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COMPLETE SPECIFICATION

Benzenesulphonyl-Ureas and Process for Preparing Them

We, FARBWERKE HOECHST AKTIENGESSELLSCHAFT, vormals Meister Lucius & Bruning, a Company recognised by German Law, of 6230 Frankfurt (Main) 80, Postfach 80 03 20, 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 provides benzenesulphonyl-ureas of the general formula

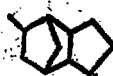


in which X, Y and R¹ have the meanings given below, and their physiologically tolerable salts. The benzenesulphonylureas, of the above formula are new compounds and, in the free form or in the form of their physiologically tolerable salts, have blood sugar lowering properties and are distinguished by a strong and long lasting hypoglycemic action.

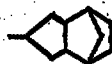
In the above formula

R¹ represents

4,7-endomethylene-perhydroindan-5-yl



which may be substituted by chlorine in 6-position,
4,7-endomethylene-perhydroindan-2-yl



2,6-endomethylene-cycloheptyl,
4,4-dimethyl-Δ²-cyclohexenyl,
Δ²-cyclopentenyl, Δ²-cycloheptenyl, Δ²-cyclooctenyl,
norcaran-7-yl



bicyclo [5,1,0] octyl-(8)



bicyclo [6,1,0] nonyl-(9)



5

bicyclo [4,2,0] octyl-(7)



5

2,5-endo-cyclobutylene-(1,2)-cyclohexyl



10

methyl-cyclopentyl,
3,3-dimethyl-cyclopentyl,
3-ethyl-cyclopentyl,
3-tert.-butyl-cyclopentyl,
2-chloro-cyclopentyl,
 Δ^2 -cyclopentenyl-methyl,
bicyclo [2,1,1] hexyl-(2)

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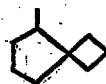


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spiro-(2-cyclopropane-cyclopentyl)



spiro-(2-cyclobutane-cyclopentyl)



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spiro-(2-cyclopentane-cyclopentyl)



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cyclopropyl, cyclobutyl,
5-methyl- Δ^2 -cyclohexenyl,

bicyclo [3,1,0] hexyl



X represents

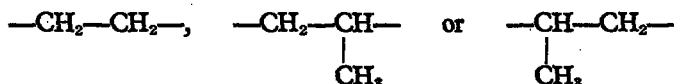
(a) a phenyl group which carries at any desired position the substituents Z and Z' defined hereafter, which may be identical or different:

Z represents hydrogen, halogen; low molecular weight alkyl, alkoxy, alkenoxy, alkoxy-alkoxy, phenalkoxy; low molecular weight acyl; benzoyl; tri-fluoromethyl; hydroxy;

Z' represents —CN; —NO₂; hydrogen; halogen; low molecular weight alkyl, alkoxy, alkoxy-alkoxy or hydroxy;

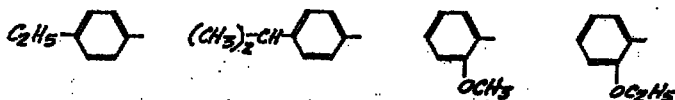
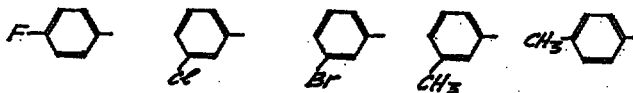
(b) a thiophen group which may be substituted by one or two substituents selected from low molecular weight alkyl, alkoxy, alkoxy-alkoxy, alkenoxy, phenalkoxy radicals and halogen atoms; the groups having the meaning given under (a) being preferred;

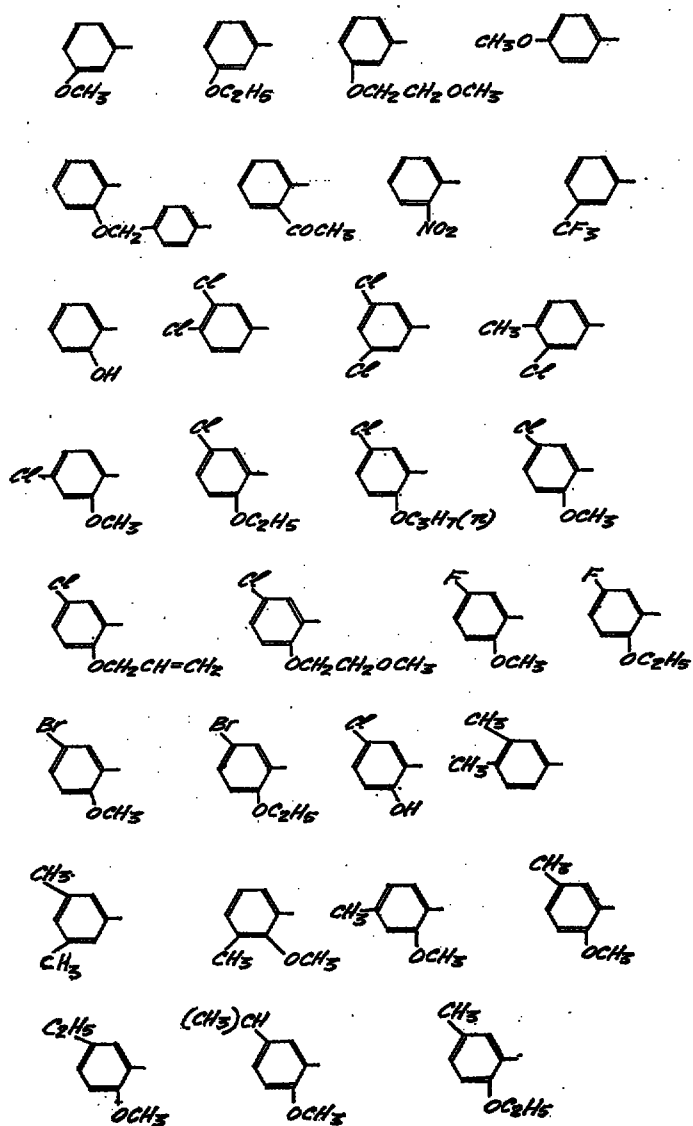
Y represents one of the groups

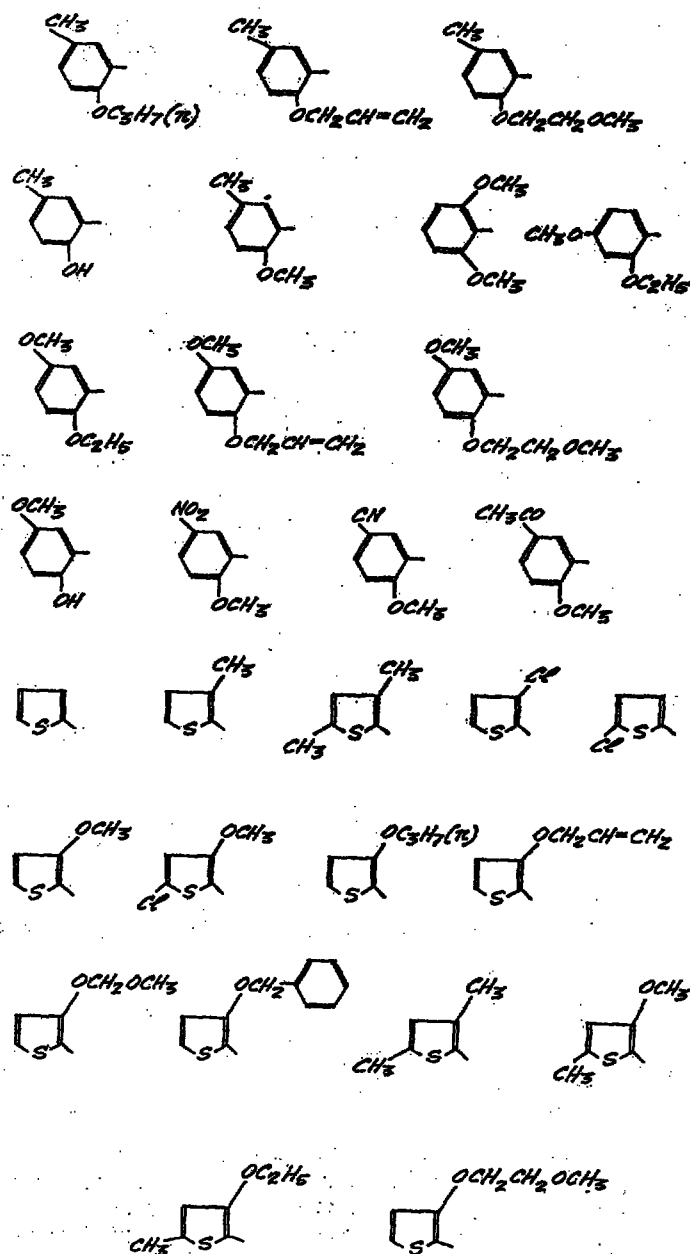


The expressions "low molecular weight alkyl" and "low molecular weight alkoxy" used throughout the specification are intended to mean respectively alkyl and alkoxy groups containing 1 to 4 carbon atoms in a straight or branched chain. The term "low molecular weight" used throughout the specification is intended to mean acyl groups (organic acid radicals) containing up to 4 carbon atoms, preferably a straight chain or branched alkanoyl radical of corresponding chain length.

