1,080,705

PATENT SPECIFICATION

NO DRAWINGS

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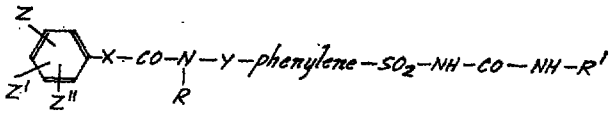
COMPLETE SPECIFICATION

Benzenesulphonyl-Ureas and process for their manufacture

We, FARBWERKE HOECHST AKTIENGESELLSCHAFT, vormals Meister Lucius & Brüning, a Body Corporate recognised under German Law, of 6230 Frankfurt (M)-Hoechst, 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 is concerned with new benzenesulphonyl-ureas and with their manufacture and use.

The present invention provides benzenesulphonyl-ureas corresponding to the general formula



in which

R represents a hydrogen atom or a lower alkyl or phenyl-lower alkyl group, R^1 represents:

(a) an alkyl, an alkenyl or a mercapto-alkyl group containing 2—8 carbon atoms;

(b) an alkoxyalkyl, alkyl-mercaptoalkyl or alkylsulphinylalkyl group containing 4—8 carbon atoms of which at least 2 belong to the alkylene-part of the alkoxyalkyl, mercaptoalkyl or alkyl-sulphinylalkyl group;

(c) a phenyl-lower alkyl or phenyl-cyclopropyl group;

(d) a cyclohexyl-lower alkyl, cycloheptylmethyl, cycloheptylethyl or cyclooctylmethyl group;

(e) an endoalkylene-cyclohexyl, endoalkylene-cyclohexenyl, endoalkylene-cyclohexylmethyl or endoalkylene-cyclohexenylmethyl group containing 1 or 2 carbon atoms in the endoalkylene part;

(f) a lower alkyl cyclohexyl or lower alkoxy cyclohexyl group;

(g) a cycloalkyl group containing 5—8 carbon atoms;

(h) a cyclohexenyl or cyclohexenylmethyl group;

(i) a heterocyclic ring containing 4 or 5 carbon atoms and 1 oxygen or 1 sulphur atom and which may contain up to 2 ethylenic double bends or

(j) a heterocyclic ring as defined under (i) linked to the nitrogen atom by means of a methylene group;

X represents a single chemical bond or an aliphatic or a cycloaliphatic hydrocarbon bridge member containing 1 to 6 carbon atoms and, if desired, one atoms or —O— or —S— atom or one —SO— or —SO_2— groups;

[*Price 4s. 6d.*]

Y represents a hydrocarbon group containing 1—4 carbon atoms;

Z represents a hydrogen or halogen atom or a lower alkyl or lower alkoxy group, a cycloalkoxy group containing 5 or 6 carbon atoms, a cyclohexyl, lower alkylmercapto, lower alkylsulphinyl, lower alkylsulphonyl, phenylsulphonyl, phenyl, phenyl-lower alkyl, lower acyl, benzoyl, trifluoromethyl, hydroxyl, lower acyloxy, benzyloxy, carboxy, lower carbalkoxy, nitrile, carbamyl, lower alkyl-carbamyl, lower dialkyl - carbamyl or nitro group;

Z′ and Z″ each represents a hydrogen atom or, if Z represents hydrogen, hydroxyl, carboxyl, alkyl, alkoxy or halogen, may also each represent a lower alkyl or lower alkoxy group or a halogen atom, or—if Z represents hydrogen—Z′ and Z″ may also together represent the methylenedienoxy group —O—CH_2—O—, and the phenylene group is unsubstituted or substituted by one or more substituents selected from halogen atoms, lower alkyl groups and lower alkoxy groups and the physiologically tolerable salts of these benzenesulphonyl-ureas with a base.

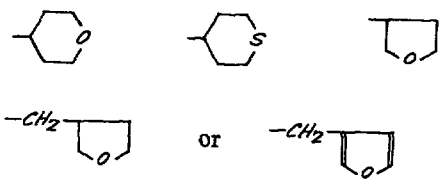
The terms "lower alkyl" and "lower alkoxy" are used herein to mean alkyl and alkoxy groups containing 1 to 4 carbon atoms in a straight or branched chain. The term "lower acyl" is used herein to mean acyl groups (organic acid groups) containing up to 4 carbon atoms, preferably a straight-chain or branched alkanoyl group of the aforesaid chain length.

In accordance with the definitions given above, R may represent, for example, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert.butyl, benzyl, α-, or β - phenylethyl, or α - β- or γ - phenylpropyl. R preferably represents a methyl or benzyl group and, in particular, a hydrogen atom.

R′ may represent, for example, ethyl, propyl, isopropyl, butyl, isobutyl, sec. butyl, straight chained or branched amyl (pentyl), hexyl, heptyl or octyl; the groups with an ethylenic double bond, for example allyl or crotyl, corresponding to the aforesaid hydrocarbon groups, and furthermore alkyl groups containing 2—8 carbon atoms, carrying, in addition, a mercapto group, for example β-mercaptoethyl or higher mercaptoalkyl groups. R′ may also represent, for example, γ-methoxypropyl, δ-methoxy-*n*-butyl, β - ethoxyethyl, γ - ethoxypropyl, δ - ethoxybutyl or higher alkoxy - ethyl, -propyl or -butyl groups as well as the corresponding groups in which the oxygen atom is replaced by a sulphur atom or the group —SO—. Furthermore, R′ may represent benzyl, α-phenylethyl, β - phenylethyl, α-, β- or γ - phenyl - propyl or phenylbutyl groups.

Within the scope of the present invention there are particularly preferred compounds containing as R′ a cycloaliphatic hydrocarbon group which may be substituted by alkyl or alkoxy or linked to the nitrogen atom by means of an alkylene group. As examples of such groups, there may be mentioned cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, methyl - cyclohexyl, ethyl - cyclohexyl, propyl - cyclohexyl, isopropyl-cyclohexyl, methoxy - cyclohexyl, ethoxy - cyclohexyl, propoxy - cyclohexyl or isopropoxy - cyclohexyl. The alkyl-groups or the alkoxy-groups may be present in the 2-, 3- or 4-position, preferably in the 4-position, and in the cis- as well as in the trans-position. Furthermore, there may be mentioned: cyclohexylmethyl, α- or β - cyclohexyl - ethyl, cyclohexylpropyl groups, endomethylene - cyclohexyl (2:2:1 - bicycloheptyl), endoethylene - cyclohexyl (2:2:2 - bicyclooctyl), endomethylene - cyclohexenyl, endoethylene - cyclohexenyl, endomethylene - cyclohexylmethyl, endoethylene-cyclohexylmethyl, endmethylene - cyclohexenylmethyl, endoethylene - cyclohexenylmethyl, or α- or β - phenyl - cyclopropyl in the cis as well as in the trans form.

Finally, the symbol R′ may represent heterocyclic rings containing, in addition to 4 or 5 carbon atoms, 1 oxygen or sulphur atom and up to 2 double bonds, and which may be bound by means of a methylene group to the adjacent nitrogen atom. Examples of these heterocyclic rings are:



As stated above, X represents a single chemical bond or a bridge member containing 1 to 6 carbon atoms belonging to an aliphatic or cycloaliphatic hydrocarbon chain and, if desired, the atom —O— or —S— or the group —SO— or —SO_2—. The two latter groupings may interrupt the hydrocarbon chain or may stand between the latter

and the phenyl nucleus. The atom —O— or —S— may likewise be present between the hydrocarbon chain and the carbonyl group. According thereto, X may represent:

$$-CH_2-,\ -CH_2-CH_2-,\ -CH(CH_3)-,\ -CH_2-CH_2-CH_2-,\ -CH(CH_3)-CH_2-,$$
$$-CH_2-CH(CH_3)-,\ -C(CH_3)_2-,\ -CH_2-CH_2-CH_2-CH_2-,$$
$$-CH(CH_3)-CH_2-CH_2-,\ -CH_2-CH(CH_3)-CH_2-,\ -CH_2-CH_2-CH(CH_3)-,$$
$$-CH(CH_3)-CH(CH_3)-,\ -C(CH_3)_2-CH_2-,\ -CH_2-C(CH_3)_2-,\ -CH(C_2H_5)-,$$
$$-C(C_2H_5)_2-\text{ or }-C(CH_3)(C_2H_5)-$$

as well as corresponding straight-chain or branched pentlene- or hexylene-bridges, and furthermore unsaturated groups such as, for example,

$$-CH=CH-,\ -CH_2-CH=CH-,\ -CH=CH-CH_2-,\ -C(CH_3)=CH-,\ -CH=C(CH_3)-$$

or higher members of the same structure which may also contain several double bonds. Examples of groups represented by X which contain one of the aforesaid heter atoms or groups are:

$$-O-CH_2-,\ -O-CH_2-CH_2-,\ -O-CH_2-CH_2-CH_2-,\ O-CH(CH_3)-,$$
$$-CH_2-O-,\ -S-CH_2-,\ -S-CH_2-CH_2-,\ -CH_2-S-CH_2-,$$
$$-S-CH(CH_3)-,\ -SO_2-CH_2-\text{ or }-O-C(C_2H_5)_2.$$

Finally, this bridge member represented by X may be of cyclic structure and may be, for example, the 1 : 1 - cyclopentylidene group

or corresponding cycloalklidene groups, preferably those containing 3 to 6 carbon atoms.

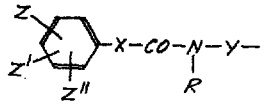
Y represents a straight-chain or branched hydrocarbon group containing 1 to 4 carbon atoms. As examples there may be mentioned those groups examplified above for the symbol X which fall within the general definition of Y.

As examples of the substituents represented by the symbols Z, Z' and Z'' there may be mentioned: methyl, ethyl, propyl, isopropyl, *n* - butyl, isobutyl or tert. butyl as well as the corresponding alkoxy groups, fluorine, chlorine, bromine, iodine, cyclohexyloxy, cyclopentyloxy, methyl - mercapto, ethyl - mercapto, propyl - mercapto or butyl - mercapto, methyl - sulphinyl, ethyl - sulphinyl, propyl - sulphinyl, butyl-sulphinyl, methyl - sulphonyl, ethyl - sulphonyl, propyl - sulphonyl, butyl - sulphonyl with straight-chained or branched alkyl groups, benzyl, phenylethyl, phenylpropyl, acetal, propionyl, butyrl, acetoxy, propionyloxy, butyryloxy, carbomethoxy, carboethoxy, carbopropoxy, methylcarbamyl, ethylcarbamyl, dimethylcarbamyl or diethylcarbamyl.

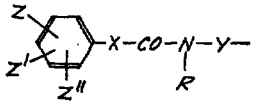
The phenylene group indicated in the formula by -phenylene- is preferablly unsubstituted but may also be substituted by one or more substituents selected from halogen atoms, lower alkyl groups and lower alkoxy groups. It may contain the remaining parts of the molecule in ortho-, meta- or para-position to one another, the para-position being preferred.

The benzenesulphonyl - ureas of the present invention can be prepared according to one of the following methods:

a) Amines of the formula $R'NH_2$ or, if desired, their salts are reacted with benzenesulphonyl - isocyanates, benzenesulphonyl - carbamic acid esters, benzenesulphonyl-thiocarbamic acid esters, benzenesulphonyl - carbamic acid halides or benzenesulphonyl-ureas carrying the substitutent

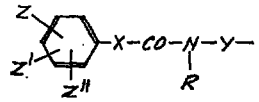


b) benzenesulphonamides or their salts carrying the substituent



are reacted with R′ - substituted isocyanates, carbamic acid esters, thiocarbamic acid esters, carbamic acid halides or ureas;

c) benzenesulphonyl - chlorides carrying the substituent

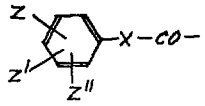


are reacted with R′-substituted ureas, isourea - ethers, isothiourea - ethers or parabanic acids, and the benzenesulphonyl - isourea - ethers, benzenesulphonyl - isothiourea-ethers or benzenesulphonyl - parabanic acids obtained in this way or by another method are hydrolysed;

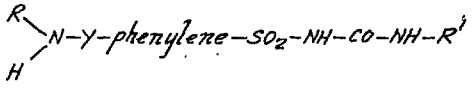
d) in correspondingly substituted benzenesulphonyl - thioureas, the sulphur atom is replaced by an oxygen atom by a known method, that is by a method known to be in actual use or described in the relevant literature;

e) correspondingly substituted benzenesulphenyl - ureas or benzenesulphinyl-ureas are oxidised;

f) in one or several reaction stages the radical



is introduced by acylation into benzenesulphonyl-ureas of the formula



g) in benzenesulphonyl - ureas of the aforesaid general formula in which Z represents a hydroxyl group or a carboxyl group protected by esterification or a hydroxyl group protected by etherification or—if X represents a single chemical bond and R represents H—a carboxyl group being in the *o*-position to the carbonimide grouping and protected by phthalimide formation, the carboxyl or hydroxyl group is set free by hydrolysis or catalytic hydrogenation; or

h) in benzenesulphonyl-ureas of the aforesaid general formula in which X contains one or more ethylenic double bonds, these are hydrogenated; and the products are treated with an alkaline agent if the corresponding salt is required.

Depending on the nature of the groups represented by Z, Z′, Z″, X and R′, one or more of the aforesaid processes may in certain cases be unsuitable for the preparation of the individual compounds covered by the general formula, or at least measures for protecting reactive groups may be required. These particular cases which are relatively unusual and are easily recognized by the expert, so that it is not difficult to select another successful method of synthesis from those described above. Thus, it may be necessary to protect hydroxyl groups represented by the symbol Z by esterification or etherification, carboxyl groups present in the corresponding position by esterification, or a carboxyl group in the ortho-position to the carbonamide group by ring closure to the phthalimide derivative. The conditions are similar if R′ represents a mercapto-alkyl group.

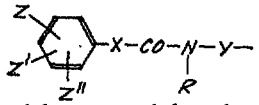
The aforesaid benzenesulphonyl-carbamic acid esters or benzenesulphonyl-thiocarbamic acid esters may contain in the alcohol component a lower alkyl group or a phenyl group. The same applies to the R^1-substitued carbamic acid esters or the corresponding monothiocarbamic acid esters.

As carbamic acid halides, the chlorides are advantageously used.

The benzenesulphonyl-ureas used as starting materials may be unsubstituted at the side of the urea molecule opposite to the sulphonyl group or may, preferably, be

mono- or disubstituted by lower alkyl groups or aryl groups. The aryl groups may be linked with one another by a chemical bond or by means of a bridge member such, for example, as $-CH_2-$, $-NH-$, $-O-$ or $-S-$. Instead of benzenesulphonyl-ureas substituted in this manner there can also be used corresponding N - benzenesulphonyl-N' - acyl - ureas which, in addition, may be alkylated or arylated at the N' - nitrogen atom, and also bis - (benzenesulphonyl) - ureas. It is, for example, possible to treat these bis - (benzenesulphonyl) - ureas or N - benzenesulphonyl - N' - acyl - ureas with amines of the formula R^1NH_2, and to heat the salts so obtained to elevated temperatures, particularly above 100°C.

It is likewise possible to start from ureas of the formula $R^1-NH-CO-NH_2$ or from acylated ureas of the formula $R^1-NH-CO-NH-$acyl, in which acyl represents an aliphatic or aromatic acid radical preferably of low molecular weight, or the nitro-group, or from phenyl-ureas of the formula $R^1-NH-CO-NH-C_6H_5$ or from diphenyl - ureas of the formula $R^1-NH-CO-N(C_6H_5)_2$, in which case the phenyl radicals may be substituted and may be linked with one another directly or by means of a bridge member such as $-CH_2-$, NH—, —O— or —S—, or from N : N - disubstituted ureas of the formula $R^1-NH-CO-NH-R^1$ and to react them with benzenesulphonamides substituted by the grouping of the formula



In the correspondingly substituted benzenesulphonyl - thioureas the sulphur atom can be replaced by an oxygen atom, for example, with the aid of oxides or salts of heavy metals or also by the use of oxidizing agents such as hydrogen peroxide, sodium peroxide or nitrous acid.

The thio-ureas can also be desulphurized by treatment with phosgene or phosphorus pentachloride. Chloroformic acid amidines or chloroformic acid carbodiimides obtained as intermediate products can be converted into the benzenesulphonyl ureas by an appropriate treatment, for example by hydrolysis or the addition of water.

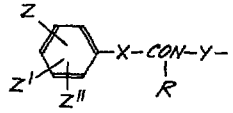
The use of phthalimide compounds if Z represents a carboxyl group in the ortho-position to the carbonamide grouping, is, in principle, possible with all types of reaction. The splitting up of the phthalimide group can be effected by alkaline agents; generally it occurs, however, even in the course of the reaction or when the reaction products are worked up. If esters or benzyl-ethers are used, the splitting may be effected later on, in order to obtain the free compounds.

In the same way, a hydroxyl group or a carboxyl group represented by the symbol Z can be protected and the subsequent splitting of the protective group can be carried out with all the types of reactions mentioned above. If Z represents a hydroxyl group, there enter into consideration as protective groups acyl groups, in particular lower alkanoyl groups and the benzoyl group as well as hydrocarbon groups, especially benzyl, which are capable of being split off by hydrolysis or catalytic hydrogenation. If Z represents a carboxyl group, the protection is realized by esterification with alcohols, especially lower aliphatic alcohols or benzyl alcohol, and the subsequent splitting by hydrolysis. If it is required to make compounds in which Z represents carbalkoxy or acyloxy or benzyloxy, hydrolysis must, of course, be avoided.

As regards the reaction conditions, the methods of carrying out the aforesaid processes may, in general, vary within wide limits and can be adapted to each individual case.

For example, the reactions can be carried out with the use of solvents, at room temperature or at an elevated temperature.

As starting materials there may be used compounds containing a benzene radical substituted by the group of the formula



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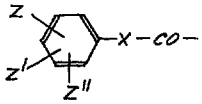
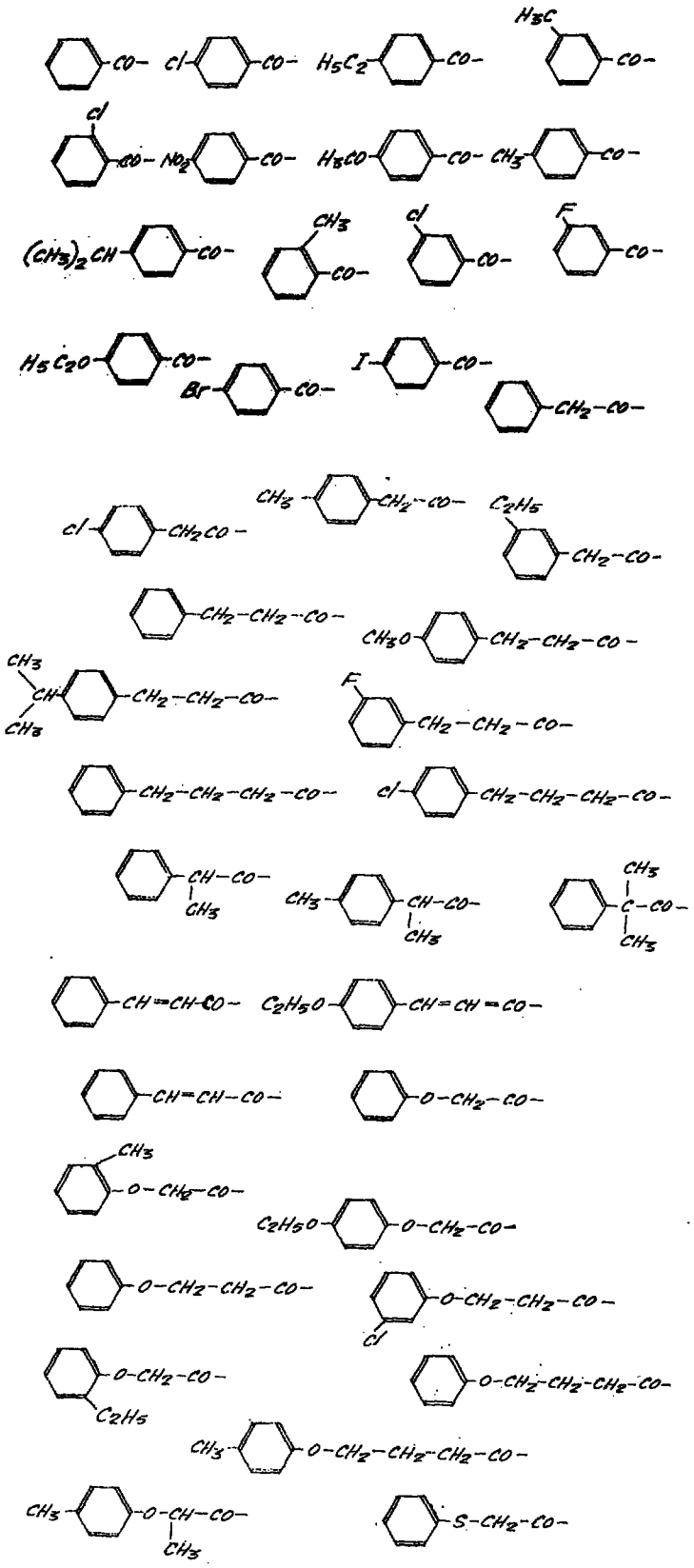
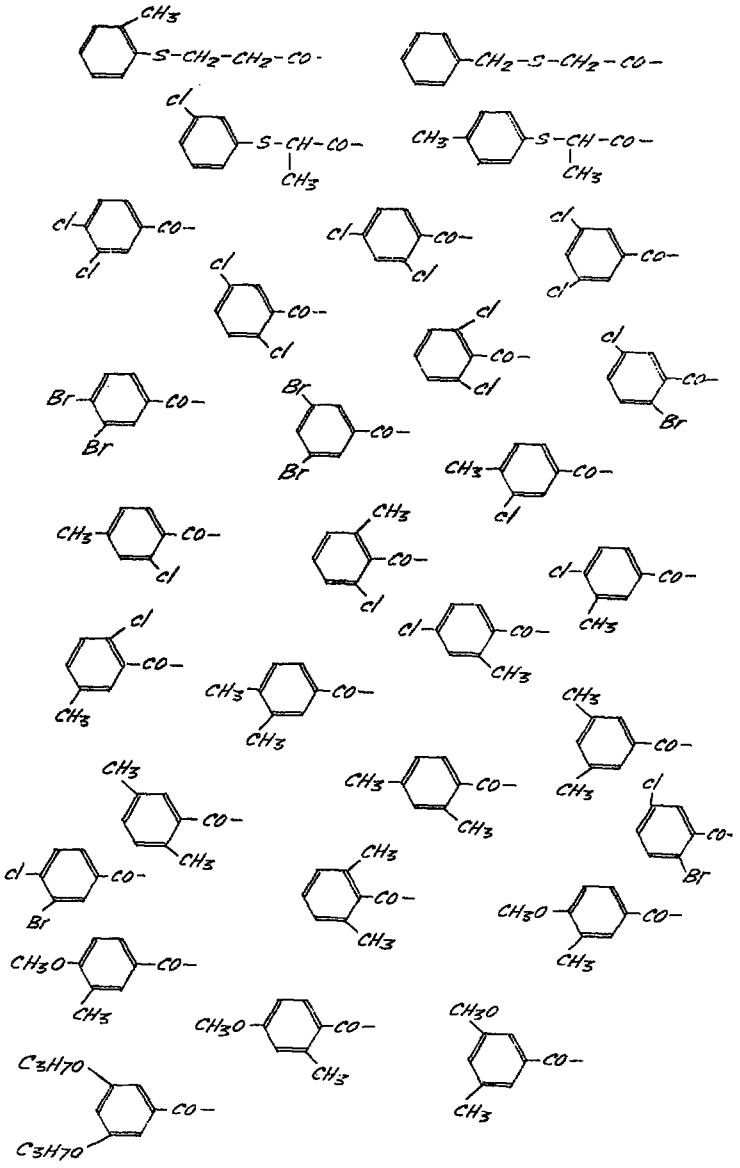
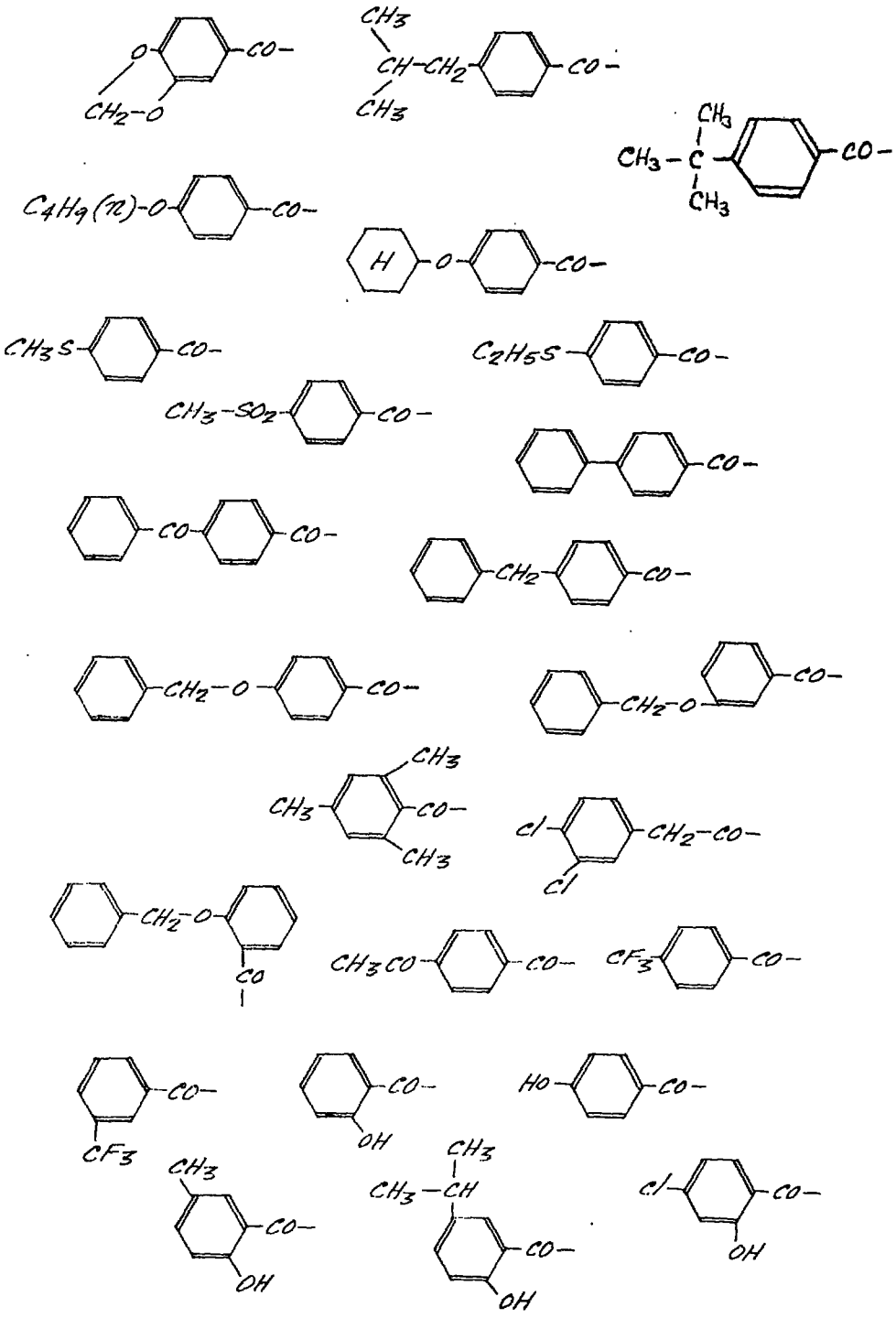
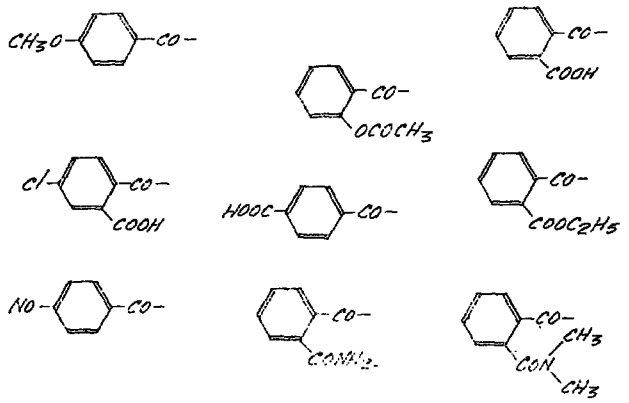


