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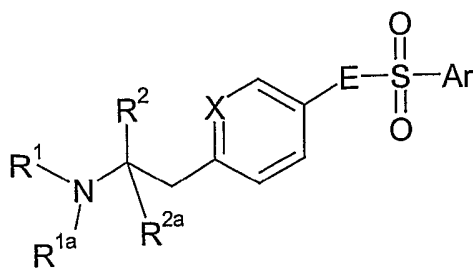
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(54) Title: AMINOETHYLAROMATIC COMPOUNDS SUITABLE FOR TREATING DISORDERS THAT RESPOND TO MODULATION OF THE DOPAMINE D₃ RECEPTOR



(I)

(57) Abstract: The present invention relates to aromatic compounds of the formula (I) wherein Ar is phenyl or an aromatic 5- or 6-membered C-bound heteroaromatic radical, wherein Ar may carry 1 radical R^a and wherein Ar may also carry 1 or 2 radicals R^b; X is N or CH; E is CR⁶R⁷ or NR³; R¹ is C₁-C₄-alkyl, C₃-C₄-cycloalkyl, C₃-C₄-cycloalkylmethyl, C₃-C₄-alkenyl, fluorinated C₁-C₄-alkyl, fluorinated C₃-C₄-cycloalkyl, fluorinated C₃-C₄-cycloalkylmethyl, fluorinated C₃-C₄-alkenyl, formyl or C₁-C₃-alkylcarbonyl;

R^{1a} is H, C₁-C₄-alkyl, C₃-C₄-cycloalkyl, C₃-C₄-cycloalkylmethyl, C₃-C₄-alkenyl, fluorinated C₁-C₄-alkyl, fluorinated C₃-C₄-cycloalkyl, fluorinated C₃-C₄-cycloalkylmethyl, fluorinated C₃-C₄-alkenyl, or R^{1a} and R² together are (CH₂)_n with n being 2, 3 or 4; R^{1a} and R^{2a} together are (CH₂)_n with n being 2, 3 or 4; R¹ and R² are independently of each other H, C₁-C₄-alkyl or fluorinated C₁-C₄-alkyl or R^{2a} and R² together are (CH₂)_m with m being 1, 2, 3, 4 or 5; R³ is H or C₁-C₄-alkyl; R⁶, R⁷ independently of each other are selected from H, fluorine, C₁-C₄-alkyl and fluorinated C₁-C₄-alkyl or together form a moiety (CH₂)_p with p being 2, 3, 4 or 5; and the physiologically tolerated acid addition salts thereof. The invention also relates to the use of a compound of the formula (I) or a pharmaceutically acceptable salt thereof for preparing a pharmaceutical composition for the treatment of a medical disorder susceptible to treatment with a dopamine D₃ receptor ligand.

AMINOETHYLAROMATIC COMPOUNDS SUITABLE FOR TREATING DISORDERS THAT RESPOND TO MODULATION OF THE DOPAMINE D₃ RECEPTOR

Background Of The Invention

5

The present invention relates to novel aminoethylaromatic compounds. The compounds possess valuable therapeutic properties and are suitable, in particular, for treating diseases that respond to modulation of the dopamine D₃ receptor.

10 Neurons obtain their information by way of G protein-coupled receptors, inter alia. A large number of substances exert their effect by way of these receptors. One of them is dopamine. Confirmed findings exist with regard to the presence of dopamine and its physiological function as a neurotransmitter. Disorders in the dopaminergic transmitter system result in diseases of the central nervous system which include, for example,
15 schizophrenia, depression and Parkinson's disease. These diseases, and others, are treated with drugs which interact with the dopamine receptors.

Up until 1990, two subtypes of dopamine receptor had been clearly defined pharmacologically, namely the D₁ and D₂ receptors. More recently, a third subtype was found,
20 namely the D₃ receptor which appears to mediate some effects of antipsychotics and antiparkinsonians (J.C. Schwartz et al., The Dopamine D₃ Receptor as a Target for Antipsychotics, in Novel Antipsychotic Drugs, H.Y. Meltzer, Ed. Raven Press, New York 1992, pages 135-144; M. Dooley et al., Drugs and Aging 1998, 12, 495-514, J.N. Joyce, Pharmacology and Therapeutics 2001, 90, pp. 231-59 "The Dopamine D₃ Receptor as a Therapeutic Target for Antipsychotic and Antiparkinsonian Drugs").
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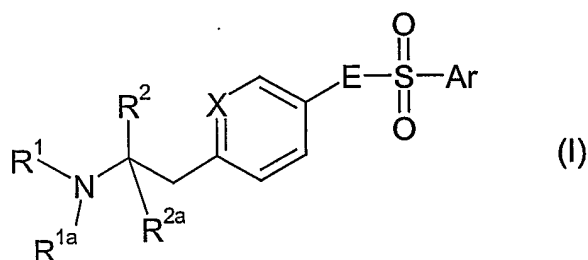
Since then, the dopamine receptors have been divided into two families. On the one hand, there is the D₂ group, consisting of D₂, D₃ and D₄ receptors, and, on the other hand, the D₁ group, consisting of D₁ and D₅ receptors. Whereas D₁ and D₂ receptors
30 are widely distributed, D₃ receptors appear to be expressed regioselectively. Thus, these receptors are preferentially to be found in the limbic system and the projection regions of the mesolimbic dopamine system, especially in the nucleus accumbens, but also in other regions, such as the amygdala. Because of this comparatively regioselective expression, D₃ receptors are regarded as being a target having few side-effects
35 and it is assumed that while a selective D₃ ligand would have the properties of known antipsychotics, it would not have their dopamine D₂ receptor-mediated neurological side-effects (P. Sokoloff et al., Localization and Function of the D₃ Dopamine Receptor,

Arzneim. Forsch./Drug Res. 42(1), 224 (1992); P. Sokoloff et al. Molecular Cloning and Characterization of a Novel Dopamine Receptor (D₃) as a Target for Neuroleptics, Nature, 347, 146 (1990)).