As the part X in the above formula, there enter into consideration the following rings systems:







The present invention furthermore provides a process for preparing the benzene-

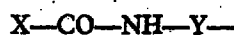
sulphonyl-ureas of the above general formula, wherein

a) a benzenesulphonyl-isocyanate, benzenesulphonyl-carbamic acid ester, benzene-

sulphonyl-thiolcarbamic acid ester, benzenesulphonyl-carbamic acid halide, benzene-

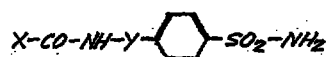
sulphonyl-urea, benzenesulphonyl-semicarbazide or benzenesulphonyl-semicarbazone,

which is substituted by the group



is reacted with an amine, $R'NH_2$, or with a salt thereof;

b) a benzenesulphonamide of the formula



or a salt thereof is reacted with an R¹-containing-isocyanate, -carbamic acid ester, -thiolcarbamic acid ester, -carbamic acid halide or -urea;

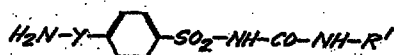
c) a correspondingly substituted benzenesulphonyl-isourea ether, benzenesulphonyl-isothiurea ether, benzenesulphonyl-isourea ester, benzenesulphonyl-parabanic acid or benzenesulphonyl-haloformic acid amidine is hydrolyzed;

d) in a correspondingly substituted benzenesulphonyl-thiourea, the sulphur atom is replaced by an oxygen atom,

e) water is added onto a correspondingly substituted carbodiimide;

f) a corresponding benzenesulphenyl-urea or benzenesulphenyl-urea is oxidized;

g) the group X—CO— is introduced by acylation, if desired in one or several steps, into a benzenesulphonyl-urea of the formula



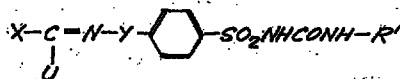
in which Y and R¹ have the meanings given above;

h) a correspondingly substituted benzenesulphonyl-halide is reacted with an R¹-substituted urea or with an alkali metal salt thereof in which R¹ has the meaning given above;

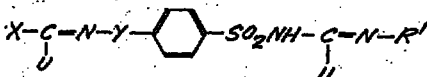
i) a correspondingly substituted benzene-sulphinic acid halide or, in the presence of an acid condensing agent, also a correspondingly substituted benzene-sulphinic acid or an alkali metal salt thereof is reacted with an N-hydroxy-N¹-R¹-urea, in which R¹ has the meaning given above;

k) in a correspondingly substituted thio-amido-alkyl-benzenesulphonyl-urea or a thio-amido-alkyl-benzenesulphonyl-thiourea, the sulphur atom or the sulphur atoms is or are replaced by an oxygen atom or oxygen atoms;

l) a compound of the formula



in which R¹ has the meaning given above, or a parabanic acid derivative thereof or a compound of the formula



in which U each time stands for one of the groups —O—low molecular weight alkyl, —S—low molecular weight alkyl or, preferably, halogen, is saponified; or

m) a corresponding benzenesulphonyl-urea which contains an unsaturated linkage in the molecule is hydrogenated; and, if desired, the reaction product so obtained is converted into a salt by treatment with a base.

Depending on the nature of the starting substances, especially on the part X, one or other of the variations of the process hereinbefore described may, in some cases, provide a desired individual benzenesulphonyl-urea only in a small yield or may be inappropriate for its synthesis or may at least require steps for the protection of active groups. In such comparatively rare cases, the expert will have no difficulty in synthesizing the desired product according to a variation of the process described.

Instead of the benzenesulphonyl-isocyanate, there may also be used reaction products of benzenesulphonyl-isocyanates with acid amides such, for example, as caprolactam or butyrolactam, furthermore with weakly basic amines such, for example, as carbazoles.

The benzenesulphonyl-carbamic acid esters or benzene-sulphonyl-thiolcarbamic acid esters may carry in the alcohol component a low molecular weight alkyl group or a phenyl group. The same applies to the R¹-substituted carbamic acid esters or to the corresponding thiolcarbamic acid esters.

As carbamic acid halides, the chlorides are advantageously used.

The benzenesulphonyl-ureas used as starting materials in the process of the

present invention may be unsubstituted at the side of the urea molecule opposite to the sulphonyl group or may be mono- or, especially, di-substituted. Since these substituents are split off during the reaction with the amines, their natures can be varied within wide limits. In addition to benzenesulphonyl-ureas which carry alkyl-, aryl-, acyl-, or heterocyclic substituents, there may also be used bis-(benzenesulphonyl)-ureas which may carry at one of the nitrogen atoms a further substituent, for example, a methyl group. Such bis-(benzenesulphonyl)-ureas or also N-benzenesulphonyl-N'-ureas may be treated with amines of the formula R^1NH_2 and the salts obtained may be heated to elevated temperatures, in particular to temperatures above $100^\circ C$.

Furthermore, it is possible to start from ureas of the formula $R^1-NH-CO-NH_2$ or from such ureas which are mono- or especially di-substituted at the free nitrogen atom and to react them with benzenesulphonamides which carry the substituent $X-CO-NH-Y$. As such starting materials, there may be used, for example, N'-acetyl- or N'-nitro-ureas, N',N'-diphenyl-ureas (in which case the two phenyl radicals may also be substituted or be linked with each other either directly or by means of a bridge member such as $-CH_2-$, $-NH-$, $-O-$ or $-S-$), N'-methyl-N'-phenyl-ureas or N',N'-dicyclohexyl-ureas, which are substituted at the N-nitrogen atom by R^1 , as well as corresponding carbamoyl-imidazoles or carbamoyl-triazoles, and finally also ureas of the formula $R^1-NH-CO-NH-R^1$.

The hydrolysis of the benzenesulphonyl-parabanic acids, benzenesulphonyl-isourea ethers, benzenesulphonyl-isothiurea ethers, benzenesulphonyl-isourea esters or benzenesulphonyl-haloformic acid amidines mentioned as starting substances is suitably carried out in an alkaline medium. Isourea ethers and isourea esters may also be hydrolyzed successfully in an acid medium.

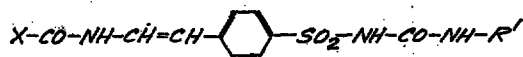
The reaction of the benzenesulphohalides with R^1 -substituted ureas is suitably effected using strongly condensing agents such, for example, as alkali metals, alkali metal amides or, preferably, alkali metal hydrides in inert solvents.

The reaction of the sulphinic acids or sulphinic acid chlorides with hydroxy-ureas can be suitably effected in inert solvents; when sulphinic acids or their alkali metal salts are used as starting substances, acid condensing agents such, for example, as thionyl chloride, polyphosphoric acids, anhydrous phosphoric acid or sulphuric acid, are necessary.

The replacement of the sulphur atom in correspondingly substituted benzene-sulphonyl-thioureas by an oxygen atom can be effected in known manner, for example, with the aid of an oxide or salt of a heavy metal or with the use of an oxidizing agent such, for example, as hydrogen peroxide, sodium peroxide or nitrous acid.