of this formula there may be mentioned, for example:









The benzenesulphonyl - urea derivatives of the present invention are valuable medicaments characterized by a strong and, in particular, a long-lasting blood sugar lowering action. Their hypoglycemic action can be determined, for example, in rabbits by feeding to them the compounds of the invention in the usual doses of 400 milligrams/kilogram of body weight and determining the blood sugar value according to the known method of Hagedorn-Jensen over a prolonged period.

Thus, it is observed, for example, that N - [4 - (β - benzamidoethyl - benzenesulphonyl] - N' - cyclohexyl - urea provokes a maximum lowering of the blood sugar (measured after 6 hours) of 32%. After 24 hours it still amounts to 32%. By administering N - [4-(β - benzamido - ethyl) - benzenesulphonyl] - N'-(4'-methylcyclohexyl)-urea the blood sugar level is lowered by 34% as a maximum, after 24 hours the lowering still amounts to 31% and after 48 hours still to 20%. In contradistinction thereto, N - (4 - methyl - benzenesulphonyl) - N' - butyl - urea, which has been known as an antidiabetic for oral administration and used as a medicament over the whole world, in a comparison test when administered in the aforesaid dose shows a blood sugar lowering amounting to 40% as a maximum but which, however, after 24 hours falls to zero. Upon the administration of a considerably lower dose of 50 mg/kg of body weight to rabbits—which dose allows the determination of the hypoglycemic action in a more differentiating manner and approaches the therapeutical dose—it is found that the new N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea 24 hours after the administration shows a lowering of the blood sugar amounting to 17% and after 48 hours a lowering of 11%, and the new N - [4 - (β - benzamido - ethyl) - benzenezenesulphonyl] - N' - (4' - methyl - cyclohexyl) - urea after 24 hous even causes a lowering of 21%, whereas the blood-sugar lowering action of the known N - (4-methylbenzenesulphonyl) - N' - *n* - butyl - urea given in the same dose after 24 hours is equal to zero.

Furthermore, it has been ascertained, for example, that 50 mg/kg of N - [4 - (β-phenoxy - acetamidoethyl) - benzenesulphonyl] - N' - cyclohexyl - urea provokes in the rabbit a blood sugar lowering of 40% after 6 hours, whereas the blood sugar level is reduced by only 30% upon the administration of the known N - (4 - methyl - benzenesulphonyl) - N' - *n* - butyl - urea.

The strong action of the compounds of the present invention is particularly evident if the dose is reduced. If N - [4 - (β - phenoxyacetamidoethyl) - benzenesulphonyl]-N' - cyclohexyl - urea or N - [4 - (β - phenylacetamidoethyl) - benzenesulphonyl]-N' - cyclohexyl - urea is given to rabbits in doses of 1 mg/kg of body weight, a distinct lowering of the blood sugar can still be observed, whereas when the aforesaid N-(4 - methyl - benzenesulphonyl) - N' - *n* - butyl - urea is given to the rabbit in a dose of less than 25 milligrams/kilogram of body weight it is not sufficiently active to produce any effect.

When administering N - [4 - (β - 3 - chloro - 4 - methyl - benzamidoethyl)-benzenesulphonyl] - N' - (4 - methyl - cyclohexyl) - urea in a dose of 0.2 mg/kg of body weight, N - [4 - (β - 3:5 - dimethoxy - benzamidoethyl) - benzenesulphonyl]-N' - cyclohexyl - urea in a dose of 0.3 mg/kg of body weight or N - [4 - (β - 3:4-dirchloro - benzamidoethyl) - benzenesulphonyl] - N' - cyclohexyl - urea in a dose of 0.3 mg/kg of body weight, N - [4 - (β - 2 - hydroxy - benzamidoethyl) - benzenesulphonyl] - N' - *n* - butyl - urea in a dose of 2 mg/kg of body weight or N - [4 - (β-

2 -hydroxy-benzamidoethyl) - benzenesulphonyl] - N' - cyclohexyl - urea in a dose of 0.15 mg/kg of body weight to rabbits a distinct lowering of the blood sugar can still be observed.

The following Table shows for a number of compounds of the present invention the doses in mg/kg of body weight which, upon oral administration to rabbits, still provokes a distinctly recognizable lowering of the blood sugar level ("threshold dose"). For comparison, it is stated that the threshold dose for the known N - (4 - methyl-benzenesulphonyl) - N' - *n* - butyl - urea amounts to about 25 mg/kg of body weight.

TABLE

Compound	Threshold dose on oral administration to rabbits (mg/kg)
N-[4-(β-benzamido-ethyl)-benzene-sulphonyl]-N'-cyclohexyl-urea	0.1
N-[4-(β-benzamido-ethyl)-benzene-sulphonyl]-N'-(4'-methyl-cyclohexyl)-urea	0.04
N-[4-(β-phenoxy-acetamido-ethyl)-benzene-sulphonyl]-N'-cyclohexy-urea	0.1
N-[4-(β-phenyl-acetamido-ethyl)-benzene-sulphonyl]-N'-cyclohexyl-urea	1
N-[4-(β-<3-chloro-4-methyl-benzamido>-ethyl)-benzenesulphonyl]-N'-4-methyl-cyclohexyl)-urea	0.2
N-[4-(β-<3,4-dichloro-benzamido>-ethyl)-benzenesulphonyl]-N'-cyclohexyl-urea	0.3
N-[4-(β-<2-hydroxy-benzamido>-ethyl)-benzenesulphonyl]-N'-*n*-butyl-urea	2
N-[4-(β-<2-hydroxy-benzamido>-ethyl)-benzenesulphonyl]-N'-cyclohexyl-urea	0.15
N-[4-(β-<4-methyl-benzamido>-ethyl)-benzene-sulphonyl]-N'-cyclohexyl-urea	0.2
N-[4-(β-<4-methyl-benzamido>-ethyl)-benzene-sulphonyl]-N'-(4-methyl-cyclohexyl)-urea	0.3
N-[4-(β-<3-methyl-benzamido>-ethyl)-benzene sulphonyl]-N'-cyclohexyl-urea	0.1
N-[4-(β-<4-methoxy-benzamido>-ethyl)-benzene-sulphonyl]-N'-(4-methyl-cyclohexyl)-urea	0.2
N-[4-(β-<4-chloro-benzamido>-ethyl)-benzene-sulphonyl]-N'-cyclohexyl-urea	0.2
N-[4-(β-phenyl-acetamido-ethyl)-benzene-sulphonyl]-N'-(4-methyl-cyclohexyl)-urea	0.5
N-[4-(β-<α-phenoxy-propionamido>-ethyl)-benzene-sulphonyl]-N'-cyclohexyl-urea	0.1
N-[4-(β-benzamido-α-methyl-ethyl)-benzene-sulphonyl]-N'-cyclohexyl-urea	0.4
N-[4-phenacetamido-methyl)-benzenesulphonyl]-N'-(4-methyl-cyclohexyl)-urea	0.2

TABLE—*continued*

Compound	Threshold dose on oral administration to rabbits (mg/kg)
N-[4-(β-benzamido-ethyl)-benzenesulphonyl]-N'-(4-ethyl-cyclohexyl)-urea	0.08
N-[4-(β-<3-trifluoromethyl-benzamido>-ethyl) benzene-sulphonyl]-N'-*n*-butyl-urea	0.3
N-[4-(β-<3-trifluoromethyl-benzamido>-ethyl)-benzene-sulphonyl]-N'-(4-methyl-cyclohexyl)-urea	0.15
N-[4-(β-<3-fluoro-benzamido>-ethyl)-benzenesulphonyl]-N'-cyclohexyl-urea	0.1
N-[4-(β-<β-phenyl-propionamido>-ethyl)-benzene-sulphonyl]-N'-cyclohexyl-urea	0.3
N-[4-(β-<β-phenyl-propionamido>-ethyl)-benzene-sulphonyl]-N'-4-methyl-cyclohexyl)-urea	0.08
N-[4-(β-<4-chloro-phenoxy-acetamido>-ethyl)-benzene-sulphonyl]-N'-cyclohexyl-urea	0.2
N-[4-(β-cinnamoylamino-ethyl)-benzenesulphonyl]-N'-(4-methyl-cyclohexyl)-urea	0.2
N-[4-(β-<4-ethyl-benzamido>-ethyl)-benzenesulphonyl]-N'-4-methyl-cyclohexy)-urea	0.2
N-[4-(β-<3-chloro-benzamido>-ethyl)-benzene-sulphonyl]-N'-(4-methyl-4-cyclohexyl)-urea	0.1
N-[4-(β-<3,4-dimethyl-benzamido>-ethyl)-benzene-sulphonyl]-N' (4-methyl-cyclohexyl)-urea	0.2
N-[4-(β-benzyloxy-carbonamido-ethyl)-benzene-sulphonyl]-N'-cyclohexyl-urea	0.2
N-[4-(β-<3-methyl-benzamido>-propyl)-benzene-sulphonyl]-N'-cyclohexyl-urea	0.2
N-[4-(β-phenoxyacetamido-propyl)-benzenesulphonyl]-N'-(4-methyl-cyclohexyl)-urea	0.3
N-[4-(α,α-dimethyl-β-benzamido-ethyl)-benzene-sulphonyl]-N'-(4-methyl-cyclohexyl)-urea	1
N-[4-chloro-3-(β-benzamido-ethyl)-benzenesulphonyl]-N'-(4-methyl-cyclohexyl)-urea	0.6
N-[4-(β-phenylmercapto-acetamido-ethyl)-benzene-sulphonyl]-N'-(4-methyl-cyclohexyl)-urea	0.2
N-[4-(β-<3,4-dichloro-phenylacetamido>-ethyl)-benzenesulphonyl]-N'-(4-methyl-cyclohexyl)-urea	0.3
N-[4-(α-ethyl-β-benzamido-ethyl)benzenesulphonyl]-N'-(4-methyl-cyclohexyl)-urea	1

TABLE—*continued*

Compound	Threshold dose on oral administration to rabbits (mg/kg)
N-[4-(β-<4-ethoxy-benzamido>-ethyl)-benzene-sulphonyl]-N'-(4-methyl-cyclohexyl)-urea	0.4
N-[4-(β-<4-ethyl-benzamido>-ethyl)-benzenesulphonyl]-N'-(4-methyl-cyclohexyl)-urea	0.2
N-[4-(β-<N-methyl-benzamido>-ethyl)-benzene-sulphonyl]-N'-(4-methyl-cyclohexyl)-urea	2
N-[4-(β-<4-phenyl-benzamido>-ethyl)-benzene-sulphonyl]-N'-cyclohexyl-urea	2
N-[4-(β-<N-benzyl-benzamido>-ethyl)-benzene-sulphonyl]-N'-cyclohexyl-urea	1
N-[4-(β-benazamido-ethyl)-benzenesulphonyl]-N'-cyclo-hexylmethyl-urea	1
N-[4-(β-benzamido-ethyl)-benzenesulphonyl]-N'-(4-methoxy-cyclohexyl)-urea	2
N-[4-(γ-benzamido-propyl)-benzenesulphonyl]-N'-(4-methyl-cyclohexyl)-urea	0.8
N-[4-(γ-<4-methoxy-benzamido>-propyl)-benzene-sulphonyl]-N'-(4-methyl-cyclohexyl)-urea	0.6
N-[4-(γ-<3-chloro-4-methyl-benzamido>-propyl)-benzenesulphonyl]-N'-cyclohexyl-urea	1
N-[4-(β-<3:5-dimethoxy-benzamido>-ethyl)-benzene-sulphonyl]-N'-cyclohexyl-urea	0.3

The present invention also provides pharmaceutical preparations which comprise the benzenesulphonyl - ureas of the present invention or their physiologically tolerable salts in admixture or conjunction with a pharmaceutically suitable carrier.

The benzenesulphonyl - ureas of the present invention are preferably used for the manufacture of orally administerable pharmaceutical preparations showing blood sugar lowering action in the treatment of diabetes mellitus and can be used as such or in the form of their physiologically tolerable salts or in the presence of substances causing the formation of such salts. For the formation of salts there may be used: alkaline agents, for example alkali metal hydroxides, alkaline earth metal hydroxides, alkali metal carbonates, alkaline earth metal carbonates, alkali metal bicarbonates, alkaline earth metal bicarbonates, and also organic bases, particularly tertiary nitrogen bases, if the latter are tolerated by the organism to be treated.

The pharmaceutical preparations are preferably in the form of tablets containing, in addition to the compounds of the invention, the usual adjuvants and carriers such as talc, starch, lactose, tragacanth or magnesium stearate.

A preparation containing the aforesaid benzenesulphonyl - ureas as the active substance, for example a tablet or a powder, with or without the aforesaid additions, is advantageously compounded into a suitable unit dosage form. The dose chosen depends upon the activity of the benzenesulphonyl - urea used and the desired effect. Preferably, the dosage per unit amounts to about 0.5 to 100 milligrams, preferably to 2—10 milligrams, but considerably higher or lower dosage units can also be used which, if desired, are divided or multiplied prior to administration.

The following Examples illustrate the invention:

EXAMPLE 1

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

13.6 g of mercuric chloride (0.05 mol) were dissolved in 120 ml. of water. 50 ml. of a 2N - sodium hydroxide solution were added dropwise, while stirring. The precipitated mercury oxide was combined with 17.8 g (0.04 mol) of N - [4 - (β - benzamido-ethyl) - benzenesulphonyl] - N' - cyclohexyl - thiourea (melting point 106—108°, prepared from 4 - (β - benzamido - ethyl) - benzenesulphonamide and cyclohexyl mustard oil) dissolved in 80 ml. of a mixture of equal parts of 1N - sodium hydroxide solution and dimethyl formamide, at a temperature of 40°. Stirring was then continued for 2½ hours at 40—50°. The mercuric sulphide formed was filtered off with suction and washed with a small quantity of water. The filtrate was clarified with charcoal and acidified with dilute hydrochloric acid. A precipitate of N - [4 - (β - benzamido-ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea was obtained, which was filtered off with suction, washed with water and recrystallized from methanol. Melting point: 189—191°.

EXAMPLE 2

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

4.5 g of N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl-isourea methyl ether (melting point 151—153°C) were heated with 100 ml. of concentrated hydrochloric acid for 5 minutes on a steam bath. The precipitated N - [4 - (β-benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea was filtered off with suction, triturated with water and recrystallized from methanol. Melting point: 189—191°C.

EXAMPLE 3

N - [4 - (benzamido - methyl) - benzenesulphonyl] - N' - cyclohexyl - urea

35 g of N - (4 - benzamido - methyl - benzenesulphonyl) - methyl - urethane (melting point 170—171°) were dissolved in 50 ml. of xylene; to this solution were added dropwise, while stirring and at 70°, 10 g of cyclohexylamine. The temperature was raised to 120—130°, whereupon the reaction set in after a short time, with the evolution of methanol. After 30 minutes, the whole was cooled, and the sulphonyl urea formed was precipitated and was recrystallized twice from methanol. The melting point of N - [4 - (benzamido - methyl) - benzenesulphonyl] - N' - cyclohexyl - urea was found to be 201—202°.

In an analogous manner, there were obtained:

N - [4 - (benzamido - methyl) - benzenesulphonyl] - N' - cyclooctyl - urea (melting point: 185—186°) (from methanol);

N - [4 - (benzamido - methyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 193—194°) (from methanol) and

N - [4 - (benzamido - methyl) - benzenesulphonyl] - N' - (4' - methyl - cyclohexyl) - urea (melting point: 210—212°) (from methanol).

EXAMPLE 4

N - [4 - (β - 4' - chlorobenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea

A mixture of 9.5 g of N - [4 - (β - 4' - chloro - benzamido - ethyl) - benzenesulphonyl] - urea (melting point 194—196°), 300 ml. of toluene, 30 ml. of glycol monomethyl ether, 1.65 g of glacial acetic acid, and 2.8 g of cyclohexylamine was heated under reflux for 5 hours while stirring. The mixture was concentrated under reduced pressure and the residue was triturated with alcohol. The N-[4 - (β - 4' - chlorobenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea obtained as crude product was filtered off with suction; after recrystallization from a mixture of dimethylformamide and water, it was found to melt at 196—197.5°.

In an analogous manner, there were obtained:

N - [4 - (β - 4' - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - cyclooctyl - urea (melting point: 180—181°) (from dimethylformamide/water);

N - [4 - (β - 4' - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - butyl-urea (melting point: 166—168°) (from dimethylformamide/water) and

N - [4 - (β - 4' - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - (4'-methylcyclohexyl) - urea (melting point: 200—202°) (from dimethylformamide/water).

EXAMPLE 5

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl)-urea

60.8 g of 4 - (β - benzamido - ethyl) - benzenesulphonamide were dissolved in 100 ml. of 2N - sodium hydroxide solution and 400 ml. of acetone and to this solution, 28 g of 4 - methylcyclohexyl isocyanate were added dropwise at 0—5°. Stirring was continued for 2 hours, double the amount of water was then added, the whole was filtered over charcoal and the filtrate was acidified with dilute hydrochloric acid. The precipitated crystals of N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl - cyclohexyl) - urea were found to melt after recrystallization from methanol at 177—178°.

In an analogous manner, there were obtained:

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclooctyl - urea (melting point: 148—149°) (from methanol);

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 189—191°) (from methanol);

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 183.5—185°) (from methanol);

N - [4 - (β - 4' - methyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclooctyl - urea (melting point: 168—170°) (from methanol);

N - [4 - (β - 4' - methyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 204—206°) (from dimethylformamide/water);

N - [4 - (β - 4' - methylbenzamido - ethyl) - benzenesulphonyl] - N' - butylurea (melting point: 185.5—186.5°) (from methanol);

N - [4 - β - 4' - methyl - benzamido - ethyl) - benzenesulphonyl] - N' - (4-methyl - cyclohexyl) - urea (melting point: 183—185°) (from dimethylformamide/water);

N - [4 - (β - 4' - methoxy - benzamido - ethyl) - benzenesulphonyl] - N' - cyclooctyl - urea (melting point: 192—193°) (from dimethylformamide/water);

N - [4 - (β - 4' - methoxy - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 209—211°) (from dimethylformamide/water);

N - [4 - (β - 4' - methoxy - benzamido - ethyl) - benzenesulphonyl] - N' - butylurea (melting point: 194—195°) (from dimethylformamide/water), and

N - [4 - (β - 4' - methoxy - benzamido - ethyl) - benzenesulphonyl] - N' - (4'-methylcyclohexyl) - urea (melting point: 208—209°) (from dimethylformamide/water).

EXAMPLE 6

N - [4 - (benzamido - methyl) - benzenesulphonyl] - N' - cyclooctyl - urea

31.2 g of 4 - (benzamido - methyl) - benzenesulphonamide sodium were mixed with 15.6 g of cyclooctyl urea (prepared from cyclooctylamine and potassium cyanate, melting point 179—181°) in a mortar and then heated for 6 hous at 150° on an oil bath. After cooling, the reaction mixture was dissolved in water, the solution was filtered, acidified and the precipitate was filtered off with suction. The N - [4 - (benzamido - methyl) - benzenesulphonyl] - N' - cyclooctyl - urea was found to melt after filtration with suction and recrystallization from methanol, at 185—186°.

