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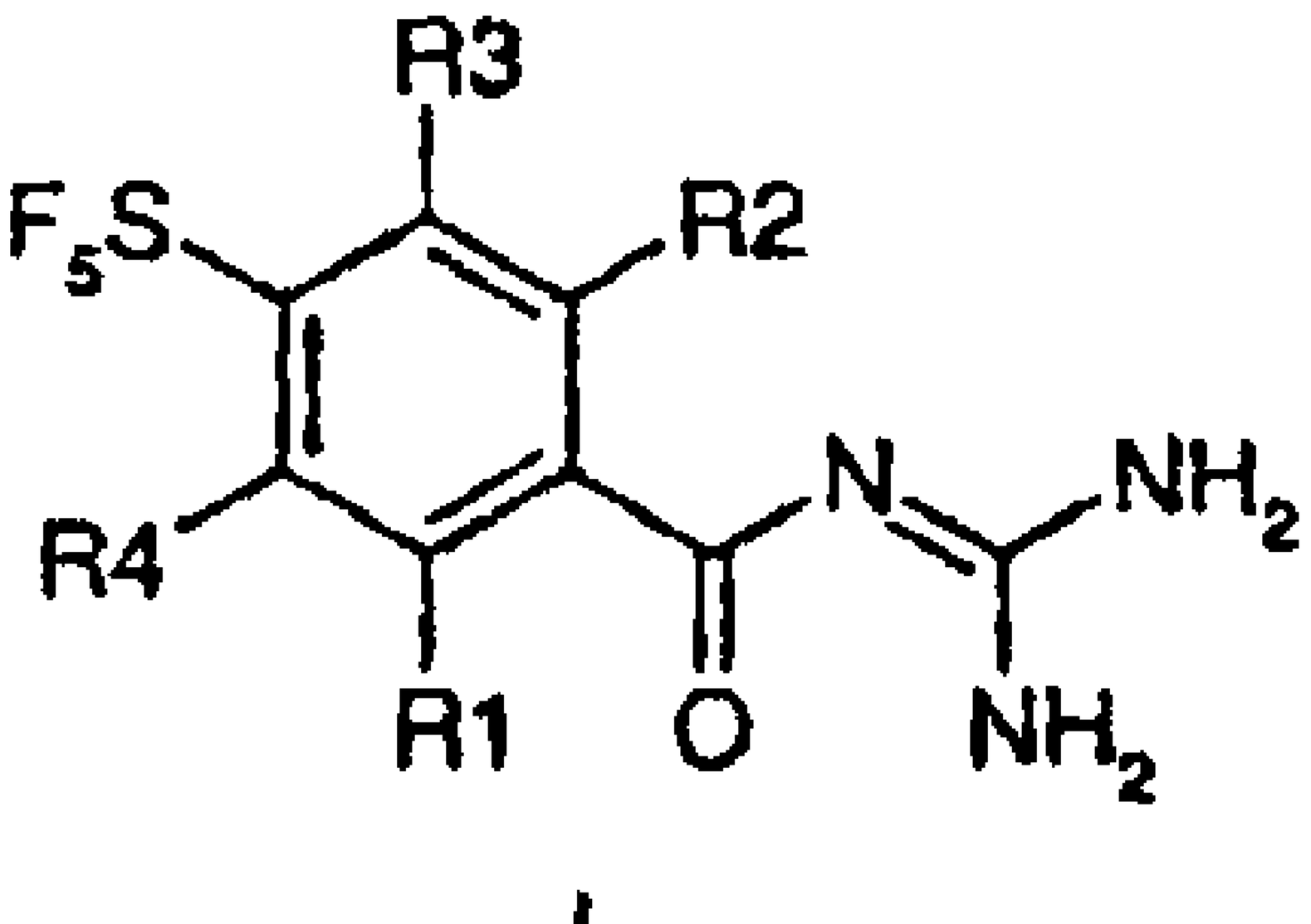
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(54) Titre : PROCEDE DE PRODUCTION DE 4-PENTAFLUOROSULFANYLBENZOYLGUANIDINES
(54) Title: METHOD FOR PRODUCING 4-PENTAFLUORIDE-SULFANYL-BENZOYLGUANIDINES




(57) Abrégé/Abstract:
The invention relates to a method for producing 4-pentafluoride-sulfanyl-benzoylguanidines of formula (I) wherein groups from R1 to R4 correspond to meanings given in claims. The compounds of the formula (I) constitute NHE1 inhibitors and can be used for curing cardiovascular diseases.

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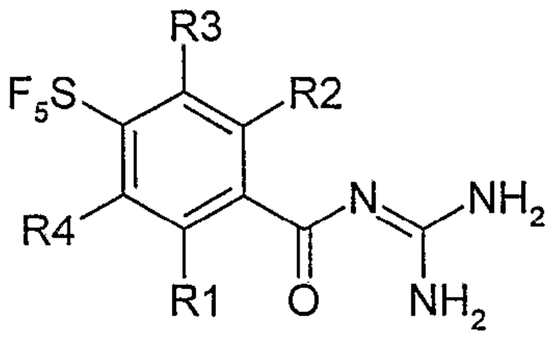
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**(54) Title:** METHOD FOR PRODUCING 4-PENTAFLUORIDE-SULFANYL-BENZOYLGUANIDINES

**(54) Bezeichnung:** VERFAHREN ZUR HERSTELLUNG VON 4-PENTAFLUORSULFANYL-BENZOYLGUANIDINEN




(I)

**(57) Abstract:** The invention relates to a method for producing 4-pentafluoride-sulfanyl-benzoylguanidines of formula (I) wherein groups from R1 to R4 correspond to meanings given in claims. The compounds of the formula (I) constitute NHE1 inhibitors and can be used for curing cardiovascular diseases.

**(57) Zusammenfassung:** Verfahren zur Herstellung von 4-Pentafluorsulfanyl-benzoylguanidinen Die vorliegende Erfindung betrifft ein Verfahren zur Herstellung von 4- Pentafluorsulfanyl-benzoylguanidinen der Formel (I), worin Rl bis R4 die in den Ansprüchen angegebenen Bedeutungen haben. Die Verbindungen der Formel (I) sind NHE1-Inhibitoren und können, beispielsweise, zur Behandlung von Herz-Kreislauferkrankungen eingesetzt werden.

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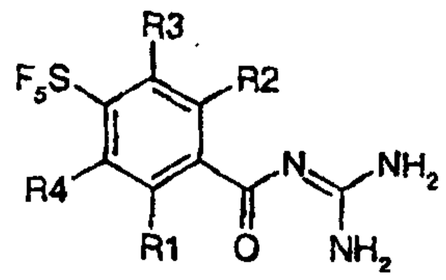
# Method for producing 4-pentafluoride-sulfanyl-benzoylguanidines

The present invention relates to a process for preparing 4-pentafluoro-sulfanylbenzoylguanidines with the formula I. The compounds of the formula I are NHE1 inhibitors and can be employed for example for the treatment of cardiovascular disorders.

DE application 10222192 describes pentafluorosulfanylbenzoylguanidines as NHE1 inhibitors. However, the processes described therein for preparing these compounds proceed with low yield and require reagents and reaction conditions which necessitate great technical complexity or are unsuitable for preparation on a relatively large scale.

It has now been found that said disadvantages can be avoided by a novel efficient synthesis which starts from 4-nitrophenylsulfur pentafluoride, which can be bought.

The present invention thus relates to a process for preparing compounds of the formula I




I

in which the meanings are:

R1 hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, NR10R11, $-O_p-(CH_2)_n-(CF_2)_o-CF_3$ or $-(SO_m)_q-(CH_2)_r-(CF_2)_s-CF_3$;

R10 and R11 independently of one another hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or $-CH_2-CF_3$;

m zero, 1 or 2

n, o, p, q, r and s independently of one another zero or 1;

R2 hydrogen, $-(SO_h)_z-(CH_2)_k-(CF_2)_l-CF_3$, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, in which 1, 2, 3 or 4 hydrogen atoms may be replaced by fluorine

atoms;

h zero, 1 or 2;

z zero or 1;

k zero, 1, 2, 3 or 4;

l zero or 1;

or

R2 $-(CH_2)_t$-phenyl or –O-phenyl,

which are unsubstituted or substituted by 1, 2 or 3 radicals selected from the group consisting of $-O_u-(CH_2)_v-CF_3$,

alkoxy having 1, 2, 3 or 4 carbon atoms, alkyl having 1, 2, 3 or 4 carbon atoms and $-SO_2CH_3$;

t zero, 1, 2, 3 or 4;

u zero or 1;

v zero, 1, 2 or 3;

or

R2 $-(CH_2)_w$-heteroaryl

which is unsubstituted or substituted by 1, 2 or 3 radicals selected from the group consisting of $-O_x-(CH_2)_y-CF_3$,

alkoxy having 1, 2, 3 or 4 carbon atoms and alkyl having 1, 2, 3 or 4 carbon atoms, $-SO_2CH_3$;

w zero, 1, 2, 3 or 4;

x zero or 1;