The thioureas may also be desulphurized by treatment with phosgene or phosphorus pentachloride. Chloroformic acid amidines or chloroformic acid carbodiimides obtained as intermediary products can be converted into the benzene-sulphonyl-ureas by suitable measures such, for example, as saponification or addition of water.

Correspondingly substituted benzenesulphonyl-ureas which contain as unsaturated linkage in the molecule, for example,



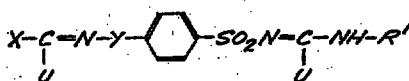
in which X and R^1 have the meanings given above, can be converted into the benzene-sulphonyl-ureas of the present invention by hydrogenation, for example, with molecular hydrogen, in the presence of a known hydrogenation catalyst.

The acylation of amino-alkyl-benzenesulphonyl-ureas may be carried out either in one step, for example, by the reaction of a correspondingly substituted acid halide, or it may be effected in several steps. As examples of the numerous possibilities of a stepwise acylation, there may be mentioned the reaction of amino-alkyl-benzenesulphonyl-ureas with 2-methoxy-benzoyl chloride and the subsequent introduction of a halogen atom into the benzene nucleus of the benzamido group. The oxidation of corresponding benzenesulphonyl-ureas or benzenesulphenyl-ureas can be effected in a particularly advantageous manner with permanganate.

The replacement of the sulphur atom in a correspondingly substituted thio-amido-alkyl-benzenesulphonyl-urea or thio-amido-alkyl-benzenesulphonyl-thiourea by an oxygen atom can be effected, for example, with the aid of an oxidizing agent such, for example, as hydrogen peroxide, sodium peroxide or other peroxide compounds.

It is also possible to desulphurize, instead of the thio-amido-alkyl-benzenesulphonyl-ureas, corresponding thio-amido-alkyl-benzenesulphonyl-isothioureas, thio-amido-alkyl-benzenesulphonyl-isoureas or esters, thio-amido-alkyl-benzenesulphonyl-parabanic acids or thio-amido-alkyl-benzenesulphonyl-haloformic acid amidines to amido-alkyl-benzenesulphonyl-ureas by treatment with an oxidizing agent in acid or alkaline medium and simultaneous hydrolytic setting free of the sulphonyl-urea grouping.

In the same manner, it is possible to convert, instead of thio-amido-alkyl-benzenesulphonyl-thioureas, compounds of the formula



in which X, Y, R¹ and U have the meanings given above, into amido-alkyl-benzene sulphonyl-ureas by treatment with an oxidizing agent in acid or alkaline medium with simultaneous desulphurisation and hydrolysis.

With regard to reaction conditions, the reactions may be carried out with the use of solvents or without solvents, at room temperature or at an elevated temperature.

The blood sugar lowering action of the benzenesulphonyl-ureas of the present invention was ascertained by administering them, for example, in form of the sodium salt, to normally fed rabbits in doses of 10 mg/kg and determining the blood sugar value according to the known method of Hagedorn-Jensen or by means of an auto-analyser for a prolonged period of time.

Thus, we have found, for example, that 10 mg/kg of N - [4 - (β - <2 - methoxy - 5 - methyl - benzamido> - ethyl) - benzenesulphonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea provoke after 3 hours a lowering of the blood sugar of 24%. In the same manner, 10 mg of N - [4 - (β - <2 - methoxy - 5 - chlorobenz - imido> - ethyl) - benzenesulphonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea provoke after 6 hours a lowering of the blood sugar of 23%, whereas the known N - [4 - methyl - benzenesulphonyl] - N' - butyl - urea has no blood sugar lowering effect when administered to rabbits in a dose of less than 25 mg/kg.

Furthermore, we have found that 10 mg of N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulphonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea provoke after 3 hours a lowering of the blood sugar of 40%.

Hence, the products of the present invention have a very strong blood lowering action and are extraordinarily well tolerated.

The benzenesulphonyl-ureas of the present invention are preferably used for the manufacture of pharmaceutical preparations suitable for oral administration and having blood sugar lowering action for the treatment of diabetes mellitus and may be used as such or in the form of their physiologically tolerable salts or in the presence of substances which cause such salt formation. For the formation of salts, there may be used, for example, bases such, for example, as alkali metal hydroxides or alkaline earth metal hydroxides or alkali metal or alkaline earth metal carbonates or bicarbonates.

The present invention, therefore, also provides pharmaceutical preparations which comprise a benzenesulphonyl-urea of the above general formula or a physiologically tolerable salt thereof, in admixture or conjunction with a pharmaceutically suitable carrier.

The pharmaceutical preparations are advantageously in the form of tablets and the pharmaceutically suitable carrier may be, for example talc, starch, lactose, tragacanth or magnesium stearate.

A pharmaceutical preparation, for example, a tablet or a powder, containing a benzenesulphonyl-urea of the invention or a physiologically tolerable salt thereof as the active substance, with or without one of the aforementioned carriers, is advantageously brought into a suitable unit dosage form. The dose chosen should comply with the activity of the benzene-sulphonyl-urea or of the physiologically tolerable salt thereof used and the desired effect. Advantageously, the dosage per unit amounts to from 0.5 to 100 mg, preferably 2 to 10 mg, but considerably higher or lower dosage units may also be used, which, if desired, are divided or multiplied prior to their administration.

The following Examples illustrate the invention:—

EXAMPLE 1

N-[4-(β-(2-methoxy-5-chlorobenzamido)-ethyl)-benzenesulfonyl]-N'-(4,7-endomethylene-perhydro-indanyl-5)-urea

8.5 g of N - [4 - (β - (2 - methoxy - 5 - chlorobenzamido) - ethyl) - benzene - sulfonyl] - methyl - urethane (melting point 189—191°C) were suspended in 100 ml of xylene and after addition of 3.3 g. of 5 - amino - 4,7 - endomethylene - perhydro - indane (boiling point: 96—98° C/8 mm) (obtained by hydrogenation of dicyclopentadiene-bis-nitroso-chloride/Raney nickel, 100°C and hydrogen under a pressure of 100 atmospheres) dissolved in 50 ml of xylene, the whole was heated for about 2 hours to 130°C, during which time the methanol which formed during the reaction was separated by distillation. The xylene was removed by distillation under reduced pressure, whereby the N - [4 - (β - (2 - methoxy - 5 - chlorobenzamido) - ethyl) - benzenesulfonyl] - N' - (4,7 - endomethylene - perhydroindanyl - 5) - urea that had formed precipitated. It was recrystallized from methanol. Melting point 196—198°C.

In analogous manner there were obtained:

from N - [4 - (β - (2 - chlorobenzamido) - ethyl) - benzenesulfonyl] - methyl - urethane (melting point: 212—215°C):

the N - [4 - (β - (4 - chlorobenzamido) - ethyl) - benzenesulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5 -) - urea, melting point 206—208°C (from methanol/dioxane);

from N - [4 - (β - (2 - methoxybenzamido) - ethyl) - benzenesulfonyl] - methyl - urethane (melting point 174—176°C):

the N - [4 - (β - (2 - methoxybenzamido) - ethyl) - benzenesulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea, melting point 195—197°C (from methanol);

from N - [4 - (β - (2 - methoxy - 5 - methylbenzamido) - ethyl) - benzene - sulfonyl] - methylurethane (melting point 175—177°C):

the N - [4 - (β - (2 - methoxy - 5 - methylbenzamido) - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea, melting point: 208—210°C (from dilute dioxane);

from N - [4 - (β - benzamido - ethyl) - benzenesulfonyl] - methyl urethane (melting point 177—179°C):

the N - [4 - (β - benzamido - ethyl) - benzenesulfonyl] - N' - (4,7 - endo - methylene - perhydro - indanyl - 5) - urea, melting point 218—220°C (decomposition);

from N - [4 - (β - (3 - trifluoromethyl - benzamido) - ethyl) - benzenesulfonyl] - methylurethane (melting point 178°—180°C):

the N - [4 - (β - (3 - trifluoromethyl - benzamido) - ethyl) - benzenesulfonyl] - N' - (4,7 - endomethylene - perhydro - indan - 2 - yl) - urea, melting point 175°—177°C (from methanol);