EXAMPLE 7

N - [4 - benzamido - methyl) - benzenesulphonyl] - N' - cyclooctyl - urea

15.6 g of 4 - (benzamido - methyl) - benzenesulphonamide sodium were thoroughly mixed with 7 g of ground potassium carbonate and 18.5 g of cyclooctyl - carbamic acid methyl ester (prepared by the reaction of cyclooctylamine with chloroformic acid methyl ester, melting point 65—66°) and the whole was heated for 3 hours at 130° on an oil bath. After cooling, the reaction mixture was combined with water, excess carbamic acid ester was removed by extraction with ether, the aqueous solution was acidified and the precipitate was filtered with suction. The crude product thus obtained was recrystallized twice from methanol. The crystals of N - [4 - (benzamido - methyl)-benzenesulphonyl] - N' - cyclooctyl - urea were found to melt at 185—186°.

EXAMPLE 8

N - [4 - (benzamido - methyl) - benzenesulphonyl] - N' - cyclohexyl - urea

3.75 g of N - [4 - (benzamido - methyl) - benzenesulphonyl] - N' - acetyl urea (melting point 161—163°) and 1.59 g of cyclohexylamine acetate were mixed thoroughly with one another and heated for 2 hours at 140—150° in an open flask. After cooling, the clear melted mass thus formed was dissolved in 1% sodium hydroxide

solution, filtered over charcoal and the filtrate was acidified. The precipitate of N - [4-(benzamido - methyl) - benzenesulphonyl] - N' - cyclohexyl - urea thus obtained was recrystallized twice from methanol and was found to melt at 201—202°.

EXAMPLE 9

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (4' - methylcyclohexyl-urea

15.4 g of N,N - diphenyl - N' - (4 - methylcyclohexyl) - urea, 8.15 g of 4 - (β-benzamido - ethyl) - benzenesulphonamide sodium and 30 ml of dimethylformamide were heated for 7 hours on an oil bath at 100°. The whole was allowed to cool, water was added, the whole was rendered alkaline and the diphenylamine formed was extracted with ether. The aqueous phase was filtered over charcoal and the filtrate was acidified. The N - [4 - (β - benzamidoethyl) - benzenesulphonyl] - N' - (4' - methylcyclohexyl) - urea obtained in a very good yield was found to melt after recrystallization from methanol at 177—178°.

EXAMPLE 10

N - [4 - (γ - benzamido - propyl) - benzenesulphonyl] - N' - cyclohexyl - urea

16 g of 4 - (γ - benzamido - propyl) - benzene sulphonamide were dissolved in 100 ml. of acetone and 25 ml. of 2N - sodium hydroxide solution; to this mixture there were added dropwise, at 0—5°C, while cooling with ice and stirring, 12.5 g of cyclohexyl isocyanate. The temperature of the reaction mixture was allowed to rise to room temperature in the course of 2 hours, the mixture was acidified and the acetone was removed by distillation under reduced pressure at room temperature. The residue was dissolved in 1% ammonia, separated from undissolved matter by filtration, the filtrate was acidified and the residue was recrystallized from a mixture of ethanol and water. (Melting point: 140°C).

In an analogous manner, there were obtained:

N - [γ - benzamido - propyl) - benzenesulphonyl] - N' - (4' - isopropylcyclohexyl) - urea (melting point: 179°C) (from ethanol/water);

N - [4 - (γ - 4' - chlorobenzamido - propyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 201°C) (from methanol), and

N - [4 - (γ - 4' - chlorobenzamido - propyl) - benzenesulphonyl] - N' - *n* - butyl-urea (melting point: 154°C) (from ethanol/water).

EXAMPLE 11

N - [4 - (β - benzamido - propyl) - benzenesulphonyl] - N' - cyclohexyl - urea

16 g of 4 - (β - benzamido - propyl) - benzenesulphonamide were dissolved in 100 ml. of acetone and 25 ml. of 2N - sodium hydroxide solution and to this solution there were added dropwise at 0—5°C, while stirring and cooling with ice, 13 g of cyclohexyl isocyanate. The temperature of the reaction mixture was allowed to rise to room temperature in the course of 2 hours, the reaction mixture was acidified with concentrated hydrochloric acid and the acetone was removed by distillation under reduced pressure at room temperature. The residue was taken up in 1% ammonia, filtered and the filtrate was combined with concentrated hydrochloric acid. The precipitate formed was then recrystallized from a mixture of ethanol and water. Melting point: 199—201°C.

In an analogous manner, there was obtained:

N - [4 - (β - benzamido - propyl) - benzenesulphonyl] - N' - *n* - butyl - urea (melting point: 159—161°C) (from ethanol).

EXAMPLE 12

N - [4 - (β - benzamido - propyl) - benzenesulphonyl] - N' - cyclooctyl - urea

17 g of N - [4 - (β - benzamido - propyl) - benzenesulphonyl - methyl - urethane were heated in 90 ml. of dioxan with 5.8 g of cyclooctylamine and the methanol formed was continuously removed by distillation. As soon as pure dioxan only was passing over, the reaction was complete. The reaction mixture was concentrated under reduced pressure and the residue was treated with 1% ammonia, precipitated with concentrated hydrochloric acid and the precipitate was recrystallized from a mixture of ethanol and water. Melting point: 158°C.

In an analogous manner, there were obtained:

by heating 36.2 g of N - [4 - (β - benzamido - ethyl) - benzenesulphonyl]-methylurethane with 13.4 g of γ - phenyl - propylamine

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - γ - phenyl - propyl-urea (melting point: 182—184°C) (from methanol) and

from the same urethane and 2,5 - endomethylene - Δ^3 - cyclohexenyl - 1 - methyl-amine

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl) - N' - (2,5 - endomethylene-Δ^3 - cyclohexenyl - 1 - methyl) - urea (melting point: 178—180°C) (from methanol) and

by using 2,5 - endomethylene - cyclohexyl - 1 - methylamine

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (2,5 - endomethylene-cyclohexyl - 1 - methyl - urea (melting point: 183—185°C) (from dilute methanol),

by using α - aminomethyl - thiophene

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - 2 - thenyl - urea (melting point: 205—208°C) (from methanol),

from N - [4 - (benzamidomethyl) - benzenesulphonyl] - methyl - urethane (melting point: 170—171°C) the

N - [4 - (benzamidomethyl) - benzenesulphonyl] - N' - cycloheptylmethylurea (melting point: 203°C) (from ethanol) and

N - [4 - (benzamidomethyl) - benzenesulphonyl] - N' - cycloheptyl - ethyl - urea (melting point: 197—198° C) (from ethanol),

from N - [4 - (β - benzamidoethyl) - benzenesulphonyl] - methyl - urethane (melting point: 177—179°C)

N - [4 - (β - benzamidoethyl) - benzenesulphonyl] - N' - cycloheptyl - methyl-urea (melting point: 188—189°C) (from ethanol) and

N - [4 - (β - benzamidoethyl) - benzenesulphonyl] - N' - cycloheptylethyl - urea (melting point: 205—206°C) (from ethanol),

from N - [4 - (β - benzamidopropyl) - benzenesulphonyl] - methyl - urethane (melting point: 112°C)

N - [4 - (β - benzamidopropyl) - benzenesulphonyl] - N' - cycloheptylmethyl - urea (melting point: 195—196°C) (from ethanol) and

N - [4 - (β - benzamidopropyl) - benzenesulphonyl] - N' - cycloheptylethyl - urea (melting point: 174—176° C) (from ethanol/water), and

from N - [4 - (γ - benzamidopropyl) - benzenesulphonyl] - methyl - urethane the N - [4 - (γ - benzamidopropyl) - benzenesulphonyl] - N' - cycloheptyl-methyl-urea.

EXAMPLE 13

N - [4 - (4' - chlorobenzamido - methyl) - benzenesulphonyl] - N' - cyclohexyl - urea

16.3 g of 4 - (4' - chloro - benzamido - methyl) - benzenesulphonamide (melting point 214—216°C) were dissolved in 25 ml. of 2N - sodium hydroxide solution and 50 ml. of acetone and 6.3 g of cyclohexyl isocyanate were added dropwise at 0—5°C, while stirring. Stirring was continued for 3 hours, the whole was diluted with a great amount of water, some methanol was added, the whole was filtered and the filtrate was acidified. The N - [4 - (4' - chloro - benzamido - methyl) - benzenesulphonyl] - N'-cyclohexyl - urea obtained was found to melt after recrystallization from methanol at 192—192.5°C.

In an analogous manner, there were obtained:

N - [4 - (4' - chloro - benzamido - methyl) - benzenesulphonyl] - N' - cyclo-octyl - urea (melting point: 188—189°C) (from dimethylformamide/water);

N - [4' - chlorobenzamido - methyl) - benzenesulphonyl] - N' - *n* - butyl - urea (melting point: 183—184°C) (from methanol);

N - [4 - (4' - chloro - benzamido - methyl) - benzenesulphonyl] - N' - (4'-methyl-cyclohexyl) - urea (melting point: 211—212°C) (from methanol);

N - [4 - (α - benzamidoethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 190—190.5°C) (from methanol);

N - [4 - (α - benzamido - ethyl) - benzenesulphonyl] - N' - cyclooctyl - urea (melting point: 171—173°C) (from methanol/dimethylformamide);

N - [4 - (α - benzamido - ethyl) - benzenesulphonyl] - N' - *n* - butyl - urea (melting point: 190—191°C) (from dimethylformamide/water);

N - [4 - (α - benzamido - ethyl) - benzenesulphonyl] - N' - (4' - methyl - cyclo-hexyl) - urea (melting point: 201—202°C) (from methanol/dimethylformamide);

N - [4 - (α - 4' - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - cyclo-hexyl - urea (melting point: 206—208°C) (from methanol);

N - [4 - (β - 3' - methyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclo-hexyl - urea (melting point: 169—170°C) (from methanol);

N - [4 - (β - 3' - methyl - benzamido - ethyl) - benzenesulphonyl] - N' - *n*-butyl - urea (melting point: 139—140°C) (from methanol);

N - [4 - (β - 3' - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 190—191°C) (from methanol);

N - [4 - (β - 3' - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - *n*-butyl-urea (melting point: 155—156°C) (from methanol);

N - [4 - (β - 2' - chloro - benzamino - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 204—205°C) (from methanol);

N - [4 - (β - 3' - fluoro - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 198—199°C) (from methanol), and

N - [4 - (β - 3' - fluoro - benzamido) - ethyl) - benzenesulphonyl] - N' - *n*-butyl - urea (melting point: 182—183°C) (from methanol).

In an analogous manner, there were, furthermore, obtained:

from 4 - (β - 4 - methylbenzamido - ethyl) - benzenesulphonamide (melting point: 216—218°C)

N - [4 - (β - 4' - methylbenzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethyl-cyclohexyl) - urea (trans) (melting point: 208—210°C) (from methanol/dimethylformamide);

from 4 - (β - 3 - methylbenzamido - ethyl) - benzenesulphonamide (melting point: 165°C)

N - [4 - (β - 3 - methylbenzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl-cyclohexyl) - urea (melting point: 165.5—167.5°C) (from methanol) and

N - [4 - (β - 3 - methylbenzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethyl-cyclohexyl) - urea (trans) (melting point: 170—172.5°C) (from methanol);

from 4 - (β - 2 - methylbenzamido - ethyl) - benzenesulphonamide (melting point: 186—188°C)

N - [4 - (β - 2 - methylbenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 182—183°C) (from methanol),

N - [4 - (β - 2 - methylbenzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl-cyclohexyl) - urea (trans) (melting point: 179—180°C) (from methanol/dimethylformamide) and

N - [4 - (β - 2 - methylbenzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethyl-cyclohexyl) - urea (trans) (melting point: 169—171°C) (from dimethylformamide/methanol);

from 4 - (β - 4 - ethylbenzamido - ethyl) - benzenesulphonamide (melting point: 149°C)

N - [4 - (β - 4 - ethylbenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 190—192°C) (from dimethylformamide/water).

N - [4 - (β - 4 - ethylbenzamido - ethyl) - benzenesulphonyl] - N' - *n* - butyl - urea (melting point: 137—138°C) (from methanol), the

N - [4 - (β - 4 - ethylbenzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl-cyclohexyl) - urea (melting point: 184—185.5°C) (from dimethylformamide/water) and

N - [4 - (β - 4 - ethylbenzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethyl-cyclohexyl) - urea (trans) (melting point: 181—182.5°C) (from methanol);

from 4 - (β - 4 - isopropylbenzamido - ethyl) - benzenesulphonamide (melting point: 184°C)

N - [4 - (β - 4 - isopropylbenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 195—196°C) (from dimethylformamide/water) and

N - [4 - (β - 4 - isopropylbenzamido - ethyl) - benzenesulphonyl] - N' - (4-methyl-cyclohexyl) - urea (melting point: 196—197°C) (from dimethylformamide/water);

from 4 - (β - 4 - methoxybenzamido - ethyl) - benzenesulphonamide (melting point: 229—231°C)

N - [4 - (β - 4 - methoxybenzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethyl-cyclohexyl) - urea (trans) (melting point: 218—219.5°C) (from dimethylformamide/water);

from 4 - (β - 3 - methoxybenzamido - ethyl) - benzensulphonamide (melting point: 162°C)

N - [4 - (β - 3 - methoxybenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 184—185°C) (from dimethylformamide/water);

N - [4 - (β - 3 - methoxybenzamido - ethyl) - benzenesulphonyl] - N' - *n* - butyl-urea (melting point: 155—156°C) (from methanol);

N - [4 - (β - 3 - methoxybenzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (trans) (melting point: 197—198°C) (from dimethylformamide/water) and
N - [4 - (β - 3 - methoxybenzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (trans) (melting point: 202—203°C) (from dimethylformamide/water);
from 4 - (β - 2 - methoxybenzamido - ethyl) - benzenesulphonamide (melting point: 173—174°C)
N - [4 - (β - 3 - methoxybenzamido - ethyl) - benzenesulphonyl] - N'-cyclohexylurea (melting point: 184°C) (from methanol),
N - [4 - (β - 2 - methoxybenzamido - ethyl) - benzenesulphonyl] - N' - *n* - butylurea (melting point: 124—126°C) (from methanol),
N - [4 - (β - 2 - methoxybenzamido - ethyl) - benzenesulphonyl] - N' - (4-methylcyclohexyl) - urea (trans) (melting point: 179—181°C) (from methanol) and
N - [4 - (β - 2 - methoxybenzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (trans) (melting point: 131—132°C) (from methanol);
from 4 - (β - 4 - ethoxybenzamido - ethyl) - benzenesulphonamide (melting point: 212—213°C)
N - [4 - (β - 4 - ethoxybenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexylurea (melting point: 199—200°C) (from methanol/dimethylformamide),
N - [4 - (β - 4 - ethoxybenzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point 203—204°C) (from methanol/dimethylformamide) and
N - [4 - (β - 4 - ethoxybenzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (trans) (melting point: 212—213°C) (from dimethylformamide/water);
from 4 - (β - 4 - fluorobenzamido - ethyl) - benzenesulphonamide (melting point: 173—174°C)
N - [4 - (β - 4 - fluorobenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexylurea (melting point: 189—190°C) (from methanol) and
N - [4 - (β - 4 - fluorobenzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 190.5—191.5°C) (from methanol);
from 4 - (β - 3 - fluorobenzamido - ethyl) - benzenesulphonamide (melting point: 218—218.5°C)
N - [4 - (β - 3 - fluorobenzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 182—184°C) (from methanol) and
N - [4 - (β - 3 - fluorobenzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (trans) (melting point: 196°C) (from dimethylformamide/water);
from 4 - (β - 3 - chlorobenzamido - ethyl) - benzenesulphonamide (melting point: 166—167°C)
N - [4 - (β - 3 - chlorobenzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 173—175°C) (from methanol) and
N - [4 - (β - 3 - chlorobenzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (trans) (melting point: 164—166°C) (from methanol);
from 4 - (β - 2 - chlorobenzamido - ethyl) - benzenesulphonamide (melting point: 195—196°C)
N - [4 - (β - 2 - chlorobenzamido - ethyl) - benzenesulphonyl] - N' - *n* - butylurea (melting point: 139.5—141°C) (from methanol),
N - [4 - (β - 2 - chlorobenzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 180—182°C) (from dimethylformamide/water) and
N - [4 - (β - 2 - chlorobenzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (trans) (melting point: 156°C) (from dimethylformamide/water);
from 4 - (α - benzamido - ethyl) - benzenesulphonamide (melting point: 215—216°C) the
N - [4 - (α - benzamido - ethyl) - benzenesulphonyl] - N' - *n* - butyl - urea (melting point: 190—191°C) (from dimethylformamide/water) and
N - [4 - (α - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl)-urea (melting point: 201—201.5°C) (from methanol/dimethylformamide); and
from 4 - (α - 4 - chlorobenzamido - ethyl) - benzenesulphonamide (melting point: 211—214°C)
N - [4 - (α - 4 - chlorobenzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 210—211°C) (from dimethylformamide/water).

In an analogous manner, there were, furthermore, obtained:
from 4 - (γ - benzamidopropyl) - benzenesulphonamide (melting point: 155°C)
N - [4 - (γ - benzamidopropyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl)-urea (melting point: 189°C) (from ethanol/water) and
N - [4 - (γ - benamidopropyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl)-urea (trans), (melting point: 179°C) (from ethanol/water);
from 4 - (β - 4 - chlorobenzamidopropyl) - benzenesulphonamide (melting point: 191°C)
N - [4 - (β - 4 - chlorobenzamidopropyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 240°C) (from dimethylformamide/water) and
N - [4 - (β - 4 - chlorobenzamidopropyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 210°C) (from ethanol);
from 4 - (β - 4 - methylbenzamidopropyl) - benzenesulphonamide (melting point: 209—210°C)
N - [4 - (β - 4 - methylbenzamidopropyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 229°C) (from dimethylformamide/water),
N - [4 - (β - 4 - methylbenzamidopropyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 201°C) (from ethanol), and
N - [4 - (β - 4 - methylbenzamidopropyl) - benzenesulphonyl] - N' - *n* - butyl-urea (melting point: 178°C) (from methanol/water);
from 4 - (β - 4 - methoxybenzamidopropyl) - benzenesulphonamide (melting point: 163—165°C)
N - [4 - (β - 4 - methoxybenzamidopropyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 210°C) (from dimethylformamide/water) and
N - [4 - (β - 4 - methoxybenzamidopropyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 193—194°C) (from ethanol/water);
from 4 - (γ - 4 - isopropylbenzamidopropyl) - benzenesulphonamide (melting point: 147°C)
N - [4 - (γ - 4 - isopropylbenzamidopropyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 142°C) (from methanol), and
N - [4 - (γ - 4 - isopropylbenzamidopropyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 148°C) (from methanol/water);
from 4 - (β - 3 - methylbenzamidopropyl) - benzenesulphonamide (melting point: 164°C)
N - [4 - (β - 3 - methylbenzamidopropyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 188°C) (from methanol), and
N - [4 - (β - 3 - methylbenzamidopropyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 162—163°C) (from ethanol/water);
from 4 - (β - benzamidopropyl) - benzenesulphonamide (melting point: 209°C)
N - [4 - (β - benzamidopropyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl)-urea (melting point: 204°C) (from methanol/water);
from 4 - (γ - 4 - methoxybenzamidopropyl) - benzenesulphonamide (melting point: 175°C)
N - [4 - (γ - 4 - methoxybenzamidopropyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 152°C) (from ethanol/water),
N - [4 - (γ - 4 - methoxybenzamidopropyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 160°C) (from ethanol),
N - [4 - (γ - 4 - methoxybenzamidopropyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (trans) (melting point: 172°C) (from methanol/water);
from 4 - (γ - 4 - methylbenzamidopropyl) - benzenesulphonamide (melting point: 150°C)
N - [4 - (γ - 4 - methylbenzamidopropyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 194°C) (from methanol/water) and
N - [4 - (γ - 4 - methylbenzamidopropyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 165°C) (from methanol/water);
from 4 - (β - benzamidopropyl) - benzenesulphonamide (melting point: 208°C)
N - [4 - (β - benzamidopropyl) - benzensulphonyl] - N' - cyclopentyl - urea (melting point: 176°C) (from ethanol/water),
N - [4 - (β - benzamidopropyl) - benzenesulphonyl] - N' - cyclooctyl - urea (melting point: 158°C) (from ethanol/water),
N - [4 - (β - benzamidopropyl) - benzenesulphonyl] - N' - (4 - isopropylcyclohexyl) - urea (melting point: 183°C) (from isopropanol),
N - [4 - (β - benzamidopropyl) - benzenesulphonyl] - N' - cycloheptyl - urea (melting point: 189°C) (from ethanol/water), and

N - [4 - (β - benzamidopropyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl)-urea (trans) (melting point: 203°C) (from ethanol);

from 4 - (β - 3 - fluorobenzamidopropyl) - benzenesulphonamide (melting point: 165°C)

N - [4 - (β - 3 - fluorobenzamidopropyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 177°C) (from ethanol), and

N - [4 - (β - 3 - fluorobenzamidopropyl) - benzenesulphonyl] - N' - (4 - methyl-cyclohexyl) - urea (melting point: 204—205°C) (from ethanol);

from 4 - (β - 3 - chlorobenzamidopropyl) - benzenesulphonamide (melting point: 168°C)

N - [4 - (β - 3 - chlorobenzamidopropyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 176—178°C) (from ethanol) and

N - [4 - (β - 3 - chlorobenzamidopropyl) - benzenesulphonyl] - N' - (4 - methyl-cyclohexyl) - urea (melting point: 169°C) (from ethanol);

from 4 - (β - 4 - iodobenzamidoethyl) - benzenesulphonamide (melting point: 260°C)

N - [4 - (β - 4 - iodobenzamidoethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 209°C) (from methanol/water);

from 1 - (β - 4 - brombenzamido - ethyl) - benzenesulphonamide (melting point: 236—238°C)

N - [4 - (β - 4 - brombenzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl-cyclohexyl) - urea (trans) (melting point: 205—207°C) (from ethanol/dioxan), and

N - [4 - (β - 4 - brombenzamido - ethyl) - benzenesulphonyl] - N' - isobutyl - urea (melting point: 181—183°C) (from ethanol/dioxan); and

from 4 - (β - 2 - brombenzamido - ethyl) - benzenesulphonamide (melting point: 176—178°C)

N - [4 - (β - 2 - brombenzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl-cyclohexyl) - urea (trans) (melting point: 184—186°C) (from methanol) and

N - [4 - (β - 2 - brombenzamido - ethyl) - benzenesulphonyl] - N' - isobutyl-urea (melting point: 165—167°C) (from methanol).

Furthermore, by the reaction of 4 - (β - benzamido - α - methylethyl) - benzenesulphonamide with cyclohexyl isocyanate there was obtained N - [4 - (β - benzamido-α - methyl - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 176—178°C) (from methanol) and when using butyl isocyanate there was obtained N - [4-(β - benzamido - α - methyl - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 184—185°C) (from methanol).

Furthermore, there was obtained, by the reaction of 4 - (β - 4' - chloro - benzamido - α - methyl - ethyl - benzenesulphonamide with cyclohexyl isocyanate, N - [4-(β - 4' - chloro - benzamido - α - methyl - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 196—198°C) (from methanol) and when using butyl isocyanate there was obtained the corresponding N - [4 - (β - 4' - chloro - benzamido - α-methyl-ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 159—161°C) (from methanol).

Example 14

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (4' - ethylcyclohexyl)-urea

18.1 g of N - [4 - (β - benzamido - ethyl) - benzensulphonyl] - methylurethane and 6.4 g of 4 - ethyl - cyclohexylamine were suspended in 200 ml. of dioxan and heated for 1.5 hours at 120—130°C. The methanol formed during the reaction was removed by distillation over a small column. As soon as the passing-over temperature had risen to 100°C, the whole was allowed to cool and water was added. The N - [4-(β - benzamido - ethyl) - benzenesulphonyl] - N' - (4' - ethylcyclohexyl) - urea obtained in crystalline form was recrystallized from methanol and found to melt at 190—192°C.

