1 505 636

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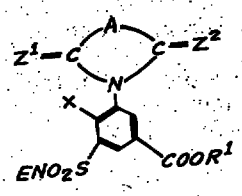
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(54) SULPHAMOYLBENZOIC ACID DERIVATIVES AND A PROCESS FOR THEIR PRODUCTION

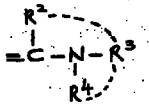
(71) We, HOECHST AKTIENGESELLSCHAFT, a body corporate organised according to the laws of the Federal Republic of Germany, of 6230 Frankfurt (Main) 80, Postfach 80 03 20, Federal Republic of Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to sulphamoyl benzoic acid derivatives and to a process for their preparation.

The present invention provides a compound of the general formula I



in which Z^1 and Z^2 each independently represents one oxygen atom or two hydrogen atoms, E represents the group



in which R^2, R^3 and R^4 represent identical or different lower alkyl groups and in which R^2 may also represent a hydrogen atom and/or two of the substituents R^2, R^3 and R^4 may be bound and, with the atom(s) to which they are attached, form a ring,

R^1 represents a hydrogen atom, a straight or branched chain alkyl group having from 1 to 4 carbon atoms, a cycloalkyl group having 5 or 6 ring members, one of which may be replaced by an oxygen or sulphur atom, a phenyl or benzyl group which may be substituted in the phenyl nucleus by one or more substituents selected from nitro groups, alkyl groups having from 1 to 3 carbon atoms, alkoxy groups having from 1 to 5 carbon atoms and halogen atoms, or represents a benzhydryl group or an alkanoyloxymethyl group having 2 to 4 carbon atoms in the alkanoyl part,

X represents a halogen atom, a CF_3 or CCl_3 group, a straight of branched chain, saturated or unsaturated aliphatic hydrocarbon group having up to 6 carbon atoms, a benzyl group which may be substituted in the phenyl nucleus by one or more substituents selected from halogen atoms, hydroxy, amino, alkylamino and dialkylamino groups, and lower alkyl and lower alkoxy groups, or represents one of the groups —O—R^5, —S—R^5, SO—R^5, SO_2—R^5 and NR^5R^6, in which R^5 represents a phenyl group which may be substituted by one or more substituents

selected from halogen atoms, CF_3, OH, amino alkylamino and dialkylamino groups, alkyl and alkoxy groups having from 1 to 4 carbon atoms, and SO_2NH_2 groups, or represents a straight or branched chain alkyl group having from 1 to 4 carbon atoms which may be substituted by a phenyl, pyridyl, furyl or thienyl group, and R^6 represents a hydrogen atom, a straight or branched chain alkyl group having from 1 to 4 carbon atoms, and the group NR^5R^6 may also represent a saturated, heterocyclic, 5- or 6-membered ring which may be interrupted by an O—, N— or S—atom.

A represents a single bond, or an alkylene chain of 1 to 3 carbon atoms which may be unsaturated, interrupted by O—, N— or S—atoms or substituted by one or more substituents selected from halogen atoms, alkyl, alkoxy, aralkyl, and aryl groups and mono-nuclear hetero-aromatic rings, or A represents an ortho-phenylene radicals or the grouping



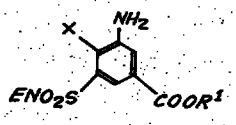
in which Y represents a single bond or an alkylene group having from 1 to 4 carbon atoms, and R^8 and R^7, which may be identical or different, each represents a hydrogen or halogen atom or an alkyl group having from 1 to 4 carbon atoms.

Preferred compounds of the formula I are those in which the radical R^1 represents a hydrogen atom, a lower alkyl group or a benzyl group which may be substituted as above; X represents a benzyl, $—OR^5$, $—SR^5$, or $—SO—R^5$, R^5 preferably representing a phenyl radical the phenyl moiety of which may be substituted in any position, and once or several times, by substituents selected from chlorine atoms, OH and CF_3 groups, straight or branched chain alkyl groups having from 1 to 3 carbon atoms, alkylamino, dialkylamino or alkoxy groups having 1 or 2 carbon atoms in the or each alkyl moiety or NH_2; and A represents a single bond or an alkylene or alkenylene chain of 1 or 2 carbon atoms which may be substituted once or several times by substituents selected from halogen atoms, phenyl and aralkyl groups, and lower alkyl and alkoxy groups.

The term "lower" is used herein to denote groups having up to 4 carbon atoms.

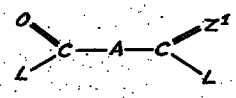
The invention also provides a process for the manufacture of a compound of the general formula I, which comprises

a) (i) reacting a compound of formula V



(V)

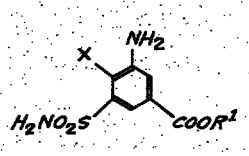
in which E, X and R^1 have the meanings given above, with a compound of the formula VI



(VI)

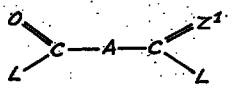
in which A and Z^1 have the meanings given above and L represents a "leaving group" or both symbols L together represent an oxygen atom, to give a compound of formula I in which Z^1 represents an oxygen atom or two hydrogen atoms and Z^2 represents an oxygen atom, or

a) (ii) reacting a compound of formula Va



(Va)

in which X and R^1 have the meanings given above, with a compound of formula VI



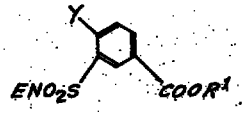
(VI)

in which A, Z^1 and L have the meanings given above and introducing the group E, which has the meaning given above, into the resulting compound to give a compound of formula I in which Z^1 represents an oxygen atom or two hydrogen atoms and Z^2 represents an oxygen atom and, if desired,

b) reducing the compound of formula I resulting from (a) (i) or (a) (ii) by means of a boron hydride to give the corresponding compound of formula I in which Z^1 and Z^2 each represents two hydrogen atoms.

The compound of formula V may be prepared by a reaction sequence which comprises

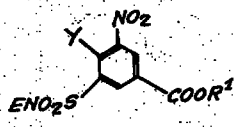
(x) nitrating a sulphamoylbenzoic acid derivative of the general formula II



(ii)

in which Y represents a halogen atom and E and R^1 are as defined above,

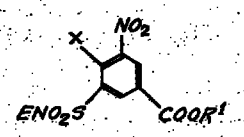
(y) reacting the resulting compound of formula III



(iii)

in which R^1, Y and E are as defined above, with a compound of formula XH in which X is as defined above,

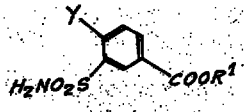
(z) reducing the resulting compound of formula IV



(iv)

in which E, X and R^1 have the meanings given above, to give a compound of formula V.

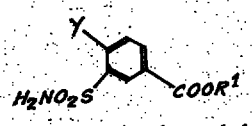
A compound of formula Va may be prepared by carrying out the reactions (x), (y) and (z) described above using the corresponding, unprotected compound of formula IIa



(iia)

as starting material. This process may be modified to produce a compound of formula V by introducing the group E into any of the intermediates i.e. into the unprotected compounds corresponding to compounds III, IV and V.