from N - [4 - (β - (3 - chlorobenzamido) - ethyl) - benzenesulfonyl] - methyl - urethane (melting point 173°—175°C):

the N - [4 - (β - (3 - chlorobenzamido) - ethyl) - benzenesulfonyl] - N' - (4,7 - endomethylene - perhydro - indan - 2 - yl) - urea, melting point 191°—192°C (from methanol);

the N - [4 - (β - (3 - chlorobenzamido) - ethyl) - benzenesulfonyl] - N' - (2,6 - endomethylene - cycloheptyl) - urea, melting point 186°—187°C (from methanol);

the N - [4 - (β - (3 - chlorobenzamido) - ethyl) - benzenesulfonyl] - N' - cyclo - pentene - (2) - yl - urea, melting point 195°—196°C (from methanol);

the N - [4 - (β - (3 - chlorobenzamido) - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexene - (2) - yl) - urea, melting point 188°—190°C (from methanol);

the N - [4 - (β - (3 - chlorobenzamido) - ethyl) - benzenesulfonyl] - N' - cycloheptene - (2) - yl - urea, melting point 170°—172°C (from methanol) and the N - [4 - (β - (3 - chlorobenzamido) - ethyl) - benzenesulfonyl] - N' - cyclo - octene - (2) - yl - urea, melting point 179°—181°C (from methanol);

from N - [4 - (β - (3 - methoxythiophen - 2 - carbonamido) - ethyl) - benzene - sulfonyl] - methylurethane (melting point 226°—228°C):

the N - [4 - (β - (3 - methoxythiophen - 2 - carbonamido) - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - perhydro - indan - 2 - yl) - urea, melting point 199°—200°C (from methanol/dimethylformamide);

the N - [4 - (β - (3 - methoxythiophen - 2 - carbonamido) - ethyl) - benzene -

- sulfonyl] - N' - cyclopentene - 2 - yl - urea, melting point F 204—205°C (from methanol);
- from N - [4 - (β - <3 - ethoxythiophen - 2 - carbonamido> - ethyl) - benzene - sulfonyl] - methyl - urethane (melting point 163—165°C):
- 5 the N - [4 - (β - <3 - ethoxythiophen - 2 - carbonamido> - ethyl) - benzene - sulfonyl] - N' - (4,4 - dimethylcyclohexene - 2 - yl) - urea, melting point 140—142°C (from methanol);
- from N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulfonyl] - methyl - urethane (melting point 174—176°C):
- 10 the N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - 4,7 - endomethylene - perhydro - indan - 2 - yl) - urea, melting point 187—189°C (from methanol/dimethylformamide);
- the N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - (2,6 - endomethylene - cycloheptyl) - urea, melting point 170—172°C (from methanol);
- 15 the N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - cyclopentene - 2 - yl - urea, melting point 170—172°C (from methanol);
- the N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexene - 2 - yl) - urea, melting point 178—179°C (from methanol);
- 20 the N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - cycloheptene - (2) - yl - urea, melting point 174—176°C (from methanol); and,
- the N - [4 - (β - <2 - methoxy - benzamido - ethyl) - benzenesulfonyl] - N' - cyclo - octene - (2) - yl - urea, melting point 168—170°C (from methanol);
- 25 from N - [4 - (β - <2 - ethoxy - benzamido> - ethyl - benzenesulfonyl] - methyl - urethane (melting point 172—174°C):
- the N - [4 - (β - <2 - ethoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexene - (2) - yl) - urea, melting point 141—142°C (from methanol); and
- the N - [4 - (β - <2 - ethoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - cycloheptene - (2) - yl - urea, melting point 162—164°C (from methanol);
- 30 from N - [4 - (β - <3 - methyl - benzamido> - ethyl) - benzenesulfonyl] - methyl - urethane (melting point 200—202°C):
- the N - [4 - (β - <3 - methyl - benzamido> - ethyl) - benzenesulfonyl] - N' - (4,7 - endomethylene - perhydro - indan - 2 - yl) - urea, melting point 175—177°C (from methanol);
- 35 from N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzene - sulfonyl] - methylurethane (melting point 189—191°C):
- the N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - perhydro - indan - 2 - yl) - urea, melting point 177—179°C (from methanol);
- 40 the N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzene - sulfonyl] - N' - (2,6 - endomethylene - cycloheptyl) - urea, melting point 140—142°C (from methanol);
- the N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzene - sulfonyl] - N' - cyclopenten - (2) - yl - urea, melting point 188—189°C (from methanol);
- 45 the N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzene - sulfonyl] - N' - (4,4 - dimethyl - cyclohexene - (2) - yl) - urea, melting point 170—172°C (from methanol);
- 50 the N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzene - sulfonyl] - N' - cycloheptene - (2) - yl - urea, melting point 142—144°C (from methanol); and
- the N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzene - sulfonyl] - N' - cyclooctene - (2 - yl - urea, melting point 171—172°C (from methanol);
- 55 from N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzene - sulfonyl] methylurethane (melting point 175—177°C):
- the N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - perhydro - indan - 2 - yl) - urea, melting point 204—206°C (from methanol/dimethylformamid);
- 60 the N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzene - sulfonyl] - N' - (2,6 - endomethylene - cycloheptyl) - urea, melting point 189—191°C (from methanol/dimethylformamide);
- the N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzene -

- sulfonyl] - N' - cyclopentene - (2) - urea, melting point 201—203°C (from methanol/dimethylformamid);
- the N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzene - sulfonyl] - N' - (4,4 - dimethyl - cyclohexene - (2) - yl) - urea melting point 152—154°C (from methanol);
- the N - [4 - (β - <2 - methoxy - 5 - methyl - benzamido> - ethyl) - benzene - sulfonyl] - N' - cycloheptene - (2) - yl - urea, melting point 177—178°C (from methanol); and
- the N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzene - sulfonyl] - N' - cyclooctene - (2) - yl - urea, melting point 178—180°C (from methanol/dimethylformamide);
- from N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzene - sulfonyl] - methylurethane (melting point 197—199°C):
- the N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - perhydro - indan - 2 - yl) - urea, melting point 178—180°C (from methanol);
- the N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzene - sulfonyl] - N' - (2,6 - endomethylene - cycloheptyl) - urea, melting point 170—172°C (from methanol);
- the N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzene - sulfonyl] - N' - cyclopentene - (2) - yl - urea, melting point 188—190°C (from methanol);
- the N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzene - sulfonyl] - N' - (4,4 - dimethylcyclohexene - (2) - yl) - urea, melting point 118—120°C (from methanol);
- the N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzene - sulfonyl] - N' - cycloheptene - (2) - yl - urea, melting point 142—144°C (from methanol); and
- the N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzene - sulfonyl] - N' - cyclooctene - (2) - yl - urea, melting point 175—176°C (from methanol);
- from N - [4 - (β - <2 - methoxyethoxy - benzamido> - ethyl) - benzene - sulfonyl] - methylurethane (melting point 123—125°C):
- the N - [4 - (β - <2 - methoxyethoxy - benzamido> - ethyl) - benzene - sulfonyl] - N' - (4,4 - dimethylcyclohexene - (2) - yl) - urea, melting point 153—155°C (from methanol); and
- the N - [4 - (β - <2 - methoxy - ethoxy - benzamido> - ethyl) - benzene - sulfonyl] - N' - cycloheptene - (2) - yl - urea, melting point 166—168°C (from methanol);
- from N - [4 - (β - <2 - ethoxy - 5 - chlorobenzamido> - ethyl) - benzene - sulfonyl] - methylurethane (melting point 203—205°C):
- the N - [4 - (β - <2 - ethoxy - 5 - chlorobenzamido> - ethyl) - benzene - sulfonyl] - N' - (2,6 - endomethylene - cycloheptyl) - urea, melting point 172—174°C (from methanol);
- from N - [4 - (β - <3,5 - dimethyl - benzamido> - ethyl) - benzene - sulfonyl] - methylurethane (melting point 223—225°C):
- the N - [4 - (β - <3,5 - dimethyl - benzamido> - ethyl) - benzenesulfonyl] - N' - (4,7 - endomethylene - perhydro - indan - 2 - yl) - urea, melting point 190—192°C (from methanol); and
- the N - [4 - (β - <3,5 - dimethyl - benzamido> - ethyl) - benzenesulfonyl] - N' - cycloheptene - (2) - yl - urea, melting point 196—198°C (from methanol);
- from N - [4 - (β - <2 - ethoxy - 5 - fluorobenzamido> - ethyl) - benzene - sulfonyl] - methylurethane (melting point 193—195°C):
- the N - [4 - (β - <2 - ethoxy - 5 - fluorobenzamido> - ethyl) - benzene - sulfonyl] - N' - (4,4 - dimethyl - cyclohexene - (2) - yl) - urea, melting point 140—141°C (from methanol);
- from N - [4 - (β - <3 - methoxy - 5 - chlorothiophen - 2 - carbonamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 186—188°C):
- the N - [4 - (β - <3 - methoxy - 5 - chlorothiophen - 2 - carbonamido> - ethyl) - benzenesulfonyl] - N' - cycloheptene - (2) - yl - urea, melting point 164—166°C (from methanol);
- Furthermore, there were prepared in a manner analogous to that of example 1:
- the N[4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzene - sulfonyl] - N' - cyclopropyl - urea, melting point 165°C (methanol/water); and