- 5 WO 99/58499 discloses phenylsulfonamide substituted phenethylamines having an affinity for the dopamine D₃ receptor. The phenyl ring of the phenylsulfonamide moiety preferably carries a radical selected from C₁-C₃-alkyl, halogen, OCH₃, OCF₃, CF₃, CN, SCH₃ or NHCOCH₃. These compounds are selective for the Dopamine D₃ receptor and possess only modest affinities for the dopamine D₂ receptor. They have therefore been
- 10 proposed as being suitable for treating diseases of the central nervous system. Unfortunately their affinity for the D₃ receptor or their pharmacological profile are not satisfactory. Consequently there is an ongoing need to provide new compounds, which either have an high affinity and an improved selectivity. The compounds should also have good pharmacological profile, e.g. a high brain plasma ratio, a high bioavailability,
- 15 metabolic stability or a decreased inhibition of the mitochondrial respiration.

Summary Of The Invention

- The invention is based on the object of providing compounds which act as highly selective dopamine D₃ receptor ligands. This object is surprisingly achieved by means of
- 20 aminoethylaromatic compounds of the formula I



wherein

- 25 Ar is phenyl or an aromatic 5- or 6-membered C-bound heteroaromatic radical, wherein Ar may carry 1 radical R^a and wherein Ar may also carry 1 or 2 radicals R^b;
- 30 R^a being selected from the group consisting of C₁-C₆-alkyl, C₂-C₆-alkenyl, fluorinated C₂-C₆-alkenyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, fluorinated C₁-C₆-alkyl, fluorinated C₃-C₆-cycloalkyl, fluorinated C₁-C₆-alkoxy, C₁-C₆-hydroxyalkyl, C₁-C₆-alkoxy-C₁-C₄-alkyl, C₁-C₆-hydroxyalkoxy, C₁-C₆-alkoxy-C₁-C₄-alkoxy, COOH, NR⁴R⁵,

- CH₂NR⁴R⁵, ONR⁴R⁵, NHC(O)NR⁴R⁵, C(O)NR⁴R⁵, SO₂NR⁴R⁵, C₁-C₆-alkylcarbonyl, fluorinated C₁-C₆-alkylcarbonyl, C₁-C₆-alkylcarbonylamino, fluorinated C₁-C₆-alkylcarbonylamino, C₁-C₆-alkylcarbonyloxy, fluorinated C₁-C₆-alkylcarbonyloxy, C₁-C₆-alkoxycarbonyl, C₁-C₆-alkylthio, fluorinated C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, fluorinated C₁-C₆-alkylsulfinyl, fluorinated C₁-C₆-alkylsulfonyl, phenylsulfonyl, phenyl, phenoxy, benzyloxy and a 3- to 7-membered heterocyclic radical, wherein the five last mentioned radicals may carry 1, 2, 3 or 4 radicals selected from halogen, cyano, OH, oxo, CN, and the radicals R^a,
- R^b being, independently from each other, selected from halogen, cyano, nitro, OH, methyl, methoxy, fluoromethyl, difluoromethyl, trifluoromethyl, fluormethoxy, difluoromethoxy and trifluoromethoxy,
- the radical R^a and one radical R^b, if present and bound to two adjacent carbon atoms of phenyl, may form a 5- or 6-membered heterocyclic or carbocyclic ring which is fused to the phenyl ring and which is unsubstituted or which may carry 1, 2 or 3 radicals selected from halogen, NO₂, NH₂, OH, CN, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, fluorinated C₁-C₆-alkyl, fluorinated C₃-C₆-cycloalkyl, fluorinated C₁-C₆-alkoxy, C₁-C₆-hydroxyalkyl, C₁-C₄-alkoxy-C₂-C₄-alkyl, C₁-C₆-hydroxyalkoxy, C₁-C₄-alkoxy-C₂-C₄-alkoxy, C₁-C₆-alkylcarbonyl, C₁-C₆-alkylamino, di-C₁-C₆-alkylamino, C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, fluorinated C₁-C₆-alkylcarbonyl, C₁-C₆-alkylcarbonylamino, fluorinated C₁-C₆-alkylcarbonylamino, C₁-C₆-alkylcarbonyloxy, fluorinated C₁-C₆-alkylcarbonyloxy, C₁-C₆-alkoxycarbonyl, C₁-C₆-alkylthio, fluorinated C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, fluorinated C₁-C₆-alkylsulfinyl and fluorinated C₁-C₆-alkylsulfonyl,
- X is N or CH;
- E is CR⁶R⁷ or NR³;
- R¹ is C₁-C₄-alkyl, C₃-C₄-cycloalkyl, C₃-C₄-cycloalkylmethyl, C₃-C₄-alkenyl, fluorinated C₁-C₄-alkyl, fluorinated C₃-C₄-cycloalkyl, fluorinated C₃-C₄-cycloalkylmethyl, fluorinated C₃-C₄-alkenyl, formyl or C₁-C₃-alkylcarbonyl;