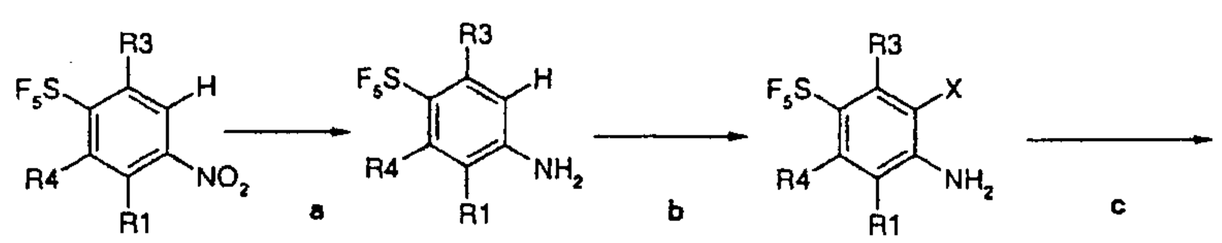
y zero, 1, 2 or 3;

R3 and R4,

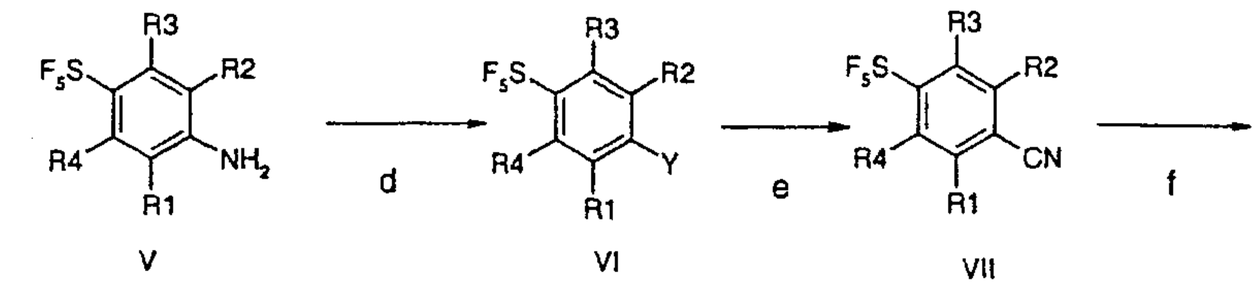
independently of one another hydrogen or F;

and the salts thereof;

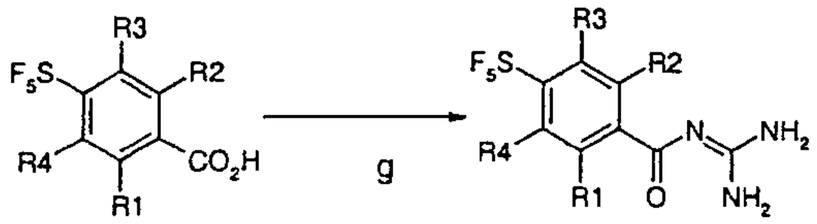
which comprises, as depicted in scheme 1,




II III IV




V VI VII




VIII I

Scheme 1

a) reducing a 4-nitrophenylsulfur pentafluoride derivative of the formula II to the amine of formula III, and
b) halogenating the compound of the formula III in the ortho position to the amino group with a halogenating agent to give the compound of the formula IV, and
c) replacing the halogen substituent in the compound of the formula IV with a suitable nucleophile or an organoelement compound, for example an alkylboron compound, where appropriate with catalysis, by a substituent R2, and
d) replacing the amino function in the compound of the formula V by a halogen substituent, and
e) replacing the halogen substituent in the compound of the formula VI by a nitrile function, and
f) hydrolyzing the nitrile function of the compound of the formula VII to the carboxylic acid, and
g) converting the carboxylic acid of the formula VIII into the acylguanidine of the formula I,
where in the compounds of the formulae II, III, IV, V, VI, VII and VIII
R1 to R4 are as defined in formula I and
X and Y are independently of one another F, Cl, Br or I.

In one embodiment, preference is given to compounds of the formula I in which R1 is described by hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, NR10R11, -O-$CH_2$-$CF_3$ or –$SO_m$-$(CH_2)_r$–$CF_3$ where R10 and R11 are independently of one another hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or –$CH_2$-$CF_3$, and where m is zero, 1 or 2 and r is zero or 1, with particular preference for compounds in which R1 are described by hydrogen or methyl. In a further embodiment, preference is given to compounds of the formula I in which R2 is described by hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or –$SO_h$-$(CH_2)_k$-$CF_3$ where h is zero, 1 or 2 and k is zero or 1, phenyl or –O-phenyl, which are unsubstituted or substituted as indicated, with particular preference for compounds in which R2 is described by hydrogen or methyl.
In a further embodiment, preference is given to compounds of the formula I in which R3 and R4 are described by hydrogen.

The procedure for preparing the compounds of the formula I is initially in

step a (Scheme 1) to convert the compounds of the formula II by methods known in principle for the reduction of aromatic nitro compounds to aromatic amines into compounds of the formula III. Such methods are described, for example, in: R.C. Larock, Comprehensive Organic Transformations: A Guide to Functional Group Preparations, VCH Publishers, New York, Weinheim, 1999, 821-828 and the literature cited therein.

Subsequently (step b), the compounds of the formula III are dissolved in an organic solvent A and reacted with a halogenating agent, for example a brominating agent. The reaction temperature in this case is generally from -30°C to +150°C, preferably 0°C to 40°C. The reaction time is generally from 10 min to 20 h, depending on the composition of the mixture and the chosen temperature range. The resulting reaction mixture can be worked up by subsequent filtration through a layer of silica gel, washing with organic solvent A and, after removal of the solvent in vacuo, purifying the product by conventional purification methods such as recrystallization, distillation or chromatography.

From 0.1 to 10 mol of the compound of the formula II for example are dissolved in 1000 ml of organic solvent A. For example, from 0.8 to 1.2 equivalents of the halogenating agent are used for 1 mol of the compound of the formula II to be halogenated.

The term "halogenating agent" means for example elemental halogens, halogen-amine complexes, cyclic and acyclic N-halogenated carboxamides and –imides, and ureas, as described, for example, in R.C. Larock, Comprehensive Organic Transformations: A Guide to Functional Group Preparations, VCH Publishers, New York, Weinheim, 1999, 619-628, and the literature cited therein or M.B. Smith and J. March, March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, Wiley, New York, 2001, 704-707, and the literature cited therein, such as, for example, N-bromosuccinimide, N-chlorosuccinimide, HBr in $H_2SO_4$ or 1,3-dibromo-5,5-dimethylimidazolidine-2,4-dione, the latter being able to transfer 2 bromine atoms per molecule. The term "brominating agent" means, for example, elemental bromine, bromine-amine complexes, cyclic and acyclic N-brominated carboxamides and –imides, and ureas, as described, for example, in R.C. Larock, Comprehensive Organic Transformations: A Guide to Functional Group Preparations, VCH Publishers, New York, Weinheim, 1999, 622-624, and the literature cited therein or M.B. Smith and J. March, March's Advanced Organic Chemistry: Reactions,

Mechanisms, and Structure, Wiley, New York, 2001, 704-707, and the literature cited therein, for example N-bromosuccinimide, HBr in $H_2SO_4$ or 1,3-dibromo-5,5-dimethylimidazolidine-2,4-dione, the latter being able to transfer 2 bromine atoms per molecule.

The term "organic solvent A" preferably means aprotic solvents such as, for example, dichloromethane, chloroform, tetrachloromethane, pentane, hexane, heptane, octane, benzene, toluene, xylene, chlorobenzene, 1,2-dichloroethane, trichloroethylene or acetonitrile.

Any HX produced in the reaction can be trapped by organic or inorganic bases.

In step c, the compounds of the formula IV are subsequently dissolved in an organic solvent B and reacted with a nucleophile $R2^-$ or an element compound comprising the substituent R2 to give compounds of the formula V. It is possible in this case to add a base A and to add a catalyzing metal salt A.

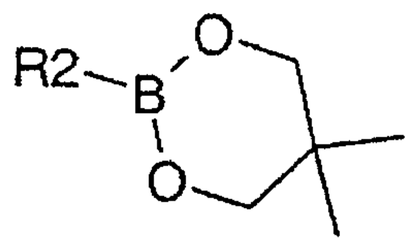
The reaction temperature in this case is generally between -20°C and +150°C, preferably between 30°C and 100°C. The reaction time is generally from 0.5 h to 20 h, depending on the composition of the mixture and the chosen temperature range. The resulting reaction mixture can be worked up by subsequent filtration through a layer of silica gel, washing with an organic solvent B and, after removal of the solvent in vacuo, purifying the product by conventional purification processes such as recrystallization, chromatography, for example on silica gel, distillation or steam distillation.