- the N - [4 - (β - $\langle$ 2 - methoxy - 5 - methylbenzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - cyclopropyl - urea, melting point 188°C (from methanol/dimethylformamide/water).
- 5 from N - [4 - (β - $\langle$ 2 - methoxy - 5 - chlorobenzamido $\rangle$ - ethyl) - benzene - sulfonyl] - methyl - urethane: 5
- the N - [4 - (β - $\langle$ 2 - methoxy - 5 - chlorobenzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (2 - chloro - cyclopentyl) - urea, melting point 196—198°C (from methanol);
- 10 the N - [4 - (β - $\langle$ 2 - methoxy - 5 - chlorobenzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (1 - methyl - cyclopentyl) - urea, melting point 171—173°C (from methanol); 10
- the N - [4 - (β - $\langle$ 2 - methoxy - 5 - chlorobenzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (cyclobutyl) - urea, melting point 177°C (from methanol);
- 15 the N - [4 - (β - $\langle$ 2 - methoxy - 5 - chlorobenzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (5 - methyl - cyclohexene - (2) - yl) - urea, melting point 173—175°C (from methanol); 15
- the N - [4 - (β - $\langle$ 2 - methoxy - 5 - chlorobenzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (3 - tert.butyl - cyclopentyl) - urea, melting point 140—142°C (from methanol);
- 20 the N - [4 - (β - $\langle$ 2 - methoxy - 5 - chlorobenzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (3 - methyl - cyclopentyl) - urea, melting point 152—153°C (from isopropanol); 20
- the N - [4 - (β - $\langle$ 2 - methoxy - 5 - chlorobenzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - [spiro - (2 - cyclobutane) - cyclopentyl] - urea, melting point 176—178°C (from methanol/dimethylformamide/water);
- 25 the N - [4 - (β - $\langle$ 2 - methoxy - 5 - chloro - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - [spiro - (2 - cyclopropane) - cyclopentyl] - urea, melting point 167°C (from methanol/dimethylformamide/water); 25
- the N - [4 - (β - $\langle$ 2 - methoxy - 5 - chloro - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - bicyclo - [5,1,0] - octyl - (8) - urea, melting point 150°C (decomposition) (from methanol/dimethylformamide/water);
- 30 from N - [4 - (β - $\langle$ 2 - methoxy - 5 - methyl - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - methyl - urethane: 30
- the N - [4 - (β - $\langle$ 2 - methoxy - 5 - methyl - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (2 - chloro - cyclopentyl) - urea, melting point 209—210°C (from methanol/dimethylformamide/water);
- 35 the N - [4 - (β - $\langle$ 2 - methoxy - 5 - methyl - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (1 - methyl - cyclopentyl) - urea, melting point 156—158°C (from methanol); 35
- the N - [4 - (β - $\langle$ 2 - methoxy - 5 - methyl - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - cyclobutyl - urea, melting point 209—211°C (from methanol);
- 40 the N - [4 - (β - $\langle$ 2 - methoxy - 5 - methyl - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (5 - methyl - cyclohexene - (2) - yl) - urea, melting point 171—173°C (from methanol); 40
- the N - [4 - (β - $\langle$ 2 - methoxy - 5 - methyl - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (3 - tert. butyl - cyclopentyl) - urea, melting point 143—145°C (from methanol);
- 45 the N - [4 - (β - $\langle$ 2 - methoxy - 5 - methyl - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (3 - methyl - cyclopentyl) - urea, melting point 151—153°C (from methanol); 45
- the N - [4 - (β - $\langle$ 2 - methoxy - 5 - methyl - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - [spiro - (2 - cyclobutane) - cyclopentyl] - urea, melting point 174°C (from methanol/dimethylformamide/water);
- 50 the N - [4 - (β - $\langle$ 2 - methoxy - 5 - methyl - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - [spiro - (2 - cyclopropane) - cyclopentyl] - urea, melting point 188°C (from methanol/dimethylformamide/water); 50
- from N - [4 - (β - $\langle$ 2 - methoxy - 5 - bromobenzamido $\rangle$ - ethyl) - benzene - sulfonyl] - methyl - urethane:
- the N - [4 - (β - $\langle$ 2 - methoxy - 5 - bromo - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (2 - chloro - cyclopentyl) - urea, melting point 191—193°C (from methanol/dimethylformamide);
- 60 the N - [4 - (β - $\langle$ 2 - methoxy - 5 - bromo - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - cyclobutyl - urea, melting point 174—176°C (from methanol); 60
- the N - [4 - (β - $\langle$ 2 - methoxy - 5 - bromo - benzamido $\rangle$ - ethyl) - benzene -

- sulfonyl] - N' - (3 - tert. butyl - cyclopentyl) - urea, melting point 144—146°C (from methanol);
- the N - [4 - (β - <2 - methoxy - 5 - bromo - benzamido> - ethyl) - benzene - sulfonyl] - N' - (3 - methyl - cyclopentyl) - urea, melting point 144—145°C (from methanol);
- from N - [4 - (β - <3 - chloro - benzamido> - ethyl) - benzenesulfonyl] - methyl - urethane:
- the N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chloro - cyclopentyl) - urea, melting point 192—193°C (methanol);
- the N - [4 - (β - <3 - chloro - benzamido> - ethyl) - benzenesulfonyl] - N' - (1 - methyl - cyclopentyl) - urea, melting point 191—193°C (from methanol);
- the N - [4 - (β - <3 - chloro - benzamido> - ethyl) - benzenesulfonyl] - N' - (3 - tert. butyl - cyclopentyl) - urea, melting point 174—175°C (from methanol);
- the N - [4 - (β - <3 - chloro - benzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methyl - cyclopentyl) - urea, melting point 164—166°C (from methanol);
- the N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - [spiro - <2 - cyclobutane> - cyclopentyl] - urea, melting point 192°C (from methanol/dimethylformamide/water);
- the N - [4 - (β - <3 - chloro - benzamido> - ethyl) - benzenesulfonyl] - N' - [spiro - <2 - cyclopropane> - cyclopentyl] - urea, melting point 187°C (from methanol/dimethylformamide/water);
- from N - [4 - (β - <3,5 - dimethyl - benzamido> - ethyl) - benzenesulfonyl] - methyl - urethane:
- the N - [4 - (β - <3,5 - dimethyl - benzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclopentyl) - urea, melting point 207—209°C (from methanol);
- the N - [4 - (β - <3,5 - dimethyl - benzamido> - ethyl) - benzenesulfonyl] - N' - (3 - tert. butyl - cyclopentyl) - urea, melting point 150—152°C (from methanol);
- the N - [4 - (β - <3,5 - dimethyl - benzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methyl - cyclopentyl) - urea, melting point 183—185°C (from methanol);
- from N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulfonyl] - methyl - urethane:
- the N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chloro - cyclopentyl) - urea, melting point 182—183°C (from methanol);
- the N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - (3 - tert. butyl - cyclopentyl) - urea, melting point 175—177°C (from methanol);
- the N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methyl - cyclopentyl) - urea, melting point 164—165°C (from methanol);
- the N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - [spiro - (2 - cyclobutane) - cyclopentyl] - urea, melting point 175°C (from methanol/dimethylformamide/water);
- the N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - [spiro - (2 - cyclopropane) - cyclopentyl] - urea, melting point 165°C (from methanol/water);
- from N - [4 - (β - <2 - ethoxy - benzamido> - ethyl) - benzenesulfonyl] - methyl - urethane:
- the N - [4 - (β - <2 - ethoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methyl - cyclopentyl) - urea, melting point 139—141°C (from methanol);
- from N - [4 - (β - <2 - ethoxy - 5 - chloro - benzamido> - ethyl) - benzene - sulfonyl] - methyl - urethane:
- the N - [4 - (β - <2 - ethoxy - 5 - chloro - benzamido> - ethyl) - benzene - sulfonyl] - N' - (3 - tert. butyl - cyclopentyl) - urea, melting point 152—153°C (from methanol);
- the N - [4 - (β - <2 - ethoxy - 5 - chloro - benzamido> - ethyl) - benzene - sulfonyl] - N' - (3 - methyl - cyclopentyl) - urea, melting point 144—146°C (from methanol);
- from N - [4 - (β - <3,4 - dichloro - benzamido> - ethyl) - benzenesulfonyl] - methyl - urethane:
- the N - [4 - (β - <3,4 - dichloro - benzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methyl - cyclopentyl) - urea, melting point 180—181°C (from methanol);
- from N - [4 - (β - <2 - methoxymethoxy - benzamido> - ethyl) - benzene - sulfonyl] - methyl - urethane:
- the N - [4 - (β - <2 - methoxymethoxy - benzamido> - ethyl) - benzene - sulfonyl] - N' - (3 - methyl - cyclopentyl) - urea, melting point 147—149°C (from methanol);