The benzoic acid derivatives of formula II used in the method of the invention may be prepared by various methods. The reaction is particularly simple to carry out when starting from a known sulphamoylbenzoic acid derivative of the formula IIa



(iia)

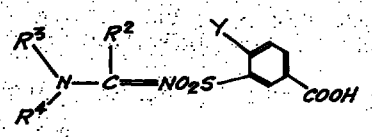
i.e. a compound which is unsubstituted in the sulphamoyl group, using one of the various known condensation methods. The compound of formula IIa is the starting material for producing the compound Va and also for the alternative method of producing compound V.

The following literature is cited by way of example of documents disclosing such methods which may also be used for introducing the group E into later intermediates.

J. Org. Chem. *25* (1960), 352—356; Zh. Org. Khim *8* (1972), 286—291; Liebigs Ann. Chem. *750* (1971), 42; Zh. Org. Khim. *6* (1970), 9,1855; B. *94* (1961), 2731—2737; Ang. Ch. *78* (1966), 147—148; Ang. Ch. *80* (1968), 281—282; B. *97* (1964),

483—389; B. *96* (1963), 802—812; J. Org. Chem. *27* (1962), 4566—4570; Ang. Ch. *74* (1962), 781—782, and Doklady Akad. SSSR *145* (1962), 584.

As the compound of the general formula II, there may be used, for example, any of the following derivatives:



Compound No.	R^2	R^3	R^4	Y
1	H	CH_3	CH_3	Cl
2	CH_3	CH_3	CH_3	Cl
3	H	C_2H_5	C_2H_5	Cl
4	C_4H_9	CH_3	CH_3	Cl
5	H	CH_3	CH_3	F
6	H	CH_3	CH_3	Br
7	CH_3	$-CH_2-CH_2-CH_2-CH_2-CH_2-$		Cl
8	$-CH_2-CH_2-CH_2-$		CH_3	Cl

A compound of the formula II may be prepared according to any of the above methods described in the literature or by an analogous method. Instead of the acids listed above as compounds 1 to 7, there may be used, for example, the corresponding methyl or ethyl ester.

Nitration of the benzoic acid derivatives of the formula II can be effected in various ways, for example, the benzoic acid derivative may be introduced into one of the nitrating mixtures conventionally used for the nitration of inert aromatic substances (cf. manual "Organicum", page 288, Edition 1967). The process may also be carried out by dissolving the benzoic acid derivative of the formula II in oleum and controlling the nitration by dropwise addition of nitric acid.

It is surprising that it is possible to nitrate a benzoic acid derivative of the general formula II without modification of other groups in the molecule merely by the introduction of the protective group E into the sulphonamide radical.

The reaction temperature is relatively low; preferably, temperatures in the range of from 55° to 70°C are maintained.

It is advantageous first to introduce into a suitable vessel a nitrating acid of oleum and fuming nitric acid, then to add the compound of formula II and to heat the reaction mixture to 55° to 60°C.

The course of the nitration can be followed by thin-layer chromatography. Isolation of the final product may be carried out in the usual manner, for example, by pouring the reaction mixture onto ice and separating by filtration the crystals that have precipitated.

As mentioned above, an acid or ester of the general formula II may be used. When an ester is used small amounts of the acid of the formula IIIa are generally obtained in addition to the ester. Such a resulting mixture can be separated in the usual manner, for example, by treatment with aqueous sodium carbonate. Any resulting acid of the formula IIIa may then be esterified in the usual manner, for example, it is converted into its acid chloride which, upon addition of an alcohol, yields the corresponding ester of the formula III. Esterification of the carboxylic acid group is preferable, especially for the optional final reduction step, but it can be carried out at a later stage, for example, immediately prior to reduction.

Suitable alcohols for the esterification are, in particular, alkyl alcohols having

from 1 to 4 carbon atoms, for example, methanol, ethanol, propanol, butanol, isopropanol or isobutanol, and aralkyl-alcohols, for example, benzyl-alcohols or benzhydrol. It is advantageous to use the alcohol in a 5- to 20-fold molar excess or to use it simultaneously as solvent. A tert. butyl ester or benzhydryl ester can be prepared according to other known methods.

In the next step, the compound of formula III is converted by reaction with a compound of the formula XH into a compound of formula IV. It is surprising that an ester of the general formula III especially one in which R^3 represents an alkyl group can be reacted under anhydrous conditions with good yields with compounds of the general formula XH.

As the compound of the formula XH, there may be used, for example, phenol, 4 - methylphenol, 3 - methylphenol, 2 - methylphenol, 4 -chlorophenol, 3 - trifluoromethylphenol, 3,5 - dimethylphenol, 2,4 - dimethylphenol, 4 - methoxyphenol, 3 - methoxyphenol, 4 - propylphenyl; thiophenol or a thiophenol substituted in the same manner as the phenols listed above; N - methylaniline, benzenesulphinic acid, pyrrolidine, N - methyl - piperazine, 5 - methyl - 2 - mercapto - 1,3,4 - thiadiazole, or 1 - methyl - 5 - mercapto - 1,2,3,4 - tetrazole. Any additionally present functional groups in XH as well as other OH-groups and/or NH_2 groups are blocked by the usual protective groups, for example by acylation.

Compounds of the general formula HOR^5 and HSR^5, in which the radical R^5 has the meanings given above, are of great importance. Among them, the thiophenol and phenol derivatives, which may be substituted as already indicated, are of particular importance.

The reaction may be carried out without a solvent, but it is advantageous to use a solvent. Particularly suitable solvents are organic solvents, for example, ether and tert. carboxamide, in particular diglym, dimethylformamide or hexamethylphosphoric acid-tris-amide (HMPT).

The compound X—H may be used as such in the presence of a base or may be used in the form of an alkali metal salt or alkaline earth metal salt thereof. As the base, an alcoholate or an alkali metal amide may be used.

The thiophenol or phenol derivative is reacted in the form of the anions thereof, among these, the alkali metal salts, especially the sodium and potassium salts, have proved particularly useful.

The reaction may be carried out in the presence or in the absence of a solvent. Without a solvent, the components are heated, for example, to a temperature within the range of from 100° to 200°C, preferably from 140° to 180°C. The resulting product can be isolated in the usual manner, for example, by dissolving the molten products in a solvent and subsequently precipitating them by the addition of water or of an organic non-solvent.

The reaction with a phenolate or thiophenolate in a solvent at a temperature within the range of from 100° to 200°C, preferably from 120° to 160°C, however, is particularly advantageous.

As the solvent, there may be used an organic solvent, in particular a tertiary carboxamide, polyether or high-boiling point solvent, for example, HMPT or tetramethylenesulphone. Particularly advantageous is the reaction of an ester of the formula III in a tertiary carboxamide, for example, dimethylformamide or dimethylacetamide. Depending on the reaction temperature selected, the reaction is generally completed after 1 to 6 hours.