In an analogous manner, there were obtained:

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (β - phenylethyl)-urea (melting point: 193—194°C) (from methanol);

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (cyclohexylmethyl)-urea (melting point: 198—200°C) (from dimethylformamide/water).

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclopentyl - urea (melting point: 188—190°C) (from methanol);

N - [4 - (β - benzamidoethyl) - benzenesulphonyl] - N' - (4 - methoxy - cyclohexyl) - urea (melting point: 161—163°C);

N - [4 - (β - benzamidoethyl) - benzenesulphonyl] - N' - (4 - ethoxy - cyclohexyl) - urea (melting point: 176—178°C);

N - [4 - (β - benzamidoethyl) - benzenesulphonyl] - N' - (4 - isopropoxy - cyclohexyl) - urea (melting point: 186—188°C);

N - [4 - (β - benzamidoethyl) - benzenesulphonyl] - N' - (γ - methoxypropyl)-urea (melting point: 162—164°C);

N - [4 - (β - 4' - chloro - benzamidoethyl) - benzenesulphonyl] - N' - (4 - methoxy - cyclohexyl) - urea (melting point: 183—185°C);

N - [4 - (β - 4' - chloro - benzamidoethyl) - benzenesulphonyl] - N' - (4 - ethoxy - cyclohexyl) - urea (melting point: 200—202°C) and

N - [4 - (β - 4' - chloro - benzamidoethyl) - benzenesulphonyl] - N' - (γ - methoxy - propyl) - urea (melting point: 173—174°C).

In an analogous manner, there were, furthermore, obtained:

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

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - ethyl - urea (melting point: 210—210.5°C) (from methanol),

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - *n* - propyl - urea (melting point: 200—201°C) (from methanol/dimethylformamide), the

N - [4 - (β - benzamidoethyl) - benzenesulphonyl] - N' - *n* - hexyl - urea (melting point: 170—171.5°C) (from methanol),

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (trans) (melting point: 184—186°C) (from methanol) and

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl)-urea (cis) (melting point: 186°C) (from methanol);

from N - [4 - (β - 4 - chlorobenzamido - ethyl) - benzenesulphonyl] - methylurethane (melting point: 212—215°C)

N - [4 - (3 - 4 - chlorobenzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (melting point: 207—208°C) (from methanol);

from N - [4 - (β - benzamidoethyl) - benzenesulphonyl] - methyl - urethane

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (tetrahydro - pyranyl-2 - methyl) - urea (melting point: 166—167.5°C) (from methanol),

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (trans - 2 - phenylcyclopropyl) - urea (melting point: 182—183°C) (from methanol) and

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (β - phenyl - isopropyl)-urea (melting point: 190—192.5°C) (from methanol;

from N - [4 - (β - 4 - chlorobenzamido - ethyl) - benzenesulphonyl] - methylurethane

N - [4 - (β - 4 - chlorobenzamido - ethyl) - benzenesulphonyl] - N' - (Δ3 - tetrahydrobenzyl) - urea (melting point: 200—202°C) (from methanol/dimethylformamide); and

from N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - methylurethane

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - allyl - urea (melting point: 203—204°C) (from dimethylformamide/water) and

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (β - cyclohexylethyl)-urea (melting point: 211—212.5°C) (from dimethylformamide/water).

Example 15

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclooctyl - urea

72.4 g of N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - methyl - urethane were suspended in 500 ml. of dioxan; 25.4 g of cyclooctylamine were added and the whole was then heated to 120—130°C. The methanol formed during the reaction was removed by distillation over a small column. As soon as the passing-over temperature had risen to 100°C, the whole was allowed to cool and water was slowly added, while stirring, until the urea precipitation ceased. The product was recrystallized from methanol. The N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclooctyl-urea obtained in a very good yield was found to melt at 172.5—174°C (from methanol) and constituted thus another form of the urea defined in Example 5 under the same nomenclature, which had a melting point of 148—149°C. Both forms can be converted into each other by crystallization.

Example 16

N - [4 - (benzamido - methyl) - benzenesulphonyl] - N' - cyclohexyl - urea

2.2 g of N - [4 - aminomethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 199°C), 1.1 g of pyridine and 1.0 g of benzoyl chloride were heated

for 6 hours at 35°C in 10 ml of chloroform. The chloroform was evaporated *in vacuo* and the residue was treated with an equimolar quantity of 1% aqueous sodium carbonate solution. The sodium salt of the urea specified in the heading formed while heating and was dissolved in the aqueous solution. The solution was heated and filtered over charcoal. After cooling, the sodium salt crystallized out. It was suction-filtered, dissolved in a great amount of water and the free compound was precipitated by means of gaseous HCl. Melting point: 209—210°C.

EXAMPLE 17

N - [4 - (α - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

1.6 mol of N - benzoyl - α - phenylethylamine were introduced at 20—25°C, while stirring, into 7 mols of chlorosulphonic acid. Stirring was continued for 15 minutes at room temperature and then for 30 minutes at 60°. The whole was then poured onto ice and the crude sulphonyl chloride obtained was removed by suction-filtration. The moist sulphonyl chloride was heated for half an hour on a steam bath, while stirring, with 1 litre of 12% ammonia. Undissolved matter was removed by filtration and, after cooling, the pH value of the reaction mixture was adjusted to 9 by means of dilute acetic acid. The 4 - (α - benzamidoethyl) - benzene - sulphonamide obtained was suction - filtered, washed with water and recrystallised from 90% ethyl alcohol. Yield: 65% of the theory, melting point: 214—216°.

1/10 mol of this amide were heated under reflux for 7 hours with 41 g of potash, 200 cc. of acetone and 13 cc. of chloroformic acid ester. After cooling, 200 cc. of water were added and the upper aqueous - acetonic layer was separated. After evaporation of the acetone, the pH was adjusted to 6 by adding dilute acetic acid and the separated starting material was suction - filtered and the filtrate was adjusted to a pH of 3. The 4 - (α - benzamidoethyl) - benzenesulfonyl - ethylurethane which separated in crystalline form was then suction-filtered, washed with water and dried under reduced pressure. Yield: 54% of the theory, melting point: 145—146°.

37 g of this sulphonylurethane were suspended in 30 cc. of dimethylformamide. After the addition of 10 g of cyclohexylamine, there was obtained a clear solution which was heated for 1 hour at 90° and for half an hour at 110°. The solution was diluted with hot water while still hot. Upon cooling, the above-defined benzenesulphonyl urea crystallised out. It was suction-filtered, washed with water and dried *in vacuo*. Yield: 63% of the theory, melting point (from methanol): 198—199°.

In an analogous manner, there was obtained, from N - [4 - (β - benzamido-ethyl)-benzenesulphonyl] - methylurethane and 4 - amino - tetrahydrothiopyran, N - [4 - (β-benzamido - ethyl) - benzenesulphonyl] - N' - thiacyclohexyl - urea.

EXAMPLE 18

N - [4 - (β - benzamidopropyl) - benzenesulphonyl] - N' - cyclohexyl - urea

N - acetyl - 1 - phenyl - 2 - amino - propane was reacted in the manner described in Example 17 with chlorosulphonic acid to yield the corresponding sulphonyl chloride and the latter was reacted with ammonia to yield 4 - (β - acetamidopropyl) - benzenesulphonamide (melting point: 176—177°C) (yield: 84% of the theory).

123 g of this acetyl compound were heated at the boil for 5 hours with 500 cc. of 5N - sodium hydroxide solution. After cooling, 250 cc. of 6N - hydrochloric acid were added and 75 g of benzoyl chloride were dropped in at 20—25° and while stirring. The forming crystalline precipitate was redissolved by the addition of 2N - sodium hydroxide solution. Upon careful adjustment to a pH value of 10—11, there was obtained 4 - (β-benzamidopropyl) - benzenesulphonamide melting at 208—210° in a yield of 65% of the theory. A mixture of 100 g. of this sulphonamide, 129 g of potash, 1000 cc. of acetone and 41 cc. of chloroformic acid ethyl ester was heated for 6 hours at the boil and worked up as described in Example 17. There was obtained 4 - (β - benzamidopropyl) - benzenesulphonylethylurethane in a yield of 81.6% of the theory. Melting point: 124—126°.

50 g of this sulphonylurethane were reacted as described in Example 17 in 30 cc. of dimethylformamide with 12.7 g of cyclohexylamine. There was obtained the product identified in the heading (melting point: 203—204°C) in a yield of 65% of the theory.

EXAMPLE 19

N - [4 - (γ - benzamidopropyl) - benzenesulphonyl] - N' - cyclohexyl - urea

In a manner analogous to that described in Example 18, there was obtained from 8 g of 4 - (γ - benzamidopropyl) - benzenesulphonamide, 12 g of potash, 4 cc. of chloroformic acid ethyl ester and 100 cc. of acetone after a 6 hours heating, 4 - (γ-

benzamidopropyl) - benzenesulphonyl - ethyl - urethane in a yield of 51% (melting point: 112—113°C).

5 g of this urethane were suspended in 3 cc. of dimethylformamide and heated with 1.3 g of cyclohexylamine for 1 hour at 90° as well as for half an hour at 110°. The desired sulphonyl urea was obtained in a yield of 60% of the theory (melting point: 152—159°) (from methanol).

EXAMPLE 20

N - [4 - (β - 4' - chlorobenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

3 g of N - [4 - (β - aminoethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 203°) were heated with 1.6 g of *p* - chlorobenzoyl chloride and 1.5 g of pyridine in 20 ml. of chloroform for 15 hours at 35—40°. The chloroform was then evaporated under reduced pressure and the residue was dissolved in an excess of 1% aqueous sodium carbonate solution. The solution was then extracted by shaking with ether. The aqueous layer was then separated, treated with charcoal, filtered and precipitated with the aid of an excess of hydrochloric acid. The sulphonyl urea was recrystallized from alcohol (melting point: 209°).

In an analogous manner, there were obtained:

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 168—170°C),

N - [4 - (β - 4' - methylbenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 214—215°C), and

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl)-urea (melting point: 173—174°C).

EXAMPLE 21

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

16.2 g of N - 4 - (β - benzamido - ethyl) - benzenesulphonic acid chloride, 250 ml. of benzene, 10 g of cyclohexyl - parabanic acid (melting point: 184°) and 5 g of triethylamine were heated for 2 hours at boiling temperature under reflux. From the solution which at first was clear, crystals separated after about 2 minutes. After termination of the heating, the whole was allowed to cool and the separated crystals were suction-filtered. They were washed with water and dried on clay. 1 - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - 3 - cyclohexyl - parabanic acid was obtained in a yield of about 75%, and, after recrystallization from a mixture of methanol and dioxan, was found to melt at 246—247°C.

5 g of the parabanic acid derivative thus obtained were heated for 45 minutes on a steam bath in 50 ml. of dioxan and 100 ml. of 1N - sodium hydroxide solution. A clear solution was obtained which, after termination of heating, was combined with dilute hydrochloric acid. The crystals that had separated were filtered off with suction. The N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea thus obtained was found to melt at 189—191°C. Yield upon saponification: about 94%. After recrystallization, the compound was found to melt at 191—193°C.

EXAMPLE 22

N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

16.2 g of 4 - (β - benzamido - ethyl) - benzenesulphonic acid chloride, 2.7 g of sodium methylate, 10 g of cyclohexyl - parabanic acid and 250 ml. of benzene were heated for 2 hours at the boiling temperature under reflux. After cooling, the whole was concentrated to dryness, the residue obtained was digested with water, 50 ml. of dioxan and 100 ml. of 1N - sodium hydroxide solution were added and the whole was heated for 45 minutes on a steam bath. By adding water, acidifying with hydrochloric acid and recrystallizing the precipitated product, there was obtained N - [4 - (β - benzamido-ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea in a yield of about 36%.

EXAMPLE 23

N - [4 - (β - 4' - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

18 g of 4 - (β - 4' - chloro - benzamido - ethyl) - benzenesulphonic acid chloride (melting point: 134—136°C), 250 ml. of benzene, 10 g of cyclohexyl - parabanic acid and 5 g of triethylamine were heated for 2 hours at the boiling temperature under reflux. The products dissolved at first and after some minutes crystals separated out. After a 2 hours heating under reflux, the whole was allowed to cool, and the separated

crystals were filtered off with suction, washed with water and dried. 1 - [4 - (β - 4'-Chloro - benzamido - ethyl) - benzenesulphonyl] - 3 - cyclohexyl - parabanic acid was obtained in a yield of about 77%. The compound was found to melt after recrystallization from a mixture of methanol and dioxan at 226—228°C.

5 g of the parabanic acid derivative thus obtained were heated for 45 minutes on a steam bath in 50 ml. of dioxane and 100 ml. of 1N - sodium hydroxide solution. The clear solution was diluted with water and acidified with hydrochloric acid. The crystalline precipitate obtained constituting N - [4 - (β - 4' - chloro - benzamido - ethyl)-benzenesulphonyl] - N' - cyclohexyl - urea, was suction - filtered, washed with water and dried. The yield of saponification product was 91.5% of the theory. The N - [4 - (β- 4' - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea obtained was found to melt after recrystallization from a mixture of dioxan and methanol at 196—197.5°C.

EXAMPLE 24

N - [4 - (β - phenoxy - acetamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

13.7 g of 4 - (β - phenoxy - acetamido - ethyl) - benzenesulphonamide (melting point: 172—174°C) (from dimethylformamide/methanol) obtained by the reaction of phenoxyacetic acid chloride with 4 - β - aminoethyl - benzenesulphonamide - sodium) were suspended in 19 ml. of 2N-sodium hydroxide solution and 50 ml. of acetone and, at 0—5°C, 4.8 g of cyclohexylisocyanate were added dropwise. The whole was stirred for 3 hours at room temperature, then diluted with 150 ml. of water and 50 ml. of methanol, filtered and the filtrate was acidified with dilute hydrochloric acid. The N - [4 - (β - phenoxy - acetamido - ethyl) - benzenesulphonyl] - N' - cyclohexylurea thus obtained was recrystallized from methanol and found to melt at 176—177°C.

In an analogous manner, there were obtained:

N - [4 - (β - phenoxy - acetamido - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 114—116°C) (from methanol),

N - [4 - (β - phenoxy - acetamido - ethyl) - benzenesulphonyl] - N' - (4' - methyl - cyclohexyl) - urea (melting point: 161°C) (from methanol)

N - [4 - (phenyl - acetamido - methyl) - benzenesulphonyl] - N' - cyclooctyl - urea (melting point: 196—197°C) (from dimethylformamide/water),

N - [4 - (phenyl - acetamido - methyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 212—213°C) (from dimethylformamide/water),

N - [4 - (phenyl - acetamido - methyl) - benzenesulphonyl] - N' - *n* - butyl - urea (melting point: 197—198°C) (from dimethylformamide/water),

N - [4 - (phenyl - acetamido - methyl) - benzenesulphonyl] - N' - (4' - methyl - cyclohexyl) - urea (melting point: 194—195°C) (from dimethylformamide/water),

N - [4 - (β - hydroxy - cinnamoylamino - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 184—186°C) (from methanol),

N - [4 - (β - cinnamoylamino - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 183—184°C) (from methanol), and

N - {4 - [β - (α - phenoxy - propionylamino) - ethyl] - benzenesulphonyl} - N' - cyclohexyl - urea (melting point: 158—159°C) (from methanol).

In an analogous manner, there were obtained:

from 4 - (β - phenoxyacetamido - ethyl) - benzenesulphonamide (melting point: 171—173°C)

N - [4 - (β - phenoxyacetamido - ethyl) - benzenesulphonyl] - N' - (4 - ethyl - cyclohexyl) - urea (melting point: 160—161°C) (from dimethylformamide/water);

from 4 - (β - <β - phenylpropionamido> - ethyl) - benzenesulphonamide (melting point: 165—166.5°C)

N - [4 - (β - <β - phenylpropionamido> - ethyl) - benzenesulphonyl] - N' - *n* - butyl - urea (melting point: 129—130.5°C) (from methanol),

N - [4 - (β - <β - phenylpropionamido> - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 190.5°C) (from methanol) and

N - [4 - (β - <β - phenylpropionamido> - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (melting point: 184—186°C) (from methanol);

from 4 - (β - phenylpropionamidomethyl) - benzenesulphonamide (melting point: 131—133°C)

N - [4 - (β - phenylpropionamidomethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 174—176°C) (from methanol) and the N - [4 - (β - phenylpro-

pionamidomethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 192—193°C) (from methanol/dimethylformamide);

from 4 - (β - 4 - chlorophenylacetamido - ethyl) - benzenesulphonamide (melting point: 115—118°C (crude)),

N - [4 - (β - 4 - chlorophenylacetamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 164—166°C) (from methanol) and

N - [4 - (β - 4 - chlorophenylacetamido - ethyl) - benzenesulphonyl] - N' - (4-ethylcyclohexyl) - urea (trans) melting point: 180—181.5°C) (from methanol);

from 4 - [β - (β - phenylisobutyramido) - ethyl] - benzenesulphonamide (melting point: 157—160°C)

N - [4 - (β - <β - phenylisobutyramido> - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 163—166°C) (from methanol) and

N - [4 - (β - <β - phenylisobutyramido> - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (trans) (melting point: 187—189°C) (from methanol);

from 4 - (β - cinnamoylamino - ethyl) - benzenesulphonamide (melting point: 236—237.5°C)

N - [4 - (β - cinnamoylamino - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 162—163°C) (from methanol),

N - [4 - (β - cinnamoylamino - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 204—206°C) (from methanol) and

N - [4 - (β - cinnamoylamino - ethyl) - benzenesulphonyl] - N' - (4 - ethyl - cyclohexyl) - urea (trans) (melting point: 205—206°C) (from methanol);

from 4 - (β - 4 - chlorocinnamoylamino - ethyl) - benzenesulphonamide (melting point: 214—215°C)

N - [4 - (β - 4 - chlorocinnamoylamino - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 206—208°C) (from dimethylformamide/water),

N - [4 - (β - 4 - chlorocinnamoylamino - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (trans) (melting point: 225—226°C) (from dimethylformamide/water) and

N - [4 - (β - 4 - chlorocinnamoylamino - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (trans) (melting point: 223—224°C) (from methanol/dimethylformamide);

from 4 - [β - (β - methylcinnamoylamino) - ethyl] - benzenesulphonamide (melting point: 190—192°C)

N - [4 - (β - <β - methylcinnamoylamino> - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 167—169°C) (from methanol),

N - [4 - (β - <β - methylcinnamoylamino> - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 172—174°C) (from methanol),

N - [4 - (β - <β - methylcinnamoylamino> - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (trans) (melting point: 174—175.5°C) (from methanol) and

N - [4 - (β - <β - methylcinnamoylamino> - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (trans) (melting point: 168—170°C) (from methanol);

from 4 - [β - (α - methylcinnamoylamino) - ethyl] - benzenesulphonamide (melting point: 207°C)

N - [4 - (β - <α - methylcinnamoylamino> - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 175—177.5°C) (from methanol);

from 4 - (β - 4 - methylphenoxyacetamido - ethyl) - benzenesulphonamide (melting point: 160—161°C)

N - [4 - (β - 4 - methylphenoxyacetamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 167—168°C) (from methanol),

N - [4 - (β - 4 - methylphenoxyacetamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 173—175°C) (from dimethylformamide/water) and

N - [4 - (β - 4 - methylphenoxyacetamido - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (melting point: 195—196.5°C) (from dimethylformamide/water);

from 4 - (β - 4 - chlorophenoxyacetamido - ethyl) - benzenesulphonamide (melting point: 159—161°C)

N - [4 - (β - 4 - chlorophenoxyacetamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 174—176°C) (from dimethylformamide/water) and

N - [4 - (β - 4 - chlorophenoxyacetamido - ethyl) - benzenesulphonyl] - N' - (4 -

methylcyclohexyl) - urea (melting point: 173—174°C) (from methanol/dimethylformamide);

from 4 - (β - <α - phenoxypropionamido> - ethyl) - benzenesulphonamide (melting point: 146—147°C)

N - [4 - (β - <α - phenoxypropionamido> - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 139—141°C) (from methanol),

N - [4 - (β - <α - phenoxypropionamido> - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 202—204°C) (from methanol/dimethylformamide) and

N - [4 - (β - <α - phenoxypropionamido> - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (trans) (melting point: 209.5—211.5°C) (from methanol/dimethylformamide);

from 4 - (α - phenoxypropionamido - methyl) - benzenesulphonamide (melting point: 145—146°C)

N - [4 - (α - phenoxy - propionamidomethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 176—177°C) (from methanol/dimethylformamide) and

N - [4 - (α - phenoxy - propionamidomethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 205—206°C) (from dimethylformamide/water);

from 4 - [β - (γ - phenoxybutyramido) - ethyl] - benzenesulphonamide (melting point: 168—170°C)

N - [4 - (β - <γ - phenoxybutyramido> - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 173—175°C) (from methanol) and

N - [4 - (β - <γ - phenoxybutyramido> - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (trans) (melting point: 154—157°C) (from methanol);

from 4 - (β - benzyloxycarbonamido - ethyl) - benzenesulphonamide (melting point: 157—158°C)

N - [4 - (β - benzyloxycarbonamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 170—170.5°C) (from methanol),

N - [4 - (β - benzyloxycarbonamido - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 120—122°C) (from methanol) and the

N - [4 - (β - benzyloxycarbonamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 178—179.5°C) (from methanol);

from 4 - (benzyloxycarbonamido - methyl) - benzenesulphonamide (melting point: 156—157°C)

N - [4 - (benzyloxycarbonamidomethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 170—171°C) (from methanol),

N - [4 - (benzyloxycarbonamidomethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (trans) (melting point: 185—185.5°C) (from methanol) and

N - [4 - (benzyloxycarbonamidomethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (trans) (melting point: 184—186°C) (from methanol);

from 4 - (β - phenylmercaptoacetamido - ethyl) - benzenesulphonamide (melting point: 139—142°C)

N - [4 - (β - phenylmercaptoacetamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 151—152°C) (from methanol),

N - [4 - (β - phenylmercaptoacetamido - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 124—125°C) (from methanol),

N - [4 - (β - phenylmercaptoacetamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (trans) (melting point: 179—180°C) (from dimethylformamide/water) and

N - [4 - (β - phenylmercaptoacetamido - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (trans) (melting point: 193—194.5°C) (from dimethylformamide/water);

from 4 - [β - (β - phenylmercaptopropionamido) - ethyl] - benzenesulphonamide (melting point: 113—115°C)

N - [4 - (β - <β - phenylmercaptopropionamido> - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 160—161°C) (from methanol),

N - [4 - (β - <β - phenylmercaptopropionamido> - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (trans) (melting point: 152—153°C) (from methanol) and

N - [4 - (β - <β - phenylmercaptopropionamido> - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (trans) (melting point: 150—151°C) (from methanol);

from 4 - [β - 4 - chlorobenzylmercaptoacetamido - ethyl] - benzenesulphonamide (melting point: 157°C)

N - [4 - (β - 4 - chlorobenzylmercaptoacetamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 139—141°C) (from methanol) and

N - [4 - (β - 4 - chlorobenzylmercaptoacetamido - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 133—134.5°C) (from methanol);

from 4 - (β - 3 - methoxy - phenylacetamido - ethyl) - benzenesulphonamide (melting point: 125°C)

N - [4 - (β - 3 - methoxy - phenylacetamidoethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 190—192°C) (from ethanol/water),

N - [4 - (β - 3 - methoxy - phenylacetamidoethyl) - benzene sulphonyl] - N' - butyl - urea (melting point: 128—130°C) (from ethanol/water),

N - [4 - (β - 3 - methoxy - phenylacetamidoethyl) - benzenesulphonyl] - N' - (4 - methyl - cyclohexyl) - urea (melting point: 170—172°) (from ethanol/water) and

N - [4 - (β - 3 - methoxy - phenylacetamidoethyl) - benzenesulphonyl] - N' - (4 - ethyl - cyclohexyl) - urea (melting point: 157—159°C) (from ethanol/water);

from 4 - (3 - methoxy - phenylacetamidomethyl) - benzenesulphonamide (melting point: 140—142°C)

N - [4 - (3 - methoxy - phenylacetamidomethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 202—204°C) (from ethanol/water) and

N - [4 - (3 - methoxy - phenylacetamidomethyl) - benzene sulphonyl] - N' - butyl - urea (melting point: 184—187°C) (from ethanol/water);

from N - 4 - (β - phenylacetamido) - propyl - benzenesulphonamide (melting point: 161°C)

N - [4 - (β - phenylacetamido - propyl) - benzenesulphonyl] - N' - *n* - butyl - urea (melting point: 179—180°C) (from methanol/water) and the

N - [4 - (β - phenylacetamido - propyl) - benzenesulphonyl] - N' - (4 - methyl - cyclohexyl) - urea (melting point: 186—187°C) (from methanol/water);

from N - 4 - (β - <β - phenyl> - propionamdio - propyl) - benzenesulphonamide (melting point: 131°C)

N - [4 - (β - <β - phenyl> - propionamido - propyl) - benzenesulphonyl] - N' - (4 - methyl - cyclohexyl) - urea (melting point: 165°C) (from methanol/water);

from N - 4 - (β - phenoxyacetamido) - propyl - benzenesulphonamide (melting point: 172—173°C)

N - [4 - (β - phenoxyacetamido - propyl) - benzenesulphonyl] - N' - (4 - methyl - cyclohexyl) - urea (melting point: 137°C) (from methanol/water);

from N - 4 - (γ - <α - phenoxy> - propionamido - propyl) - benzenesulphonamide (melting point: 116—117°C)

N - [4 - (γ - <α - phenoxy> - propionamido - propyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 148°C) (from methanol/water);

from N - 4 - (β - <α - phenoxy> - propionamido - propyl) - benzenesulphonamide (melting point: 172°C)

N - [4 - (β - <α - phenoxy> - propionamido - propyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 188°C) (from ethanol) and the

N - [4 - (β - <α - phenoxy> - propionamido - propyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 180°C) (from methanol/water); and

from N - 4 - (β - 2 - chlorophenoxyacetamido - propyl) - benzenesulphonamide (melting point: 121°C)

N - [4 - (β - 2 - chlorophenoxyacetamidopropyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 152°C) (from methanol/water);

EXAMPLE 25

N - [4 - (β - phenyl - acetamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

9 g of N - [4 - (β - phenyl - acetamido - ethyl) - benzenesulphonyl] - urea (melting point: 174—176°C, from dimethylformamide/water, obtained from 4 - (β - phenyl - acetamido - ethyl) - benzenesulphonamide and potassium cyanate) were heated under reflux for 5 hours, while stirring, with a mixture of 250 ml. of toluene, 30 ml. of glycol monomethyl ether, 1.65 g of glacial acetic acid and 2.8 g of cyclohexylamine. The reaction mixture was concentrated under reduced pressure and the residue was treated with 1 litre of 1% aqueous ammonia. It was filtered over charcoal and the filtrate was acidified. After recrystallization from methanol and the N - [4 - (β - phenyl -

acetamidoethyl) - benzenesulphonyl] - N' - cyclohexyl - urea obtained as crude product was found to melt at 176°C.