From 0.1 to 10 mol of the compound of the formula IV for example are dissolved in 1000 ml of organic solvent B. For example, from 0.8 to 3 equivalents of the nucleophile $R2^-$ or of the element compound comprising the substituent R2 are used for 1 mol of the starting compound of the formula IV.

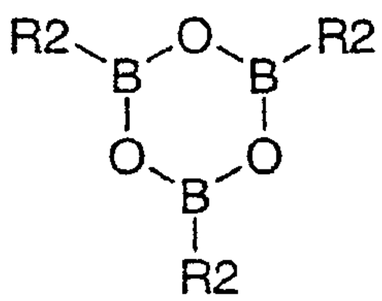
The term "nucleophile $R2^-$" means compounds which result on deprotonation of a compound R2-H with strong bases such as, for example, alkyl- or aryllithium compounds, organomagnesium compounds, alcoholates or lithium diisopropylamide.

"Organoelement compounds comprising the substituent R2" mean for example organolithium compounds R2-Li, organomagnesium compounds R2-Mg-Hal, with Hal = Cl, Br, I, organoboron compounds such as $R2\text{-}B(OH)_2$, R2-boronic esters such as, for example,

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R2-boronic anhydrides such as, for example,



or organozinc compounds R2-Zn-Z, with Z = Cl, Br, I.

The term "base A" means bases like those used as auxiliary bases in cross-coupling reactions and mentioned for example in A. Suzuki et al., Chem. Rev. 1995, *95*, 2457-2483 or M. Lamaire et al., Chem. Rev. 2002, *102*, 1359-1469 or S.P. Stanforth, Tetrahedron 1998, *54*, 263-303 and the literature cited therein in each case, for example $Na_2CO_3$, $Cs_2CO_3$, KOH, NaOH, $K_3PO_4$, N(ethyl)$_3$.

The term "organic solvent B" means protic or aprotic solvents such as diethyl ether, dimethoxyethane, THF, alcohols, water or mixtures thereof. In one embodiment, mixtures with water are preferred.

The term "catalyzing metal salt A" means inter alia Pd and Ni catalysts like those used for Suzuki and Negishi reactions and described for example in A. Suzuki et al., Chem. Rev. 1995, *95*, 2457-2483 or M. Lamaire et al., Chem. Rev. 2002, *102*, 1359-1469 or S.P. Stanforth, Tetrahedron 1998, *54*, 263 or G.C. Fu et al., J. Am. Chem. Soc. 2001, *123*, 10099 or G.C. Fu et al., J. Am. Chem. Soc. 2002, *124*, 13662 and the literature cited therein in each case, including the added ligands such as $Pd(OAc)_2$, $PdCl_2$(dppf) or $Pd_2(dba)_3$.

In step d, the compounds of the formula V are subsequently converted into the compounds of the formula VI by a diazotization-halogenation process with a diazotizing-halogenating agent, for example with a diazotizing-brominating agent, as described for other aromatic amines to replace the amine function by a halogen function for example in M.B. Smith and J. March, March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, Wiley, New York, 2001, 935-936 or R.C. Larock, Comprehensive Organic Transformations: A Guide to Functional Group Preparations, VCH Publishers, New York, Weinheim, 1999, 678-679 and

the literature cited therein, for example by the Sandmeyer or Gattermann reaction. The process of M. Doyle et al., J. Org. Chem. 1977, *42*, 2426 or of S. Oae et al., Bull. Chem. Soc. Jpn. 1980, *53*, 1065 is preferred.

In step e, the compounds of the formula VI are reacted in a solvent C with a cyanidating agent, for example with addition of a catalyzing metal salt B. The reaction temperature is generally from 20°C to 200°C, preferably 80°C to 150°C. The reaction time is generally from 1 h to 20 h, depending on the composition of the mixture and the chosen temperature range. The resulting reaction mixtures can be filtered with suction through a layer of silica gel or kieselguhr and the filtrate can be worked up by aqueous extraction. After evaporation of the solvent in vacuo, the compound of the formula VII is purified by conventional purification processes such as recrystallization, chromatography on silica gel, distillation or steam distillation.

From 0.1 to 10 mol of the compound of the formula VI for example are dissolved in 1000 ml of organic solvent C. For example, from 1 to 10 equivalents of the cyanidating agent are used for 1 mol of the compound having the formula VI to be reacted.

The term “cyanidating agent” means, for example, alkali metal cyanides or $Zn(CN)_2$ either alone or mixed with metallic zinc, preferably in the form of zinc dust.

The term “organic solvent C” preferably means aprotic polar solvents such as, for example, DMF, dimethylacetamide, NMP, DMSO.

The term “catalyzing metal salt B” means inter alia Pd and Ni catalysts like those employed in Suzuki reactions and described for example in A. Suzuki et al., Chem. Rev. 1995, *95*, 2457-2483 or M. Lamaire et al., Chem. Rev. 2002, *102*, 1359-1469 or S.P. Stanforth, Tetrahedron 1998, *54*, 263 and the literature cited therein, for example $PdCl_2(dppf)$, $Pd(OAc)_2$, $Pd_2(dba)_3$.

The resulting compounds of the formula VII are subsequently hydrolyzed in step f to the carboxylic acids of the formula VIII, for example in the presence of a base. This can take place by processes known to the skilled worker for hydrolyzing aromatic nitriles, as described, for example, in R.C. Larock, Comprehensive Organic Transformations: A Guide to Functional Group Preparations, VCH Publishers, New York, Weinheim, 1999, 1986-1987 or M.B. Smith and J. March, March’s Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, Wiley, New York, 2001, 1179-1180 and the literature cited therein.

In step g, the carboxylic acids of the formula VIII are then subsequently converted into the acylguanidines having the formula IX. For this purpose, the carboxylic acids are converted into activated acid derivatives such as carbonyl halides, preferably carbonyl chlorides, esters, preferably methyl esters, phenyl esters, phenylthio esters, methylthio esters, 2-pyridylthio esters, or a nitrogen heterocycle, preferably 1-imidazolyl. The esters and nitrogen heterocycles are advantageously obtained in a manner known to the skilled worker from the underlying carbonyl chlorides, which in turn themselves can be prepared in a known manner from the underlying carboxylic acids, for example with thionyl chloride.

Besides the carbonyl chlorides, it is also possible to prepare other activated acid derivatives in a known manner directly from the underlying benzoic acids, such as the methyl esters by treatment with gaseous HCl in methanol, the imidazolides by treatment with carbonyldiimidazole the mixed anhydrides with Cl-$COOC_2H_5$ or tosyl chloride in the presence of triethylamine in an inert solvent, as well as activations of benzoic acids with dicyclohexylcarbodiimide (DCC) or with O-[(cyano(ethoxycarbonyl)-methylene)amino]-1,1,3,3-tetramethyluronium tetrafluoroborate ("TOTU") are possible. A number of suitable methods for preparing activated carboxylic acid derivatives are indicated with indication of source literature M.B. Smith and J. March, March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, Wiley, New York, 2001, 506-516 or R.C. Larock, Comprehensive Organic Transformations: a Guide to Functional Group Preparations, VCH Publishers, New York, Weinheim, 1999, 1941-1949.

Reaction of an activated carboxylic acid derivative with guanidine preferably takes place in a manner known per se in a protic or aprotic polar but inert organic solvent either with free guanidine base or with guanidinium chloride in the presence of a base. In this connection, methanol, isopropanol or THF at temperatures from 20°C to the boiling point of these solvents have proved suitable for the reaction of the methyl benzoates with guanidine. Most reactions of carboxylic acid derivatives with salt-free guanidine are advantageously carried out in aprotic inert solvents such as THF, dimethoxyethane, dioxane. However, water can also be used as solvent in the reaction with guanidine on use of a base such as, for example, NaOH.

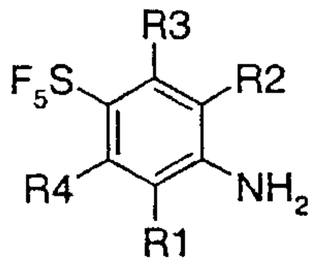
If a carbonyl chloride is employed as carboxylic acid derivative, it is

advantageous to add an acid scavenger, for example in the form of excess guanidine, to bind the hydrohalic acid.

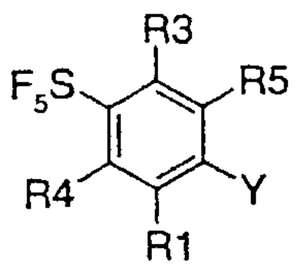
For preparing compounds of the formula I in which R2 is hydrogen, can the synthesis takes place without steps b and c.
In order to prepare compounds of the formula I with R2 = $-(SO_h)_z-(CH_2)_k-(CF_2)_l-CF_3$, where h is 1 or 2, as described above compounds in which R2 is $-(SO_h)_z-(CH_2)_k-(CF_2)_l-CF_3$, where h is zero, are synthesized and subsequently converted by generally known oxidation reactions into the desired compounds of the formula I.