The isolation of the compound of formula IV may be effected in the usual manner; for example, the inorganic salts are first filtered off and the reaction product is then precipitated by the addition of a non-solvent or the reaction mixture is poured into water or onto ice and the reaction product that has precipitated is isolated.

A compound of the formula IV in which X represents the group SOR^5 or SO_2R^5 may be obtained from the corresponding compound in which X represents the group SR^5 by oxidation according to a known method, for example, an S-oxide is obtained by oxidation with peracetic acid in dimethylformamide at a low temperature, while an S-dioxide is formed upon addition of an excess of an oxidizing agent at a more elevated temperature.

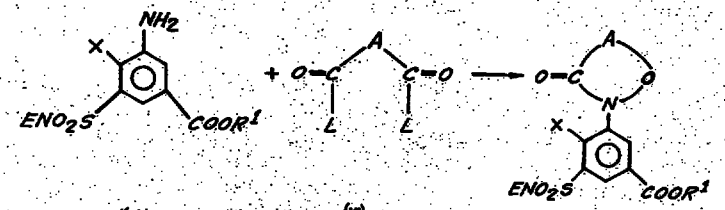
The reduction of the nitro group in a benzoic acid derivative of the formula IV may be effected in the usual manner, for example, by catalytic hydrogenation. As the catalyst, Raney nickel or a noble metal catalyst, for example, palladium on charcoal or platinum oxide, is preferably used (cf. for example Organokum, pages 271—277 pages 507—510).

As the solvent for the reduction, an organic solvent, for example, methanol or

ethanol, ethyl acetate, dioxane or another polar solvent, in particular an amide, for example, dimethylformamide, dimethylacetamide or HMPT, is preferably used. Hydrogenation may be effected at room temperature and increased pressure, for example, at 50°C and 100 atmospheres gauge in an autoclave.

A 3-imidobenzoic acid derivative of the general formula I (Z^1=O, Z^2=O) may be prepared in various ways. For example, it may be obtained by reacting the amino compound V with a dicarboxylic acid derivative of the general formula VI which is capable of forming an imide.

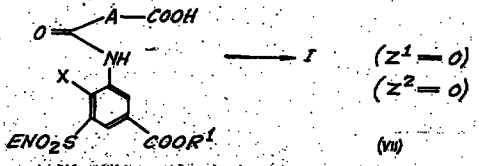
In the compound of formula VI, Z^1 represents an oxygen atom and the "leaving group" L is preferably a halogen atom, a trialkyl-ammonium group or the radical of an activated ester or of a mixed anhydride. For this acylation reaction, any hydroxyl and/or amino mercapto groups in other positions of the molecule should be blocked by means of customary protective groups.



(v) (vi) (I)

Examples of dicarboxylic acids which can be converted into the corresponding dicarboxylic acid halides are succinic acid, methylsuccinic acid, 2,3-dimethylsuccinic acid, glutaric acid, 2-methylglutaric acid, phthalic acid, cis-cyclopropanedicarboxylic acid, cyclobutane-1,2-cis-dicarboxylic acid, cyclohexane-1,2-cis-dicarboxylic acid, bromosuccinic acid and diglycolic acid. The reaction of such a dicarboxylic acid derivative with an amino compound of the formula V is generally carried out under the conditions of the known Schotten-Baumann reaction.

It is also possible to use an anhydride of a dicarboxylic acid as the compound of formula IV, especially an anhydride of one of the acids listed above or of maleic acid. The carboxylic acid derivative of the formula VII which is formed initially in many cases, changes into the imido compound of formula I directly, with elimination of water, generally on further increasing the temperature.

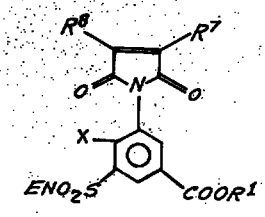


(vii)

The compound of formula VII may be isolated.

The reaction can be followed easily by thin layer chromatography because the compound of formula V fluoresces at 366 mμ, while the compounds of formulae VI and I show no fluorescence. Depending on the reaction conditions chosen, particularly if the reaction mixture is heated to a temperature of from 150 to 250°C, the cyclised product is obtained in high yields.

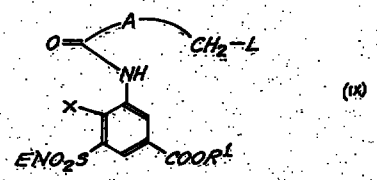
An anhydride is advantageously used in a substantial excess, for example, in a 2- or 3-fold excess, and the reaction is preferably carried out in the absence of a solvent. If an unsaturated dicarboxylic acid anhydride is used as compound VI, the corresponding unsaturated imido compound of formula I is obtained, for example, if maleic anhydride is used as the compound of formula VI, a viscous oil is formed on reaction with the amino compound of the formula V at a temperature from 150 to 200°C, and this oil changes after some time, with elimination of water, into the saturated imido compound of the formula VIII



(viii)

in which the radicals E, R^1, R^7, R^8 and X have the meanings given above. The double bond present in this imido compound makes possible a larger number of reactions, for example, it can be hydrogenated to give an imido compound of formula I in which Z^1 and Z^2 both represent oxygen atoms and A represents an ethylene group.

Compounds of formula I in which Z^1 represents two hydrogen atoms may be prepared by various processes, for example, from an amino compound of the formula V by reaction with an ω-substituted carboxylic acid derivative of the formula VI in which Z^1 represents two hydrogen atoms, according to the conditions of the Schotten-Baumann reaction and subsequent cyclisation of the resulting amido compound of the formula IX



(IX)

with elimination of H—L, for example, as described above by increasing the temperature.

The following are examples of carboxylic acid derivatives of the formula VI: ω-chloropropionic acid chloride, ω-chloropropionic acid bromide, ω-chlorobutyric acid chloride, ω-bromobutyric acid chloride, ω-bromobutyric acid phenyl ester and the chloride of trimethylammoniumbutyric acid chloride.

The base used for the elimination of the grouping H—L is preferably a tertiary organic base, for example, pyridine, triethylamine or N,N-dimethylaniline. The base may be used in a stoichiometric quantity or in a substantial excess, for example, when it is also used as the solvent.

An amido or imido derivative of the formula I (Z^1=O or H_2, Z^2=O) may be reduced according to the invention to give the corresponding compound in which Z^1 and Z^2 each represents two hydrogen atoms. The compound may be in the form of a free acid or in the form of a salt which does not interfere with the reduction, for example, an alkali metal salt or an alkaline earth metal salt.

In order to obtain particularly pure reaction products in high yield, it is advantageous to use a 5-sulphamoylbenzoic acid ester for the reduction. Such an ester can be prepared from the corresponding acid by a known process. Suitable esters are especially alkyl esters having from 1 to 5 carbon atoms, for example, methyl, ethyl, propyl, butyl and *n*-pentyl ester, benzyl, *p*-methoxybenzyl and *t*-butyl esters, benzhydryl esters, and acyloxymethyl esters wherein the acyl radical represents the radical of a lower aliphatic carboxylic acid, for example, an acetyl or tert.-butyryl radical.