In an analogous manner, there were obtained:

N - [4 - (β - phenylacetamido - ethyl) - benzenesulphonyl] - N' - cyclooctyl - urea (melting point: 178—180°C) (from methanol),

N - [4 - (β - phenyl - acetamido - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 140—141°C) (from methanol), and

N - [4 - (β - phenyl - acetamido - ethyl) - benzenesulphonyl] - N' - (4' - methyl-cyclohexyl) - urea (melting point: 183—184°C) (from methanol).

EXAMPLE 26

N - [4 - (β - 4' - chlorophenyl - acetamido - α - methyl - ethyl) - benzene - sulphonyl] - N' - cyclohexyl - urea

26.5 g of 4 - [β - 4' - chlorophenyl - acetamido - α - methyl - ethyl] - benzenesulphonamide were suspended in 250 ml. of acetone. 9.6 g. of finely ground potassium carbonate were added, while stirring, and the whole was heated for 1 hour at the boiling temperature. 12.5 g of cyclohexyl isocyanate were added dropwise and stirring was continued for 5 hours at the boiling temperature. After removing the acetone by distillation the residue was taken up in water. The whole was filtered and the filtrate was acidified. The N - [4 - (β - 4' - chlorophenyl - acetamido - α - methyl - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea obtained in a yield of 21 g was found to melt after recrystallization from methanol at 180—182°C.

EXAMPLE 27

N - [4 - (β - cinnamoylamino - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea

A sample of 4.7 g of N - [4 - (β - cinnamoylamino - ethyl) - benzenesulphonyl] - N' - cyclohexyl - thiourea, prepared from 4 - (β - cinnamoylamido - ethyl) - benzenesulphonamide and cyclohexyl - mustard oil, melting point: 175—176°C) was dissolved in excess 1N-sodium hydroxide solution, an excess of 3% hydrogen peroxide was added and the whole was heated for a short time on a steam bath. After cooling, the separated sulfur was filtered off, the whole was clarified with charcoal and the filtrate was acidified with dilute hydrochloric acid. The N - [4 - (β - cinnamoylamino - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea obtained in a good yield was found to melt after recrystallization from methanol at 183—184°C.

EXAMPLE 28

N - [4 - (β - cinnamoylamino - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

4.6 g of N - [4 - (β - cinnamoylamino - ethyl) - benzenesulphonyl] - N' - cyclohexyl - isourea methyl ether prepared from the thiourea used as starting material according to Example 4 by the reaction of mercuric oxide in methanol at 60°C (melting point: 133—135°C) (from methanol) were heated for some minutes on a steam bath with 100 ml. of concentrated hydrochloric acid. The mass which was at first smeary solidified and immediately crystallized. After suction-filtration and recrystallization from methanol the N - [4 - (β - cinnamoylaminoethyl) - benzenesulphonyl] - N' - cyclohexyl - urea obtained was found to melt at 183—184°C.

EXAMPLE 29

N - [4 - (γ - phenacetamido - propyl) - benzenesulphonyl] - N' - cyclohexyl - urea

18 g of 4 - (γ - phenacetamido - propyl) - benzenesulphonamide (melting point: 167°C) were combined with 110 ml. of acetone and 27 ml. of 2N-sodium hydroxide solution and cooled down to 0—5°C. At this temperature, 7 g of cyclohexyl isocyanate were added dropwise, while stirring. The dropwise addition being complete, stirring was continued for 3 hours, while allowing the temperature to rise to 20°C by removing the ice bath. The reaction solution was acidified, the acetone was removed at room temperature under reduced pressure and the residue was extracted with 1% ammonia. The extract was acidified, and the precipitate formed was suction-filtered and recrystallized from a mixture of ethanol and water. (Melting point: 156°C).

In an analogous manner, there were obtained:

N - [4 - (γ - phenacetamido - propyl) - benzenesulphonyl] - N' - *n* - butyl - urea (melting point: 167—168°C) (from ethanol),

N - [4 - (β - phenacetamido - propyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 178°C) (from ethanol),

N - [4 - (β - phenoxyacetamido - propyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 181°C) (from methanol),

N - [4 - (γ - phenoxyacetamido - propyl) - benzenesulphonyl] - N' - (4' - methyl-cyclohexyl) - urea (melting point: 161°C) (from ethanol), and

N - [4 - (β - phenoxyacetamido - propyl) - benzenesulphonyl] - N' - *n* - butyl - urea (melting point: 149°C) (from ethanol).

EXAMPLE 30

N - [4 - (phenoxyacetamidomethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

32 g of 4 - (phenoxyacetamidomethyl) - benzenesulphonamide (melting point: 177—178°C), prepared from 4 - aminomethylbenzenesulphonamide and phenoxyacetyl chloride, were suspended in 200 ml. of acetone. This suspension was combined with a solution of 4 g of sodium hydroxide in 60 ml. of water and to the clear solution obtained were added dropwise while stirring and at room temperature 12.5 g of cyclohexyl isocyanate. Stirring was continued for 2 hours, and the batch from which the reaction product had already precipitated was combined with water and hydrochloric acid and suction-filtered. The N - [4 - (phenoxyacetamidomethyl) - benzenesulphonyl] - N' - cyclohexyl - urea was found to melt after recrystallization from a mixture of methanol and dimethylformamide at 170—172°C.

In an analogous manner, there were obtained:

N - [4 - (phenoxyacetamidomethyl) - benzenesulphonyl] - N' - (4 - isopropyl - cyclohexyl) - urea (melting point: 180—182°C), and

N - [4 - (phenoxyacetamidomethyl) - benzenesulphonyl] - N' - isobutyl - urea (melting point: 140—142°C).

EXAMPLE 31

N - [4 - {β - (4 - methoxy - phenylacetamido) - ethyl} - benzenesulphonyl] - N' - cyclohexyl - urea

17.4 g of 4 - [β - (4 - methoxy - phenylacetamido) - ethyl] - benzenesulphonamide (melting point: 134—135°C), prepared from 4 - (β - aminoethyl) - benzenesulphonamide and *p*-methoxyphenylacetyl chloride), were introduced into 200 ml. of acetone and an aqueous solution of 2 g of sodium hydroxide was added. Water was added in such an amount that a nearly clear solution was obtained, 6.5 g of cyclohexyl isocyanate were added dropwise, while stirring, and stirring was continued for 2 hours. A small amount of impurities appeared as solid particles which rendered the solution turbid. These impurities filtered off with suction, the filtrate was treated with water and hydrochloric acid and the resulting benzenesulphonyl urea which solidified was separated from the liquid and recrystallized from ethanol. The N - [4 - {β - (4 - methoxy - phenylacetamido) - ethyl} - benzenesulphonyl] - N' - cyclohexyl - urea was found to melt at 166—168°C.

In an analogous manner, there were obtained:

N - [4 - {β - (4 - methoxy - phenylacetamido) - ethyl} - benzenesulphonyl] - N' - butyl - urea (melting point: 131—133°C),

N - [4 - (4 - methoxy - phenylacetamidomethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 192—194°C), and

N - [4 - (4 - methoxy - phenylacetamidomethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 171—173°C).

EXAMPLE 32

N-[4-(phenoxyacetamidomethyl)benzenesulphonyl]-N'-cyclohexyl-urea

19 g of N - [4 - (phenoxyacetamidomethyl) - benzene sulphonyl] - methyl - urethane (melting point: 163—165°C, prepared from 4 - (phenoxyacetamidomethyl) - benzenesulphonamide and chloroformic acid methyl ester in the presence of potassium carbonate in acetone) were heated on an oil bath with 5 g of cyclohexylamine until a clear melted mass had formed (melting point: 150—160°C) from which methanol escaped. The temperature was maintained at 140—150°C; after the termination of the reaction, the whole was cooled and the reaction product was recrystallized from a mixture of methanol and dimethylformamide. The N - [4 - (phenoxyacetamidomethyl) - benzenesulphonyl] - N' - cyclohexyl - urea was found to melt at 170—172°C.

EXAMPLE 33

N - [4 - (phenoxyacetamidomethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

9 g of 4 - (phenoxy - acetamidomethyl) - benzenesulphonyl - urea (melting point: 169—171°C, prepared from 4 - (phenoxyacetamidomethyl) - benzenesulphonamide and potassium cyanate) were heated for 5 hours at the boiling temperature in a mixture of 300 ml. of toluene and 30 ml. of monomethyl glycol with 1.65 g of glacial acetic acid and 2.8 g. of cyclohexylamine, while stirring. Then the whole was concentreated under a reduced pressure, the residue was triturated with alcohol and, after suction-filtration, and the reaction product was recrystallized from a mixture of methanol and dimethylformamide. The N - [4 - (phenoxy - acetamidomethyl) - benzenesulphonyl] - N' - cyclohexyl - urea was found to melt at 170—172°C.

EXAMPLE 34

N - [4 - (β - cinnamoylamino - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

7.35 g of N - N - diphenyl - N' - cyclohexyl - urea and 8.8 g of the sodium salt of 4 - (β - cinnamoylamino - ethyl) - benzenesulphonamide were suspended in 50 ml. of dimethylformamide and heated for 6 hours at 100°C, while stirring. The clear solution was then diluted with a small quantity of water; the whole was rendered alkaline with dilute sodium hydroxide solution and was twice shaken out with ether. The aqueous phase was filtered over charcoal and acidified, the precipitated N - [4-(β-cinnamoylamino - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea was suction-filtered and recrystallized from a mixture of dimethylformamide and water. (Melting point: 182—184°C).

EXAMPLE 35

N - [4 - (β - 3,5 - dimethoxy - benzamidoethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

18.2 g of 4 - (β - 3,5 - dimethoxy - benzamidoethyl) - benzene - sulphonamide (melting point: 151—153°C, prepared from 4 - (β - amino - ethyl) - benzenesulphonamide and 3,5 - dimethoxybenzoyl chloride) were combined in 200 ml. of acetone with a solution of 2 g of sodium hydroxide in a small quantity of water. The addition of water was continued until a clear solution had formed, 6.5 g of cyclohexyl isocyanate were added dropwise at room temperature, while stirring and stirring was continued for 2 hours at room temperature. A slight precipitate formed which was suction-filtered and the filtrate was combined with water and hydrochloric acid. The precipitated product was suction-filtered and recrystallized from a mixture of ethanol and water. The N - [4 - (β - 3,5 - dimethoxy - benzamidoethyl) - benzenesulphonyl] - N' - cyclohexyl - urea was found to melt at 184—186°C.

In an analogous manner, there were obtained:

N - [4 - (β - 3,5 - dimethoxy - benzamidoethyl) - benzenesulphonyl] - N' - (4 - ethyl - cyclohexyl) - urea (melting point: 209—210°C) and

N - [4 - (β - 3,5 - dimethoxy - benzamido - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 178—180°C).

In an analogous manner, there were obtained: from 4 - (3,5 - dimethoxybenzamido - methyl) - benzenesulphonamide (melting point: 189—191°C)

N - [4 - (3,5 - dimethoxy - benzamido - methyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 160—162°C), and

N - [4 - (3,5 - dimethoxy - benzamido - methyl) - benzenesulphonyl] - N' - (4-ethyl - cyclohexyl) - urea (melting point: 190—192°C).

EXAMPLE 36

N - [4 - (3 - methyl - 4 - chlorobenzamidomethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

12 g of 4 - (3 - methyl - 4 - chlorobenzamidomethyl) - benzenesulphonamide (melting point: 204°C) were dissolved in 110 ml. of acetone and 18 ml. of 2N-sodium hydroxide solution and, at 0—5°C, 5 g of cyclohexyl isocyanate were slowly added dropwise, while stirring. Stirring was continued for 3 hours while allowing the temperature to rise to room temperature. The whole was acidified with 2N-hydrochloric acid and the solvent was distilled off under reduced pressure. The residue was extracted with 1% ammonia, the extract was acidified and the precipitate was recrystallized from ethanol by adding a small quantity of water. (Melting point: 187°C).

In an analogous manner, there were obtained:
N - [4 - (3 - methyl - 4 - chlorobenzamidomethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 180°C) (from ethanol);
from 4 - (β - 3 - methyl - 4 - chlorobenzamidoethyl) - benzenesulphonamide (melting point: 180—181°C),
N - [4 - (β - 3 - methyl - 4 - chlorobenzamidoethyl) - benzenesulphonyl] - N' - *n* - butyl - urea (melting point: 178°C) (from methanol/water),
N - [4 - (β - 3 - methyl - 4 - chlorobenzamidoethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 184°C) (from ethanol/water) and
N - [4 - (β - 3 - methyl - 4 - chlorobenzamidoethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 191°C) (from ethanol);
from 4 - (β - 3 - chloro - 4 - methylbenzamidopropyl) - benzenesulphonamide (melting point: 159°C):
N - [4 - (β - 3 - chloro - 4 - methylbenzamidopropyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 209°C) (from ethanol/water);
from 4 - (γ - 3 - chloro - 4 - methylbenzamidopropyl) - benzenesulphonamide (melting point: 145°C):
N - [4 - (γ - 3 - chloro - 4 - methylbenzamidopropyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 151°C) (from methanol) and
N - [4 - (γ - 3 - chloro - 4 - methylbenzamidopropyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 168°C) (from ethanol);
from 4 - (2,4 - dimethylbenzamidomethyl) - benzenesulphonamide (melting point: 202°C):
N - [4 - (2,4 - dimethylbenzamidomethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 197—199°C) (from ethanol);
from 4 - (β - 2,4 - dimethylbenzamidoethyl) - benzenesulphonamide (melting point: 173°C):
N - [4 - (β - 2,4 - dimethylbenzamidoethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 208°C) (from much ethanol or dimethylformamide/water) and
N - [4 - (β - 2,4 - dimethylbenzamidoethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 177°C) (from ethanol); and
from 4 - (γ - 2,5 - dimethylbenzamidopropyl) - benzenesulphonamide (melting point: 141°C):
N - [γ - 2,5 - dimethylbenzamidopropyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 184°C) (from ethanol)

Example 37

N - [4 - (β - 2 - methyl - 6 - chloro - benzamido - ethyl) - benzenesulphonyl] cyclohexyl - urea

17.5 g of 4 - (β - 2 - methyl - 6 - chloro - benzamido - ethyl) - benzenesulphonamide (melting point: 176—178°C) were heated for 1 hour at the boiling temperature in 250 ml. of acetone with 13.8 g of finely ground potassium carbonate, while stirring. Then 6.3 g of cyclohexyl isocyanate were added dropwise and stirring was continued for 6 hours at the boiling temperature. The acetone was distilled off under reduced pressure, the residue was taken up in about 3 litres of water, filtered and the filtrate was acidified with dilute hydrochloric acid. The crystalline precipitate of N - [4 - (β - 2 - methyl - 6 - chloro - benzamido - ethyl) - benzenesulphonyl] - cyclohexyl - urea obtained was suction-filtered, washed with water and dissolved in 1% ammonia for further purification. After filtering again, the filtrate obtained was acidified and, after suction-filtration, the crystallization product was recrystallized from methanol. Melting point: 203—204°C.

In an analogous manner, there was obtained:
from 4 - (β - 2 - methyl - 6 - chloro - benzamido - ethyl) - benzenesulphonamide and 4 - methyl - cyclohexyl isocyanate,
N - [4 - (β - 2 - methyl - 6 - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl - cyclohexyl) - urea (melting point: 190—191°C) (from methanol).

In an analogous manner, there were obtained:
N - [4 - (β - 3,5 - dipropoxy - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 172—174°C) (from methanol) by reacting 4 - (β - 3,5 - dipropyoxybenzamido - ethyl) - benzenesulphonamide (melting point: 185—187°C) with cyclohexyl isocyanate, and
N - [4 - (β - 3,5 - dipropoxy - benzamido - ethyl) - benzene sulphonyl] - N' - (4 - methyl - cyclohexyl) - urea from the above - defined sulphonamide and 4 - methyl - cyclohexyl - isocyanate, (melting point: 170—172°C) (from methanol), as well as

N - [4 - (β - 3,5 - dipropoxy - benzamido - ethyl) - benzenesulphonyl] - N' - *n* - butyl - urea from the above-defined sulphonamide and *n*-butyl isocyanate (melting point: 170—172°C) (from isopropanol).

EXAMPLE 38

N - [4 - (β - 2,6 - dimethyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

a) N - [4 - (β - 2,6 - dimethyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - thiourea

16.6 g of 4 - (β - 2,6 - dimethyl - benzamido - ethyl) - benzenesulphonamide (melting point: 174—175°C) and 13.8 g of potassium carbonate were heated under reflux for 2 hours at the boiling temperature in 200 ml. of acetone, while stirring. Then 7 g of cyclohexyl mustard oil were added dropwise and stirring was continued for 16 hours at the boiling temperature. After concentration under reduced pressure, the residue obtained was dissolved at 45°C on a steam bath in about 3 litres of water. The whole was clarified with charcoal, filtered and the filtrate was acidified with dilute hydrochloric acid. For further purification the N - [4 - (β - 2,6 - dimethyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexylthiourea was dissolved in 1% ammonia and, after filtration, the solution was acidified with hydrochloric acid. After suction-filtration, drying and recrystallization from methanol, the crystallization product was found to melt at 171—173°C.

b) N - [4 - (β - 2,6 - dimethyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

3.4 g. of mercuric chloride were dissolved in 30 ml. of water. 12.5 ml. of 2N-sodium hydroxide solution were added dropwise, while stirring. The precipitated mercuric oxide was combined, at a temperature of 40°C, with 4.5 g of N - [4 - (β - 2,6 - dimethyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - thiourea dissolved in 20 ml. of a mixture of equal parts of 1N-sodium hydroxide solution and dimethylformamide. Stirring was continued for 2½ hours at 40—50°C. The mercuric sulphide obtained was suction-filtered and washed with a small quantity of water. The filtrate was clarified with charcoal and acidified with dilute hydrochloric acid. A precipitate of N - [4 - (2,6 - dimethyl - benzamidoethyl) - benzenesulphonyl] - N' - cyclohexyl - urea was obtained which was suction-filtered, washed with water and recrystallized from ethanol. (Melting point: 191—193°C).

c) N - [4 - (β - 2,6 - dimethyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - isourea - methyl ether

2.5 g of mercuric oxide were suspended in 40 ml. of methanol. The whole was heated to 40°C and then 4.73 g of N - [4 - (β - 2,6 - dimethyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - thiourea dissolved in 60 ml. of methanol and 25 ml. of dioxan were added. The suspension was stirred for 5 hours at 40°C. The mercuric sulfide was filtered off and from the filtrate the N-[4-(β-2,6-dimethylbenzamido-ethyl)-benzenesulphonyl]-N'-cyclohexyl-isourea-methyl ether was precipitated as crystallization product by sprinkling with water. The substance was suction-filtered and dried. After recrystallization from ethyl acetate it was found to melt at 136—138°C. The same substance may be obtained by reacting 4-(β-2,6-dimethyl-benzamido-ethyl)-benzenesulphonic acid chloride with N - cyclohexylisourea - methyl - ether.

d) N - [4 - (β - 2,6 - dimethyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

3.7 g of N - [4 - (β - 2,6 - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - isourea - methyl ether were heated for 5 minutes on a steam bath with 100 ml. of concentrated hydrochloric acid. The precipitated N - [4 - (β - 2,6 - dimethylbenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea was suction-filtered, triturated with water and recrystallized from ethanol. (Melting point: 191—193°C).

EXAMPLE 39

N - [4 - (β - 2 - methyl - 6 - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

a) N - [4 - (β - 2 - methyl - 6 - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - parabanic acid

14.9 g of 4 - (β - 2 - methyl - 6 - chloro - benzamido - ethyl) - benzenesulphonic acid chloride were heated under reflux for 2 hours at the boiling temperature in 200 ml. of benzene with 8 g of cyclohexyl - parabanic acid and 4 g of triethylamine. At first a clear solution was obtained, and then N - [4 - (β - 2 - methyl - 6 - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl parabanic acid separated

in crystalline form. It was allowed to stand overnight; it was then suction-filtered and recrystallized from a mixture of methanol and dioxan. The substance obtained was found to melt at 211—213°C.

b) N - [4 - (β - 2 - methyl - 6 - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

5 g of the parabanic acid derivative obtained according to a) were heated for 45 minutes on a steam bath in 50 ml. of dioxan and 100 ml. of 1N-sodium hydroxide solution. A clear solution was obtained, which, after termination of the heating was combined with dilute hydrochloric acid. The precipitated crystals were suction-filtered. The melting point of the N - [4 - (β - 2 - methyl - 6 - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea thus obtained was found, after recrystallization from methanol, to be 203—204°C.