The reaction mixture can be worked up after each of process steps a), b), c), d), e), f) and g) or after two or more process steps. Synthesis of the compounds of the formula I by the process of the invention can, however, also take place in two or more consecutive process steps without isolation of the compounds III, IV, V, VI, VII or VIII obtained in the individual process steps, in which case workup after each process step is unnecessary. The workup and, if desired, the purification of the products takes place by the usual methods such as extraction, pH separation, chromatography or crystallization and the usual dryings.
The starting compounds of the formulae II are obtainable by purchase or can be prepared by or in analogy to processes described in the literature and known to the skilled worker, for example as described in Bowden, R.D., Comina, P.J., Greenhall, M.P., Kariuki, B.M., Loveday, A., Philip, D. Tetrahedron 2000, 56, 5660. Functional groups in the starting compounds may also be present in protected form or in the form of precursors, and then be converted into the desired groups in the compounds of the formula I prepared by the process of the invention. Appropriate protective group techniques are known to the skilled worker. For example, the $NH_2$ group in compounds of the formula II in which R1 is $NH_2$ can be present in a form protected by an acetyl, trifluoroacetyl or trityl group and be deprotected again.

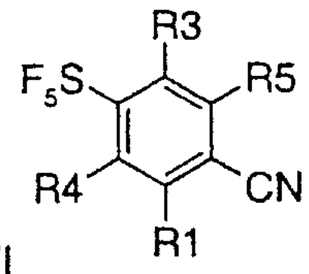
A further aspect of the invention relates to novel compounds of the formulae V, VI, VII and VIII.



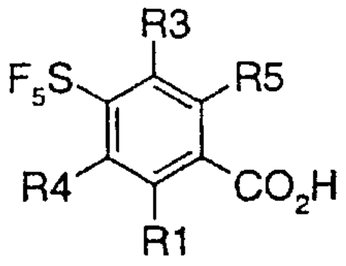
V



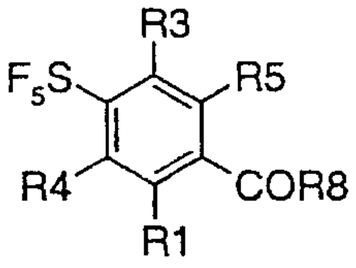
VI



VII

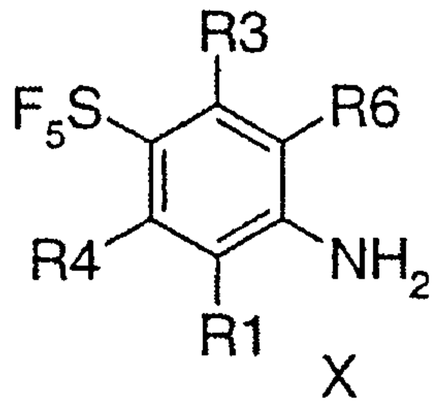


VIII



IX

The invention thus relates to 4-pentafluorosulfanyl-substituted compounds of the formula X



X

in which the meanings are:

R1 hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, NR10R11, $-O_p-(CH_2)_n-(CF_2)_o-CF_3$ or $-(SO_m)_q-(CH_2)_r-(CF_2)_s-CF_3$;

R10 and R11

independently of one another hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or $-CH_2-CF_3$;

m zero, 1 or 2

n, o, p, q, r and s

independently of one another zero or 1;

R6 $-(SO_h)_z-(CH_2)_k-(CF_2)_l-CF_3$, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, in which 1, 2, 3 or 4 hydrogen atoms may be replaced by fluorine atoms;

h zero, 1 or 2;

z zero or 1;

k zero, 1, 2, 3 or 4;

l zero or 1;

or

R6 $-(CH_2)_t$-phenyl or –O-phenyl,

which are unsubstituted or substituted by 1, 2 or 3 radicals selected from the group consisting of $-O_u-(CH_2)_v-CF_3$,

alkoxy having 1, 2, 3 or 4 carbon atoms, alkyl having 1, 2, 3

or 4 carbon atoms and $-SO_2CH_3$;

t zero, 1, 2, 3 or 4;

u zero or 1;

v zero, 1, 2 or 3;

or

R6 $-(CH_2)_w$-heteroaryl

which is unsubstituted or substituted by 1, 2 or 3 radicals selected from the group consisting of $-O_x-(CH_2)_y-CF_3$, alkoxy having 1, 2, 3 or 4 carbon atoms and alkyl having 1, 2, 3 or 4 carbon atoms, $-SO_2CH_3$;

w zero, 1, 2, 3 or 4;

x zero or 1;

y zero, 1, 2 or 3;

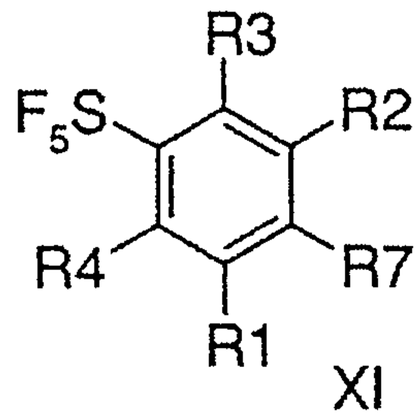
R3 and R4,

independently of one another hydrogen or F;

and the salts thereof;

In one embodiment, preference is given to compounds of the formula X in which R1 is described by hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, NR10R11, $-O-CH_2-CF_3$ or $-SO_m-(CH_2)_r-CF_3$, where R10 and R11 are independently of one another hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or $-CH_2-CF_3$, and where m is zero, 1 or 2 and r is zero or 1, with particular preference for compounds in which R1 are described by hydrogen or methyl. In a further embodiment, preference is given to compounds of the formula X in which R6 is described by hydrogen, F, Cl, Br, I, alkyl having 1, 2, 3 or 4 carbon atoms or $-SO_h-(CH_2)_k-CF_3$ where h is zero, 1 or 2 and k is zero or 1, phenyl or –O-phenyl, which are unsubstituted or substituted as indicated, with particular preference for compounds in which R6 is described by hydrogen or methyl, for example by hydrogen. In a further embodiment, preference is given to compounds of the formula X in which R6 is described by F, Cl, Br or I, in particular by Br. In a further embodiment, preference is given to compounds of the formula X in which R3 and R4 are described by hydrogen.

The invention likewise relates to 4-pentafluorosulfanyl-substituted compounds of the formula XI



XI

in which the meanings are:

R1 hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, NR10R11, $-O_p-(CH_2)_n-(CF_2)_o-CF_3$ or $-(SO_m)_q-(CH_2)_r-(CF_2)_s-CF_3$;

R10 and R11

independently of one another hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or $-CH_2-CF_3$;

m zero, 1 or 2

n, o, p, q, r and s

independently of one another zero or 1;

R2 hydrogen, F, Cl, Br, I,$-(SO_h)_z-(CH_2)_k-(CF_2)_l-CF_3$ or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms;

h zero, 1 or 2;

z zero or 1;

k zero, 1, 2, 3 or 4;

l zero or 1;

R3 and R4,

independently of one another hydrogen or F;

R7 CN;

and the salts thereof.

In one embodiment, preference is given to compounds of the formula XI in which R1 is described by hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, NR10R11, $-O-CH_2-CF_3$ or $-SO_m-(CH_2)_r-CF_3$, where R10 and R11 are independently of one another hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or $-CH_2-CF_3$, and where m is zero, 1 or 2 and r is zero or 1, with particular preference for compounds in which R1 are described by hydrogen or methyl. In a further embodiment, preference is given to compounds of the formulae XI in which R2 is described by hydrogen, F, Cl, Br, I, alkyl having 1, 2, 3 or 4 carbon atoms or $-SO_h-(CH_2)_k-CF_3$, where h is zero, 1 or 2 and k is zero or 1, with particular preference for compounds in which R2 is described by hydrogen or methyl, for example by hydrogen.

In a further embodiment, preference is given to compounds of the formula XI in which R2 is described by F, Cl, Br or I, in particular by Br.
In a further embodiment, preference is given to compounds of the formula XI in which R3 and R4 are described by hydrogen.

If the substituents R1, R2, R3, R4 and R6 contain one or more centers of asymmetry, these may have independently of one another either the S or R configuration. The compounds can exist as optical isomers, as diastereomers, as racemates or mixtures thereof in all ratios.

The present invention encompasses all tautomeric forms of the compounds of the formula I.

Alkyl radicals may be straight-chain or branched. This also applies if they carry substituents or occur as substituents of other radicals, for example in fluoroalkyl radicals or alkoxy radicals. Examples of alkyl radicals are methyl, ethyl, n-propyl, isopropyl (= 1-methylethyl), n-butyl, isobutyl (= 2-methylpropyl), sec-butyl (= 1-methylpropyl), tert-butyl (= 1,1-dimethylethyl), n-pentyl, isopentyl, tert-pentyl, neopentyl and hexyl. Preferred alkyl radicals are methyl, ethyl, n-propyl and isopropyl. One or more, for example 1, 2, 3, 4 or 5, hydrogen atoms in alkyl radicals may be replaced by fluorine atoms. Examples of such fluoroalkyl radicals are trifluoromethyl, 2,2,2-trifluoroethyl and pentafluoroethyl. Substituted alkyl radicals may be substituted in any positions.