Suitable boron hydride reducing agents are complex borohydrides or diborane in the presence of Lewis acids, and the diborane alone. In the reduction of a lactam of the formula II (Z^1=2H), it is possible to use diborane in the presence of a Lewis acid. An imide (Z^1=O), on the other hand, requires the use of a complex borohydride in the presence of a Lewis acid in order to obtain good yield. The reducing agent may be introduced into the reaction mixture while taking suitable protective measures, for example, the use of nitrogen as an inert gas. When diborane is used, it is simpler to take it up in a solvent and to use the resulting solution for the reduction. Suitable solvents are ethers, for example, tetrahydrofuran or diethylene glycol dimethyl ether.

The complex hydrides of boron used in this method of reduction are, for example, the alkali metal borohydrides, for example, lithium borohydride, sodium borohydride or potassium borohydride, the alkaline earth metal borohydrides, for example, calcium borohydride, and also zinc borohydride and aluminium borohydride. If a Lewis acid is added, this borohydride reduces the amide or imide groups present in the compound of formula I, and it is surprising that the carboxylic acid ester function is not appreciably attacked.

Suitable Lewis-acids are especially aluminium chloride, titanium tetrachloride, tin tetrachloride, cobalt-II chloride, iron-III chloride, mercury-I chloride, zinc chloride, and boron trifluoride and its addition products, for example, boron trifluoride etherate. In this case there is the possibility that diborane may be formed *in situ* in the reaction of the boron trifluoride etherate, for

example with sodium borohydride (c.f. Fieser, Fieser: Reagents for Organic Synthesis, John Wiley and Sons, Inc., New York, Vol. 1, page 199).

In order to obtain a particularly high yield and particularly pure end products, it is advantageous first to introduce the Lewis acid together with the compound of the formula I and then to add the complex borohydride.

It is particularly advantageous to use the Lewis acid in excess and the complex borohydride, in an at least stoichiometric quantity, relative to the amide group to be reduced. Thus, advantageous results are obtained by adding, for example in the case of titanium tetrachloride, three times the stoichiometric quantity of $NaBH_4$, and when using boron trifluoride etherate, by using the complex borohydride in the stoichiometric quantity, relative to the particular number of amide groups to be reduced.

In carrying out the reduction it is unimportant whether the substances to be reduced are introduced as imido compounds of the formula I i.e. Z^1 represents an oxygen atom or as amido compounds i.e. Z^1 represents two hydrogen atoms. The reduction is carried out in a solvent. Examples of suitable solvents are ethers, for example, tetrahydrofuran and diethylene glycol dimethyl ether (diglym). The solvent is which the reduction is carried out may be the same as that in which the boron hydride is dissolved, but can also be different therefrom.

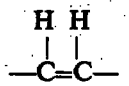
The reduction may be carried out within a wide range of temperatures, for example, at room temperature or at a slightly elevated temperature. While a secondary amine reacts with diborane and a lactam with diborane and a Lewis acid preferably at a slightly elevated temperature (40° to 60°C), the reduction with a complex borohydride and a Lewis acid, in particular with an imide, often proceeds favourably in the temperature range of from 0° to 20°C. If somewhat longer reaction times are acceptable, it is also possible to carry out the reduction in the cold. The duration of the reduction depends on the reaction components used and on the temperature selected.

In a preferred method of the process of the invention, the compound of formula I is first introduced together with the Lewis acid, in an inert solvent and then a solution of the complex borohydride or, if appropriate, a suspension of the complex borohydride in the same or a different solvent is added at room temperature and the mixture is stirred for a short time. The complex borohydride can also be added directly in solid form. In order to accelerate the reaction, it may also be carried out at elevated temperature or the mixture may be heated to 50° to 80°C for about 1 hour after completing the addition of the reducing agent.

Another method comprises first introducing the substance to be reduced together with the complex borohydride and then adding the Lewis acid at room temperature. Sodium borohydride is particularly suitable as the complex borohydride. Here too, it may be advantageous, to achieve a faster conversion, to heat the mixture to 40°—70°C for about 1 hour after the end of the addition of the Lewis acid. With the aid of thin layer chromatography it is possible to follow the progress of the reaction by the appearance of the intense light-blue fluorescence (in the region of 366 nm) of the resulting compound of the formula I. In the reduction according to the invention it is possible that any double bonds which may be present in the group A may be reduced simultaneously.

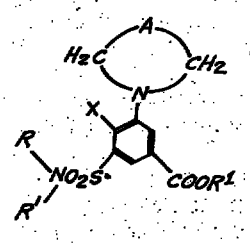
The resulting compound of formula I can be isolated in any of several ways. A preferred method of working up comprises adding water and small quantities of an acid in order to free the solution of the reaction product from any reducing agent which may still be present and then precipitating the resulting 5-sulphamoyl-benzoic acid ester by adding a non-solvent. When diethylene glycol dimethyl ether is used, a particularly suitable non-solvent is water. The resulting 5-sulphamoyl-benzoic acid ester of the formula I generally crystallises almost quantitatively with high purity. Subsequently, any substituents which are present in the radical X of the sulphamoylbenzoic acid derivatives of the general formula I and which are protected by protective groups may be liberated.

The reduction can be carried equally successfully with an imide or amide of formula I if the C—C chain contains substituents which are split off easily with formation of a carbon-carbon double bond. Thus, for example, a 3-pyrroline derivative of the formula I in which A represents a



group, is obtained when 2-bromosuccinic acid is used as the starting material for the reactant of the formula II.

The compounds of the general formula may be used in the production of compounds of the formula X



(X)

in which R^1, X and A are as defined above and R and R', which may be identical or different, each represents a hydrogen atom or an alkyl group having from 1 to 4 carbon atoms and, if R represents a hydrogen atom, R' may also represent an alkoxymethyl group having from 1 to 4 carbon atoms in the alkoxy radical, a phenoxymethyl group or a phenylthiomethyl group.

Compounds of formula X and processes for their production are described and claimed in our Co-pending Application No. 17337/75, (Serial No. 1,504,505).

Example 1:

a) 4 - Chloro - 5 - N,N - dimethylaminomethyleneaminosulphonylbenzoic acid.

90 ml (1.25 mols) of thionyl chloride are added dropwise, at –10°C, to a solution of 58.9 g (0.25 mol) of 4-chloro-5-sulphamoylbenzoic acid in 183 g (2.5 mols) of dimethylformamide (DMF). The solution is then allowed to reach room temperature, stirred for 2 hours and poured onto ice, the precipitate is filtered off and washed with water until neutral. 4-Chloro-5-N,N-dimethylaminomethyleneamino-sulphonylbenzoic acid is obtained (with a very good yield) in the form of crystals having a melting point of 266—267°C.

b) 3 - Nitro - 4 - chloro - 5 - N,N - dimethylaminomethyleneaminosulphonyl - benzoic acid.