R^{1a} is H, C₁-C₄-alkyl, C₃-C₄-cycloalkyl, C₃-C₄-cycloalkylmethyl, C₃-C₄-alkenyl, fluorinated C₁-C₄-alkyl, fluorinated C₃-C₄-cycloalkyl, fluorinated C₃-C₄-cycloalkylmethyl, fluorinated C₃-C₄-alkenyl, or R^{1a} and R^2 together are (CH₂)_n with n being 2, 3 or 4, or R^{1a} and R^{2a} together are (CH₂)_n with n being 2, 3 or 4;

5 R^2 and R^{2a} are independently of each other H, C₁-C₄-alkyl or fluorinated C₁-C₄-alkyl or R^{2a} and R^2 together are (CH₂)_m with m being 2, 3, 4 or 5;

R^3 is H or C₁-C₄-alkyl;

10 R^4 , R^5 independently of each other are selected from H, C₁-C₃-alkyl, C₁-C₃-alkoxy and fluorinated C₁-C₃-alkyl;

15 R^6 , R^7 independently of each other are selected from H, fluorine, C₁-C₄-alkyl and fluorinated C₁-C₄-alkyl or together form a moiety (CH₂)_p with p being 2, 3, 4 or 5;

provided that for R^1 being C₁-C₄-alkyl, $R^2 = R^{2a}$ being H, E being NH, X being CH and Ar = substituted phenyl Ar carries at least one substituent R^a which is different from linear C₁-C₃-alkyl, OCH₃, OCF₃, CF₃, SCH₃ or NHC(O)CH₃, and which is preferably
 20 selected from secondary C₃-C₆-alkyl, fluorinated C₂-C₆-alkyl, fluorinated C₃-C₆-cycloalkyl, fluorinated C₂-C₆-alkoxy, CHF₂, CF₂, OCHF₂, OCF₂, NR⁴R⁵, 1-aziridinyl, azetidin-1-yl, pyrrolidin-1-yl or piperidin-1-yl, wherein the last for mentioned radicals may be fluorinated or may carry 1 or 2 radicals selected from OH, oxo, C₁-C₂-alkyl, fluorinated C₁-C₂-alkyl or C₁-C₂-alkoxy, a phenyl group and an aromatic 5- or 6-
 25 membered C-bound heteroaromatic radical, comprising 1 nitrogen atom as ring member and 0, 1, 2 or 3 further heteroatoms, independently of each other, selected from O, S and N, wherein the last two mentioned radicals may carry 1, 2, 3 or 4 radicals selected from halogen, NO₂, OH, CN, and the radicals R^a such as NH₂, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, fluorinated C₁-C₆-alkyl, fluorinated C₃-C₆-cycloalkyl, fluorinated C₁-C₆-alkoxy, C₁-C₆-hydroxyalkyl, C₁-C₄-alkoxy-C₂-C₄-alkyl, C₁-C₆-hydroxyalkoxy, C₁-C₄-alkoxy-C₂-C₄-alkoxy, C₁-C₆-alkylcarbonyl, C₁-C₆-alkylamino, di-C₁-C₆-alkylamino, C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, fluorinated C₁-C₆-alkylcarbonyl, C₁-C₆-alkylcarbonylamino, fluorinated C₁-C₆-alkylcarbonylamino, C₁-C₆-alkylcarbonyloxy, fluorinated C₁-C₆-alkylcarbonyloxy, C₁-C₆-alkoxycarbonyl, C₁-C₆-alkylthio, fluorinated C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, fluorinated C₁-C₆-alkylsulfinyl and fluorinated C₁-C₆-alkylsulfonyl;

and the physiologically tolerated acid addition salts of these compounds.

The present invention therefore relates to aminoethylaromatic compounds of the general formula I and to their physiologically tolerated acid addition salts.

5

The present invention also relates to a pharmaceutical composition which comprises at least one aminoethylaromatic compound of the formula I and/or at least one physiologically tolerated acid addition salt of I, where appropriate together with physiologically acceptable carriers and/or auxiliary substances.

10

The present invention also relates to a method for treating disorders which respond to influencing by dopamine D₃ receptor antagonists or dopamine D₃ agonists, said method comprising administering an effective amount of at least one aminoethylaromatic compound of the formula I and/or at least one physiologically tolerated acid addition salt of I to a subject in need thereof.

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Detailed Description Of The Invention

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The diseases which respond to the influence of dopamine D₃ receptor antagonists or agonists include, in particular, disorders and diseases of the central nervous system, in particular affective disturbances, neurotic disturbances, stress disturbances and somatoform disturbances and psychoses, especially schizophrenia and depression and, in addition, disturbances of kidney function, in particular kidney function disturbances which are caused by diabetes mellitus (see WO 00/67847).

25

According to the invention, at least one compound of the general formula I having the meanings mentioned at the outset is used for treating the above mentioned indications. Provided the compounds of the formula I of a given constitution may exist in different spatial arrangements, for example if they possess one or more centers of asymmetry, polysubstituted rings or double bonds, or as different tautomers, it is also possible to use enantiomeric mixtures, in particular racemates, diastereomeric mixtures and tautomeric mixtures, preferably, however, the respective essentially pure enantiomers, diastereomers and tautomers of the compounds of formula I and/or of their salts.