Examples of cycloalkyl radicals are cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl or cyclooctyl. One or more, for example 1, 2, 3 or 4, hydrogen atoms in cycloalkyl radicals may be replaced by fluorine atoms. Substituted cycloalkyl radicals may be substituted in any positions.

Phenyl radicals may be unsubstituted or be substituted one or more times, for example once, twice or three times, by identical or different radicals. If a phenyl radical is substituted, it preferably has one or two identical or different substituents. This likewise applies to substituted phenyl radicals in groups such as, for example, phenylalkyl or phenyloxy. The substituent in monosubstituted phenyl radicals may be in position 2, position 3 or position 4. Disubstituted phenyl may be substituted in the 2,3 position, 2,4 position, 2,5 position, 2,6 position, 3,4 position or 3,5 position. The substituents in trisubstituted phenyl radicals may be in the 2,3,4 position, 2,3,5 position,

2,4,5 position, 2,4,6 position, 2,3,6 position or 3,4,5 position. Heteroaryl radicals are aromatic ring compounds in which one or more ring atoms are oxygen atoms, sulfur atoms or nitrogen atoms, e.g. 1, 2 or 3 nitrogen atoms, 1 or 2 oxygen atoms, 1 or 2 sulfur atoms or a combination of various heteroatoms. The heteroaryl radicals may be attached by all positions, for example by the 1 position, 2 position, 3 position, 4 position, 5 position, 6 position, 7 position or 8 position. Heteroaryl radicals may be unsubstituted or be substituted one or more times, for example once, twice or three times, by identical or different radicals. This applies likewise to heteroaryl radicals such as, for example, in the radical heteroarylalkyl. Examples of heteroaryl are furanyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl and cinnolinyl.

Heteroaryl radicals are, in particular, 2- or 3-thienyl, 2- or 3-furyl, 1-, 2- or 3-pyrrolyl, 1-, 2-, 4- or 5-imidazolyl, 1-, 3-, 4- or 5-pyrazolyl, 1,2,3-triazol-1-, -4- or -5-yl, 1,2,4-triazol-1-, -3- or -5-yl, 1- or 5-tetrazolyl, 2-, 4- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 1,2,3-oxadiazol-4- or -5-yl, 1,2,4-oxadiazol-3- or -5-yl, 1,3,4-oxadiazol-2-yl or -5-yl, 2-, 4- or 5-thiazolyl, 3-, 4- or 5-isothiazolyl, 1,3,4-thiadiazol-2- or -5-yl, 1,2,4-thiadiazol-3- or -5-yl, 1,2,3-thiadiazol-4- or -5-yl, 2-, 3- or 4-pyridyl, 2-, 4-, 5- or 6-pyrimidinyl, 3- or 4-pyridazinyl, pyrazinyl, 1-, 2-, 3-, 4-, 5-, 6- or 7-indolyl, 1-, 2-, 4- or 5-benzimidazolyl, 1-, 3-, 4-, 5-, 6- or 7-indazolyl, 2-, 3-, 4-, 5-, 6-, 7- or 8-quinolyl, 1-, 3-, 4-, 5-, 6-, 7- or 8-isoquinolyl, 2-, 4-, 5-, 6-, 7- or 8-quinazolinyl, 3-, 4-, 5-, 6-, 7- or 8-cinnolinyl, 2-, 3-, 5-, 6-, 7- or 8-quinoxalinyl, 1-, 4-, 5-, 6-, 7- or 8-phthalazinyl. Also encompassed are the corresponding N-oxides of these compounds, i.e. for example 1-oxy-2-, 3- or 4-pyridyl.

Particularly preferred heteroaromatic radicals are 2- or 3-thienyl, 2- or 3-furyl, 1-, 2- or 3-pyrrolyl, 1-, 2-, 4- or 5-imidazolyl, 2-, 3-, 4-, 5-, 6-, 7- or 8-quinolyl, 1-, 3-, 4- or 5-pyrazolyl, 2-, 3- or 4-pyridyl, 2- or 3-pyrazinyl, 2-, 4-, 5- or 6-pyrimidinyl and 3- or 4-pyridazinyl.

The compounds of the formula I may be isolated in the form of their salts. These are obtained by conventional methods by reaction with acids or bases. Examples of suitable acid addition salts in this connection are halides, especially hydrochlorides, hydrobromides, lactates, sulfates,

citrates, tartrates, acetates, phosphates, methylsulfonates, benzenesulfonates, p-toluenesulfonates, adipates, fumarates, gluconates, glutamates, glycerolphosphates, maleates, benzoates, oxalates and pamoates and trifluoroacetates, in the case of the preparation of active ingredients preferably pharmaceutically suitable salts. If the compounds contain an acidic group, they can form salts with bases, for example alkali metal salts, preferably sodium or potassium salts, or ammonium salts, for example of salts with ammonia or organic amines or amino acids. They may also be in the form of a zwitterion.

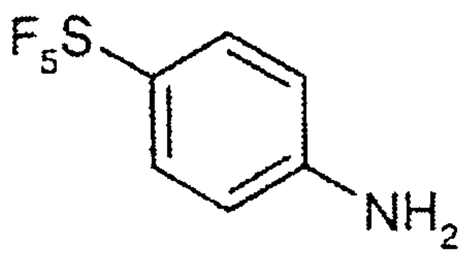
List of abbreviations:

| | |
|---|---|
| DMF | N,N-Dimethylformamide |
| DMSO | Dimethyl sulfoxide |
| dba | Dibenzylideneacetone |
| OAc | Acetate |
| M.p. | Melting point |
| MTB | tert-Butyl methyl ether |
| NMP | N-Methyl-2-pyrrolidone |
| dppf | 1,1'-Bis-(diphenylphosphino)-ferrocene |
| THF | Tetrahydrofuran |

Experimental section

Example 1:

a) 4-Aminophenylsulfur pentafluoride

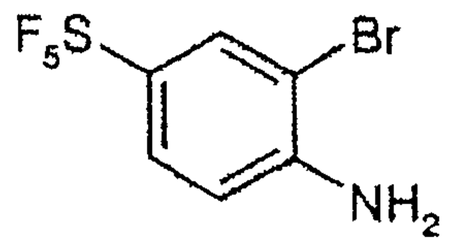



A solution of tin(II) chloride (1465 g, 7.73 mol) in concentrated (32 percent) aqueous HCl solution was heated with stirring to 80°C and then, with ice cooling, 4-nitrophenylsulfur pentafluoride (584 g, 2.344 mol) was introduced in 8 portions over the course of 1 h. The internal temperature was kept below 100°C during this. Subsequently, the mixture was stirred at an internal temperature of 85°C for 1.5 h and then cooled to 45°C over the course of a further hour. A mixture of ice (12 kg), NaOH (2 kg) and dichloromethane (1.5 l) was prepared and added to the reaction mixture with vigorous stirring. The phases were separated, the aqueous phase was

extracted 3 times with 1 l of dichloromethane each time, and the combined organic phases were dried over $Na_2SO_4$ and evaporated in vacuo. 510 g (99%) of 4-aminophenylsulfur pentafluoride were obtained as a pale yellow crystalline powder, m.p. 63-65°C (Bowden, R.D., Comina, P.J., Greenhall, M.P., Kariuki, B.M., Loveday, A., Philip, D. Tetrahedron 2000, 56, 3399: 57-59°C).

$^1$H-NMR 400 MHz, $CDCl_3$: $\delta$ = 3.99 (bs, 2H), 6.61 (d, J=9 Hz, 2H), 7.52 (d, J=9 Hz, 2H) ppm.

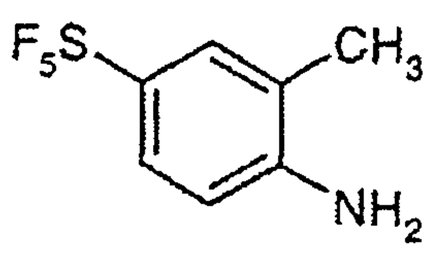
b) 4-Amino-3-bromophenylsulfur pentafluoride




4-Aminophenylsulfur pentafluoride (510 g, 2.327 mol) was dissolved in dichloromethane (7 l), the solution was cooled to 5°C and, while stirring, 1,3-dibromo-5,5-dimethylimidazolidine-2,4-dione (326 g, 1.14 mol) was introduced in several portions with ice cooling so that the internal temperature was kept at 3-8°C (approx. 1 h). The mixture was then left to stir and warm to room temperature without external cooling for 1 h. The mixture was filtered through a bed of silica gel (volume about 1 l) and washed with dichloromethane (5.5 l), and the filtrate was evaporated in vacuo. About 700 g of a red-brown crystalline mass was obtained and was dissolved in n-heptane (600 ml) at 60°C and then crystallized in a refrigerator at 4°C. Filtration with suction resulted in 590 g (85%) of 4-amino-3-bromphenylsulfur pentafluoride as brownish crystals, m.p. 59-59.5°C.