EXAMPLE 40

N - [4 - (β - 2 - methyl - 4 - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

41 g of N - [4 - (β - 2 - methyl - 4 - chloro - benzamido - ethyl) - benzenesulphonyl] - methylurethane (melting point: 175—177°C) were suspended in 50 ml. of xylene and, at 70°C, 10 g of cyclohexylamine were added dropwise, while stirring. The temperature was raised to 120—130°C, whereupon the reaction set in after a short time, with the evolution of methanol. After 30 minutes, the whole was cooled; the sulphonylurea formed was precipitated and was recrystallized from a mixture of dimethylformamide and water. The melting point of N - [4 - (β - 2 - methyl - 4 - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea was found to be 195—196°C.

In an analogous manner, there was obtained:

from N - [4 - (β - 3,4 - dichlorobenzamido - ethyl) - benzenesulphonyl] - methylurethane (melting point: 197—200°C)

N - [4 - (β - 3,4 - dichlorobenzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethoxycyclohexyl) - urea (melting point: 206—207.5°C) (from methanol).

EXAMPLE 41

N - [4 - (β - 2 - methyl - 4 - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl - cyclohexyl) - urea

A mixture of 9.9 g of N - [4 - (β - 2 - methyl - 4 - chloro - benzamidoethyl) - benzenesulphonyl] - urea (melting point: 194°C), 300 ml. of toluene, 30 ml. of glycol monomethyl ether, 1.65 g of glacial acetic acid and 3.2 g of 4-methylcyclohexylamine were heated under reflux for 5 hours, while stirring. The mixture was concentrated under reduced pressure and the residue was triturated with alcohol. The N - [4 - (β - 2 - methyl - 4 - chloro - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl - cyclohexyl) - urea obtained as crude product was suction-filtered and found to melt, after recrystallization from a mixture of dimethylformamide and water, at 196—197°C.

EXAMPLE 42

N - [4 - (β - 3,4 - dimethyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

16.6 g of 4 - (β - 3,4 - dimethyl - benzamido - ethyl) - benzenesulphonamide (melting point: 190°C) were combined, at 0—5°C, in 25 ml. of 2N-sodium hydroxide solution and 50 ml. of acetone with 6.5 g of cyclohexyl isocyanate, while stirring. Stirring was continued for 3 hours, the whole was diluted with water and a small quantity of methanol, the undissolved matter was filtered off, the filtrate was acidified and the precipitate obtained was recrystallized from a mixture of dimethylformamide and water. The melting point of N - [4 - (β - 3,4 - dimethyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea was found to be 194—195°C.

In an analogous manner, there were obtained:

N - [4 - (β - 3,4 - dimethyl - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl - cyclohexyl) - urea (melting point: 172—174°C) from dimethylformamide/water);

from 4 - (β - 3,4 - dichlorobenzamido - ethyl) - benzenesulphonamide (melting point: 171—172°C)

N - [4 - (β - 3,4 - dichloro - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 187—189°C) (from dimethylformamide/water) and

N - [4 - (β - 3,4 - dichloro - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl - cyclohexyl) - urea (melting point: 192—194°C) (from dimethylformamide/water);

from 4 - (β - 3 - chloro - 4 - methyl - benzamido - ethyl) - benzenesulphonamide (melting point: 198—200°C)

N - [4 - (β - 3 - chloro - 4 - methyl - benzamido - ethyl) - benzenesulphonyl] - N - cyclohexyl - urea (melting point: 207—209°C) (from dimethylformamide/water) and

N - [4 - (β - 3 - chloro - 4 - methyl - benzamido - ethyl) - benzenesulphonyl] - N'- (4 - methyl - cyclohexyl) -urea (melting point: 200—202°) (from dimethylformamide/water);

from 4 - (β - 2,6 - dichloro - benzamido - ethyl) - benzenesulphonamide (melting point: 182—184°C)

N - [4 - (β - 2,6 - dichloro - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 206—207°C) (from dimethylformamide/water),

N - [4 - (β - 2,6 - dichloro - benzamido - ethyl) - benzenesulphonyl] - N - butyl - urea (melting point: 189—191°C) (from dimethylformamide/water) and

N - [4 - (β - 2,6 - dichloro - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl - cyclohexyl) - urea (melting point: 180—181°C) (from methanol);

from 4 - (β - 2,5 - dimethyl - benzamido - ethyl) - benzenesulphonamide (melting point: 162°C)

N - [4 - (β - 2,5 - dimethyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 184—185°C) (from methanol) and

N - [4 - (β - 2,5 - dimethyl - benzamido - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 169—171°C) (from methanol);

from 4 - (β - 2,4 - dichloro - benzamido - ethyl) - benzenesulphonamide (melting point: 162—164°C)

N - [4 - (β - 2,4 - dichloro - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 197—198°C) (from dimethylformamide/water) and

N - [4 - (β - 2,4 - dichloro - benzamido - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 186—188°C) (from dimethylformamide/water);

from 4 - (β - 3 - chloro - 4 - methylbenzamido - ethyl) - benzenesulphonamide (melting point: 198—200°C) the

N - [4 - (β - 3 - chloro - 4 - methylbenzamido - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 174—175°C) (from methanol/dimethylformamide) and

N - [4 - (β - 3 - chloro - 4 - methylbenzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (trans) (melting point: 196—197°C) (from methanol/dimethylformamide); and

from 4 - (β - 3,4 - dimethylbenzamido - ethyl) - benzenesulphonamide (melting point: 190°C)

N - [4 - (β - 3,4 - dimethylbenzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (trans) (melting point: 177.5—179°C) (from methanol).

EXAMPLE 43

N - [4 - (β - 4 - n - butoxy - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

18.8 g of 4 - (β - 4 - n - butoxy - benzamido - ethyl) - benzenesulphonamide (melting point: 208—209°C) were stirred for 1 hour together with 13.8 g of potassium carbonate and 300 ml. of acetone, while heating at the boiling temperature of the acetone. Then 6.3 g of cyclohexyl isocyanate were added dropwise at the boiling temperature of acetone and stirring was continued for 4 hours, while further boiling. The whole was concentrated under reduced pressure, the residue obtained was dissolved in about 2 litres of water on a steam bath, filtered and the filtrate was acidified with dilute hydrochloric acid. The residue obtained was taken up in 1% aqueous ammonia and re-precipitated by acidifying the filtrate with hydrochloric acid. The N - [4 - (β - 4 - *n* - butoxy - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea thus obtained was found to melt, after recrystallization from a mixture of methanol and dioxan, at 197—199°C.

In an analogous manner, there were obtained from the same 4 - (β - 4 - *n* - butoxy - benzamido - ethyl) - benzenesulphonamide and 4 - methyl - cyclohexyl isocyanate, N - [4 - (β - 4 - *n* - butoxy - benzamido - ethyl) - benzenesulphonyl] - N' - 4 - methyl - cyclohexyl - urea (melting point: 202—204°C) (from methanol/dioxan), and by using *n* - butyl isocyanate N - [4 - (β - 4 - *n* - butoxy - benzamido - ethyl) - benzenesulphonyl] - N' - *n* - butyl - urea (melting point: 203—205°C) (from methanol).

EXAMPLE 44

N - [4 - (β - 4 - *n* - butoxy - benzamido - ethyl) - benzenesulphonyl] - N′ - isobutyl - urea

13.6 g of mercuric chloride were dissolved in 120 ml. of water. 50 ml. of 2N-sodium hydroxide solution were added dropwise, while stirring. To the precipitated mercuric oxide, 18 g of N - [4 - (β - 4 - *n* - butoxy - benzamido - ethyl) - benzenesulphonyl] - N′ - isobutyl - thiourea (melting point: 124—126°C, prepared from β - 4 - *n* - butoxy - benzamido - ethyl - benzenesulphonamide and isobutyl mustard oil in the presence of potassium carbonate) dissolved in 80 ml. of a mixture of equal parts of 1N-sodium hydroxide solution and dimethylformamide were added at a temperature of 40°C. Stirring was continued for 2½ hours at 40—50°C, and the mercuric sulphide formed was suction-filtered and washed with a small quantity of water. The filtrate was clarified with charcoal and acidified with dilute hydrochloric acid. A precipitate of N - [4 - (β - 4 - *n* - butoxy - benzamido - ethyl) - benzenesulphonyl] - N′ - isobutyl - urea was obtained which was washed with water and recrystallized from methanol. (Melting point: 210—212°C).

EXAMPLE 45

N - [4 - (β - 4 - n - butoxy - benzamido - ethyl) - benzenesulphonyl] - N′ - cyclohexyl - urea

A mixture of 10 g of N - [4 - (β - 4 - *n* - butoxy - benzamido - ethyl) - benzenesulphonyl] - urea (melting point: 219—220°C), 300 ml. of toluene, 30 ml. of glycol monomethyl ether, 1.7 g of glacial acetic acid and 8.8 g of cyclohexylamine was heated under reflux for 5 hours, while stirring. The mixture was concentrated under reduced pressure and the residue was triturated with alcohol. The N - [4 - (β - 4 - *n* - butoxy - benzamido - ethyl) - benzenesulphonyl] - N′ - cyclohexyl - urea obtained as crude product was suction-filtered. After recrystallization from a mixture of dimethylformamide and water it was found to melt at 190—192°C.

EXAMPLE 46

N - [4 - (β - 2 - benzyloxy - benzamido - ethyl) - benzenesulphonyl] - N′ - cyclohexyl - urea

20.5 g of 4 - (β - 2 - benzyloxy - benzamido - ethyl) - benzene - sulphonamide (melting point: 180—183°C) were suspended in 250 ml. of acetone. 13.8 g of ground potassium carbonate were added and the whole was heated under reflux for 1½ hours at the boiling temperature. Then 6.25 g of cyclohexyl isocyanate were added dropwise. Stirring was continued for 7½ hours at the boiling temperature of the acetone which was then distilled off under reduced pressure. The residue was taken up in water, the undissolved matter was filtered off, the whole was clarified with charcoal and the filtrate was acidified. The crude N - [4 - (β - 2 - benzyloxy - benzamido - ethyl) - benzenesulphonyl] - N′ - cyclohexyl - urea obtained was found to melt after recrystallization from methanol at 175—177°C.

In an analogous manner, there was obtained, by using the above-defined sulphonamide and methyl - cyclohexyl isocyanate,

N - [4 - (β - 2 - benzyloxy - benzamido - ethyl) - benzenesulphonyl] - N′ - 4 - methyl - cyclohexyl - urea (melting point: 165—167°C).

EXAMPLE 47

N - [4 - (β - 2 - hydroxy - benzamido - ethyl) - benzenesulphonyl] - N′ - cyclohexyl - urea

1 g of the N - [4 - (β - 2 - benzyloxy - benzamido - ethyl) - benzenesulphonyl] - N′ - cyclohexyl - urea obtained according to Example 46 was dissolved in about 150 ml. of methanol. After the addition of palladium black the solution was shaken in a hydrogenation duck with hydrogen. After the completion of the absorption of hydrogen, the reaction solution was filtered off from the catalyst and concentrated. The N - [4 - (β - 2 - hydroxy - benzamido - ethyl) - benzenesulphonyl] - N′ - cyclohexyl - urea obtained was found to melt, after recrystallization from methanol, at 191—193°C.

EXAMPLE 48

N - [4 - (β - 2 - carboxy - benzamido - α - methyl - ethyl) - benzenesulphonyl] - N′ - cyclohexyl - urea

34.4 g of 4 - (β - phthalimido - α - methyl - ethyl) - benzenesulphonamide (melting point: 165—171°C) were dissolved in 500 ml. of acetone. 27.6 g of ground potassium carbonate were added and the whole was heated under reflux for 1 hour at the

boiling temperature, while stirring. Then 12.5 g of cyclohexyl isocyanate were added dropwise. After heating for 6 hours under reflux and simultaneously stirring, the acetone was distilled off from the reaction mixture and the residue was dissolved in water. By acidifying with hydrochloric acid a precipitate was obtained which was re-dissolved in 1% ammonia. After filtering and acidifying, N - [4 - (β - 2-carboxy - benzamido - α - methyl - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea crystallized out. The melting point of the substance was found to be after recrystalliztion from methanol, 170—171°C) (under decomposition).

In an analogous manner, there were obtained, by using 4 - (β - phthalimidoethyl)-benzenesulphonamide (melting point: 225—227°C), N - [4 - (β - 2 - carboxy - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 161—163°C) (with decomposition) and, by using the above-defined benzenesulphonamide and isobutylisocyanate, N - [4-(β - 2 - carboxy - benzamido-ethyl)-benzenesulphonyl]-N' - isobutyl - urea (melting point: 145—146°C) (with decomposition).

The same compound was obtained by reacting instead of the phthalimide 4 - (β-2 - carboxy - benzamido - ethyl) - benzenesulphonamide in acetone with isobutyl isocyanate by using an excess of potassium carbonate.

In an analogous manner, there were obtained:

from 4 - (β - 2 - carboxy - 4 - chloro - benzamido - ethyl) - benzenesulphonamide and cyclohexyl isocyanate

N - [4 - (β - 2 - carboxy - 4 - chloro - benzamido - ethyl) - benzenesulphonyl]-N' - cyclohexyl - urea (melting point: 117—118°C) (with decomposition) and

from 4 - (β - 2 - carboxy - 4 - chloro - benzamido - ethyl) - benzenesulphonamide and 4 - methyl - cyclohexyl isocyanate

N - [4 - (β - 2 - carboxy - 4 - chloro - benzamido - ethyl) - benzenesulphonyl]-N' - (4 - methyl - cyclohexyl) - urea (melting point: 109—110°C) with decomposition).

Example 49

N - [4 - (β - 3 - trifluoromethyl - benzamido - ethyl) - benzenesulphonyl] - N'-cyclohexyl - urea

18.6 g of 4 - (β - 3 - trifluoromethyl - benzamido - ethyl) - benzenesulphonamide (melting point: 145—147°C) (from methanol) were dissolved in 25 ml. of 2N-sodium hydroxide solution and 50 ml. of acetone and, at 0—5°C, 6.3 g of cyclohexyl isocyanate were added dropwise. Stirring was continued for 3 hours, the whole was diluted with water and a small quantity of methanol, filtered and the filtrate was acidified. The N-[4 - (β - 3 - trifluoromethyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea precipitating in crystalline form was found to melt, after recrystallization from methanol at 160—162°C.

In an analogous manner, there were obtained:

N - [4 - (β - 3 - trifluoromethyl - benzamido - ethyl) - benzenesulphonyl] - N'-butyl - urea (melting point: 145—146°C) (from methanol), and

N - [4 - (β - 3 - trifluoromethyl - benzamido - ethyl) - benzenesulphonyl] - N'-(4 - methyl - cyclohexyl) - urea (melting point: 176—177°C) (from methanol).

In an analogous manner, there were obtained:

from 4 - (β - 4 - cyano - benzamido - ethyl) - benzenesulphonamide (melting point: 237—238°C) (from dimethylformamide/water)

N - [4 - (β - 4 - cyano - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 198°C) (from dimethylformamide/water);

N - [4 - (β - 4 - cyano - benzamido - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 192—193°C) (from methanol) and

N - [4 - (β - 4 - cyano - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 198°C) (from dimethylformamide water);

N - [4 - (β - 4 - cyano - benzamido - ethyl) - benzenesulphonyl] - N' - butyl-urea (melting point: 192—193°C) (from methanol) and

N - [4 - (β - 4 - cyano - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl-cyclohexyl - urea (melting point: 198—199°C) (from methanol);

from 4 - (β - 4 - trifluoromethyl - benzamido - ethyl) - benzenesulphonamide (melting point: 216—217°C)

N - [4 - (β - 4 - trifluoromethyl - benzamido - ethyl) - benzenesulphonyl] - N'-cyclohexyl - urea (melting point: 205—206°C) (from dimethylformamide/water) and

N - [4 - (β - 4 - trifluoromethyl - benzamido - ethyl) - benzenesulphonyl] - N' - (4-methyl - cyclohexyl) - urea (melting point: 213—214°C) (from dimethylformamide/water);

from 4 - (β - 4 - methylsulphonyl - benzamido - ethyl) - benzenesulphonamide (melting point: 238—240°C)

N - [4 - (β - 4 - methylsulphonyl - benzamido - ethyl) - benzenesulphonyl] - N'- cyclohexyl - urea (melting point: 212°C) (from dimethylformamide/methanol) and trans N - [4 - (β - 4 - methylsulphonyl - benzamido - ethyl) - benzenesulphonyl] - N'- (4 - methyl - cyclohexyl) - urea (melting point: 210—211°C) (from dimethylformamide/methanol);

from 4 - (β - (4 - benzyloxybenzamido - ethyl) - benzenesulphonamide (melting point: 242°C)

N - [4 - (β - 4 - benzyloxybenzamido - ethyl) - benzenesulphonyl] - N' - butyl-urea (melting point: 218°C) (from dimethylformamide/water) and

trans N - [4 - (β - 4 - benzyloxy - benzamido - ethyl) - benzenesulphonyl]- N' - (4 - methyl - cyclohexyl) - urea (melting point: 224°C) (from dimethylformamide/water);

from 4 - (β - 3 - trifluoromethylbenzamido - ethyl) - benzenesulphonamide (melting point: 145—147°C)

N - [4 - (β - 3 - trifluoromethylbenzamido - ethyl) - benzenesulphonyl] - N' - (4-ethylcyclohexyl) - urea (trans) (melting point: 181—182.5°C) (from methanol);

from 4 - (β - 4 - methylsulphonylbenzamido - ethyl) - benzenesulphonamide (melting point: 238—240°C)

N - [4 - (β - 4 - methyl - sulphonylbenzamido - ethyl) - benzenesulphonyl] - N'-butyl - urea (melting point: 190—191°C) (from methanol/dimethylformamide);

from 4 - (β - 4 - benzyloxybenzamido - ethyl) - benzenesulphonamide (melting point: 242°C)

N - [4 - (β - 4 - benzyloxybenzamido - ethyl) - benzenesulphonyl] - N' - butyl-urea (melting point: 206—207°C) (from dimethylformamide/water);

from 4 - (β - 4 - phenylbenzamido - ethyl) - benzenesulphonamide (melting point: 281—283°C)

N - [4 - (β - 4 - phenylbenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 222°) (with decomposition) (from methanol);

from 4 - (β - 4 - tert.butylbenzamido - ethyl) - benzenesulphonamide (melting point: 208°C)

N - [4 - (β - 4 - tert.butylbenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 201—202.5°C) (from methanol),

N - [4 - (β - 4 - tert.butylbenzamido - ethyl) - benzenesulphonyl] - N' - butyl-urea (melting point: 160—161°C) (from methanol), the

N - [4 - (β - 4 - tert.butylbenzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl-cyclohexyl) - urea (trans) (melting point: 190—191°C) (from methanol and

N - [4 - (β - 4 - tert.butylbenzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethyl-cyclohexyl) - urea (trans) (melting point: 180—181°C) (from methanol);

from 4 - (β - 2 - acetylbenzamido - ethyl) - benzenesulphonamide (melting point: 213—215°C)

N - [4 - (β - 2 - acetylbenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 181°C) (with decomposition) (from methanol) and

N - [4 - (β - 2 - acetylbenzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl-cyclohexyl) - urea (trans) (melting point: 184—185°C) (from methanol);

from 4 - (4 - methylmercaptobenzamidomethyl) - benzenesulphonamide (melting point: 195°C)

N - [4 - (4 - methylmercaptobenzamidomethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 191—192°C) (from dimethylformamide/water) and

N - [4 - (4 - methylmercaptobenzamidomethyl) - benzenesulphonyl] - N' - (4-methylcyclohexyl) - urea (trans) (melting point: 204—205°C) (from dimethylformamide/water); and

from 4 - (β - 2 - hydroxy - 4 - chloro - benzamido - ethyl) - benzenesulphonamide (melting point: 172: 174°C)

N - [4 - (β - 2 - hydroxy - 4 - chloro - benzamido - ethyl) - benzenesulphonyl]- N' - cyclohexyl - urea (melting point: 204—206°C) (from methanol dioxan),

N - [4 - (β - 2 - hydroxy - 4 - chloro - benzamido - ethyl) - benzenesulphonyl]- N' - 4 - methylcyclohexyl - urea (trans) (melting point: 203—205°C) (from methanol) and

N - [4 - (β - 2 - hydroxy - 4 - chloro - benzamido - ethyl) - benzenesulphonyl]- N' - *n* - butyl - urea (melting point: 171—173°C) (from ethanol).

EXAMPLE 50

N - [4 - (β - 4 - methylmercapto - benzamido - ethyl) - benzenesulphonyl] - N' cyclohexyl - urea

40.8 g of N - [4 - (β - 4 - methylmercapto - benzamido - ethyl) - benzenesulphonyl] - methylurethane (melting point: 195—197°C) (from dimethylformamide/water) were suspended in 50 ml. of xylene and, at 70°, 10 g of cyclohexylamine were added dropwise, while stirring. The temperature was raised to 120—130°, whereupon the reaction set in after a short time, with the evolution of methanol. After 1 hour the whole was cooled. The sulphonyl - urea formed precipitated and was recrystallized from a mixture of dimethylformamide and water. The N - [4 - (β - 4 - methylmercapto - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea thus obtained was found to melt at 212—213°.

In an analogous manner, there was obtained trans - N - [4 - (β-4-methylmercapto-benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl - cyclohexyl) - urea (melting point: 213°) (from dimethylformamide/water).

EXAMPLE 51

N - [4 - (γ - 4 - carboxy - benzamido - propyl) - benzenesulphonyl] - N' - cyclohexyl - urea

7 g of N - 4 - (γ - 4 - carboxy - benzamido - propyl) - benzenesulphonamide melting point: 148—149°C) were dissolved in 100 ml. of acetone and 19.4 ml. of 2N-sodium hydroxide solution and 2.5 g of cyclohexyl isocyanate were added dropwise, while stirring and cooling (0—5°). After the completion of the dropwise addition, stirring was continued for 3 hours while allowing the temperature to rise to 20°C. Then the whole was acidified, the acetone was removed under reduced pressure at room temperature and the residue was extracted with 1% ammonia. The urea precipitated with acid was recrystallized from methanol and a small quantity of water. (Melting point: 163—164°)

EXAMPLE 52

N - [4 - (2 - hydroxy - benzamido - methyl) - benzenesulphonyl] - N' - (4 - methyl-cyclohexyl) - urea

10 g of N - [4 - (2 - hydroxy - benzamido - methyl) - benzenesulphonamide melting point: 184°) were dissolved in 80 ml. of acetone and 32.5 ml. of 2N - sodium hydroxide solution, cooled down to 0—5° and 4.6 g of methylcyclohexyl isocyanate were added dropwise, while stirring. Stirring was continued for 3 hours while allowing the temperature to rise to 20°, the whole was acidified and the acetone was removed at room temperature on a rotation evaporator. The residue was extracted with 1% ammonia, the extract was acidified and the precipitate was suction-filtered. By recrystallization from a mixture of ethanol and water crystals having a melting point of 180—181° were obtained.

In an analogous manner, there were obtained:

from N - [4 - (β - 2 - hydroxy - benzamido - ethyl) - benzenesulphonamide (melting point: 207°)

N - [4 - (β - 2 - hydroxy - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 193°) (from ethanol),

N - [4 - (β - 2 - hydroxy - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 188°) (from ethanol/water), and

N - [4 - (β - 2 - hydroxy - benzamido - ethyl) - benzenesulphonyl] - N' - *n* - butyl-urea (melting point: 152°) (from isopropanol/water),

from N - [4 - (β - 2 - hydroxy - benzamido - propyl) - benzenesulphonamide (melting point: 196°)

N - [4 - (β - 2 - hydroxy - benzamido - propyl) - benzenesulphonyl] - N' - (4-methyl - cyclohexyl) - urea (melting point: 158°) (from ethanol/water), and

from N - [4 - (γ - 3 - acetoxy - benzamido - propyl) - benzenesulphonamide (melting point: 137°)

N - [4 - (γ - 3 - hydroxy - benzamido - propyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 173—174.5°) (from ethanol/water).