from N - [4 - (β - <3 - trifluoromethyl - benzamido> - ethyl) - benzenesulfonyl] - methyl - urethane:

the N - [4 - (β - <3 - trifluoromethyl - benzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methyl - cyclopentyl) - urea, melting point 166—168°C (from methanol);

5 from N - [4 - (β - <3 - methoxy - 5 - chloro - thiophen - 2 - carbonamido> - ethyl) - benzenesulfonyl] - methyl - urethane:

the N - [4 - (β - <3 - methoxy - 5 - chloro - thiophen - 2 - carbonamido> - ethyl) - benzenesulfonyl] - N' - (3 - methyl - cyclopentyl) - urea, melting point 169—170°C (from methanol);

10 from N - [4 - (β - <3 - methoxy - thiophen - 2 - carbonamido> - ethyl) - benzenesulfonyl] - methyl - urethane:

the N - [4 - (β - <3 - methoxy - thiophen - 2 - carbonamido> - ethyl) - benzenesulfonyl] - N' - (3 - methyl - cyclopentyl) - urea, melting point 178—179°C;

15 from N - [4 - (β - <2 - methoxy - 5 - chloro - benzamido> - ethyl) - benzene - sulfonyl] - methyl - urethane:

the N - [4 - (β - <2 - methoxy - 5 - chloro - benzamido> - ethyl) - benzene - sulfonyl] - N' - (bicyclo - [3,1,0] - hexyl - (6)) - urea, melting point 175—177°C (from methanol).

EXAMPLE 2:

20 N-[4-(β-(2-methoxy-5-chlorobenzamido)-ethyl)-benzenesulfonyl]-N'-(4,7-endomethylene-perhydro-indanyl-5)-urea

A mixture of 10.3 g of N-[4-(β-(2-methoxy-5-chlorobenzamido)-ethyl)-benzenesulfonyl]-urea, 300 ml of toluene, 30 ml of glycol-monomethyl ether, 1.65 g of glacial acetic acid and 4.2 g of 4,7-endomethylene-perhydro-indanyl-5-amine was heated for 5 hours under reflux. The whole was then concentrated under reduced pressure the residue was treated with alcohol and the crystals obtained, constituting the N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea, were recrystallized from methanol. Melting point 196—198°C.

30 In analogous manner, there was obtained:

the N - [4 - (β - <2 - methoxy - 5 - chloro - benzamido> - ethyl) - benzene - sulfonyl] - N' - bicyclo - (6,1,0) - nonyl - (9) - urea, melting point 110°C (from methanol/dimethylformamide/water).

EXAMPLE 3

35 N-[4-(β-(2-methoxy-5-chlorobenzamido)-ethyl)-benzenesulfonyl]-N'-(4,7-endomethylene-perhydro-indanyl-5)-urea

8.2 g of N - [4 - (β - acetamidoethyl) - benzenesulfonyl] - N' - (4,7 - endo - methylene - perhydro - indanyl - 5) - urea were heated for 2 hours under reflux with a solution of 1.6 g of sodium hydroxide in 30 ml of water. The whole was allowed to cool to room temperature, combined with 20 ml of acetone and 1.3 g of glacial acetic acid and then, 4.1 g of 2-methoxy-5-chlorobenzoyl chloride were added portionwise. After having stirred for 2 hours at room temperature, the whole was suction-filtered, the precipitate was treated with bicarbonate solution and then dissolved and reprecipitated utilizing dilute mixtures of ammonia and hydrochloric acid. The N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4,7 - endo - methylene - perhydro - indanyl - 5) - urea thus obtained was found to melt, after recrystallization from a mixture of methanol and dimethylformamide, at 196—198°C.

EXAMPLE 4

50 N-[4-(β-(2-methoxy-5-chlorobenzamido)-ethyl)-benzenesulfonyl]-N'-(4,7-endomethylene-6-chloro-perhydro-indanyl-5)-urea

7.8 g of N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzene - sulfonyl] - methylurethane (melting point 189—191°C) were suspended in 50 ml of xylene and combined with 2.7 g of 4,7 - endomethylene - 6 - chloro - perhydro - indanyl - 5 - amine (boiling point 134—138°C/8 mm). The reaction mixture was heated for 2 hours to the boiling temperature, during which time the methanol that had formed during the reaction was distilled off; after removal by distillation of the xylene under reduced pressure, the residue was treated with strongly diluted sodium hydroxide solution. Undissolved matter was filtered off and the filtrate was acidified. The N - [4 - (β - <2 - methoxy - 5 - chloro - benzamido> - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - 6 - chloro - perhydro - indanyl - 5) - urea thus formed was filtered off with suction and recrystallized from aqueous dioxane. The substance was found to melt at 189—191°C.

In analogous manner, there were obtained:

from N - [4 - (β - $\langle$ 3 - methoxythiophen - 2 - carbonamido $\rangle$ - ethyl) - benzene - sulfonyl] - methylurethane (melting point 226—228°C):

the N - [4 - (β - $\langle$ 3 - methoxythiophen - 2 - carbonamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea, melting point 163—165°C (from methanol);

from N - [4 - (β - $\langle$ 5 - chlorothiophen - 2 - carbonamido $\rangle$ - ethyl) - benzene - sulfonyl] - methylurethane (melting point 174—176°C):

the N - [4 - (β - $\langle$ 5 - chlorothiophen - 2 - carbonamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea, melting point (from methanol/dimethylformamid). 190—192°C.

EXAMPLE 5

N-[4-(β - $\langle$ 2-methoxy-5-chlorobenzamido $\rangle$ -ethyl)-benzenesulfonyl]-
N'-(4,7-endomethylene-perhydro-indanyl-5)-urea

5 g of 4 - (β - $\langle$ 2 - methoxy - 5 - chlorobenzamido $\rangle$ - ethyl) - benzene - sulfonamide were dissolved in 7 ml of binormal sodium hydroxide solution and 50 ml of acetone and to this solution, there were added dropwise, while stirring and at 0—5°C, 2.7 g of 4,7-endomethylene-perhydro-indanyl-5-isocyanate. The whole was stirred for 3 hours, diluted with water and methanol, undissolved matter was filtered off and the filtrate was acidified with dilute hydrochloric acid. The N - [4 - (β - $\langle$ 2 - methoxy - 5 - chlorobenzamido $\rangle$ - ethyl) - benzenesulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea that had precipitated was found to melt, after recrystallization from methanol, at 196—198°C.