$^1$H-NMR 400 MHz, $CDCl_3$: $\delta$ = 4.45 (bs, 2H), 6.72 (d, J=9 Hz, 1H), 7.49 (dd, $J_1$=9 Hz, $J_2$=2.5 Hz, 1H) 7.81 (d, J=2.5 Hz, 1H) ppm.
$C_6H_5BrF_5NS$ (298.07): calc. C 24.18, H 1.69, N 4.70; found C 24.39, H 1.45, N 4.77.

c) 4-Amino-3-methylphenylsulfur pentafluoride



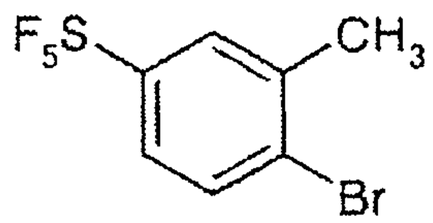

A mixture of $Cs_2CO_3$ (794 g, 2.7 mol), dimethoxyethane (2 l), water (300 ml) and trimethylboroxine (50 percent solution in THF, 225 g, 0.9 mol)

was heated to 70°C, $PdCl_2$ (dppf) × $CH_2Cl_2$ (37 g, 45 mmol) was added, and a solution of 4-amino-3-bromophenylsulfur pentafluoride (270 g, 0.9 mol) in dimethoxyethane (400 ml) was added dropwise over the course of 2 h while the reaction mixture was heated to reflux. It was subsequently heated under reflux for a further 3 h and then cooled to room temperature, diluted with MTB ether (500 ml), filtered through a silica gel column (14 × 7 cm, 70-200 µm) and washed with MTB ether (2500 ml). The filtrate was evaporated in vacuo. 490 g of a black, semicrystalline mass was obtained and was subjected to a steam distillation. A total of 5.5 l of condensate was collected, from which the crystals of the product separated out. The condensate was extracted 3 × with MTB ether, and the combined organic phases were dried over $Na_2SO_4$ and evaporated in vacuo. 4-Amino-3-methylphenylsulfur pentafluoride (181 g, 76%) was obtained as colorless crystals, m.p. 65-66°C,

$^1$H-NMR 400 MHz, $CDCl_3$: $\delta$ = 2.18 (s, 3 H), 3.92 (bs, 2 H), 6.60 (d, J=8.5 Hz, 1 H), 7.40 (dd, $J_1$=8.5 Hz, $J_2$=2.5 Hz, 1 H), 7.43 (d, J=2.5 Hz, 1 H) ppm

$C_7H_8F_5NS$ (233.20): calc. C 36.05, H 3.46, N 6.01; found C 36.43 H 3.30 N 6.09.

d) 4-Bromo-3-methylphenylsulfur pentafluoride

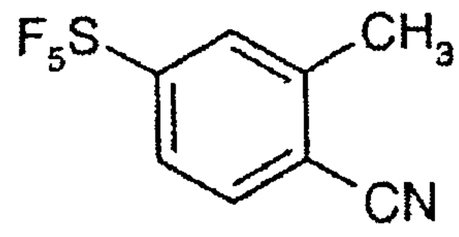



A mixture of tert-butyl nitrite (90 percent pure, 37 ml, 280 mmol) and $CuBr_2$ (35.8 g, 160 mmol) in acetonitrile (260 ml) was cooled to 5°C and, while stirring and cooling with ice, a solution of 4-amino-3-methylphenylsulfur pentafluoride (30.9 g, 132.5 mmol) in MTB ether (140 ml) was added dropwise at 5-8°C over the course of 1 h. Evolution of nitrogen started after about 2 min. The mixture was then allowed to warm with stirring to room temperature over the course of 1 h, a mixture of ice (250 g), 26 percent aqueous $NH_3$ solution (50 ml) and MTB ether (250 ml) was added, and the mixture was stirred for 10 min. The phases were separated, the aqueous was extracted 3 × with MTB ether (150 ml each time), and the combined organic phases were shaken once with 400 ml of water. Drying with $Na_2SO_4$ and evaporation of the organic phase resulted in 39 g of 4-bromo-3-methylphenylsulfur pentafluoride as a red-brown oil which, according to 1H-NMR, was contaminated with 8 mol% of 4,5-dibromo-

3-methylphenylsulfur pentafluoride, but was used further without further purification. Yield 89% based on a purity of 90%. For combustion analysis, a sample was purified by chromatography on silica gel (35-70 µm, heptane).

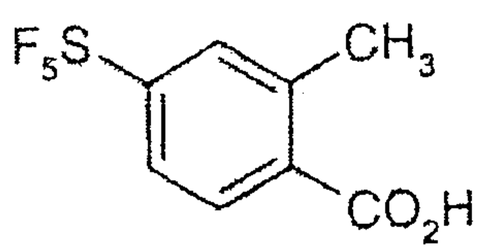
$^1$H-NMR 400 MHz, $CDCl_3$: $\delta$ = 2.47 (s, 3 H), 7.43 (dd, $J_1$=9 Hz, $J_2$=3 Hz, 1 H), 7.62 (m, 2 H) ppm. Signals of 4,5-dibromo-3-methylphenylsulfur pentafluoride (contaminant):
2.56 (s, 3 H), 7.56 (d, J=2.5 Hz, 1 H), 7.85 (d, J=2.5 Hz, 1 H).
$C_7H_6BrF_5S$ (297.09): calc. C 28.30, H 2.04; found C 28.42, H 1.78.

e) 4-Cyano-3-methylphenylsulfur pentafluoride



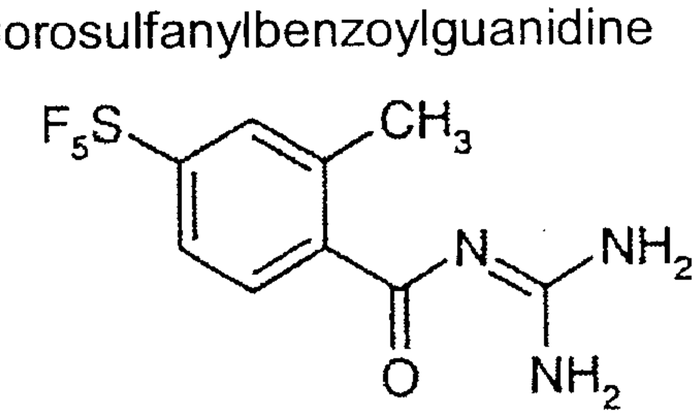

A mixture of 4-bromo-3-methylphenylsulfur pentafluoride (136.4 g, purity 80%, 0.367 mol), $Zn(CN)_2$ (72.8 g, 0.62 mol) and Zn dust (7.2 g, 0.11 mol) in dimethylacetamide (900 ml) and water (40 ml) was heated with stirring and nitrogen blanketing to 125°C, and $PdCl_2$(dppf) × $CH_2Cl_2$ (32.7 g, 40 mmol) was added. After stirring at 125°C for one hour, $PdCl_2$(dppf) × $CH_2Cl_2$ (16.3 g, 20 mmol) and Zn dust (3.6 g, 55 mmol) were again added, and stirring was continued at 125°C for 2 h. The mixture was then cooled to room temperature, diluted with n-heptane (400 ml) and stirred vigorously with addition of 5 N aqueous $NH_4Cl$ solution (250 ml) and water (450 ml) for 15 min. The mixture was filtered with suction through a layer of kieselguhr, the phases were separated, and the aqueous was extracted 2 × with n-heptane (200 ml). The combined organic phases were shaken with water (450 ml), dried over $MgSO_4$ and evaporated in vacuo. The resulting black residue was dissolved in 200 ml of n-heptane, filtered and again evaporated in vacuo. 78 g of a dark brown liquid were obtained and were purified by chromatography on a silica gel column (7 × 55 cm, 60-200 µm, n-heptane/dichloromethane 4:1 to 3:2). The first fraction obtained was 6.5 g of 4-bromo-3-methylphenylsulfur pentafluoride (precursor) as yellowish liquid, and then 71.1 g (80%) of 4-cyano-3-methyl-phenylsulfur pentafluoride as pale yellow oil.
$^1$H-NMR 400 MHz, $CDCl_3$: $\delta$ = 2.65 (s, 3 H), 7.71 (m, 3H) ppm.

