2 - isobutylimino - 1,3 - thiazolidine - 4 - ol (decomposition beginning at 125°C). By treating with methanolic hydrochloric acid and following crystallization under acetone there was obtained the corresponding 3-ethyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - isobutylimino - 1,3 - thiazolidine-4 - ole - hydrochloride from this compound in ether. Melting point: 175°C (decomposition).

EXAMPLE 123.

from 6.3 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and
2.6 g of 1-methyl-3-propargylthiourea (melting point: 65°C, prepared from 2.8 g of propargyl amine and 3.4 g of methyl mustard oil in 34 ml of toluene) in the presence of a small amount of methanol
4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - propargyl - imino - 1,3 - thiazolidine - 4 - ol-hydrobromide, melting point: 168°C (decomposition).

EXAMPLE 124.

from 7.2 g of 2,4'-dibromo-3'-sulfamoylacetophenone and
2.1 g of 1,3-dimethylthiourea
4 - (4 - bromo - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide, melting point: 169°C (decomposition).
(Preparation of 2,4'-dibromo-3'-sulfamoylacetophenone:
5.35 g of 3'-amino-4'-bromoacetophenone, melting point: 113°C, were diazotized in 50 ml of semi-concentrated hydrochloric acid with 1.75 g of sodium nitrite at 0—5°C and then decomposed according to Meerwein with 62 ml of sulfur-dioxide-saturated glacial acetic acid solution and 2 g of copper-II-chloride-dihydrate. After the addition of 62 ml of water, the 4'-bromo-3'-chlorosulfonylacetophenone was obtained which melted at 107°C and could be introduced without further purification into about 50 ml of liquid ammonia. After evaporation of the ammonia and treatment with water, 4'-bromo-3'-sulfamoylacetophenone were obtained which melted at 161°C.

In an analogous manner as described under Example 12, 4.8 g of 4'-bromo-3'-sulfamoylacetophenone were reacted with 2.8 g of bromine and the 2,4'-dibromo-3'-sulfamoylacetophenone was recrystallized from isopropanol. Melting point: 179°C).

EXAMPLE 125.

from 7.2 g of 2,4'-dibromo-3'-sulfamoylacetophenone and
3.5 g of 1-cyclohexyl-3-methylthiourea
4 - (4 - bromo - 3 - sulfamoylphenyl) - 2 - cyclohexylimino - 3 - methyl - 1,3 - thiazolidine - 4 - ol - hydrobromide, melting point: 172°C, decomposition.

EXAMPLE 126.

from 7.2 g of 2,4'-dibromo-3'-sulfamoylacetophenone and
3 g of 1-ethyl-3-isopropylthiourea and following precipitation with diisopropyl ether
the 3 - ethyl - 4 - (4 - bromo - 3 - sulfamoylphenyl) - 2 - isopropylimino - 1,3 - thiazolidine - 4 - ol -hydrobromide, (decomposition beginning at 135°C).

EXAMPLE 127.

from 7.2 g of 2,4'-dibromo-3'-sulfamoylacetophenone and
3.2 g of 1,3-diallylthiourea and following precipitation with diisopropyl ether
the 3 - allyl - 2 - allylimino - 4 - (4 - bromo - 3 - sulfamoylphenyl) - 1,3 - thiazolidine - 4 - ol -hydrobromide, melting point: 156°C (decomposition).

EXAMPLE 128.