30

It is likewise possible to use physiologically tolerated salts of the compounds of the formula I, especially acid addition salts with physiologically tolerated acids. Examples of suitable physiologically tolerated organic and inorganic acids are hydrochloric acid,

35

hydrobromic acid, phosphoric acid, sulfuric acid, C₁-C₄-alkylsulfonic acids, such as methanesulfonic acid, aromatic sulfonic acids, such as benzenesulfonic acid and toluenesulfonic acid, oxalic acid, maleic acid, fumaric acid, lactic acid, tartaric acid, adipic acid and benzoic acid. Other utilizable acids are described in Fortschritte der Arzneimittelforschung [Advances in drug research], Volume 10, pages 224 ff., Birkhäuser Verlag, Basel and Stuttgart, 1966.

The organic moieties mentioned in the above definitions of the variables are - like the term halogen - collective terms for individual listings of the individual group members.

10 The prefix C_n-C_m indicates in each case the possible number of carbon atoms in the group.

The term halogen denotes in each case fluorine, bromine, chlorine or iodine, in particular fluorine or chlorine.

15 C₁-C₄ Alkyl (and likewise in C₁-C₄ hydroxyalkyl, C₁-C₆ alkoxy-C₁-C₄-alkyl, C₁-C₄ alkylcarbonyl, C₁-C₄ alkylcarbonylamino, C₁-C₄ alkylcarbonyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl etc.) is a straight-chain or branched alkyl group having from 1 to 4 carbon atoms. Examples of an alkyl group are methyl, ethyl, n-propyl, iso-propyl, n-butyl, 2-butyl, iso-butyl or *tert*-butyl.

C₁-C₆ Alkyl (and likewise in C₁-C₆ hydroxyalkyl, C₁-C₆ alkoxy-C₁-C₄-alkyl, C₁-C₆ alkylcarbonyl, C₁-C₆ alkylcarbonylamino, C₁-C₆ alkylcarbonyloxy, C₁-C₆ alkylthio, C₁-C₆ alkylsulfinyl, C₁-C₆ alkylsulfonyl etc.) is a straight-chain or branched alkyl group having from 1 to 6 carbon atoms. Examples include C₁-C₄ alkyl as mentioned above and also pentyl, 1-methylbutyl, 2-methylbutyl, 3-methylbutyl, 2,2-dimethylpropyl, 1-ethylpropyl, hexyl, 1,1-dimethylpropyl, 1,2-dimethylpropyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 1,1-dimethylbutyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, 2,2-dimethylbutyl, 2,3-dimethylbutyl, 3,3-dimethylbutyl, 1-ethylbutyl, 2-ethylbutyl, 1,1,2-trimethylpropyl, 1,2,2-trimethylpropyl, 1-ethyl-1-methylpropyl and 1-ethyl-2-methylpropyl;

Fluorinated C₁-C₆ alkyl (and likewise in fluorinated C₁-C₆ alkylcarbonyl, fluorinated C₁-C₆ alkylcarbonylamino, fluorinated C₁-C₆ alkylcarbonyloxy, fluorinated C₁-C₆ alkylthio, fluorinated C₁-C₆ alkylsulfinyl, fluorinated C₁-C₆ alkylsulfonyl etc.) is a straight-chain or branched alkyl group having from 1 to 6, in particular 1 to 4 carbon atoms, more preferably 1 to 3 carbon atoms, wherein at least one, e.g. 1, 2, 3, 4 or all of the hydrogen

atoms are replaced by a fluorine atoms such as in fluoromethyl, difluoromethyl, trifluoromethyl, (R)-1-fluoroethyl, (S)-1-fluoroethyl, 2-fluoroethyl, 1,1-difluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, (R)-1-fluoropropyl, (S)-1-fluoropropyl, 2-fluoropropyl, 3-fluoropropyl, 1,1-difluoropropyl, 2,2-difluoropropyl, 3,3-difluoropropyl, 3,3,3-trifluoropropyl, (R)-2-fluoro-1-methylethyl, (S)-2-fluoro-1-methylethyl, (R)-2,2-difluoro-1-methylethyl, (S)-2,2-difluoro-1-methylethyl, (R)-1,2-difluoro-1-methylethyl, (S)-1,2-difluoro-1-methylethyl, (R)-2,2,2-trifluoro-1-methylethyl, (S)-2,2,2-trifluoro-1-methylethyl, 2-fluoro-1-(fluoromethyl)ethyl, 1-(difluoromethyl)-2,2-difluoroethyl, (R)-1-fluorobutyl, (S)-1-fluorobutyl, 2-fluorobutyl, 3-fluorobutyl, 4-fluorobutyl, 1,1-difluorobutyl, 2,2-difluorobutyl, 3,3-difluorobutyl, 4,4-difluorobutyl, 4,4,4-trifluorobutyl, etc.;

Branched C₃-C₆ alkyl is alkyl having 3 to 6 carbon atoms at least one being a secondary or tertiary carbon atom. Examples are isopropyl, tert.-butyl, 2-butyl, isobutyl, 2-pentyl, 2-hexyl, 3-methylpentyl, 1,1-dimethylbutyl, 1,2-dimethylbutyl 1-methyl-1-ethylpropyl.