42 ml of fuming nitric acid are added dropwise, while cooling with ice, to 60 ml of a 20% oleum, then 34.9 g (0.12 mol) of 4-chloro-5-N,N-dimethylaminomethyleneaminosulphonylbenzoic acid are introduced slowly. After having stirred for 24 hours at 55—60°C, the solution is cooled to room temperature, poured onto ice and the precipitate is washed with water until neutral. 3-Nitro-4-chloro-5-N,N-dimethylaminomethyleneaminosulphonylbenzoic acid is obtained in the form of crystals, m.p. 274—276°C.

c) 3 - Nitro - 4 - chloro - 5 - N,N - dimethylaminomethyleneaminosulphonyl - benzoic acid methyl ester.

50.4 g (0.15 mol) of 3-nitro-4-chloro-5-N,N-dimethylaminomethyleneaminosulphonylbenzoic acid are boiled for 1 hour under reflux in a solution of 150 ml of thionyl chloride which contains 5 drops of DMF. After removal of the excess thionyl chloride in vacuo, the solid acid chloride is suspended in 200 ml of methanol. The suspension is boiled for 1/2 hour under reflux, then cooled, filtered and washed with cold methanol. 3-Nitro-4-chloro-5-N,N-dimethylaminomethyleneaminosulphonylbenzoic acid methyl ester is obtained in the form of crystals, m.p. 168—169°C.

d) 3 - Nitro - 4 - phenoxy - 5 - N,N - dimethylaminomethyleneaminosulphonyl - benzoic acid methyl ester.

A solution of 105 g (0.3 mol) of 3-nitro-4-chloro-5-N,N-dimethylaminomethyleneaminosulphonylbenzoic acid methyl ester and 47.5 g (0.36 mol) of potassium phenolate in 600 ml of DMF is boiled for 2 hours under reflux. After cooling and removal of the potassium chloride by filtration, the solution is poured onto ice/water and stirred for 1 hour. The precipitate is filtered, washed with water and dried.

After dissolution of the raw product in 900 ml of acetone, the solution is clarified with charcoal, evaporated to 500 ml and diluted with 1 l of methanol. After having stirred for 1 hour at 10°C, the precipitate is filtered and washed with cold methanol. 3-Nitro-4-phenoxy-5-N,N-dimethylaminomethyleneamino-sulphonylbenzoic acid methyl ester is obtained in the form of crystals, m.p.: 191—193°C.

e) 3 - Amino - 4 - phenoxy - 5 - N,N - dimethylaminomethyleneaminosulphonyl - benzoic acid methyl ester.

61 g (0.15 mol) of 3-nitro-4-phenoxy-5-N,N-dimethylaminomethyleneamino-sulphonyl-benzoic acid methyl ester are hydrogenated with Raney nickel in methanol at room temperature and normal pressure for 8 hours. After filtration, the catalyst is suspended in warm DMF, filtered and the DMF filtrate is poured onto ice/water.

3 - Amino - 4 - phenoxy - 5 - N,N-dimethylaminomethyleneaminosulphonyl - benzoic acid methyl ester is obtained in the form of crystals, m.p.: 255—256°C.

f) 3 - N - Succinimido - 4 - phenoxy - 5 - N,N - dimethylaminomethyleneamino - sulphonyl - benzoic acid methyl ester.

30 g of 3-amino-4-phenoxy-5-N,N-dimethylaminomethyleneaminosulphonyl-benzoic acid methyl ester are fused at 180°C with 26 g of succinic anhydride. After a reaction time of about 2 hours the imide that has formed is precipitated with methanol. By recrystallization from *n*-butanol, the imide is obtained with a very good yield, m.p.: 283—284°C.

g) 4 - Phenoxy - 3 - (1 - pyrrolidinyl) - 5 - N,N - dimethylaminomethyleneamino - sulphonyl - benzoic acid methyl ester.

23 g (0.05 mol) of 3-N-succinimido-4-phenoxy-5-N,N-dimethylamino-methyleneaminosulphonyl-benzoic acid methyl ester are suspended in 200 ml of diethylene glycol dimethyl ether (diglyme) and 13 ml of BF_3-etherate (0.1 mol) are added. Then, a solution of 3.8 g (0.1 mol) of $NaBH_4$ in 200 ml of diglym is slowly added dropwise while cooling and keeping the temperature in the range of from −10 to +5°C. The mixture is allowed to reach room temperature, whereupon a clear solution is formed. The reaction is completed after 1.25 hours. The product precipitates by the addition of water. By recrystallization from methanol, there is obtained the 4-phenoxy-3-(1-pyrrolidinyl)-5-N,N-dimethylaminomethylene-amino-sulphonyl-benzoic acid ester, m.p.: 189—190°C.

Example 2:

The reaction sequence indicated in Example 1 is repeated until step c). The 3-nitro-4-chloro-5-N,N-dimethylaminomethyleneamino-sulphonyl-benzoic acid methyl ester obtained is subsequently heated with potassium phenolate for 2 hours to 190—200°C. The reaction mixture is cooled, taken up in acetone and, after having separated the inorganic components, worked up in the manner described in step d). 3-Nitro-4-phenoxy-5-N,N-dimethylaminomethyleneamino-sulphonyl-benzoic acid methyl ester is obtained, which is converted in the manner described in Example 1 into the final product described therein.

Example 3:

a) The reaction sequence indicated in Example 1 is repeated with the difference that the catalytic hydrogenation of the 3-nitro-4-phenoxy-5-N,N-dimethylaminomethyleneamino-sulphonyl-benzoic acid methyl ester is carried out in the autoclave at 50°C and 50 atmospheres. After cooling, the desired 3-amino-4-phenoxy-5-N,N-dimethylaminomethyleneamino-sulphonyl-benzoic acid methyl ester is isolated in the manner described in Example 1 e).

b) The reaction sequence indicated in Example 1 is repeated with the difference that the catalytic hydrogenation of the 3-nitro-4-phenoxy-5-N,N-dimethylaminomethyleneamino-sulphonyl-benzoic acid methyl ester is carried out in dimethylformamide (DMF) with Raney nickel at room temperature and normal pressure. After removal of the catalyst by filtration, the DMF solution is poured onto ice. 3-Amino-4-phenoxy-5-N,N-dimethylaminomethyleneamino-sulphonyl-benzoic acid methyl ester is obtained, m.p.: 255—256°C.

In each case, the 3-amino compound was converted to the 3-(1-pyrrolidinyl) compound described in Example 1.

Example 4:

The reaction sequence indicated in Example 1 is repeated with the difference that the 4-chloro-5-N,N-dimethylaminomethyleneamino-sulphonyl-benzoic acid methyl ester is used as the starting compound.

a) 4 - Chloro - 5 - N,N - dimethylaminomethyleneaminosulphonyl - benzoic acid methyl ester.