During the preparation in the alkaline medium the hydroxyl group was de-acylated.

EXAMPLE 53

N - [4 - (β - 4 - n - butoxy - benzamidoethyl) - benzenesulphonyl] - N' - isobutyl-urea

3.8 g of N - [4 - (β - 4 - n - butoxy - benzamidoethyl) - benzenesulphonyl] - N'-isobutyl - isourea - methyl ether (obtained as an oily crude product by reacting N-[4-

(β - 4 - *n* - butoxy - benzamido - ethyl) - benzenesulphonyl] - N' - isobutyl - thiourea with mercuric oxide in methanol) were heated for 10 minutes on a steam bath with 50 ml. of concentrated hydrochloric acid. The whole was cooled, diluted with water and the N - [4 - (β - 4 - n - butoxy - benzamido - ethyl) - benzenesulphonyl] - N' - isobutyl-urea which, after recrystallization from methanol was found to melt at 210—212°, was suction-filtered.

EXAMPLE 54

N - [- (β - 2,4,6 - trimethyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

11.3 g of 4 - (β - 2,4,6 - trimethyl - benzamido - ethyl) - benzenesulphonamide (melting point: 193—195°C, prepared from 2,4,6 - trimethyl - benzoylchloride and 4-(β - amino - ethyl) - benzenesulphonamide) were heated at the boil with 9.2 g of potassium carbonate in 100 ml. of acetone, while stirring. 4.2 g of cyclohexyl isocyanate were added dropwise and stirring was continued for 3 hours at the boiling temperature. The batch was then concentrated under reduced pressure, the residue was dissolved in water, and the solution was filtered and acidified with dilute hydrochloric acid. The precipitated product was reprecipitated from 1% ammonia and recrystallized from methanol. The N - [4 - (β - 2,4,6 - trimethyl - benzamido - ethyl) - benzenesulphonyl] - N'-cyclohexyl - urea was found to melt at 214—216°C.

In an analogous manner, there were obtained:

N - [4 - (β - 2,4,6 - trimethyl - benzamidoethyl) - benzenesulphonyl] - N' - (4-methyl - cyclohexyl) - urea (melting point: 206—208°C), and

N - [4 - (β - 2,4,6 - trimethyl - benzamido - ethyl) - benzenesulphonyl] - N' - *n*-butyl - urea (melting point: 210—212°C).

In an analogous manner, there were obtained:

from 4 - (β - 3,4,5 - trimethoxybenzamido - ethyl) - benzenesulphonamide (melting point: 170—172°C)

N - [4 - (β - 3,4,5 - trimethoxybenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 180—181°C) (from methanol),

N - [4 - (β - 3,4,5 - trimethoxybenzamido - ethyl) - benzenesulphonyl] - N' - butyl-urea (melting point: 165—167°C) (from methanol),

N - [4 - (β - 3,4,5 - trimethoxybenzamido - ethyl) - benzenesulphonyl] - N' - (4-methyl - cyclohexyl) - urea (trans) (melting point: 208—209°) (from methanol/dimethylformamide) and

N - [4 - (β - 3,4,5 - trimethoxybenzamido - ethyl) - benzenesulphonyl] - N' - (4-ethyl - cyclohexyl) - urea (trans) (melting point: 205—206.5°) (from methanol).

In an analogous manner, there were, furthermore, obtained:

from N - 4 - (β - 3,4,5 - trimethoxybenzamidopropyl - benzenesulphonamide (melting point: 176°C)

N - [4 - (β - 3,4,5 - trimethoxybenzamidopropyl) - benzenesulphonyl] - N'-cyclohexyl - urea (melting point: 215°C) (from acetone/water); and

from N - 4 - (γ - 3,4,5 - trimethoxybenzamidopropyl) - benzenesulphonamide (melting point: 181—183°C)

N - [4 - (γ - 3,4,5 - trimethoxybenzamidopropyl) - benzenesulphonyl] - N' - (4-methylcyclohexyl) - urea (melting point: 166°C) from ethanol/water).

EXAMPLE 55

N - [4 - (β - N - methyl - benzamido - ethyl) - benzenesulphonyl]- N' - cyclohexyl-urea

15.9 g of 4 - (β - N - methylbenzamido - ethyl) - benzenesulphonamide (melting point: 184—185.5°) (from methanol) were suspended in 25 ml. of 2N-sodium hydroxide solution and 50 ml. of acetone and, at 0—5°, 6.5 g of cyclohexyl isocyanate were added dropwise, while stirring. Stirring was continued for 3 hours at room temperature, the whole was diluted with water, filtered and the filtrate was acidified. The N-[4 - (β - N - methyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea obtained in crystalline form was found to melt, after recrystallization from a mixture of dimethylformamide and water, at 199—200°.

In an analogous manner, there was obtained:

N - [4 - (β - N - methylbenzamido - ethyl) - benzenesulphonyl] - N' - (4-methyl-cyclohexyl) - urea (melting point: 172—174°C) (from dimethylformamide/water).

In an analogous manner, there were obtained:

from the 4 - (β - N - methyl - 4 - chloro - benzamido - ethyl) - benzenesulphonamide (melting point: 198—199°) (from methanol)

N - [4 - (β - N - methyl - 4 - chlorobenzamido - ethyl) - benzenesulphonyl] - N'-cyclohexyl - urea (melting point: 164—166°) (from dimethylformamide/water) and
N - [4 - (β - N - methyl - 4 - chlorobenzamido - ethyl) - benzenesulphonyl] - N'-(4 - methylcyclohexyl) - urea (trans) (melting point: 187—188°) (from methanol/dimethylformamide).

In an analogous manner, there were obtained:

from 4 - (β - N - methyl - 3 - methyl - benzamido - ethyl) - benzenesulphonamide (melting point: 146°) (from methanol/water)
N - [4 - (β - N - methyl - 3 - methylbenzamido - ethyl) - benzenesulphonyl] - N'-cyclohexyl - urea (melting point: 142—144.5°) (from methanol) and
N - [4 - (β - N - methyl - 3 - methyl - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (trans) (melting point: 155—157°) from methanol).

In an analogous manner, there were obtained:

from 4 - (N - methyl - benzamido - methyl) - benzenesulphonamide (melting point: 197°) (from methanol/dimethylformamide)
N - [4 - (N - methyl - benzamido - methyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 179—181°) (from dimethylformamide/water) and
N - [4 - (N - methyl - benzamido - methyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (melting point: 137—138°) (from methanol).

In an analogous manner, there was obtained:

from 4 - (N - methyl - 4 - chlorobenzamido - methyl) - benzenesulphonamide (melting point: 144°) (from alcohol)
N - [4 - (N - methyl - 4 - chlorobenzamido - methyl) - benzenesulphonyl] - N'-(4 - methylcyclohexyl) - urea (trans) (melting point: 199—201°) (from methanol).

In an analogous manner, there was obtained:

from 4 - (β - N - benzyl - 4 - benzamido - ethyl) - benzenesulphonamide (melting point: 174—175°) (from methanol)
N - [4 - (β - N - benzyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 135—137°) (with decomposition) (from methanol).

EXAMPLE 56

N - [4 - (β - 3,5 - dimethylphenoxyacetamido - ethyl) - benzenesulphonyl] - N' - (4-methylcyclohexyl) - urea (trans)

18.1 g of 4 - (β - 3,5 - dimethylphenoxyacetamido - ethyl) - benzenesulphonamide (melting point: 172°) were dissolved in 25 ml. of 2N - sodium hydroxide solution and 50 ml. of acetone and, at 0—5°, 7 g of 4 - methylcyclchexyl isocyanate (trans) were added dropwise, while stirring. Stirring was continued for 3 hours, the whole was diluted with methanol and a small quantity of dimethylformamide, filtered, and the filtrate was combined with water and acidified with dilute hydrochloric acid. The N[4-(β - 3,5 - dimethylphenoxyacetamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea obtained in crystalline form was suction-filtered and recrystallized from methanol. (Melting point: 188—190°).

In an analogous manner, there was obtained:

N - [4 - (β - 3,5 - dimethylphenoxyacetamido - ethyl) - benzenesulphonyl] - N'-cyclohexyl - urea (melting point: 162—163°) (from methanol).

In an analogous manner, there were obtained:

from 4 - (β - 3,4 - dimethylphenoxyacetamido - ethyl) - benzenesulphonamide (melting point: 150—151°)
N - [4 - (β - 3,4 - dimethylphenoxyacetamido - ethyl) - benzenesulphonyl] - N'-cyclohexyl - urea (melting point: 176—177.5°) (from methanol) and
N - [4 - (β - 3,4 - dimethylphenoxyacetamido - ethyl) - benzenesulphonyl] - N'-(4 - methylcyclohexyl) - urea (trans) (melting point: 184—185.5°) (from methanol),
from 4 - (β - 2,4 - dichlorophenoxyacetamido - ethyl) - benzenesulphonamide (melting point: 147°)
N - [4 - (β - 2,4 - dichlorophenoxyacetamido - ethyl) - benzenesulphonyl] - N'-cyclohexyl - urea (melting point: 156—158°) (from methanol) and
N - [4 - (β - 2,4 - dichlorophenoxyacetamido - ethyl) - benzenesulphonyl] - N' - (4-methylcyclohexyl) - urea (trans) (melting point: 173—174°) (from methanol),
from 4 - (β - 2 - methyl - 4,6 - dichloro - phenoxyacetamido - ethyl) - benzenesulphonamide (melting point: 85°)
N - [4 - (β - 2 - methyl - 4,6 - dichloro - phenoxyacetamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 189—190.5°) (from methanol),
N - [4 - (β - 2 - methyl - 4,6 - dichloro - phenoxyacetamido - ethyl) - benzene-

sulphonyl] - N' - (4 - methylcyclohexyl) - urea (trans) melting point: 173—175°) (from methanol) and

N - [4 - (β - 2 - methyl - 4,6 - dichlorophenoxyacetamido - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (trans) (melting point: 180—180.5°C) (from methanol),

from 4 - (β - 3,4 - dichlorophenylacetamido - ethyl) - benzenesulphonamide (melting point: 132—134°)

N - [4 - (β - 3,4 - dichlorophenylacetamido - ethyl) - benzenesulphonyl] - N' cyclohexyl - urea (melting point: 192—194°) (from dimethylformamide/water) and

N - [4 - (β - 3,4 - dichlorophenylacetamido - ethyl) - benzenesulphonyl] - N' - (4-methylcyclohexyl) - urea (trans) (melting point: 178—179°) (from dimethylformamide/water),

from 4 - (β - 3,4 - dimethoxyphenylacetamido - ethyl) - benzenesulphonamide (melting point: 158—160°)

N - [4 - (β - 3,4 - dimethoxyphenylacetamido - ethyl) - benzenesulphonyl] - N'-cyclohexyl - urea (melting point: 174—176°) (from methanol) and

N - [4 - (β - 3,4 - dimethoxyphenylacetamido - ethyl) - benzenesulphonyl] - N' - (4-methylcyclohexyl) - urea (trans) (melting point: 161—163°) (from methanol/dimethylformamide), and

from 4 - (β - 3,4 - dichlorocinnamoylamino - ethyl) - benzenesulphonamide (melting point: 201—203°)

N - [4 - (β - 3,4 - dichlorocinnamoylamino - ethyl) - benzenesulphonyl] - N'-cyclohexyl - urea (melting point: 203—204°) (from dimethylformamide/water) and the

N - [4 - (β - 3,4 - dichlorocinnamoylamino - ethyl) - benzenesulphonyl] - N' - (4-methylcyclohexyl) - urea (trans) (melting point: 196—198°) (from dimethylformamide/water).

EXAMPLE 57

N - [4 - (β - <α,α - diethyl - 4 - chlorophenylacetamido> - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (trans)

15 g of 4 - [β - (α,α - diethyl - 4 - chlorophenylacetamido) - ethyl] - benzenesulphonamide (melting point: 118—119°) (from alcohol/water) were dissolved in 18.4 ml. of 2N - sodium hydroxide solution and 35 ml. of acetone and, at 0—5°, 5.4 g of 4 - methylcyclohexyl isocyanate (trans) were added dropwise, while stirring. The stirring of the reaction mixture was continued for 3 hours, the whole was diluted with water and methanol and the undissolved matter was filtered off. The N - [4 - (β-<α,α - diethyl - 4 - chloro - phenylacetamido>ethyl) - benzenesulphonyl] - N' - (4-methylcyclohexyl) - urea (trans) obtained in crystalline form by acidifying the filtrate was found to melt after recrystallization from a mixture of dimethlformamide and water at 190—191°.

In the same manner, there was obtained:

N - [4 - (β - <α,α - diethyl - 4 - chlorophenylacetamido> - ethyl) - benzenesulphonyl] - N' - (cyclohexyl) - urea (melting point: 189—191°) (from dimethylformamide/water).

In an analogous manner, there were obtained:

from 4 - [β - (α,α - diethylphenylacetamido) - ethyl] - benzenesulphonamide (melting point: 134—136°)

N - [4 - (β - <α,α - diethylphenylacetamido> - ethyl) - benzenesulphonyl] - N'-cyclohexyl - urea (melting point: 198—198.5°) (from methanol),

N - [4 - (β - <α,α - diethylphenylacetamido> - ethyl) - benzenesulphonyl] - N'-butyl - urea (melting point: 150—152°) (from methanol) and

N - [4 - (β - <α,α - diethylphenylacetamido> - ethyl) - benzenesulphonyl] - N'-(4 - methylcyclohexyl) - urea (melting point: 170—172°) (from methanol);

from 4 - [β - (γ - phenylvaleramido) - ethyl] - benzenesulphonamide (melting point: 105°)

N - [4 - (β - <γ - phenylvaleramido> - ethyl) - benzenesulphonyl] - N' - (4-methylcyclohexyl) - urea (trans) melting point: 141—143°) (from methanol);

from 4 - [β - (α - benzylbutyramido) - ethyl] - benzenesulphonamide (melting point: 132—134°) (from methanol/water),

N - [4 - (β - <α - benzylbutyramido> - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 172—174°) (from methanol),

N - [4 - β - <α - benzylbutyramido>-ethyl)-benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (trans) (melting point: 187—188°C) (from methanol) and

N - [4 - (β - <α - benzylbutyramido> - ethyl) - benzenesulphonyl] - N' - (4-ethylcyclohexyl) - urea (trans) (melting point: 168—170°C) (from methanol);

from 4 - (α,α - diethylphenylacetamido - ethyl) - benzenesulphonamide (melting point: 128—129°C)

N - [4 - (α,α - diethylphenylacetamidomethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 184—185°C) (from dimethylformamide/water),

N - [4 - (α,α - diethylphenylacetamido - methyl) - benzenesulphonyl] - N' - butyl-urea (melting point 160°C) (from methanol) and

N - [4 - (α,α - diethylphenylacetamido - methyl) - benzenesulphonyl] - N' - (4-methylcyclohexyl) - urea (trans) (melting point: 202—203°C) (from dimethylformamide/water); and

from 4 - (β - <3 - methoxy - α,α - diethyl - phenylacetamido> - ethyl) - benzenesulphonamide (melting point: 129°C)

N - [4 - (β - <3 - methoxy - α,α - diethyl - phenylacetamido> - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 191—193°C) (from ethanol/water), and

N - [4 - (β - <3 - methoxy - α,α - diethyl - phenylacetamido> - ethyl) - benzenesulphonyl] - N' - (4 - methyl - cyclohexyl) - urea (melting point: 151—153°C) (from ethanol/water).

In an analogous manner, there were obtained:

from 4 - [β - (β - methyl - β - phenylbutyramido) - ethyl] - benzenesulphonamide (melting point: 133—135°C) (from dilute methanol)

N - (4 - (β - <β - methyl - β - phenylbutyramido> - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 157.5—159.5°C) (from dilute methanol),

N - [4 - (β - <β - methyl - β - phenylbutyramido> - ethyl) - benzenesulphonyl] - N' - 4 - methyl - cyclohexyl - urea (melting point: 194—196°C) (from dilute methanol) and

N - [4 - (β - <β - methyl - β - phenylbutyramido> - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 134—136°C) (from dilute methanol).

EXAMPLE 58

N - [4 - (β - <α - phenyl - β - methyl - butyramido> - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

18 g of 4 - (β - <α - phenyl - β - methyl - butyramido> - ethyl) - benzenesulphonamide (melting point: 163—165°C) (from dilute methanol) were dissolved in 250 ml. of acetone. After the addition of 13.8 g of potassium carbonate the whole was heated under reflux in the course of 1 hour at the boil, while stirring.

After the addition of 6.25 g of cyclohexyl isocyanate, stirring and heating were continued for 8 hours. The solvent was then distilled off and the residue was taken up in water. By acidifying the filtrated solution a crystalline precipitate of N - [4 - (β-<α - phenyl - β - methyl - butyramido> - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea was obtained. The substance was found to melt, after recrystallization from dilute methanol, at 176—178°C.

In the same manner there was obtained from the same sulphonamide by using 4-methyl - cyclohexyl isocyanate (trans) the N - [4 - (β - (α - phenyl - β - methyl-butyramido> - ethyl) - benzenesulphonyl] - N' - (4 - methyl - cyclohexyl) - urea (melting point: 224—226°C) (from dilute methanol) and by using *n* - butyl isocyanate N - [4 - (β - <α - phenyl - β - methyl - butyramido> - ethyl) - benzenesulphonyl] - N' - *n* - butyl - urea (melting point: 137—139°C) (from acetic ester).

In an analogous manner, there were obtained:

from 4 - (β - (<β - methyl - β - phenyl - butyramido> - ethyl) - benzenesulphonamide (melting point: 133—135°C)

N - 4 - [β - (<β - methyl - β - phenyl - butyramido> - ethyl) - benzenesulphonyl] - N' - butyl - urea (melting point: 134—136°C) (from dilute methanol),

N - 4 - [β - (<β - methyl - β - phenyl - butyramido> - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 157.5—159.5°C) from dilute methanol) and

N - 4 - [β - (<β - methyl - β - phenyl - butyramido> - ethyl) - benzenesulphonyl] - N' - 4 - methyl - cyclohexyl - urea (trans) (melting point: 194—196°C) (from dilute methanol);

from 4 - (β - 3,4,5 - trimethoxybenzamidopropyl) - benzenesulphonamide (melting point: 176°C)

N - [4 - (β - 3,4,5 - trimethoxybenzamidopropyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 215°C) (from acetone/water); and

from 4 - (γ - 3,4,5 - trimethoxybenzamidopropyl) - benzenesulphonamide (melting point: 181—183°C)

N - [4 - (γ - 3,4,5 - trimethoxybenzamidopropyl) - benzenesulphonyl] - N' - (4-methylcyclohexyl) - urea (melting point: 166°C) (from ethanol/water).

EXAMPLE 59

N - [4 - (β - benzophenone - 4 - carbonamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

11.5 g of 4 - (β - benzophenone - 4 - carbonamido - ethyl) - benzenesulphonamide (melting point: 240—242°C) were introduced into 100 ml. of acetone together with 8 g of finely ground potassium carbonate. The whole was stirred and heated under reflux at the boil. After 1 hour, 3.6 g of cyclohexyl isocyanate were added dropwise while further stirring and heating, and stirring were continued for 4 hours at the boiling temperature of the acetone. The acetone was distilled off *in vacuo*, and the residue obtained was treated with water and hydrochloric acid. The crystal paste obtained was suction-filtered and washed with water. The N - [4 - (β - benzophenone - 4 - carbonamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea was obtained as crude product in a good yield. After recrystallization from a mixture of methanol and dioxan, the substance was found to melt at 222—224°C.

In an analogous manner, there was obtained from the above-defined benzenesulphonamide by using 4 - methyl - cyclohexyl isocyanate N - [4 - (β - benzophenone - 4 - carbonamido - ethyl) - benzenesulphonyl] - N - 4 - methyl - cyclohexyl - urea (melting point: 217—219°C) (from methanol/dioxan).

EXAMPLE 60

N - [4 - (α - ethyl - β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

16.6 g of 4 - (α - ethyl - β - benzamido - ethyl) - benzenesulphonamide (melting point: 185—187°C, obtained from benzoic acid - (β - phenylbutyl) - amide by the reaction with chlorosulphonic acid and subsequent treatment with ammonia) were dissolved in 25 ml. of 2N-sodium hydroxide solution and 50 ml. of acetone and, at 0—5°C, 6.5 g of cyclohexyl isocyanate were added dropwise. Stirring was continued for 2—3 hours, the whole was diluted with water, filtered and the filtrate was acidified with dilute hydrochloric acid. The precipitated product was suction-filtered and recrystallized from methanol. (Melting point: 189—190°C).

In an analogous manner, there were obtained:

N - [4 - (α - ethyl - β - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (trans) (melting point: 184°C) (from methanol),

from 4 - (α - ethyl - β - 4 - chlorobenzamido - ethyl) - benzenesulphonamide (melting point: 177°C)

N - [4 - (α - ethyl - β - 4 - chlorobenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 201.5—203°C) (from methanol/dimethylformamide),

N - [4 - (α - ethyl - β - 4 - chlorobenzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea (trans) (melting point: 206—207°C) (from methanol/dimethylformamide) and

N - [4 - (α - ethyl - β - 4 - chlorobenzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethylcyclohexyl) - urea (trans) (melting point: 205—207°C) (from dimethylformamide/water);

from 4 - (α,α - dimethyl - β - benzamido - ethyl) - benzenesulphonamide (melting point: 223—216°C)

N - [4 - (α,α - dimethyl - β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 195—197°C) (from methanol) and

N - [4 - (α,α - dimethyl - β - benzamido - ethyl) - benzenesulphonyl] - N' - 4 - methylcyclohexyl - urea (trans) (melting point: 190—191°C); and

from 4 - (δ - benzamidobutyl) - benzenesulphonamide (melting point: 193°C)

N - [4 - (δ - benzamidobutyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 173°C) (from methanol/water).

EXAMPLE 61

N - [4 - (β - benzenesulphonyl acetamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

15.3 g of 4 - (β - benzenesulphonylacetamido - ethyl) - benzenesulphonamide (melting point: 184—187°C) were suspended in 20 ml. of 2N-sodium hydroxide solution and 40 ml. of acetone and, at 0—5°C, 5.5 g of cyclohexyl isocyanate were added dropwise. Stirring was continued for 3 hours, the whole was diluted with water and methanol, filtered and the filtrate was acidified. The N - [4 - (β - benzenesul-

phonylacetamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea precipitating in crystalline form was found to melt, after recrystallization from methanol, at 187—188°C.

In an analogous manner, there were obtained:

N - [4 - (β - benzenesulphonylacetamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl - cyclohexyl) - urea (trans) (melting point: 193—194°C) (from methanol/dimethylformamide);

from 4 - [β - (β - benzenesulphonyl - propionamido) - ethyl] - benzenesulphonamide (melting point: 128°C)

N - [4 - (β - <β - benzenesulphonyl - propionamido> - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 193—194°) (from methanol) and

N - [4 - (β - <β - benzenesulphonyl - propionamido> - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl - urea (trans) (melting point: 188—189.5°C) (from methanol).

EXAMPLE 62

N - [4 - (β - benzamido - propyl) - benzenesulphonyl] - N' - (3 - methoxypropyl)-urea

6 g of N - [4 - (β - benzamido - propyl) - benzenesulphonyl] - urethane (melting point: 76°C, prepared by the reaction of 4 - (β - benzamidopropyl) - benzenesulphonamide with chloroformic acid ethyl ester in acetone) were heated at the boil in 35 ml. of dioxan and 1.4 g of methoxypropylamine, while stirring, until the expected quantity of methanol had distilled off. The whole was concentrated under reduced pressure by half the volume, the residue was dissolved in 1% ammonia, filtered and the filtrate was acidified with hydrochloric acid.