C₁-C₆ Alkoxy (and likewise in C₁-C₆ alkoxy carbonyl, C₁-C₆ alkoxy-C₁-C₄ alkyl, C₁-C₆ alkoxy-C₁-C₄ alkoxy and C₁-C₆ hydroxyalkoxy) is a straight-chain or branched alkyl group having from 1 to 6, in particular 1 to 4 carbon atoms, which is bound to the remainder of the molecule via an oxygen atom. Examples include methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, 2-butoxy, iso-butoxy, tert.-butoxy pentyloxy, 1-methylbutoxy, 2-methylbutoxy, 3-methylbutoxy, 2,2-dimethylpropoxy, 1-ethylpropoxy, hexyloxy, 1,1-dimethylpropoxy, 1,2-dimethylpropoxy, 1-methylpentyloxy, 2-methylpentyloxy, 3-methylpentyloxy, 4-methylpentyloxy, 1,1-dimethylbutyloxy, 1,2-dimethylbutyloxy, 1,3-dimethylbutyloxy, 2,2-dimethylbutyloxy, 2,3-dimethylbutyloxy, 3,3-dimethylbutyloxy, 1-ethylbutyloxy, 2-ethylbutyloxy, 1,1,2-trimethylpropoxy, 1,2,2-trimethylpropoxy, 1-ethyl-1-methylpropoxy and 1-ethyl-2-methylpropoxy;

Fluorinated C₁-C₆ alkoxy (and likewise in fluorinated C₁-C₆ alkoxy carbonyl) is a straight-chain or branched alkoxy group having from 1 to 6, in particular 1 to 4 carbon atoms, wherein at least one, e.g. 1, 2, 3, 4 or all of the hydrogen atoms are replaced by a fluorine atoms such as in fluoromethoxy, difluoromethoxy, trifluoromethoxy, (R)-1-fluoroethoxy, (S)-1-fluoroethoxy, 2-fluoroethoxy, 1,1-difluoroethoxy, 2,2-difluoroethoxy, 2,2,2-trifluoroethoxy, (R)-1-fluoropropoxy, (S)-1-fluoropropoxy, 2-fluoropropoxy, 3-fluoropropoxy, 1,1-difluoropropoxy, 2,2-difluoropropoxy, 3,3-difluoropropoxy, 3,3,3-trifluoropropoxy, (R)-2-fluoro-1-methylethoxy, (S)-2-fluoro-1-methylethoxy, (R)-2,2-difluoro-1-methylethoxy, (S)-2,2-difluoro-1-methylethoxy, (R)-1,2-difluoro-1-

methylethoxy, (S)-1,2-difluoro-1-methylethoxy, (R)-2,2,2-trifluoro-1-methylethoxy, (S)-2,2,2-trifluoro-1-methylethoxy, 2-fluoro-1-(fluoromethyl)ethoxy, 1-(difluoromethyl)-2,2-difluoroethoxy, (R)-1-fluorobutoxy, (S)-1-fluorobutoxy, 2-fluorobutoxy, 3-fluorobutoxy, 4-fluorobutoxy, 1,1-difluorobutoxy, 2,2-difluorobutoxy, 3,3-difluorobutoxy, 4,4-difluorobutoxy, 4,4,4-trifluorobutoxy, etc.;

C_3 - C_6 Cycloalkyl is a cycloaliphatic radical having from 3 to 6 C atoms, such as cyclopropyl, cyclobutyl and cyclopentyl. The cycloalkyl radical may be unsubstituted or may carry 1, 2, 3 or 4 C_1 - C_4 alkyl radicals, preferably a methyl radical. One alkyl radical is preferably located in the 1-position of the cycloalkyl radical, such as in 1-methylcyclopropyl or 1-methylcyclobutyl.

Fluorinated C_3 - C_6 cycloalkyl is a cycloaliphatic radical having from 3 to 6 C atoms, such as cyclopropyl, cyclobutyl and cyclopentyl, wherein at least one, e.g. 1, 2, 3, 4 or all of the hydrogen atoms are replaced by a fluorine atoms such as in 1-fluorocyclopropyl, 2-fluorocyclopropyl, 2,2-difluorocyclopropyl, 1,2-difluorocyclopropyl, 2,3-difluorocyclopropyl, pentafluorocyclopropyl, 1-fluorocyclobutyl, 2-fluorocyclobutyl, 3-fluorocyclobutyl, 2,2-difluorocyclobutyl, 3,3-difluorocyclobutyl, 1,2-difluorocyclobutyl, 1,3-difluorocyclobutyl, 2,3-difluorocyclobutyl, 2,4-difluorocyclobutyl, or 1,2,2-trifluorocyclobutyl.

C_3 - C_6 Cycloalkylmethyl is methyl which carries a cycloaliphatic radical having from 3 to 6 C atoms as mentioned above

Fluorinated C_3 - C_6 cycloalkylmethyl is methyl which carries a cycloaliphatic radical having from 3 to 6 C atoms, wherein at least one, e.g. 1, 2, 3, 4 or all of the hydrogen atoms are replaced by a fluorine atoms.

C_2 - C_6 -Alkenyl is a singly unsaturated hydrocarbon radical having 2, 3, 4, 5 or 6 C-atoms, e.g. vinyl, allyl(2-propen-1-yl), 1-propen-1-yl, 2-propen-2-yl, methallyl(2-methylprop-2-en-1-yl) and the like. C_3 - C_4 -Alkenyl is, in particular, allyl, 1-methylprop-2-en-1-yl, 2-buten-1-yl, 3-buten-1-yl, methallyl, 2-penten-1-yl, 3-penten-1-yl, 4-penten-1-yl, 1-methylbut-2-en-1-yl or 2-ethylprop-2-en-1-yl.