90 ml (1.25 mols) of thionyl chloride are added dropwise, at −10°C, to a

solution of 74.9 g (0.3 mol) of 4-chloro-5-sulphamoyl-benzoic acid methyl ester in 183 g (2.5 mlos) of dimethylformamide, and working up is effected as described in Example 1. In this way, 4-chloro-5-N,N-dimethylaminomethyleneamino-sulphonyl-benzoic acid methyl ester is obtained, m.p.: 174—176°C.

b) 3 - Nitro - 4 - chloro - 5 - N,N - dimethylaminomethyleneaminosulphonyl - benzoic acid methyl ester.

36.5 g (0.12 mol) of 4-chloro-5-N,N-dimethylaminomethyleneaminosulphonyl-benzoic acid methyl ester are reacted under the same conditions as those indicated in Example 1 b). A mixture of 3-nitro-4-chloro-5-N,N-dimethylamino-methyleneamino-sulphonyl-benzoic acid and 3-nitro-4-chloro-5-N,N-dimethyl-aminomethyleneaminosulphonyl-benzoic acid methyl ester is obtained. The mixture is separated by treating it with a 5% aqueous sodium carbonate. 3-Nitro-4-chloro-5-N,N-dimethylaminomethyleneamino-sulphonyl-benzoic acid methyl ester having a melting point of 168—169°C and, after acidification, 3-nitro-4-chloro-5-N,N-dimethylaminomethyleneamino-sulphonyl-benzoic acid having a melting point of 270—272°C are obtained; the latter can also be converted into the ester in the manner described in Example 1 c).

The further reactions are then effected according to the reaction sequence described in Example 1 to give the final product described therein.

Example 5:

The nitration described in Example 1 is carried out with the difference that the ethyl ester is used instead of the methyl ester.

a) 4 - Chloro - 5 - N,N - dimethylaminomethyleneaminosulphonylbenzoic acid ethyl ester.

90 ml (1.25 mols) of thionyl chloride are added dropwise at −10°C to a solution of 65 g (0.25 mol) of 4-chloro-4-sulphamoyl-benzoic acid ethyl ester in 183 g (2.5 mols) of DMF and working up is effected as in Example 1. 4-Chloro-5-N,N-dimethylaminomethyleneamino-sulphonyl-benzoic acid ethyl ester is obtained in the form of crystals, m.p.: 119—121°C.

b) 3 - Nitro - 4 - chloro - 5 - N,N - dimethylaminomethyleneaminosulphonyl - benzoic acid ethyl ester.

38.3 g (0.12 mol) of 4-chloro-5-N,N-dimethylaminomethyleneaminosulphonyl-benzoic acid ethyl ester are reacted under the same conditions as indicated in Example 4. Separation of the nitro ester and the nitro acid is effected as indicated in Example 5. 3-Nitro-4-chloro-5-N,N-dimethylaminomethyleneamino-sulphonyl-benzoic acid ethyl ester is obtained in the form of crystals having a melting point of 182—184°C, and, after acidification of the aqueous solution, 3-nitro-4-chloro-5-N,N-dimethylaminomethyleneaminosulphonyl-benzoic acid is obtained in the form of crystals having a melting point of 270—272°C, which, according to melting point and mixture is identical with the carboxylic acid described in Example 1 b). This is then reacted according to Example 1 to give the final product described therein.

Example 6:

4 - Phenylthio - 3 - (1 - pyrrolidinyl) - 5 - sulphamoylbenzoic acid.

The reaction sequence described in Example 1 for the preparation of 3-nitro-4-chloro-5-N,N-dimethylaminomethyleneaminosulphonylbenzoic acid methyl ester is repeated.

a) 3 - Nitro - 4 - phenylthio - 5 - N,N - dimethylaminomethyleneaminosulphonyl - benzoic acid methyl ester.

A solution of 21 g (0.06 mol) of 3-nitro-4-chloro-5-N,N-dimethylamino-methyleneaminosulphonylbenzoic acid methyl ester, 7.7 g (0.07 mol) of thiophenol and 8.2 g (0.077 mol) of sodium carbonate in 100 ml of DMF is boiled for 2 hours under reflux. After cooling and filtration, the solution is poured onto a mixture of ice and water and stirred for 1 hour. The precipitate is filtered off, washed with water and dried. The raw product is recrystallized from acetone/methanol. 3-Nitro-4-phenylthio-5-N,N-dimethylaminomethyleneaminosulphonyl-benzoic acid methyl ester is obtained in the form of crystals melting at 207°C.

b) 3 - Amino - 4 - phenylthio - 5 - N,N - dimethylaminomethyleneaminosulphonyl - benzoic acid methyl ester.

2 g (0.0047 mol) of 3-nitro-4-phenylthio-5-N,N-dimethylaminomethyleneaminosulphonylbenzoic acid methyl ester are hydrogenated for 8 hours with Raney nickel in 30 ml of DMF at room temperature and normal pressure. The catalyst is removed by filtration with suction, washed with warm DMF and the DMF filtrate is poured onto a mixture of ice and water.

3 - Amino - 4 - phenylthio - 5 - N,N - dimethylaminomethyleneamino - sulphonylbenzoic acid methyl ester is obtained from acetone in the form of crystals melting at 214—215°C.

c) 3 - N - Succinimido - 4 - phenylthio - 5 - N,N - dimethylaminomethylene - aminosulphonylbenzoic acid methyl ester.

35 g (0.089 mol) of 3-amino-4-phenylthio-5-dimethylaminomethyleneamino-sulphonyl-benzoic acid methyl ester are finely triturated with 26.6 g (0.2668 mol) of succinic anhydride and fused for 2 hours at 175°C. After cooling to 150°C, the whole is diluted with 100 ml of DMF and the solution is poured slowly onto a mixture of ice and water. The precipitate is filtered off with suction, dried and recrystallised from DMF/CH_3OH. M.p. 261—263°C.

d) 4 - Phenylthio - 3 - (1 - pyrrolidinyl) - 5 - N,N - dimethylaminomethylene - aminosulphonyl - benzoic acid methyl ester.

A solution of 5.1 g of $NaBH_4$ in 135 ml of absolute diglym is added dropwise, at a temperature of 0°—10°C, while stirring well, to a solution of 32 g of 3-N-succinimido - 4 - phenylthio - 5 - N,N - dimethylaminomethyleneaminosulphonyl - benzoic acid methyl ester and 17.5 ml of BF_3-etherate in 135 ml of absolute diglyme. After 2 hours, the whole is hydrolysed and the product is precipitated by further addition of water.

e) The raw product that has precipitated is heated under reflux with a 2 N—NaOH until a clear solution is formed. The 4-phenylthio-3-(1-pyrrolidinyl)-5-sulphamoylbenzoic acid is precipitated with the aid of 2N—HCl and recrystallised from CH_3OH/H_2O. M.p. 237—238°C (see also Example 33).

Example 7.

4 - Phenylthio - 3 - [1 - (3 - methylpyrrolidinyl)] - 5 - sulphamoylbenzoic acid.

a) 3 - Amino - 4 - phenylthio - 5 - N,N - dimethylaminomethyleneaminosulphonyl - benzoic acid methyl ester.