from 3 g of 2-bromo-4'-fluoro-3'-sulfamoylacetophenone and
1 g of 1,3-dimethylthiourea
the 4 - (4 - fluoro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide, melting point: 164°C (decomposition).
(Preparation of 2-bromo-4'-fluoro-3'-sulfamoylacetophenone:
a) 39 g of 4'-fluoro-3'-nitroacetophenone, melting point: 44°C, were hydrogenated in 390 ml of methanol at 20 atm. and 40°C in the presence of Raney-Nickel to give the 3'-amino-4'-fluoro-acetophenone, melting point: 70°C).
b) 4.9 g of 3'-amino-4'-fluoroacetophenone were diazotized in 25 ml of concentrated hydrochloric acid at 0 to 5°C with a solution of 2.3 g of $NaNO_2$ in 5 ml of water and treated with a solution, prepared from 2.7 g of sodium bisulfite in 5 ml of water and 25 ml of concentrated hydrochloric acid and the oily 3'-chlorosulfonyl-4'-fluoroacetophenone was reacted with 20 ml of liquid ammonia to give the 4'-fluoro-3'-sulfamoylacetophenone, melting point: 135°C from glacial acetic acid.
c) 12.5 g of 4'-fluoro-3'-sulfamoylacetophenone were reacted as described in Example 12 with 9.2 g of bromine to give the 2-bromo-4'-fluoro-3'-sulfamoylacetophenone, melting point: 125°C.

EXAMPLE 129.

from 3 g of 2-bromo-4'-fluoro-3'-sulfamoylacetophenone and
1.2 g of 1,3-diethylthiourea
the 3 - ethyl - 2 - ethylimino - 4 - (4 - fluoro - 3 - sulfamoylphenyl) - 1,3 - thiazolidine - 4 - ol - hydrobromide, decomposition beginning at 120°C.

EXAMPLE 130.

from 3.6 g of 2-bromo-4'-chloro-3'-propylsulfamoylacetophenone and
1.1 g of 1,3-dimethylthiourea
the 4 - (4 - chloro - 3 - propylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3-thiazolidine - 4 - ol - hydrobromide, decomposition beginning at 120°C.
(Preparation of 2-bromo-4'-chloro-3'-propylsulfamoylacetophenone:
a) 12.5 g of 4'-chloro-3'-chlorosulfonylacetophenone were reacted in 150 ml of ethanol with 18 g of n-propylamine and the 4'-chloro-3'-propylsulfamoylacetophenone was filtered off (melting point: 115°C from a small amount of isopropanol).
b) 13.8 g of 4'-chloro-3'-propylsulfamoylacetophenone were reacted as described in Example 1a) with 8 g of bromine to give the 2-bromo-4'-chloro-3'-propylsulfamoylacetophenone, melting point: 96°C, from isopropanol).

EXAMPLE 131.

from 6.2 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone
3.8 g of 1-methyl-4,4-pentamethylenethiosemicarbazide (prepared from methylisothiocyanate and N-aminohomopiperidine, melting point: 192°C)
the 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 4 hydroxy - 1,3 - thiazolidine-2 - one - N,N - pentamethylenehydrazone - hydrobromide, melting point: 165°C, decomposition.
In an analogous manner to Example 15b) there were obtained in the following Examples:

EXAMPLE 132.

from 4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and
2.2 g of 1-ethyl-3-cyclopropylthiourea (melting point: 106°C), prepared from 9 g of ethylisothiocyanate and 5.7 g of cyclopropyl amine in toluene,
the 3 - ethyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - cyclohexylimino - 1,3-thiazolidine - 4 - ol - hydrobromide, which was converted after dissolution in water and with sodium bicarbonate solution in an analogous manner as to Example 2c) into the 3 - ethyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - cyclopropylimino - 1,3-thiazolidine - 4 - ol, melting point 125°C, decomposition.

EXAMPLE 133.

from 4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and
2.8 g of 1-ethyl-3-cyclohexylthiourea
the 3 - ethyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - cyclohexylimino - 1,3 - thiazolidine - 4 - ol - hydrobromide, which was converted after dissolution in water in an analogous manner to Example 2c) into the 3 - ethyl - 4 - (4 - chloro - 3-sulfamoylphenyl) - 2 - cyclohexylimino - 1,3 - thiazolidine - 4 - ol, (decomposition beginning at 125°C).

EXAMPLE 134.

from 4.7 g of 2-bromo-4'-chloro-3'-sulfamoylacetophenone and
2.8 g of 1-ethyl-3-(2-methoxypropyl)-thiourea
the 3 - ethyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - (2 - methoxypropylimino-1,3 - thiazolidine - 4 - ol - hydrobromide, which yielded a solid substance after dissolution in water and lyophilization, (decomposition beginning at 120°C).

EXAMPLE 135.