f) 2-Methyl-4-pentafluorosulfanylbenzoic acid



A mixture of 4-cyano-3-methylphenylsulfur pentafluoride (41.2 g, 169.4 g), NaOH (20.4 g, 510 mmol) and water (60 ml) in ethylene glycol (160 ml) was heated to 130°C and stirred at this temperature for 4 h. It was then cooled to room temperature and diluted with MTB ether (150 ml) and water (250 ml), and the mixture was filtered with suction. The phases of the filtrate were separated, and the aqueous was acidified with concentrated aqueous HCl solution, and the precipitated solid was filtered off with suction. 41.1 g (93%) of 2-methyl-4-pentafluorosulfanylbenzoic acid were obtained as colorless crystals, m.p. 138-139°C.
$^1$H-NMR 400 MHz, DMSO-$d_6$: $\delta$ = 2.60 (s, 3 H), 7.81 (dd, $J_1$=8.5 Hz, $J_2$=2 Hz, 1 H), 7.89 (d, J=2 Hz, 1 H), 7.97 (d, J=8.5 Hz, 1 H), 13.43 (bs, 1 H) ppm.
$C_8H_7F_5O_2S$ (262.20): calc. C 36.65, H 2.69; found C 36.85, H 2.59.

g) 2-Methyl-4-pentafluorosulfanylbenzoylguanidine



2-Methyl-4-pentafluorosulfanylbenzoic acid (77.5 g, 295 mmol) was suspended in toluene (300 ml), thionyl chloride (36 ml, 0.5 mol) and 5 drops DMF were added, and the mixture was heated under reflux with stirring for 2 h. It was then filtered with suction, the filtrate was evaporated in vacuo, the residue was taken up 2 × in toluene (100 ml each time) and evaporated in vacuo each time. 78.8 g of the acid chloride were obtained as a pale brown liquid, which was used further without purification.

Guanidine hydrochloride (172 g, 1.8 mol) was added to a solution of NaOH (84 g, 2.1 mol) in water (600 ml), and the mixture was cooled to -3°C. Then, while stirring and ice cooling, the solution of the crude acid chloride in dichloromethane (600 ml) was added dropwise over the course of 1 h. The mixture was left to stir at room temperature for a further 30 min, and then the precipitated solid was filtered off with suction, washed with dichloromethane and dried at room temperature in vacuo. 74.3 g (87%) of 2-methyl-4-pentafluorosulfanylbenzoylguanidine were obtained as beige

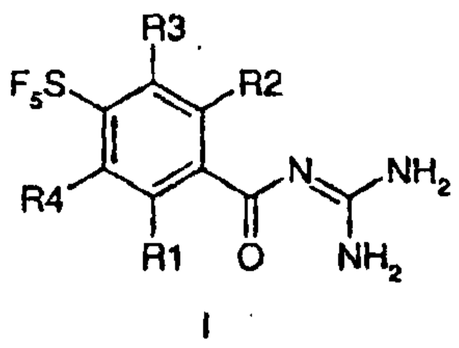
crystals, m.p. 183-183.5°C.

$^1$H-NMR 400 MHz, $CD_3OD$: $\delta$ = 2.51 (s, 3 H), 4.84 (bs, 5 H), 7.62 (m, 2 H), 7.65 (s, 1 H) ppm.

$C_9H_{10}F_5N_3OS$ (303.26): calc. C 35.65, H 3.32, N 13.86; found C 35.69, H 3.18, N 14.04.

Claims

1. A process for preparing compounds of the formula I



in which the meanings are:

R1 hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, NR10R11, $-O_p-(CH_2)_n-CF_2)_o-CF_3$ or $-(SO_m)_q-(CH_2)_r-(CF_2)_s-CF_3$;

R10 and R11

independently of one another hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or $-CH_2-CF_3$;

m zero, 1 or 2

n, o, p, q, r and s

independently of one another zero or 1;

R2 hydrogen, $-(SO_h)_z-(CH_2)_k-(CF_2)_l-CF_3$, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, in which 1, 2, 3 or 4 hydrogen atoms are optionally replaced by fluorine atoms;

h zero, 1 or 2;

z zero or 1;

k zero, 1, 2, 3 or 4;

l zero or 1;

or

R2 $-(CH_2)_t$-phenyl or –O-phenyl,

which are unsubstituted or substituted by 1, 2 or 3 radicals selected from the group consisting of $-O_u-(CH_2)_v-CF_3$, alkoxy having 1, 2, 3 or 4 carbon atoms, alkyl having 1, 2, 3 or 4 carbon atoms and $-SO_2CH_3$;

t zero, 1, 2, 3 or 4;

u zero or 1;

v zero, 1, 2 or 3;

or

R2 $-(CH_2)_w$-heteroaryl

which is unsubstituted or substituted by 1, 2 or 3 radicals selected from the group consisting of $-O_x-(CH_2)_y-CF_3$, alkoxy having 1, 2, 3 or 4 carbon atoms and alkyl having 1, 2, 3 or 4 carbon atoms, $-SO_2CH_3$;

w zero, 1, 2, 3 or 4;

x zero or 1;

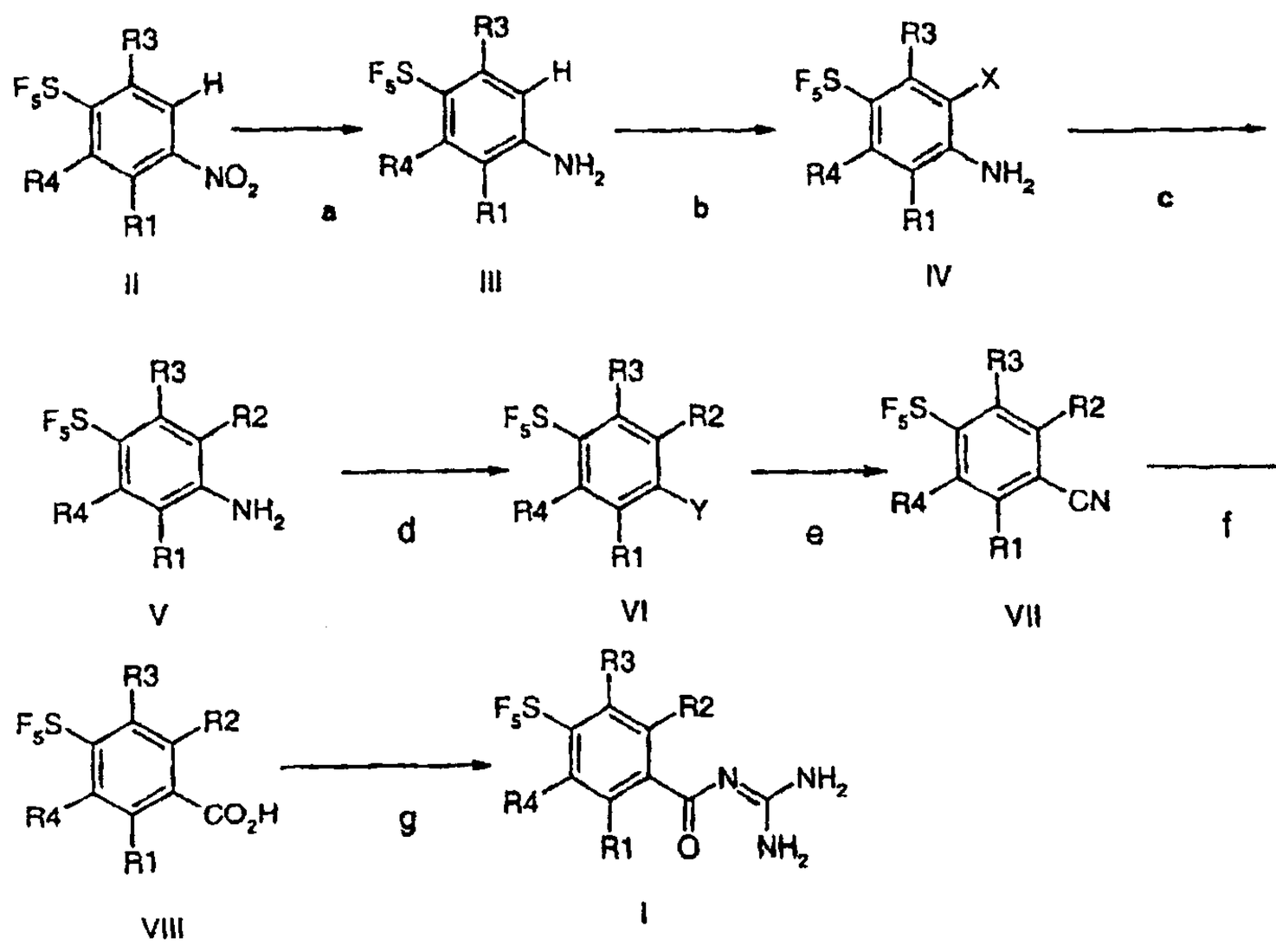
y zero, 1, 2 or 3;