A solution of 110 g of 3-nitro-4-phenylthio-5-N,N-dimethylaminomethyleneaminosulphonylbenzoic acid methyl ester in 400 ml of DMF is hydrogenated for 8 hours over ~ 10 g of Raney nickel at 40°C and 100 atmospheres gauge pressure. The catalyst is filtered off and the solution is poured onto ice. The precipitate is filtered off, dried and recrystallised from acetone. M.p. 214°—215°C.

b) 3 - N - (3 - Methylsuccinimido) - 4 - phenylthio - 5 - N,N - dimethylamino - methyleneaminosulphonyl - benzoic acid methyl ester.

40 g (0.1 mol) of 3-amino-4-phenylthio-5-N,N-dimethylaminomethyleneaminosulphonylbenzoic acid methyl ester are fused with 34 g (0.3 mol) of methylsuccinic anhydride for 2.5 hours at 175°C. After cooling to 150°C, the mixture is diluted with 100 ml of DMF and the solution is poured slowly onto a mixture of ice and water. The precipitate is filtered off with suction and recrystallised from CH_3OH. M.p. 206°—207°C.

c) 4 - Phenylthio - 3 - [1 - (3 - methylpyrrolidinyl)] - 5 - N,N - dimethylamino - methyleneaminosulphonyl - benzoic acid methyl ester.

A solution of 4.65 g of $NaBH_4$ in 120 ml of absolute diglym is added dropwise, at 0°—10°C, to a solution of 29.4 g of 3-N-(3-methylsuccinimido)-4-phenylthio-5-N,N-dimethylaminomethyleneaminosulphonyl-benzoic acid methyl ester and 15.9 ml of BF_3-etherate in 120 ml of absolute diglym. After having stirred for 2 hours, the reaction product is precipitated cautiously with water. Recrystallisation from CH_3OH. M.p. 147°—148°C.

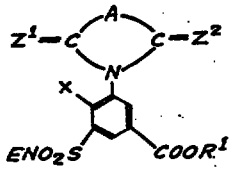
d) 4 - Phenylthio - 3 - [1 - (3 - methylpyrrolidinyl)] - 5 - sulphamoylbenzoic acid.

4 g of the ester of step c) are heated for 2 hours under reflux in 40 ml of 2NNaOH. A clear solution is formed. After cooling and acidification with 2NHCl

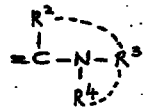
to pH 2—3, the 4-phenylthio-3-[1-(3-methylpyrrolidinyl)]-5-sulphamoylbenzoic acid precipitates. It is recrystallised from CH_3OH/H_2O. Yellow crystals melting at 216°—217°C.

WHAT WE CLAIM IS:—

1. A compound of the general formula I



in which Z^1 and Z^2 each independently represents one oxygen atom or two hydrogen atoms, E represents the group

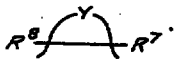


in which R^2, R^3 and R^4 represent identical or different lower alkyl groups and in whch R^2 may also represent a hydrogen atom and/or two of the constituents R^2, R^3 and R^4 may be bound and, with the atom(s) to which they are attached, form a ring.

R^1 represents a hydrogen atom, a straight or branched chain alkyl group having from 1 to 4 carbon atoms, a cycloalkyl group having 5 or 6 ring members, one of which may be replaced by an oxygen or sulphur atom, a phenyl or benzyl group which may be substituted in the phenyl nucleus by one or more substituents selected from nitro groups, alkyl groups having from 1 to 3 carbon atoms, alkoxy groups having from 1 to 5 carbon atoms and halogen atoms, or represents a benzhydryl group or a alkanoyloxymethyl group having 2 to 4 carbon atoms in the alkanoyl part,

X represents a halogen atom a CF_3 or CCl_3 group, a straight or branched chain, saturated or unsaturated aliphatic hydrocarbon group having up to 6 carbon atoms, a benzyl group which may be substituted in the phenyl nucleus by one or more substituents selected from halogen atoms, CF_3, hydroxy and amino, alkylamino and dialkylamino groups, and lower alkyl and lower alkoxy groups, or represents one of the groups —O—R^5, —S—R^5, SO—R^5, SO_2—R^5 and NR^5R^6, in which R^5 represents a phenyl group which may be substituted by one or more substituents selected from halogen atoms, CF_3, OH and amino groups, alkyl and alkoxy groups having 1 to 4 carbon atoms, and SO_2NH_2 groups, or represents a straight of branched chain alkyl group having from 1 to 4 carbon atoms which may be substituted by a phenyl, pyridyl, furyl or thienyl group, and R^6 represents a hydrogen atom, a straight or branched chain alkyl group having from 1 to 4 carbon atoms, and the group NR^5R^6 may also represent a saturated, heterocyclic, 5- or 6-membered ring which may be interrupted by an O—, N— or S—atom.

A represents a single bond, or an alkylene chain of 1 to 3 carbon atoms which may be unsaturated, interrupted by O—, N— or S—atoms or substituted by one or more substituents selected from halogen atoms, alkyl, alkoxy, aralkyl, and aryl groups and mono-nuclear hetero-aromatic rings, or A represents an ortho-phenylene radical or the grouping



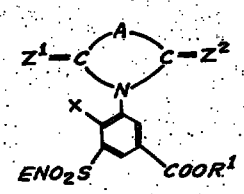
in which Y represents a single bond or an alkylene group having from 1 to 4 carbon atoms, and R^8 and R^7, which may be identical or different, each represents a hydrogen or halogen atom or an alkyl group having from 1 to 4 carbon atoms.

2. A compound as claimed in claim 1, in which X represents a benzyl, phenoxy, phenylthio, phenylsulphoxy, phenylsulphonyl or anilino group the phenyl ring of which may be substituted by one or more substituents selected from halogen atoms, OH and CF_3 groups, alkyl groups having from 1 to 4 carbo atoms, alkoxy groups having from 1 to 4 carbon atoms, and alkyl- and dialkyl-amino groups.

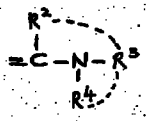
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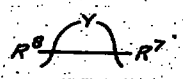


in which R^2, R^3 and R^4 represent identical or different lower alkyl groups and in whch R^2 may also represent a hydrogen atom and/or two of the constituents R^2, R^3 and R^4 may be bound and, with the atom(s) to which they are attached, form a ring.