4 - (4 - Chloro - 3 - cyclopentylmethylsulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3 - thiazolidine - 4 - ol

6.7 g of 4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino-1,3 - thiazolidine - 4 - ol (Example 2) were introduced, while stirring, into a mixture of 10 ml of absolute dimethyl sulfoxide and 1.2 g of pulverized potassium hydroxide with the exclusion of nitrogen, the temperature being maintained between 8°C and 12°C by outward cooling. While cooling and stirring were maintained, 3.3 g of cyclopentylmethylbromide were added dropwise, the mixture was stirred for 10 hours at room temperature and precipitated with 100 ml of water. The oily residue was decanted, the amorphous product was solidified under 100 ml of fresh water, suction-filtered and washed with water several times. Yellow-brown solid substance, decomposition beginning at 72°C. The IR-spectrum was identical with that of Example 76.

EXAMPLE 136.

4 - (4 - Chloro - 3 - o - chlorobenzylsulfamoylphenyl) - 3 - methyl - 2 - methylimino-1,3 - thiazolidine - 4 - ol

6.7 g of 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino-1,3 - thiazolidine - 4 - ol (Example 2) were suspended in 67 ml of absolute methanol, while stirring to which a freshly prepared solution from 0.5 g of sodium in 15 ml of absolute methanol was added. 4.1 g of o-chloro-benzyl bromide were added at +10°C while stirring and the reaction mixture was stirred for 24 hours at room temperature and for a further 2 hours at 38°C. The mixture was concentrated to a half under reduced pressure, poured into 100 ml of stirred water, filtered off and washed with water several times. Colorless substance, melting point: 161°C (decomposition). The IR-spectrum was identical with that of Example 87.

According to the operational method c) and in an analogous manner to the prescription given in Example 106 there were obtained the following compounds of the formula I of the invention as indicated in the following Table 1.

TABLE 1

| Example No. | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Y | Salt with | Melting point (decomposition) |
|---|---|---|---|---|---|---|---|---|
| 137 | $-(CH_2)_2-$ | | H | H | H | Cl | HBr | 98 to 99° C |
| 138 | $-(CH_2)_3-$ | | H | H | H | Cl | HBr | 321 to 329° C |
| 139 | $-(CH_2)_3-$ | | H | $CH_3$ | $CH_3$ | Cl | HBr | 198° C |
| 140 | $CH_3$ | $CH_3$ | H | H | H | Cl | HCl | 200 to 203° C |
| 141 | $CH_3$ | $CH_3$ | H | $CH_3$ | $CH_3$ | Cl | HCl | 165 to 167° C |
| 142 | $C_2H_5$ | $C_2H_5$ | H | $CH_3$ | $CH_3$ | Cl | HCl | 132° C |
| 143 | $C_2H_5$ | $C_2H_5$ | H | H | H | Cl | HCl | 167° C |

The mercaptoketones required for the Examples indicated above in Table 1, which are the 4′-chloro-3′-sulfamoyl-acetophenone-2-thio (melting point: 139°C) or the 2-acetylthio-4′-chloro-3′-sulfamoylacetophenone (melting point: 137°C), were obtained according to the prescription given in Example 104a). According to the operational method f) and in an analogous manner to the prescription given in Example 118, there were obtained in the following Examples:

EXAMPLE 144.

from 4 - chloro -3 - dimethylsulfamoyl - phenyllithium with N,N′ - dimethylbromoformamidine

the 4 - (4 - chloro - 3 - dimethylsulfamoylphenyl) - 3 - methyl - 2 - methylimino-1,3 - thiazolidine - 4 - ol - hydrobromide, melting point: 158—159°C, (decomposition).

EXAMPLE 145.

from 4 - chloro - 3 - dimethylsulfamoyl - phenyllithium with N,N′ - diethylbromoformamidine

the 3 - ethyl - 2 - ethylimino - 4 - (4 - chloro - 3 - dimethylsulfamoylphenyl) - 1,3-thiazolidine - 4 - ol - hydrobromide, melting point: 154°C (decomposition).