Fluorinated C_2 - C_6 -alkenyl is a singly unsaturated hydrocarbon radical having 2, 3, 4, 5 or 6 C-atoms, wherein at least one, e.g. 1, 2, 3, 4 or all of the hydrogen atoms are re-

placed by a fluorine atoms such as in 1-fluorovinyl, 2-fluorovinyl, 2,2-fluorovinyl, 3,3,3-fluoropropenyl, 1,1-difluoro-2-propenyl 1-fluoro-2-propenyl and the like.

5 C₁-C₆ hydroxyalkyl is an alkyl radical having from 1 to 6 carbon atoms as defined above, wherein one hydrogen atom is replaced by hydroxy. Examples comprise hydroxymethyl, 2-hydroxyethyl, 1-hydroxyethyl, 3-hydroxypropyl, 2-hydroxypropyl, 1-methyl-1-hydroxyethyl and the like.

10 C₁-C₆ hydroxyalkoxy is an alkoxy radical having from 1 to 6, preferably from 2 to 4 carbon atoms as defined above, wherein one hydrogen atom is replaced by hydroxy. Examples comprise 2-hydroxyethyl, 3-hydroxypropyl, 2-hydroxypropyl, 1-methyl-2-hydroxyethyl and the like.

15 C₁-C₆ alkoxy-C₁-C₄-alkyl is an alkyl radical having from 1 to 4 carbon atoms as defined above, wherein one hydrogen atom is replaced by C₁-C₆ alkoxy. Examples comprise methoxymethyl, 2-methoxyethyl, 1-methoxyethyl, 3-methoxypropyl, 2-methoxypropyl, 1-methyl-1-methoxyethyl, ethoxymethyl, 2-ethoxyethyl, 1-ethoxyethyl, 3-ethoxypropyl, 2-ethoxypropyl, 1-methyl-1-ethoxyethyl and the like.

20 C₁-C₆ alkoxy-C₁-C₄-alkoxy is an alkoxy radical having from 1 to 4 carbon atoms as defined above, wherein one hydrogen atom is replaced by C₁-C₆ alkoxy. Examples comprise methoxymethoxy, 2-methoxyethoxy, 1-methoxyethoxy, 3-methoxypropoxy, 2-methoxypropoxy, 1-methyl-1-methoxyethoxy, ethoxymethoxy, 2-ethoxyethoxy, 1-ethoxyethoxy, 3-ethoxypropoxy, 2-ethoxypropoxy, 1-methyl-1-ethoxyethoxy and the like.
25

30 C₁-C₆ alkylcarbonyl is a radical of the formula R-C(O)-, wherein R is an alkyl radical having from 1 to 6 carbon atoms as defined above. Examples comprise acetyl, propionyl, n-butyryl, 2-methylpropionyl, pivalyl and the like.

C₁-C₆ alkylcarbonylamino is a radical of the formula R-C(O)-NH-, wherein R is an alkyl radical having from 1 to 6 carbon atoms as defined above. Examples comprise acetamido, propionamido, n-butyramido, 2-methylpropionamido, 2,2-dimethylpropionamido and the like.

35 C₁-C₆ alkylcarbonyloxy is a radical of the formula R-C(O)-O-, wherein R is an alkyl radical having from 1 to 6 carbon atoms as defined above. Examples comprise acety-

loxy, propionyloxy, n-butyryloxy, 2-methylpropionyloxy, 2,2-dimethylpropionyloxy and the like.

C₁-C₆ alkylthio is a radical of the formula R-S-, wherein R is an alkyl radical having from 1 to 6 carbon atoms as defined above. Examples comprise methylthio, ethylthio, propylthio, butylthio, pentylthio, 1-methylbutylthio, 2-methylbutylthio, 3-methylbutylthio, 2,2-dimethylpropylthio, 1-ethylpropylthio, hexylthio, 1,1-dimethylpropylthio, 1,2-dimethylpropylthio, 1-methylpentylthio, 2-methylpentylthio, 3-methylpentylthio, 4-methylpentylthio, 1,1-dimethylbutylthio, 1,2-dimethylbutylthio, 1,3-dimethylbutylthio, 2,2-dimethylbutylthio, 2,3-dimethylbutylthio, 3,3-dimethylbutylthio, 1-ethylbutylthio, 2-ethylbutylthio, 1,1,2-trimethylpropylthio, 1,2,2-trimethylpropylthio, 1-ethyl-1-methylpropyl and 1-ethyl-2-methylpropyl;

C₁-C₆ alkylsulfinyl is a radical of the formula R-S(O)-, wherein R is an alkyl radical having from 1 to 6 carbon atoms as defined above. Examples comprise methylsulfinyl, ethylsulfinyl, propylsulfinyl, butylsulfinyl, pentylsulfinyl, 1-methylbutylsulfinyl, 2-methylbutylsulfinyl, 3-methylbutylsulfinyl, 2,2-dimethylpropylsulfinyl, 1-ethylpropylsulfinyl, hexylsulfinyl, 1,1-dimethylpropylsulfinyl, 1,2-dimethylpropylsulfinyl, 1-methylpentylsulfinyl, 2-methylpentylsulfinyl, 3-methylpentylsulfinyl, 4-methylpentylsulfinyl, 1,1-dimethylbutylsulfinyl, 1,2-dimethylbutylsulfinyl, 1,3-dimethylbutylsulfinyl, 2,2-dimethylbutylsulfinyl, 2,3-dimethylbutylsulfinyl, 3,3-dimethylbutylsulfinyl, 1-ethylbutylsulfinyl, 2-ethylbutylsulfinyl, 1,1,2-trimethylpropylsulfinyl, 1,2,2-trimethylpropylsulfinyl, 1-ethyl-1-methylpropyl and 1-ethyl-2-methylpropyl;