R^1 represents a hydrogen atom, a straight or branched chain alkyl group having from 1 to 4 carbon atoms, a cycloalkyl group having 5 or 6 ring members, one of which may be replaced by an oxygen or sulphur atom, a phenyl or benzyl group which may be substituted in the phenyl nucleus by one or more substituents selected from nitro groups, alkyl groups having from 1 to 3 carbon atoms, alkoxy groups having from 1 to 5 carbon atoms and halogen atoms, or represents a benzhydryl group or a alkanoyloxymethyl group having 2 to 4 carbon atoms in the alkanoyl part,

X represents a halogen atom a CF_3 or CCl_3 group, a straight or branched chain, saturated or unsaturated aliphatic hydrocarbon group having up to 6 carbon atoms, a benzyl group which may be substituted in the phenyl nucleus by one or more substituents selected from halogen atoms, CF_3, hydroxy and amino, alkylamino and dialkylamino groups, and lower alkyl and lower alkoxy groups, or represents one of the groups —O—R^5, —S—R^5, SO—R^5, SO_2—R^5 and NR^5R^6, in which R^5 represents a phenyl group which may be substituted by one or more substituents selected from halogen atoms, CF_3, OH and amino groups, alkyl and alkoxy groups having 1 to 4 carbon atoms, and SO_2NH_2 groups, or represents a straight of branched chain alkyl group having from 1 to 4 carbon atoms which may be substituted by a phenyl, pyridyl, furyl or thienyl group, and R^6 represents a hydrogen atom, a straight or branched chain alkyl group having from 1 to 4 carbon atoms, and the group NR^5R^6 may also represent a saturated, heterocyclic, 5- or 6-membered ring which may be interrupted by an O—, N— or S—atom.

A represents a single bond, or an alkylene chain of 1 to 3 carbon atoms which may be unsaturated, interrupted by O—, N— or S—atoms or substituted by one or more substituents selected from halogen atoms, alkyl, alkoxy, aralkyl, and aryl groups and mono-nuclear hetero-aromatic rings, or A represents an ortho-phenylene radical or the grouping



in which Y represents a single bond or an alkylene group having from 1 to 4 carbon atoms, and R^8 and R^7, which may be identical or different, each represents a hydrogen or halogen atom or an alkyl group having from 1 to 4 carbon atoms.

2. A compound as claimed in claim 1, in which X represents a benzyl, phenoxy, phenylthio, phenylsulphoxy, phenylsulphonyl or anilino group the phenyl ring of which may be substituted by one or more substituents selected from halogen atoms, OH and CF_3 groups, alkyl groups having from 1 to 4 carbo atoms, alkoxy groups having from 1 to 4 carbon atoms, and alkyl- and dialkyl-amino groups.

* C L M S *

3. A compound as claimed in claim 1, in which A represents a —CH_2—CH_2— or —CH=CH— group which may be substituted by one or more substituents selected from halogen atoms, lower alkyl, lower alkoxy, aralkyl and phenyl groups.

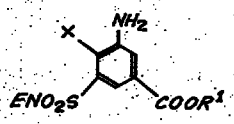
4. A compound as claimed in claim 1, in which X and A have the meanings specified in claims 2 and 3 respectively.

5. A compound as claimed in claim 1 and which is described in Example 1 or Example 6 herein.

6. A salt of a compound as claimed in any one of claims 1 to 4, in which R^1 represents a hydrogen atom.

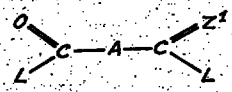
7. A process for the manufacture of a compound as claimed in claim 1, which comprises

a) (i) reacting a compound of formula V



(V)

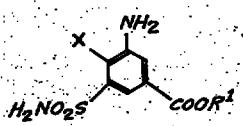
in which E, X and R^1 have the meanings given in claim 1, with a compound of the formula VI



(VI)

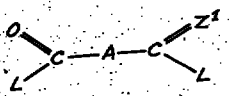
in which A and Z^1 have the meanings given in claim 1 and L represents a "leaving group" or both symbols L together represent an oxygen atom, to give a compound of formula I in which Z^1 represents an oxygen atom or two hydrogen atoms and Z^2 represents an oxygen atom, or

(ii) reacting a compound of formula Va



(Va)

in which X and R^1 have the meanings given in claim 1, with a compound of formula VI



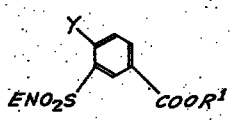
(VI)

in which A, Z^1 and L have the meanings given in claim 1 and introducing the group E, which has the meaning given in claim 1, into the resulting compound to give a compound of formula I in which Z^1 represents an oxygen atom or two hydrogen atoms and Z^2 represents an oxygen atom and, if desired,

b) reducing the compound of formula I resulting from (a) (i) or (a) (ii) by means of a boron hydride to give the corresponding compound of formula I in which Z^1 and Z^2 each represents two hydrogen atoms.

8. A process as claimed in claim 7, wherein a compound of formula V is prepared by a process which comprises

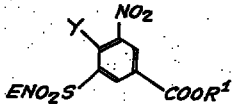
(x) nitrating a sulphamoylbenzoic acid derivative of the general formula II



(II)

in which Y represents a halogen atom and E and R^1 are as defined in claim 1,

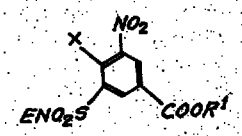
(y) reacting the resulting compound of formula III



(III)

* C L M S *

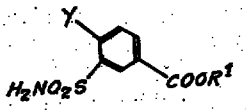
in which R^1, Y and E are as defined in claim 1, with a compound of formula XH in which X is as defined above,
(z) , reducing the resulting compound of formula IV



(IV)

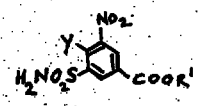
in which E, X and R^1 have the meanings given in claim 1, to give a compound of formula V.

9. A process as claimed in claim 7, wherein a compoun of formula Va is prepared by a process which comprises
(x') nitrating a sulphamoylbenzoic acid derivative of the general formula IIa



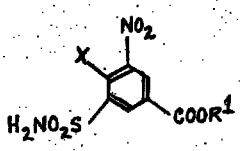
(IIa)

in which Y represents a halogen atom and R^1 is as defined in claim 1.
(y'), reacting the resulting compoud of formula IIIa



(IIIa)

in which R^1, and Y are as defined in claim 1, with a compound of formula XH in which X is as defined above,
(z') reducing the resulting compound of formula IVa



(IVa)

in which X and R^1 have the meanings given in claim 1.

10. A process as claimed in claim 7, wherein a compound of formula V is produced by a process as claimed in claim 9, wherein the group E is introduced into any one of the compounds of formulae IIIa, IVa, and Va.

11. A process as claimed in claim 8, wherein any resulting compound of formula III in which R^1 represents a hydrogen atom is esterified.

12. A process as claimed in any one of claims 8 to 11, wherein R^1 represents an alkyl group having from 1 to 4 carbon atoms.

13. A process as claimed in any one of claims 8 to 12, wherein the compound of formula XH is used in the form of an alkali metal or alkaline earth metal salt or in the presence of a base.

14. A process as claimed in any one of claims 8 to 13, wherein a resulting compound of formula IV or IVa is which X represents the group —SR^5 in which R^5 is as defined in claim 1, is converted to the corresponding compound in which X represents —SOR^5 or —SO_2R^5.

15. A process as claimed in any one of claims 7 to 14, wherein in the compound of formula VI the "leaving group" L is a halogen atom, a trialkylammonium group, or the radical of an activated ester or of a mixed anhydride.

16. A process as claimed in claim 7, carried out substantially as described in any one of the Examples herein.

17. A compound as claimed in claim 1, whenever produced by a process as claimed in any one of claims 7 to 16.

* C L M S *

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