The crude product obtained was recrystallized from a mixture of ethanol and water. (Melting point: 153°C).

In an analogous manner, there was prepared:

N - [4 - (β - benzamidopropyl) - benzenesulphonyl] - N' - furfuryl - urea (melting point: 170°C) (from ethanol/water).

EXAMPLE 63

N - [4 - chloro - 3 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl-cyclohexyl - urea (trans)

10 g of 4 - chloro - 3 - (β - benzamido - ethyl) - benzenesulphonamide (melting point: 193—195°C, obtained from 2 - (β - benzamido - ethyl) - chlorobenzene by the reaction with chlorosulphonic acid and subsequent treatment with ammonia were dissolved in 14.8 ml. of 2N - sodium hydroxide solution and 30 ml. of acetone and, at 0—5°C, 4.3 g of 4 - methylcyclohexyl isocyanate (trans) were added dropwise, while stirring. Stirring was continued for 3 hours, the whole was diluted with water and methanol, filtered and the filtrate was acidified with dilute hydrochloric acid. The urea obtained was suction-filtered and found to melt, after recrystallization from a mixture of dimethylformamide and water, at 179—180°C.

In an analogous manner, there were obtained:

N - [4 - chloro - 3 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 106—108°C) (with decomposition, contained 1 H_2O) (from methanol);

from 4 - chloro - 3 - (benzamidomethyl) - benzenesulphonamide (melting point: 163—165°C)

N - [4 - chloro - 3 - (benzamidomethyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 180°C) (from methanol) and

N - [4 - chloro - 3 - (benzamidomethyl) - benzenesulphonyl] - N' - (4 - methyl-cylohexyl) - urea (trans) (melting point: 182—183°C) (from methanol/water);

from 2,4,6 - trimethyl - 3 - (β - benzamidoethyl) - benzenesulphonamide (melting point: 198—200°C)

N - [2,4,6 - trimethyl - 3 - (β - benzamido - ethyl) - benzenesulphonyl] - N'-cyclohexyl - urea (melting point: 197—198°C) (from dimethylformamide/water),

N - [2,4,6 - trimethyl - 3 - (β - benzamido - ethyl) - benzenesulphonyl] - N'-butyl-urea (melting point: 209—211°C) (from dimethylformamide/water),

N - [2,4,6 - trimethyl - 3 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (4-methylcyclohexyl) - urea (trans) (melting point: 209—210°C) (from dimethylformamide/water), and

N - [2,4,6 - trimethyl - 3 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (4-ethylcyclohexyl) - urea (trans) (melting point: 197—199°C) (from dimethylformamide/water); and

from 4 - chloro - 3 - (4 - chlorobenzamidomethyl) - benzenesulphonamide (melting point: 130°C) (with decomposition)

N - [4 - chloro - 3 - (4 - chlorobenzamidomethyl) - benzenesulphonyl] - N' - (4-methylcyclohexyl) - urea (trans) (melting point: 210—211°C) (from dimethylformamide/water).

EXAMPLE 64

N - [4 - (β - 4 - phenyl - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea

3.2 g of N - [4 - (β - aminoethyl) - benzenesulphonyl] - N' - cyclohexyl - urea were dissolved in 5 cc. of 2N - sodium hydroxide solution; 2.2 g of *p* - diphenyl - carboxylic acid chloride were added dropwise and the whole was heated for 5 hours at 40° C. The reaction product was then suction-filtered, washed with ether and dissolved in dilute ammonia; after filtration, it was precipitated with dilute hydrochloric acid. Yield: 85%; (Melting point: 226—227°C).

EXAMPLE 65

N - [4 - (β - <α - phenylmercapto - acetamido> - ethyl) - benzenesulphonyl] - N'-cyclohexyl - urea

The compound was prepared in an analogous manner to that described in Example 64 from N - [4 - (β - aminoethyl) - benzenesulphonyl] - N' - cyclohexyl - urea and phenylmercaptoacetyl chloride. Melting point: 148—149°C after recrystallization from alcohol.

In an analogous manner, there was obtained:

N - [4 - (β - <α - phenyl - cyclopentane - carbonamido> - ethyl - benzenesulphonyl] - N' - cyclohexyl - urea. Melting point: 113—115°C after recrystallization from alcohol.

EXAMPLE 66

N - [3 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

A solution of 6.5 g of 3 - sulphamyl - benzyl cyanide was hydrogenated in 400 ml. of glacial acetic acid at normal pressure and at room temperature with palladium black as catalyst. After about 1 hour, the calculated amount of hydrogen was bound. The filtrate which had been separated from the catalyst was evaporated to dryness under reduced pressure, and syrupy-like residue was dissolved in 200 ml. of water, neutralized with sodium hydroxide solution and then combined with 2 mols of NaOH (calculated on the sulphonamide used). A slight turbidity was removed with charcoal. Subsequently, benzoyl chloride (about 10% excess) was added dropwise, while stirring. After 2 hours, the crystalline precipitate was dissolved by the addition of 2N - sodium hydroxide solution and the 3 - (β - benzamido - ethyl) - benzenesulphonamide was precipitated by adjusting the pH-value to 9. It was suction - filtered, washed with water and dried *in vacuo*. Yield: 85% of the theory, melting point: 159—160°C.

The sulphonamide thus obtained was reacted in aqueous - acetonic solution in the presence of sodium hydroxide solution with excess cyclohexyl isocyanate. On working up in the usual manner 31% of the sulphonamide used as starting material were reobtained and N - [3 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea was obtained as a product containing water of crystallization. Melting point: 115° C with decomposition. The substance contained about 1.5% of water of crystallization and was pure according to paper-chromatography.

In an analogous manner, there were obtained:

from 3 - (β - 4 - chlorobenzamido - ethyl) - benzenesulphonamide (melting point: 178—179°C)

N - [3 - (β - 4 - chlorobenzamidoethyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 118°C) (with decomposition) with a content of water of crystallization of about 1.2%;

from 3 - (β - 3,4 - dichlorobenzamidoethyl) - benzenesulphonamide (melting point: 144—145°C)

N - [3 - (β - 3,4 - dichlorobenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 130—135°C) (with decomposition) with a content of water of crystallization of about 2.3%;

from 3 - (β - 3 - fluorobenzamido - ethyl) - benzenesulphonamide (melting point: 147—148°C)

N - [3 - (β - 3 - fluorobenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 127—129°C) (from ethanol); and

from 3 - (β - 3 - methylbenzamidoethyl) - benzenesulphonamide (melting point: 149—150°C)

N - [3 - (β - 3 - methylbenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl-urea (melting point: 105—107°C) (with decomposition) with a content of water of crystallization of 0.9%.

EXAMPLE 67

N - [3 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl)-urea

30.4 g of the 3 - (β - benzamido - ethyl) - benzenesulphonamide prepared according to Example 66 were dissolved in 1 litre of acetone. After the addition of 41 g of potassium carbonate and 14 ml. of chloroformic acid ethyl ester, the whole was heated under reflux for 6 hours. After cooling, 200 ml. of water were added and the upper aqueous - acetonic layer was separated. The acetone was evaporated under reduced pressure, the residue was diluted with 600 ml. of water and the solution obtained was adjusted to a pH-value of 8.5 by means of dilute hydrochloric acid. The whole was allowed to stand for some hours and the sulphonamide used as starting material which had crystallized out was suction-filtered. The ethyl N - [3 - (β - benzamido - ethyl)-benzene sulphonyl] - urethane which, on acidifying the filtrate (pH 4) had precipitated as a viscous mass, was taken up in methylene chloride, and the solution obtained was dried over sodium sulphate and evaporated to dryness under reduced pressure. The residue (33 g) was dissolved in a mixture of 500 ml. of toluene and 100 ml. of dimethyl-formamide and, after the addition of 11.2 g of trans - 4 - methyl - cyclohexylamine, heated under reflux for 1 hour. After cooling, the whole was extracted with 500 ml. of 0.5N-sodium hydroxide solution and then once more with 250 ml. of 0.5N-sodium hydroxide solution.

The combined extracts were washed one time with ether and adjusted to a pH-value of 8.5 by means of dilute hydrochloric acid. A small quantity of a viscous precipitate was separated and then the whole was adjusted to a pH-value of 6 by the dropwise addition of dilute hydrochloric acid, while stirring. The N - [3 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methylcyclohexyl) - urea obtained as a product containing water of crystallization was found to melt at 115°C with decomposition. The substance contained about 1.2% of water of crystallization and was pure according to paper-chromatography.

In an analogous manner, there were obtained:

N - [3 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethyl) - cyclohexyl - urea (melting point: 120—125°) with a content of water of crystallization of about 1.2%;

N - [3 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - cyclooctyl - urea (melting point: 115—120°C) with a content of water of crystallization of about 1.5%, and

N - [3 - (β - benzamido - ethyl) - benzenesulphonyl] - N' - *n* - propyl - urea (melting point: 129—130°C) from ethanol).

In an analogous manner, there was, furthermore, obtained:

from ethyl N - [3 - (β - 4 - methylbenzamidoethyl) - benzenesulphonyl] - urethane (melting point: 189—190°C)

N - [3 - (β - 4 - methylbenzamidoethyl) - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 172—173°C) (from ethanol).

EXAMPLE 68

N - [2 - (β - benzamido - ethyl) - 4 - methoxy - benzenesulfonyl] - N' - n - butyl-urea

a) 65 g of 3 - β - benzamido - ethyl-methoxybenzene were dissolved in 156 ml. of chloroform. To the solution 125 g of chlorosulphonic acid were added dropwise, at −10—0°C, while vigorously stirring. The temperature of the reaction mixture was then allowed to rise to room temperature and, as soon as the evolution of hydrogen chloride and sulphur dioxide was complete, the reaction mixture was poured onto ice.

The aqueous phase was decanted, 300 ml. of concentrated ammonia were poured over the sulphochloride formed and then the whole was heated on a water bath. After a short time, the sulphonamide formed precipitated. It was cooled, suction-filtered and washed thoroughly with water. The 2 - β - benzamido - ethyl - 4 - methoxy - benzenesulphonamide having a melting point of 159—160°C was thus obtained.

b) 16.7 g of 2 - β - benzamido - ethyl - 4 - methoxy - benzenesulphonamide (melting point: 159—160°C) were suspended in 200 ml. of acetone and dissolved by the addition of 2 g of sodium hydroxide solution and water.

To this solution 5 g of *n* - butyl isocyanate were added dropwise at room temperature, while stirring, and stirring was continued for 2 hours. A slight precipitate

formed was suction-filtered and the filtrate was combined with water and hydrochloric acid. The whole was suction-filtered and the product was recrystallized from a mixture of ethanol and water. The N - [2 - (β - benzamido - ethyl) - 4 - methoxy - benzenesulphonyl] - N' - *n* - butyl - urea was found to melt at 146°C.

In an analogous manner, there were obtained:

N - [2 - (β - benzamido - ethyl) - 4 - methoxy - benzenesulphonyl] - N' - cyclohexyl - urea (melting point: 166°C) (from dilute ethanol);

N - [2 - (β - benzamido - ethyl) - 4 - methoxy - benzenesulphonyl] - N' - (4-ethyl - cyclohexyl) - urea (melting point: 168—170°C) (from dilute ethanol), and the

N - [2 - (β - benzamido - ethyl) - 4 - methoxy - benzenesulphonyl] - N' - (4-methyl - cyclohexyl) - urea (melting point: 167—169°C) (from dilute ethanol).

EXAMPLE 69

N - [-(β - 3,4 - methylenedioxybenzamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl - urea

9 g of 4 - (β - 3,4 - methylenedioxy - benzamidoethyl) - benzenesulphonamide (melting point 227°, from methanol) were suspended in 12.5 ml. of 2N - sodium hydroxide solution and 50 ml. of acetone and, at 0—5°, 3.4 g of cyclohexyl isocyanate were added dropwise. Stirring was continued for 3 hours, then the whole was dissolved by diluting with water, filtered and the filtrate was acidified with dilute acetic acid. The N - [4 - (β - 3,4 - methylenedioxy - benzamidoethyl) - benzenesulphonyl] - N'-cyclohexyl - urea obtained in crystalline form was found to melt after recrystallization from a mixture of methanol and dimethylforamamide at 208—210°.

In an analogous manner, there was obtained:

N - [4 - (β - 3,4 - methylenedioxy - benzamidoethyl) - benzenesulphonyl] - N'-(4 - methyl - cyclohexyl) - urea (trans) (melting point: 203—205°) (from methanol/dimethylformamide).

EXAMPLE 70

N - [4 - (β - benzamido - ethyl) - 2,3,5,6 - tetramethyl - benzenesulphonyl] - N'-cyclohexyl - urea

9 g of 4 - (β - benzamido - ethyl) - 2,3,5,6 - tetramethyl - benzenesulphonamide (melting point: 257°, from dimethylformamide/water) were suspended in 12.5 ml. of 2N - sodium hydroxide solution and 50 ml. of acetone and, at 0—5°, 3.2 g of cyclohexyl isocyanate were added dropwise. When stirring was continued for 3 hours the reaction mixture gradually dissolved. Subsequently, the whole was diluted with water and methanol, the undissolved matter was filtered off, the filtrate was acidified with dilute hydrochloric acid, and the precipitated N - [4 - (β - benzamido - ethyl) - 2,3,5,6-tetramethyl - benzenesulphonyl] - N' - cyclohexyl - urea was recrystallized from a mixture of dimethylformamide and water. (Melting point: 208—209°).

In an analogous manner, there was obtained:

N - [4 - (β - benzamido - ethyl) - 2,3,5,6 - tetramethyl - benzenesulphonyl] - N'-(4 - methyl - cyclohexyl) - urea (trans) melting point: 209—211°) (from dimethylformamide/water).

EXAMPLE 71

N - [4 - (β - 2 - diethylcarbamyl - benzamido - ethyl) - benzenesulphonyl] - N' - (4-methyl - cyclohexyl) - urea (trans)

12 g of 4-(β-2-diethylcarbamyl-benzamido-ethyl)-benzenesulphonamide (melting point: 190—192°, from methanol) were dissolved in the form of its sodium salt in 15 ml. of 2N - sodium hydroxide solution and 50 ml. of acetone and, at 0—5°, 4.3 g of 4 - methylcyclohexyl isocyanate (trans) were added dropwise. Stiring was continued for 3 hours; then the whole was diluted with water and a small quantity of methanol; the undissolved matter was filtered off and the filtrate was acidified. The N - [4 - (β - 2-diethylcarbamyl - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl - cyclohexyl) - urea (trans) crystallizing after a short time was recrystallized from methanol and was found to melt at 193—195°.

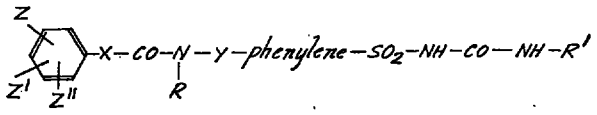
In an analogous manner, there was obtained:

from 4 - (β - 2 - benzyl - benzamido - ethyl) - benzenesulphonamide (melting point: 139—141°)

N - [4 - (β - 2 - benzyl - benzamido - ethyl) - benzenesulphonyl] - N' - (4 - methyl-cyclohexyl) - urea (trans) (melting point: 207—209°) (from methanol).

WHAT WE CLAIM IS:—

1. A compound of the general formula



in which

R represents a hydrogen atom or a lower alkyl or phenyl - lower alkyl group, R^1 represents

(a) an alkyl, an alkenyl or a mercaptoalkyl group, each containing 2 to 8 carbon atoms,

(b) an alkoxyalkyl, alkylmercaptoalkyl or alkylsulphinylalkyl group, each containing 4 to 8 carbon atoms and at least two of which carbon atoms forming the alkylene portion of the alkoxyalkyl, alkylmercaptoalkyl or alkylsulphinylalkyl group,

(c) a phenyl-lower alkyl or phenyl-cyclopropyl group,

(d) a cyclohexyl-lower alkyl, cycloheptylmethyl, cycloheptylethyl, or cyclooctylmethyl group,

(e) an endoalkylene cyclohexyl, endoalkylene cyclohexenyl, endoalkylene cyclohexyl methyl or endoalkylene cyclohexenylmethyl group, each containing 1 or 2 endoalkylene carbon atoms,

(f) a lower alkyl cyclohexyl or lower alkoxy cyclohexyl group,

(g) a cycloalkyl group containing 5 to 8 carbon atoms,

(h) a cyclohexenyl or cyclohexenylmethyl group,

(i) a heterocyclic ring containing 4 or 5 carbon atoms, 1 oxygen or sulphur atom and which may contain up to 2 ethylenic double bonds, or

(j) a heterocyclic ring as defined under (i) which is attached to the adjacent nitrogen atom via a methylene group,

X represents a single chemical bond or an aliphatic or a cycloaliphatic hydrocarbon bridge containing 1 to 6 carbon atoms and which may contain one —O— or —S— atom or one —SO— or —SO_2— group,

Y represents a hydrogen group containing 1 to 4 carbon atoms,

Z represents a hydrogen or halogen atom or a lower alkyl or lower alkoxy group, a cycloalkoxy group containing 5 or 6 carbon atoms, a cyclohexyl, lower alkyl mercapto, lower alkyl sulphinyl, lower alkyl sulphonyl, phenylsulphonyl, phenyl, phenyl - lower alkyl, lower acyl, benzoyl, trifluoromethyl, hydroxyl, lower acyloxy, benzyloxy, carboxyl, lower carbalkoxy, nitrile, carbamyl, lower alkyl carbamyl, lower dialkyl carbamyl or nitro group.

Z′ and Z″ each represents a hydrogen atom or — if Z represents a hydrogen or halogen atom or a hydroxyl, carboxyl, alkyl or alkoxy group—each may also represent a lower alkyl or lower alkoxy group or a halogen atom or—if Z represents a hydrogen atom—Z′ and Z″ may also together represent a methylenedioxy group of the formula —O—CH_2—O—, and the phenylene group is unsubstituted or is substituted by one or more substituents selected from halogen atoms, lower alkyl groups and lower alkoxy groups.

2. A compound as claimed in claim 1, wherein R represents a hydrogen atom.

3. A compound as claimed in claim 1 to 2, wherein R′ represents a cyclohexyl group.

4. A compound as claimed in claim 1 or 2, wherein R′ represents a 4 - methylcyclohexyl group.

5. A compound as claimed in any one of claims 1 to 4, wherein Z, Z′ and Z″ each represents a hydrogen atom.

6. A compound as claimed in any of claims 1 to 5, wherein Y represents a dimethylene group.

7. N - [4 - (β - Benzamidoethyl) - benzenesulphonyl] - N′ - cyclohexyl urea.

8. N - [4 - (β - Benzamidoethyl) - benzenesulphonyl] - N′ - (4 - methyl - cyclohexyl) - urea.

9. N - [4 - (β - 4 - Methyl - benzamido - ethyl) - benzenesulphonyl] - N′-cyclohexyl urea.

10. N - [4 - (β - 4 - Methyl - benzamido - ethyl) - benzenesulphonyl] - N′ - (4-methyl - cyclohexyl) - urea.

11. N - [4 - (β - 3 - Methyl - benzamido - ethyl) - benzenesulphonyl] - N′-cyclohexyl urea.

12. N - [4 - (β - 4 - Methoxy - benzamido - ethyl) - benzenesulphonyl] - N'-(4 - methyl - cyclohexyl) - urea.

13. N - [4 - (β - 4 - Chloro - benzamido - ethyl) - benzenesulphonyl] - N'-cyclohexyl urea.

14. N - [4 - (β - Phenylacetamido - ethyl) - benzenesulphonyl] - N' - (4-methyl-cyclohexyl) - urea.

15. N - [4 - (β - Phenoxyacetamido - ethyl) - benzenesulphonyl] - N' - cyclohexyl urea.

16. N - [4 - (β - <β - Phenoxypropionamido> - ethyl) - benzenesulphonyl]-N' - cyclohexyl urea.

17. N - [4 - (β - Benzamido - α - methyl - ethyl) - benzenesulphonyl] - N'-cyclohexyl urea.

18. N - [4 - (β - Benzamido - ethyl) - benzenesulphonyl] - N' - (4 - ethyl-cyclohexyl) - urea.

19. N - [4 - (Phenylacetamido - methyl) - benzenesulphonyl] - N' - (4 - methyl-cyclohexyl) - urea.

20. N - [4 - (β - <β - Phenylpropionamido>ethyl) - benzenesulphonyl] - N'-(4 - methyl - cyclohexyl) - urea.

21. N - [4 - (β - <3:4 - Dichlorophenylacetamido>ethyl) - benzenesulphonyl]-N' - cyclohexyl urea.

22. N - [4 - (β - Benzamidoethyl) - benzenesulphonyl] - N' - cyclooctyl urea.

23. A compound as claimed in claim 1, wherein R' represents a 4 - ethyl - cyclohexyl group.

24. A compound as claimed in claim 1 or 23, wherein Z represents a chlorine atom and Z' and Z'' each represents a hydrogen atom.

25. A compound as claimed in claim 1 or 23, wherein Z and Z' each represents a chlorine atom and Z'' represents a hydrogen atom.

26. A compound as claimed in claim 1 or 23, wherein Z represents a methyl group and Z' and Z'' each represents a hydrogen atom.

27. N - [4 - (β - <3 - Fluoro - benzamido>ethyl) - benzenesulphonyl] - N'-cyclohexyl urea.

28. A physiologically tolerable salt with a base of a compound as claimed in claim 1.

29. A physiologically tolerable salt with a base of a compound as claimed in any one of claims 2 to 6.

30. A physiologically tolerable salt with a base of the compound claimed in any one of claims 7 to 22.

31. A physiologically tolerable salt with a base of a compound as claimed in any one of claims 23 to 36.

32. A physiologically tolerable salt with a base of the compound claimed in claim 27.

33. A compound as claimed in claim 1 or 28 and described in any one of the Examples herein.

34. A process for the manufacture of a compound as claimed in claim 1 or 28, conducted substantially as described herein.

35. A pharmaceutical preparation which comprises a benzenesulphonyl urea as claimed in claim 1 in admixture or conjunction with a pharmaceutically suitable carrier.

36. A pharmaceutical preparation which comprises a compound as claimed in any one of claims 2 to 6 in admixture or conjunction with a pharmaceutically suitable carrier.

37. A pharmaceutical preparation which comprises the compound claimed in any one of claims 7 to 22 in admixture or conjunction with a pharmaceutically suitable carrier.

38. A pharmaceutical preparation which comprises a compound as claimed in any one of claims 23 to 26 in admixture or conjunction with a pharmaceutically suitable carrier.

39. A pharmaceutical preparation which comprises the compound claimed in claim 27 in admixture or conjunction with a pharmaceutically suitable carrier.

40. A pharmaceutical preparation which comprises a salt as claimed in claim 28 or 29 in admixture or conjunction with a pharmaceutically suitable carrier.

41. A pharmaceutical preparation which comprises a salt as claimed in claim 30 in admixture or conjunction with a pharmaceutically suitable carrier.

42. A pharmaceutical preparation which comprises a salt as claimed in claim 31 in admixture or conjunction with a pharmaceutically suitable carrier.

43. A pharmaceutical preparation which comprises a salt as claimed in claim 32 in admixture or conjunction with a pharmaceutically suitable carrier.

44. A pharmaceutical preparation as claimed in any one of claims 35 to 43, which is in a form suitable for oral administration.

45. A pharmaceutical preparation as claimed in any one of claims 35 to 44, which is in unit dosage form and contains up to 100 milligrams of the benzenesulphonyl urea or a physiologically tolerable salt thereof per unit dose.

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