The new thioureas of the formula III used in the preceding Examples as starting substances were prepared according to methods disclosed in literature (cf. Houben-Weyl, " Methoden der organischen Chemie ", vol. 9, page 884, 4th edition, (1955)). The melting points of the different compounds of the formula III are listed in the following Table 2.

TABLE 2: (thioureas III)

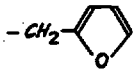
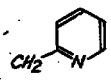
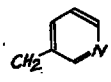
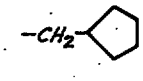
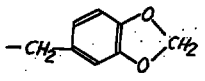
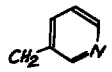
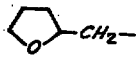
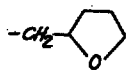
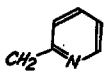
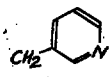
| $R^1$ | $R^2$ | Melting point |
|---|---|---|
| $CH_3-$ | | 108°C |
| $(CH_3)_2N-$ | $-N(CH_3)_2$ | 168°C |
| $CH_3O_2C-$ | $-(CH_2)_2-CH_3$ | 55°C |
| $CH_3-CH(O-CH_3)-CH_2-$ | $-CH_3$ | 32°C |
| $(CH_3)_2CH-$ | $-N(CH_3)_2$ | 134°C |
| $CH_3-$ |  | 78°C |
| $CH_2=CH-CH_2$ | | 106°C |
| | | 144°C |
| $CH_3-$ |  | 142°C |
| $CH_3-$ |  | 144°C |
| $CH_3-$ |  | 95°C |

TABLE 2: (thioureas III)

| $R^1$ | $R^2$ | Melting point |
|---|---|---|
| $CH_3-$ |  | 158°C |
| $CH_2=CH-CH_2$ |  | 75°C |
|  |  | 67°C |
| |  | 104°C |
| |  | 198°C |
| | $-N(CH_3)_2$ | 152°C |
| $CH_3-$ | | 192°C |

For the preparation of further compounds of the invention of the general formula I the sulfamoyl halogen ketones of the general formula II indicated in the following Table 3 were synthesized:

TABLE 3

Sulfamoyl halogen ketones (II) from sulfamoyl ketones (XV), prepared in a manner analogous to Example 1A).

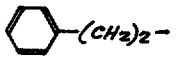
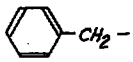
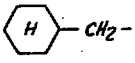
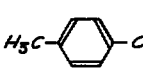
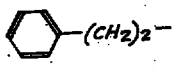
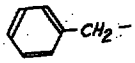
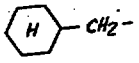
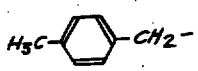
| $R^3$ | $R^4$ | $R^5$ | Y | Z | Melting point (°C) |
|---|---|---|---|---|---|
| H | $CH_3$– | H | Cl | Br | 148 |
| H | $CH_3(CH_2)_3$– | H | Cl | Br | 104 |
| H | $CH_3(CH_2)_2$– | $CH_3(CH_2)_2$– | Cl | Br | 57 |
| H | H | $CH_3$–CH(–$CH_2$–$CH_3$)– | Cl | Br | 108 |
| H | H | | Cl | Br | 114 |
| H | H |  | Cl | Br | 138 |
| H | –$(CH_2)_4$– | | Cl | Br | 127 |
| H | –$(CH_2)_5$– | | Cl | Br | 108 |
| H | $CH_3$– |  | Cl | Br | 103 |
| H | H | | Cl | Br | 108 |
| H | H |  | Cl | Br | 99 |
| H | H | $C_2H_5$– | Cl | Br | 106 |
| H | H | $(H_3C)_2$CH–$CH_2$– | Cl | Br | 100 |
| H | H |  | Cl | Br | 116 |
| H | H | H | Br | Br | 179 |

TABLE 3 (Continued)

| $R^3$ | $R^4$ | $R^5$ | Y | Z | Melting point (°C) |
|---|---|---|---|---|---|
| $C_2H_5-$ | H | $C_6H_5-CH_2-$ | Cl | Br | 111 |
| $CH_3-$ | H | | Cl | Br | 153 |
| $CH_3-$ | H | $C_6H_5-CH_2-$ | Cl | Br | 116 |
| $CH_3-$ | H | $CH_3-\underset{\displaystyle CH_3}{\underset{\vert}{CH}}-CH_2-CH_3$ | Cl | Br | 166 |
| $CH_3-$ | H | $CH_3-$ | Cl | Br | 91 |