In analogous manner, there were obtained:

from 4 - (β - $\langle$ 3,4 - dichlorobenzamido $\rangle$ - ethyl) - benzenesulfonamide (melting point 171—172°C):

the N - [4 - (β - $\langle$ 3,4 - dichlorobenzamido $\rangle$ - ethyl) - benzenesulfonyl] - N' - cycloheptene - (2) - yl - urea, melting point 197—199°C (from methanol/dimethylformamid);

from 4 - (β - $\langle$ 3,5 - dimethylthiophen - 2 - carbonamido $\rangle$ - ethyl) - benzene - sulfonamide (melting point 176—177°C):

the N - [4 - (β - $\langle$ 3,5 - dimethylthiophen - 2 - carbonamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - cycloheptene - (2) - yl - urea, melting point 184—185°C (from methanol);

from 4 - (β - $\langle$ 3 - chlorothiophen - 2 - carbonamido $\rangle$ - ethyl) - benzene - sulfonamide (melting point 190—191°C):

the N - [4 - (β - $\langle$ 3 - chlorothiophen - 2 - carbonamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - cycloheptene - (2) - yl - urea, melting point 190—191°C (from methanol/dimethylformamid);

from 4 - (β - $\langle$ 2 - methoxymethoxy - benzamido $\rangle$ - ethyl) - benzenesulfonamide (melting point 169—170°C):

the N - [4 - (β - $\langle$ 2 - methoxymethoxy - benzamido $\rangle$ - ethyl) - benzenesulfonyl] - N' - cycloheptene - (2) - yl - urea, melting point 163—164°C (from methanol);

from 4 - (β - $\langle$ 2 - methoxy - 5 - fluorobenzamido $\rangle$ - ethyl) - benzenesulfonamide (melting point 167—169°C):

the N - [4 - (β - $\langle$ 2 - methoxy - 5 - fluorobenzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - cycloheptene - (2) - yl - urea, melting point 157—159°C (from methanol);

from 4 - (β - $\langle$ 2 - ethoxy - 5 - methylbenzamido $\rangle$ - ethyl) - benzenesulfonamide (melting point 147—148°C):

the N - [4 - (β - $\langle$ 2 - ethoxy - 5 - methylbenzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - cycloheptene - (2) - yl - urea, melting point 164—166°C (from methanol/dimethylformamid);

Furthermore, there were prepared in a manner analogous to that of Example 5:

the N[4 - (β - $\langle$ 2 - methoxy - 5 - chlorobenzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - norcaran - 7 - yl - urea, melting point 158°C (from methanol/water);

from 4 - (β - $\langle$ 2 - methoxy - 5 - methylbenzamido $\rangle$ - ethyl) - benzenesulfonamide (melting point 197°C):

the N[4 - (β - $\langle$ 2 - methoxy - 5 - methylbenzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - norcaran - 7 - yl - urea, melting point 183°C (from methanol/water);

from 4(β - $\langle$ 4 - chlorobenzamido $\rangle$ - ethyl) - benzenesulfonamide (melting point 225°C):

the N[4 - (β - $\langle$ 4 - chlorobenzamido $\rangle$ - ethyl) - benzenesulfonyl] - N' - nor - caran - 7 - yl - urea, melting point 137°C (from methanol/water).

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EXAMPLE 6

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N-[4-(β - $\langle$ 2-methoxy-5-chloro-benzamido $\rangle$ -ethyl)-benzenesulfonyl]-
N'-4,7-endomethylene-perhydro-indanyl-5)-urea

1 g. of N - [4 - (β - $\langle$ 2 - methoxy - 5 - chloro - benzamido $\rangle$ - ethyl) - benzenesulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - thiourea (melting point 137—139°C) was dissolved in 100 ml of methanol which had been combined with 10 ml of dioxane. 1.1 g of mercury oxide was added and the whole was stirred for 3 hours at 50—60°C. After removal of the mercury sulfide by filtration, the whole was concentrated under reduced pressure. The N - [4 - (β - $\langle$ 2 - methoxy - 5 - chloro - benzamido $\rangle$ - ethyl) - benzenesulfonyl] - N' - (4,7 - endo - methylene - perhydro - indanyl - 5) - isourea methyl ether thus obtained was suspended in 20 ml of dioxane and 100 ml of concentrated hydrochloric acid. The whole was heated for 10 minutes on the steam bath, poured into water, the precipitate was filtered off with suction and recrystallized from methanol.

The N - [4 - (β - $\langle$ 2 - methoxy - 5 - chloro - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea was found to melt at 196—198°C.

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EXAMPLE 7

N-[4-(β - $\langle$ 2-methoxy-5-chloro-benzamido $\rangle$ -ethyl)-benzenesulfonyl]-
N'-(4,7-endomethylene-perhydro-indanyl-5)-urea

1 g of N - [4 - (β - $\langle$ 2 - methoxy - 5 - chloro - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - thiourea (melting point 137—139°C) were suspended in 20 ml of binormal sodium hydroxide solution and combined with 5 ml of hydrogen peroxide having a strength of 5%.

The whole was heated for 15 minutes on the steam bath, cooled and acidified. A precipitate was obtained which was filtered off with suction and washed with water. The N - [4 - (β - $\langle$ 2 - methoxy - 5 - chloro - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea thus obtained was found to melt, after recrystallization from a mixture of methanol and dioxane, at 196—198°C.

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EXAMPLE 8

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N-[4-(β - $\langle$ 3-methoxy-5-chloro-thiophen-2-carbonamido $\rangle$ -ethyl)-
benzenesulfonyl]-N'-(4,7-endomethylene-perhydro-indanyl-5)-urea

6.48 g of N - [4 - (β - $\langle$ 3 - methoxy - 5 - chloro - thiophen - 2 - carbonamido $\rangle$ - ethyl) - benzenesulfonyl] - methylurethane (melting point 189—191°C) together with 2.26 g of 5-amino-4,7-endomethylene-perhydro-indane and 300 ml of dioxane were heated for 1 hour to the boiling temperature under reflux. After removal of the solvent by distillation under reduced pressure, the residue obtained was treated with strongly diluted ammonia, filtered and the filtrate was acidified. The precipitate obtained was filtered off with suction and recrystallized from methanol. The N - [4 - (β - $\langle$ 3 - methoxy - 5 - chloro - thiophen - 2 - carbonamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea thus obtained was found to melt at 181—183°C.

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In analogous manner there was obtained:

from N - [4 - (β - $\langle$ 5 - chloro - thiophen - 2 - carbonamido $\rangle$ - ethyl) - benzenesulfonyl] - methylurethane (melting point 174—176°C):

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the N - [4 - (β - $\langle$ 5 - chloro - thiophen - 2 - carbonamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea, melting point 190—192°C (from methanol/water).

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WHAT WE CLAIM IS:—

1. Benzenesulphonyl-ureas of the general formula



from 4(β - $\langle$ 4 - chlorobenzamido $\rangle$ - ethyl) - benzenesulfonamide (melting point 225°C):

the N[4 - (β - $\langle$ 4 - chlorobenzamido $\rangle$ - ethyl) - benzenesulfonyl] - N' - nor - caran - 7 - yl - urea, melting point 137°C (from methanol/water).

EXAMPLE 6

N-[4-(β - $\langle$ 2-methoxy-5-chloro-benzamido $\rangle$ -ethyl)-benzenesulfonyl]-

N'-4,7-endomethylene-perhydro-indanyl-5)-urea

1 g. of N - [4 - (β - $\langle$ 2 - methoxy - 5 - chloro - benzamido $\rangle$ - ethyl) - benzenesulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - thiourea (melting point 137—139°C) was dissolved in 100 ml of methanol which had been combined with 10 ml of dioxane. 1.1 g of mercury oxide was added and the whole was stirred for 3 hours at 50—60°C. After removal of the mercury sulfide by filtration, the whole was concentrated under reduced pressure. The N - [4 - (β - $\langle$ 2 - methoxy - 5 - chloro - benzamido $\rangle$ - ethyl) - benzenesulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - isourea methyl ether thus obtained was suspended in 20 ml of dioxane and 100 ml of concentrated hydrochloric acid. The whole was heated for 10 minutes on the steam bath, poured into water, the precipitate was filtered off with suction and recrystallized from methanol.