C₁-C₆ alkylsulfonyl is a radical of the formula R-S(O)₂-, wherein R is an alkyl radical having from 1 to 6 carbon atoms as defined above. Examples comprise methylsulfonyl, ethylsulfonyl, propylsulfonyl, butylsulfonyl, pentylsulfonyl, 1-methylbutylsulfonyl, 2-methylbutylsulfonyl, 3-methylbutylsulfonyl, 2,2-dimethylpropylsulfonyl, 1-ethylpropylsulfonyl, hexylsulfonyl, 1,1-dimethylpropylsulfonyl, 1,2-dimethylpropylsulfonyl, 1-methylpentylsulfonyl, 2-methylpentylsulfonyl, 3-methylpentylsulfonyl, 4-methylpentylsulfonyl, 1,1-dimethylbutylsulfonyl, 1,2-dimethylbutylsulfonyl, 1,3-dimethylbutylsulfonyl, 2,2-dimethylbutylsulfonyl, 2,3-dimethylbutylsulfonyl, 3,3-dimethylbutylsulfonyl, 1-ethylbutylsulfonyl, 2-ethylbutylsulfonyl, 1,1,2-trimethylpropylsulfonyl, 1,2,2-trimethylpropylsulfonyl, 1-ethyl-1-methylpropyl and 1-ethyl-2-methylpropyl;

fluorinated C₁-C₆ alkylcarbonyl is a radical of the formula R-C(O)-, wherein R is a fluorinated alkyl radical having from 1 to 6 carbon atoms as defined above. Examples comprise fluoroacetyl, difluoroacetyl, trifluoroacetyl, (R)-1-fluoroethylcarbonyl, (S)-1-fluoroethylcarbonyl, 2-fluoroethylcarbonyl, 1,1-difluoroethylcarbonyl, 2,2-difluoroethylcarbonyl, 2,2,2-trifluoroethylcarbonyl, (R)-1-fluoropropylcarbonyl, (S)-1-fluoropropylcarbonyl, 2-fluoropropylcarbonyl, 3-fluoropropylcarbonyl, 1,1-difluoropropylcarbonyl, 2,2-difluoropropylcarbonyl, 3,3-difluoropropylcarbonyl, 3,3,3-trifluoropropylcarbonyl, (R)-2-fluoro-1-methylethylcarbonyl, (S)-2-fluoro-1-methylethylcarbonyl, (R)-2,2-difluoro-1-methylethylcarbonyl, (S)-2,2-difluoro-1-methylethylcarbonyl, (R)-1,2-difluoro-1-methylethylcarbonyl, (S)-1,2-difluoro-1-methylethylcarbonyl, (R)-2,2,2-trifluoro-1-methylethylcarbonyl, (S)-2,2,2-trifluoro-1-methylethylcarbonyl, 2-fluoro-1-(fluoromethyl)ethylcarbonyl, 1-(difluoromethyl)-2,2-difluoroethylcarbonyl, (R)-1-fluorobutylcarbonyl, (S)-1-fluorobutylcarbonyl, 2-fluorobutylcarbonyl, 3-fluorobutylcarbonyl, 4-fluorobutylcarbonyl, 1,1-difluorobutylcarbonyl, 2,2-difluorobutylcarbonyl, 3,3-difluorobutylcarbonyl, 4,4-difluorobutylcarbonyl, 4,4,4-trifluorobutylcarbonyl, etc.;

fluorinated C₁-C₆ alkylcarbonylamino is a radical of the formula R-C(O)-NH-, wherein R is a fluorinated alkyl radical having from 1 to 6 carbon atoms as defined above. Examples comprise fluoroacetamido, difluoroacetamido, trifluoroacetamido, (R)-1-fluoroethylcarbonylamino, (S)-1-fluoroethylcarbonylamino, 2-fluoroethylcarbonylamino, 1,1-difluoroethylcarbonylamino, 2,2-difluoroethylcarbonylamino, 2,2,2-trifluoroethylcarbonylamino, (R)-1-fluoropropylcarbonylamino, (S)-1-fluoropropylcarbonylamino, 2-fluoropropylcarbonylamino, 3-fluoropropylcarbonylamino, 1,1-difluoropropylcarbonylamino, 2,2-difluoropropylcarbonylamino, 3,3-difluoropropylcarbonylamino, 3,3,3-trifluoropropylcarbonylamino, (R)-2-fluoro-1-methylethylcarbonylamino, (S)-2-fluoro-1-methylethylcarbonylamino, (R)-2,2-difluoro-1-methylethylcarbonylamino, (S)-2,2-difluoro-1-methylethylcarbonylamino, (R)-1,2-difluoro-1-methylethylcarbonylamino, (S)-1,2-difluoro-1-methylethylcarbonylamino, (R)-2,2,2-trifluoro-1-methylethylcarbonylamino, (S)-2,2,2-trifluoro-1-methylethylcarbonylamino, 2-fluoro-1-(fluoromethyl)ethylcarbonylamino, 1-(difluoromethyl)-2,2-difluoroethylcarbonylamino, (R)-1-fluorobutylcarbonylamino, (S)-1-fluorobutylcarbonylamino, 2-fluorobutylcarbonylamino, 3-fluorobutylcarbonylamino, 4-fluorobutylcarbonylamino, 1,1-difluorobutylcarbonylamino, 2,2-difluorobutylcarbonylamino, 3,3-difluorobutylcarbonylamino, 4,4-difluorobutylcarbonylamino, 4,4,4-trifluorobutylcarbonylamino, etc.,