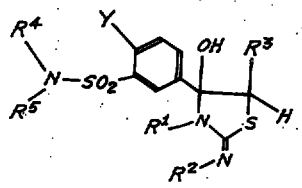
The sulfamoyl ketones (XV) required for the sulfamoyl halogen ketones (II) indicated in Table 3 were prepared by the action of amine (VII) on a sulfochloride (IV) and are indicated in Table 4:

TABLE 4: Sulfamoyl ketones (XV)

| $R^3$ | $R^4$ | $R^5$ | Y | Melting point (°C) |
|---|---|---|---|---|
| H | $CH_3$ | H | Cl | 153 |
| H | $CH_3(CH_2)_3-$ | H | Cl | 55 |
| H | $CH_3(CH_2)_2-$ | H | Cl | 74 |
| H | H | $CH_3-CH(CH_3)-CH_2-CH_3$ | Cl | 89 |
| H | H |  | Cl | 87 |
| H | H | | Cl | 109 |
| H | | $-(CH_2)_5-$ | Cl | 112 |
| H | | $-(CH_2)_4-$ | Cl | 98 |
| H | $CH_3$ |  | Cl | 97 |
| H | H | | Cl | 82 |
| H | H | $C_2H_5-$ | Cl | 116 |
| H | H |  | Cl | 114 |
| H | H | $(H_3C)_2CH-CH_2-$ | Cl | 60 |
| H | H |  | Cl | 85 |
| H | H | H | Br | 161 |
| $C_2H_5-$ | H | $C_6H_5-CH_2-$ | Cl | 112 |
| $CH_3-$ | H | | Cl | 63 |
| $CH_3-$ | H | $C_6H_5-CH_2-$ | Cl | 80 |
| $CH_3-$ | H | $CH_3-CH(CH_3)-CH_2-CH_3$ | Cl | 65 |
| $CH_3-$ | H | $CH_3-$ | Cl | 124 |

WHAT WE CLAIM IS:—

1. Thiazolidine derivatives of general formula I



(I)

in which

$R^1$ stands for an alkyl or alkenyl radical having up to 4 carbon atoms, a cycloalkyl radical having from 3 to 6 carbon atoms, or a diakylamino group having a total of 7 carbon atoms, which may form together with the nitrogen atom of the amino group a saturated heterocyclic ring;

$R^2$ stands for an alkyl, alkenyl, or alkynyl radical having up to 8 carbon atoms which may be substituted by one or more alkoxy groups having from 1 to 4 carbon atoms; a cycloalkyl radical having from 3 to 8 carbon atoms; a phenylalkyl radical having 1 or 2 carbon atoms in the alkyl moiety, which may be substituted in the phenyl ring by one or more substituents, which may be the same or different, selected from halogen atoms, alkyl and alkoxy groups having up to 4 carbon atoms, and alkylenedioxy groups; or

$R^2$ stands for an alkyl group having 1 or 2 carbon atoms which is substituted by a cycloalkyl radical having from 3 to 6 carbon atoms or by a 5- or 6-membered saturated or unsaturated heterocyclic radical containing one or more heteroatoms selected from oxygen, nitrogen and sulfur atoms; or

$R^2$ stands for a dialkylamino group having a total of up to 7 carbon atoms, which may form together with the nitrogen atom of the amino group a saturated heterocyclic ring; or

$R^1$ and $R^2$ together stand for an alkylene group having from 2 to 4 carbon atoms;

$R^3$ stands for a hydrogen atom or an alkyl group having 1 or 2 carbon atoms;