The N - [4 - (β - $\langle$ 2 - methoxy - 5 - chloro - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea was found to melt at 196—198°C.

EXAMPLE 7

N-[4-(β - $\langle$ 2-methoxy-5-chloro-benzamido $\rangle$ -ethyl)-benzenesulfonyl]-

N'-(4,7-endomethylene-perhydro-indanyl-5)-urea

1 g of N - [4 - (β - $\langle$ 2 - methoxy - 5 - chloro - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - thiourea (melting point 137—139°C) were suspended in 20 ml of binormal sodium hydroxide solution and combined with 5 ml of hydrogen peroxide having a strength of 5%.

The whole was heated for 15 minutes on the steam bath, cooled and acidified. A precipitate was obtained which was filtered off with suction and washed with water. The N - [4 - (β - $\langle$ 2 - methoxy - 5 - chloro - benzamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea thus obtained was found to melt, after recrystallization from a mixture of methanol and dioxane, at 196—198°C.

EXAMPLE 8

N-[4-(β - $\langle$ 3-methoxy-5-chloro-thiophen-2-carbonamido $\rangle$ -ethyl)-benzenesulfonyl]-N'-(4,7-endomethylene-perhydro-indanyl-5)-urea

6.48 g of N - [4 - (β - $\langle$ 3 - methoxy - 5 - chloro - thiophen - 2 - carbonamido $\rangle$ - ethyl) - benzenesulfonyl] - methylurethane (melting point 189—191°C) together with 2.26 g of 5-amino-4,7-endomethylene-perhydro-indane and 300 ml of dioxane were heated for 1 hour to the boiling temperature under reflux. After removal of the solvent by distillation under reduced pressure, the residue obtained was treated with strongly diluted ammonia, filtered and the filtrate was acidified. The precipitate obtained was filtered off with suction and recrystallized from methanol. The N - [4 - (β - $\langle$ 3 - methoxy - 5 - chloro - thiophen - 2 - carbonamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea thus obtained was found to melt at 181—183°C.

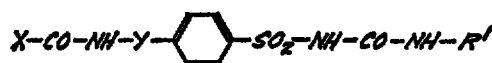
In analogous manner there was obtained:

from N - [4 - (β - $\langle$ 5 - chloro - thiophen - 2 - carbonamido $\rangle$ - ethyl) - benzenesulfonyl] - methylurethane (melting point 174—176°C):

the N - [4 - (β - $\langle$ 5 - chloro - thiophen - 2 - carbonamido $\rangle$ - ethyl) - benzene - sulfonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea, melting point 190—192°C (from methanol/water).

WHAT WE CLAIM IS:—

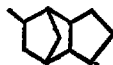
1. Benzenesulphonyl-ureas of the general formula



wherein

R¹ represents

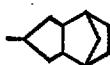
4,7-endomethylene-perhydroindan-5-yl



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which may be substituted by chlorine in 6-position
4,7-endomethylene-perhydroindan-2-yl

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2,6-endomethylene-cycloheptyl,
4,4-dimethyl-Δ²-cyclohexenyl,
Δ²-cyclopentenyl, Δ²-cycloheptenyl, Δ²-cyclooctenyl,
norcaran-7-yl

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bicyclo [5,1,0] octyl-(8)



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bicyclo [6,1,0] nonyl-(9)

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bicyclo [4,2,0] octyl-(7)



2,5-endo-cyclobutylene-(1,2-cyclohexyl

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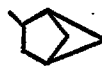
methyl-cyclopentyl,
3,3-dimethyl-cyclopentyl,
3-ethyl-cyclopentyl,
3-tertiary-butyl-cyclopentyl,
2-chloro-cyclopentyl,
Δ²-cyclopentenyl-methyl,

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bicyclo [2,1,1] hexyl-(2)



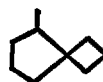
spiro-(2-cyclopropane-cyclo-pentyl)



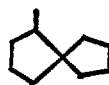
5

spiro-(2-cyclobutane-cyclopentyl)

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spiro-(2-cyclopentane-cyclopentyl)



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cyclopropyl, cyclobutyl,
5-methyl-Δ²-cyclohexenyl,
bicyclo [3,1,0] hexyl

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X represents

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(a) a phenyl group which carries at any desired position the substituents Z and Z' defined hereafter, which may be identical or different:

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Z represents a hydrogen or halogen atom or a low molecular weight alkyl, alkoxy, alkenoxy, alkoxy-alkoxy, phenalkoxy radical, or a low molecular weight acyl or benzoyl radical, or a trifluoromethyl or hydroxy group;

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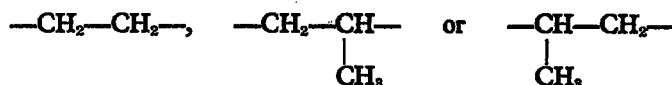
Z' represents a CN or —NO₂ group, a hydrogen or halogen atom, or a low molecular weight alkyl, alkoxy or alkoxy-alkoxy radical or a hydroxy group;

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(b) a thiophen group which may be substituted by one or two substituents selected from low molecular weight alkyl, alkoxy, alkoxy-alkoxy, alkenoxy, phenalkoxy radicals and halogen atoms; and

Y represents one of the groups

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2. Benzenesulphonyl-ureas as claimed in claim 1, wherein X is a phenyl radical which is substituted in the 2-position by an alkoxy radical having up to four carbon atoms.

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3. Benzenesulphonyl-ureas as claimed in claim 1 wherein X is a phenyl radical which is substituted in the 2-position by an alkoxy radical having up to four carbon atoms and in the 4- or 5-position by a halogen atom or by an alkyl or alkoxy radical having up to four carbon atoms.

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4. Benzenesulphonyl-ureas as claimed in claim 1, wherein X is phenyl which is substituted in the 2-position by a methoxy group and in the 4- or 5-position by a halogen atom or a methyl or methoxy group.

5. Benzenesulphonyl-ureas as claimed in claim 1, wherein X is a phenyl radical which is substituted in the 2-position by a methoxy group and in the 4- or 5-position by a chlorine atom.

6. Physiologically tolerable salts of any one of the compounds claimed in any of claims 1 to 5.

7. N - [4 - (β - $\langle$ 2 - methoxy - 5 - chlorobenzamido $\rangle$ - ethyl) - benzenesulphonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea.

8. N - [4 - (β - $\langle$ 2 - methoxy - 5 - chlorobenzamido $\rangle$ - ethyl) - benzenesulphonyl] - N' - (4,7 - endomethylene - 6 - chloro - perhydro - indanyl - 5) - urea.

9. N - [4 - (β - $\langle$ 3 - methoxy - 5 - chloro - thiophen - 2 - carbonamido $\rangle$ - ethyl) - benzenesulphonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea.

10. N - [4 - (β - $\langle$ 2 - methoxy - 5 - methyl - benzamido $\rangle$ - ethyl) - benzenesulphonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea.

11. N - [4 - (β - $\langle$ 2 - methoxy - benzamido $\rangle$ - ethyl) - benzenesulphonyl] - N' - (4,7 - endomethylene - perhydro - indanyl - 5) - urea.

12. Any one of the benzenesulphonyl-ureas of the general formula given in claim 1 which is specifically mentioned herein, other than the compounds claimed in claims 7 to 11.

13. Physiologically tolerable salts of any one of the compounds claimed in claims 7 to 11.

14. A process for the manufacture of benzenesulphonyl-ureas as claimed in claim 1, conducted substantially as described herein.

15. A pharmaceutical preparation for oral administration and lowering the blood sugar level in the treatment of diabetes mellitus, which comprises a compound as claimed in any one of claims 1 to 13 in admixture or conjunction with a pharmaceutically suitable carrier.

16. A pharmaceutical preparation as claimed in claim 15, which contains in dosage unit form from 0.5 to 100 milligrammes of the active ingredient.

17. A pharmaceutical preparation as claimed in claim 16, which contains in dosage unit form from 2 to 10 milligrammes of the active ingredient.

18. A pharmaceutical preparation as claimed in any one of claims 15 to 17, which is in the form of a tablet.

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