R3 and R4,

independently of one another hydrogen or F;

and the salts thereof;

which comprises




a) reducing a 4-nitrophenylsulfur pentafluoride derivative of the formula II to the amine of formula III, and

b) halogenating the compound of the formula III in the ortho position to the amino group with a halogenating agent to give the compound of the formula IV, and

c) replacing the halogen substituent in the compound of the formula IV with a suitable nucleophile or an organoelement compound, optionally with catalysis,

by a substituent R2, and

d) replacing the amino function in the compound of the formula V by a halogen substituent, and

e) replacing the halogen substituent in the compound of the formula VI by a nitrile function, and

f) hydrolyzing the nitrile function of the compound of the formula VII to the carboxylic acid, and

g) converting the carboxylic acid of the formula VIII into the acylguanidine of the formula I,

where in the compounds of the formulae II, III, IV, V, VI, VII and VIII

R1 to R4 are as defined in formula I and

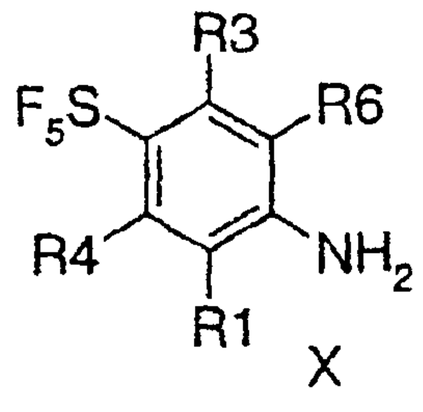
X and Y are independently of one another F, Cl, Br or I.

2. The process as claimed in claim 1, wherein the organoelement compound is an alkylboron compound.

3. The process as claimed in claim 1 or 2 where steps a), b), c), d), e), f) and g) are managed independently of one another continuously or discontinuously.

4. The process as claimed in any one of claims 1-3, in which R2 is hydrogen, and steps b) and c) are omitted.

5. A compound of the formula X




X

in which the meanings are:

R1 hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, $NR10R11$, $-O_p-(CH_2)_n-(CF_2)_o-CF_3$ or $-(SO_m)_q-(CH_2)_r-(CF_2)_s-CF_3$;

R10 and R11

independently of one another hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or $-CH_2-CF_3$;

m zero, 1 or 2

n, o, p, q, r and s

independently of one another zero or 1;

R6 $-(SO_h)_z-(CH_2)_k-(CF_2)_l-CF_3$, alkyl having 1, 2, 3, 4, 5 or 6

carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, in which 1, 2, 3 or 4 hydrogen atoms are optionally by fluorine atoms;

h zero, 1 or 2;

z zero or 1;

k zero, 1, 2, 3 or 4;

l zero or 1;

or

R6 $-(CH_2)_t$-phenyl or –O-phenyl,

which are unsubstituted or substituted by 1, 2 or 3 radicals selected from the group consisting of $-O_u-(CH_2)_v-CF_3$,

alkoxy having 1, 2, 3 or 4 carbon atoms, alkyl having 1, 2, 3 or 4 carbon atoms and $-SO_2CH_3$;

t zero, 1, 2, 3 or 4;

u zero or 1;

v zero, 1, 2 or 3;

or

R6 $-(CH_2)_w$-heteroaryl

which is unsubstituted or substituted by 1, 2 or 3 radicals selected from the group consisting of $-O_x-(CH_2)_y-CF_3$,

alkoxy having 1, 2, 3 or 4 carbon atoms and alkyl having 1, 2, 3 or 4 carbon atoms, $-SO_2CH_3$;

w zero, 1, 2, 3 or 4;

x zero or 1;

y zero, 1, 2 or 3;

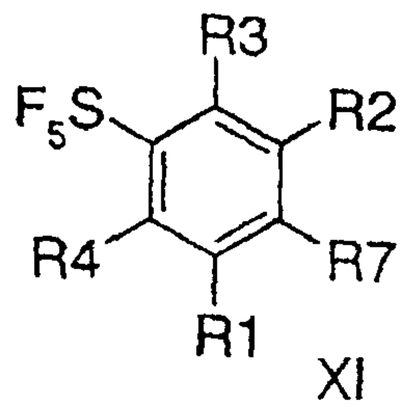
R3 and R4,

independently of one another hydrogen or F;

and the salts thereof.

6. A compound of the formula X and/or the pharmaceutically suitable salts thereof as claimed in claim 5 for use as synthesis intermediate.

7. A compound of the formula XI




XI

in which the meanings are:

R1 hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, $NR10R11$, $-O_p-(CH_2)_n-(CF_2)_o-CF_3$ or $-(SO_m)_q-(CH_2)_r-(CF_2)_s-CF_3$;

R10 and R11

independently of one another hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or $-CH_2-CF_3$;

m zero, 1 or 2

n, o, p, q, r and s

independently of one another zero or 1;

R2 hydrogen, F, Cl, Br, I, $-(SO_h)_z-(CH_2)_k-(CF_2)_l-CF_3$ or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms;

h zero, 1 or 2;

z zero or 1;

k zero, 1, 2, 3 or 4;

l zero or 1;

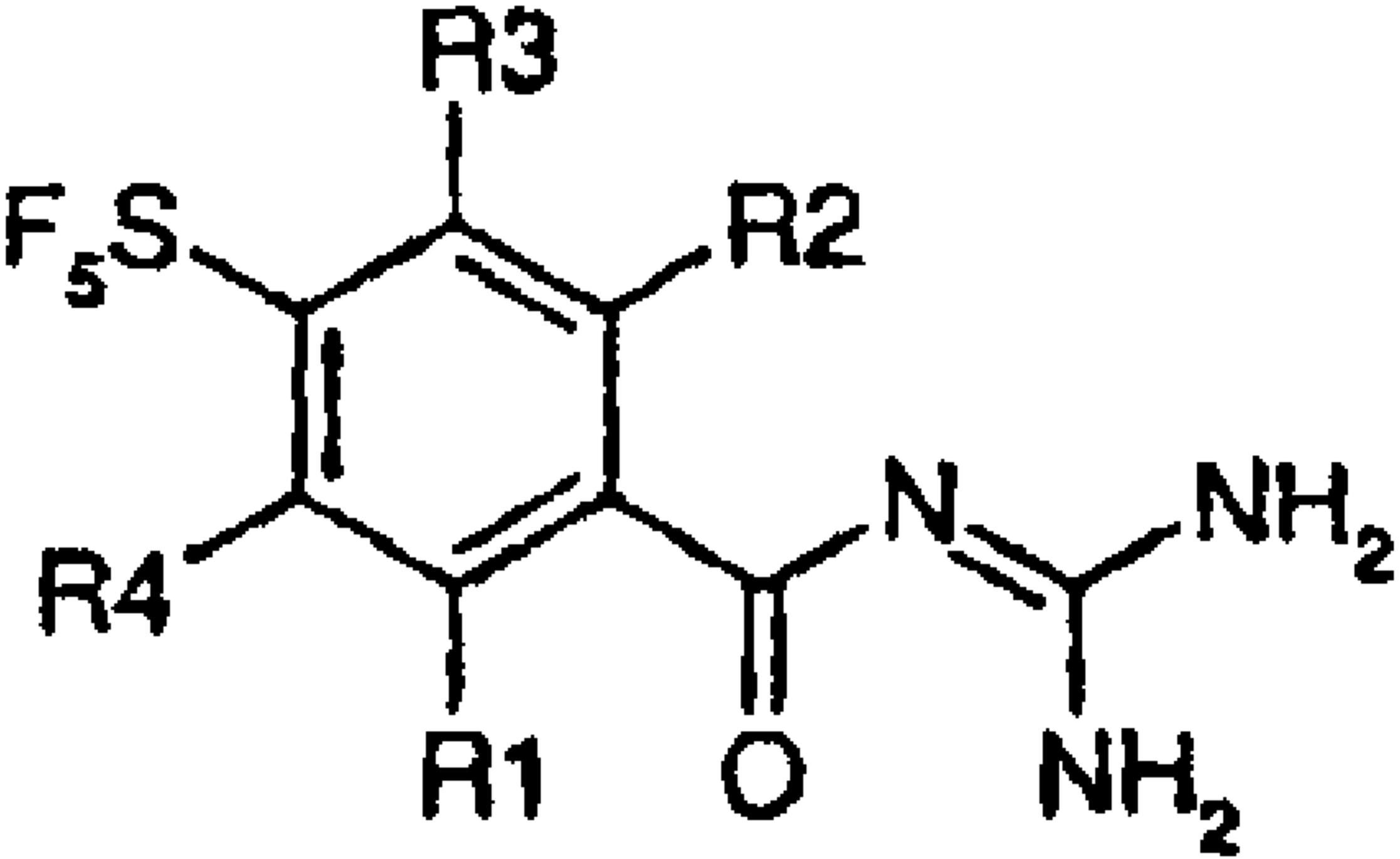
R3 and R4,

independently of one another hydrogen or F;

R7 CN;

and the salts thereof.

8. A compound of the formula XI and/or the pharmaceutically suitable salts thereof as claimed in claim 7 for use as synthesis intermediate.




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