$R^4$ and $R^5$ are identical or different, and each stands for a hydrogen atom; an alkyl or alkenyl radical having up to 6 carbon atoms, which may be substituted by one or more alkoxy groups having 1 to 4 carbon atoms; a cycloalkyl or cycloalkylalkyl group having a total of 3 to 9 carbon atoms; a phenyl group or a phenylalkyl group having 1 to 3 carbon atoms in the alkyl moiety, the phenyl ring optionally being substituted by one or more substituents, which may be the same or different, selected from halogen atoms, alkyl and alkoxy groups having up to 4 carbon atoms, and alkylenedioxy groups; or stands for an alkyl group having 1 or 2 carbon atoms which is substituted by a 5- or 6-membered unsaturated heterocyclic radical containing one or more hetero-atoms selected from oxygen, nitrogen and sulfur atoms; or

$R^4$ and $R^5$ together with the nitrogen atom form a saturated, optionally methyl-substituted, 5- or 6-membered heterocyclic ring, in which optionally a $—CH_2—$ group may be replaced by an oxygen atom; and

Y stands for a hydrogen or halogen atom or a methyl or trifluoromethyl group.

2. 4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - methylimino - 1,3-thiazolidine - 4 - ol - hydrochloride.

3. 3 - Ethyl - 2 - ethylimino - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 1,3 - thiazolidine - 4 - ol - hydrochloride.

4. 4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - propyl - 2 - propylimino - 1,3-thiazolidine - 4 - ol - hydrochloride.

5. 4 - (4 - Chloro - 3 - sulfamoylphenyl) - 2 - isopropylimino - 3 - methyl - 1,3-thiazolidine - 4 - ol - hydrochloride.

6. 3 - Ethyl - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 2 - isopropylimino - 1,3-thiazolidine - 4 - ol - hydrochloride.

7. 3 - Allyl - 2 - allylimino - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 1,3 - thiazolidine - 4 - ol -hydrochloride.

8. 4 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - methyl - 2 - (2 - methoxy - 1-propylimino) - 1,3 - thiazolidine - 4 - ol.

9. 2 - Benzylimino - 4 - (4 - chloro - 3 - sulfamoylphenyl) - 3 - methyl - 1,3-thiazolidine - 4 - ol.

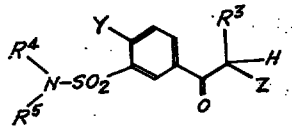
10. 3 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - hydroxy - 2,3,5,6 - tetrahydro-imidazo[2,1-b] - thiazole - hydrobromide.

11. 3 - (4 - Chloro - 3 - sulfamoylphenyl) - 3 - hydroxy - 2,3,6,7 - tetrahydro-5H - thiazolo[3,2-a] - pyrimidine - hydrochloride.

12. 3 - (4 - Chloro - 3 - sulfamoylphenyl) - 6,6 - dimethyl - 3 - hydroxy - 2,3,5,6-tetrahydro - imidazo[2,1-b] - thiazole - hydrobromide.

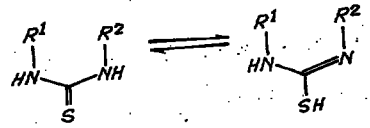
13. A process for the manufacture of a compound as claimed in claim 1 which comprises

a) reacting a compound of the general formula II



(II)

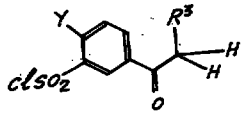
in which $R^3$, $R^4$, $R^5$ and Y are defined as in claim 1 and Z stands for the radical of an activated ester of an inorganic or organic acid, with a thiourea of the general formula III, which can be represented by formulae IIIa and IIIb



(IIIa) (IIIb)

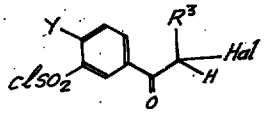
in which $R^1$ and $R^2$ are defined in claim 1 or

b) treating a compound of the general formula IV



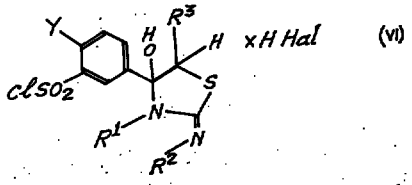
(IV)

in which $R^3$ and Y are defined as in claim 1, with a halogenating agent and reacting the $\alpha$-halogen ketone of the general formula V



(V)

thus obtained in which $R^3$ and Y are defined as in claim 1, and Hal stands for a chlorine or bromine atom, if desired without isolation or purification, with a thiourea of the formula III, and reacting the thiazolidine derivative thus obtained of the general formula VI



(VI)

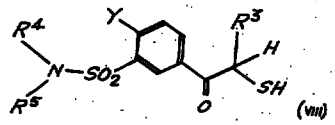
in which $R^1$, $R^2$ and $R^3$ are defined as in claim 1, with ammonia, a primary or secondary amine of the general formula VII

(VII)

in which $R^4$ and $R^5$ are defined in claim 1, or

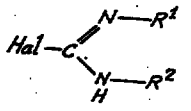
* C L M S *

c) reacting a compound of the general formula VIII



(VIII)

with a compound of the formula IX



(IX)

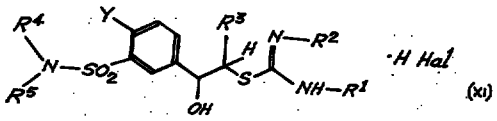
in which $R^1$, $R^2$, $R^3$ and Y are defined as in claim 1, and Hal stands for a chlorine or bromine atom,

d) reacting a compound of the formula VIII with a carbodiimide of formula X

$$R^1—N=C=N—R^2 \qquad (X)$$

in which $R^1$ and $R^2$ are defined as in claim 1,

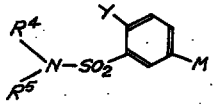
e) treating a compound of the general formula XI



(XI)

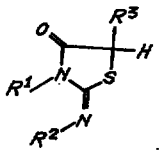
in which $R^1$, $R^2$, $R^3$, $R^4$ and $R^5$ and Y are defined as in claim 1, and Hal stands for a chlorine or bromine atom with an oxidation agent or

f) reacting a compound of the general formula XII



(XII)

in which $R^4$ and $R^5$ and Y are defined as in claim 1, but $R^4$ and $R^5$ do not stand for hydrogen atoms and Y does not stand for a bromine or iodine atom, and M stands for lithium or a MgBr-group, with a compound of the general formula XIII



(XIII)

in which $R^1$, $R^2$ and $R^3$ are defined as in claim 1, and hydrolyzing the reaction product obtained, and, if desired, converting the compound of the general formula I obtained according to any one of methods a) to f) in which $R^4$ and/or $R^5$ stands for a hydrogen atoms, by alkylation into the corresponding compound in which $R^4$ and/or $R^5$ has one of the other meanings given in claim 1, and/or converting the compound of the formula 1, prepared according to any one of methods a) to f), with an organic or inorganic acid into an acid addition salt thereof, or converting a salt of the general formula 1 with a base into the corresponding free basic compound of the formula 1.

14. A process as claimed in claim 13, carried out substantially as described in any one of the Examples herein.

15. A compound as claimed in claim 1, whenever produced by a process as claimed in claim 13 or claim 14.

16. A compound as claimed in claim 1 and which is described in the Table herein or in any one of the Examples herein, with the exception of the compounds claimed in claims 2 to 12.

17. An acid addition salt of a compound as claimed in claim 1.

18. A physiologically tolerable acid addition salt of a compound as claimed in claim 1.

19. A pharmaceutical preparation which comprises a compound as claimed in any one of claims 1 to 12, claim 15, claim 16 or claim 18 as active substance, in admixture or conjunction with a pharmaceutically suitable carrier.

20. A pharmaceutical preparation as claimed in claim 19, in unit dosage form.

21. A pharmaceutical preparation as claimed in claim 20, which comprises from 5 to 500 mg of the active substance per unit dose.

22. A pharmaceutical preparation as claimed in claim 21, which comprises from 10 to 100 mg of the active substance per unit dose.

23. A pharmaceutical preparation as claimed in any one of claims 19 to 22, which comprises one or more further active substance(s).

24. A pharmaceutical preparation as claimed in claim 23, wherein the active substance(s) is or are selected from antihypertensive agents, potassium retaining compounds, and potassium substitution substances.

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