fluorinated C₁-C₆ alkylcarbonyloxy is a radical of the formula R-C(O)-O-, wherein R is a fluorinated alkyl radical having from 1 to 6 carbon atoms as defined above fluoroacetyl, difluoroacetyl, trifluoroacetyl, (R)-1-fluoroethylcarbonyloxy, (S)-1-fluoroethylcarbonyloxy, 2-fluoroethylcarbonyloxy, 1,1-difluoroethylcarbonyloxy, 2,2-difluoroethylcarbonyloxy, 2,2,2-trifluoroethylcarbonyloxy, (R)-1-fluoropropylcarbonyloxy, (S)-1-fluoropropylcarbonyloxy, 2-fluoropropylcarbonyloxy, 3-fluoropropylcarbonyloxy, 1,1-difluoropropylcarbonyloxy, 2,2-difluoropropylcarbonyloxy, 3,3-difluoropropylcarbonyloxy, 3,3,3-trifluoropropylcarbonyloxy, (R)-2-fluoro-1-methylethylcarbonyloxy, (S)-2-fluoro-1-methylethylcarbonyloxy, (R)-2,2-difluoro-1-methylethylcarbonyloxy, (S)-2,2-difluoro-1-methylethylcarbonyloxy, (R)-1,2-difluoro-1-methylethylcarbonyloxy, (S)-1,2-difluoro-1-methylethylcarbonyloxy, (R)-2,2,2-trifluoro-1-methylethylcarbonyloxy, (S)-2,2,2-trifluoro-1-methylethylcarbonyloxy, 2-fluoro-1-(fluoromethyl)ethylcarbonyloxy, 1-(difluoromethyl)-2,2-difluoroethylcarbonyloxy, (R)-1-fluorobutylcarbonyloxy, (S)-1-fluorobutylcarbonyloxy, 2-fluorobutylcarbonyloxy, 3-fluorobutylcarbonyloxy, 4-fluorobutylcarbonyloxy, 1,1-difluorobutylcarbonyloxy, 2,2-difluorobutylcarbonyloxy, 3,3-difluorobutylcarbonyloxy, 4,4-difluorobutylcarbonyloxy, 4,4,4-trifluorobutylcarbonyloxy, etc.;

fluorinated C₁-C₆ alkylthio is a radical of the formula R-S-, wherein R is a fluorinated alkyl radical having from 1 to 6 carbon atoms as defined above. Examples comprise fluoromethylthio, difluoromethylthio, trifluoromethylthio, (R)-1-fluoroethylthio, (S)-1-fluoroethylthio, 2-fluoroethylthio, 1,1-difluoroethylthio, 2,2-difluoroethylthio, 2,2,2-trifluoroethylthio, (R)-1-fluoropropylthio, (S)-1-fluoropropylthio, 2-fluoropropylthio, 3-fluoropropylthio, 1,1-difluoropropylthio, 2,2-difluoropropylthio, 3,3-difluoropropylthio, 3,3,3-trifluoropropylthio, (R)-2-fluoro-1-methylethylthio, (S)-2-fluoro-1-methylethylthio, (R)-2,2-difluoro-1-methylethylthio, (S)-2,2-difluoro-1-methylethylthio, (R)-1,2-difluoro-1-methylethylthio, (S)-1,2-difluoro-1-methylethylthio, (R)-2,2,2-trifluoro-1-methylethylthio, (S)-2,2,2-trifluoro-1-methylethylthio, 2-fluoro-1-(fluoromethyl)ethylthio, 1-(difluoromethyl)-2,2-difluoroethylthio, (R)-1-fluorobutylthio, (S)-1-fluorobutylthio, 2-fluorobutylthio, 3-fluorobutylthio, 4-fluorobutylthio, 1,1-difluorobutylthio, 2,2-difluorobutylthio, 3,3-difluorobutylthio, 4,4-difluorobutylthio, 4,4,4-trifluorobutylthio, etc.;

fluorinated C₁-C₆ alkylsulfinyl is a radical of the formula R-S(O)-, wherein R is a fluorinated alkyl radical having from 1 to 6 carbon atoms as defined above. Examples comprise fluoromethylsulfinyl, difluoromethylsulfinyl, trifluoromethylsulfinyl, (R)-1-fluoroethylsulfinyl, (S)-1-fluoroethylsulfinyl, 2-fluoroethylsulfinyl, 1,1-difluoroethylsulfinyl, 2,2-difluoroethylsulfinyl, 2,2,2-trifluoroethylsulfinyl, (R)-1-fluoropropylsulfinyl, (S)-1-

fluoropropylsulfinyl, 2-fluoropropylsulfinyl, 3-fluoropropylsulfinyl, 1,1-difluoropropylsulfinyl, 2,2-difluoropropylsulfinyl, 3,3-difluoropropylsulfinyl, 3,3,3-trifluoropropylsulfinyl, (R)-2-fluoro-1-methylethylsulfinyl, (S)-2-fluoro-1-methylethylsulfinyl, (R)-2,2-difluoro-1-methylethylsulfinyl, (S)-2,2-difluoro-1-methylethylsulfinyl, (R)-1,2-difluoro-1-methylethylsulfinyl, (S)-1,2-difluoro-1-methylethylsulfinyl, (R)-2,2,2-trifluoro-1-methylethylsulfinyl, (S)-2,2,2-trifluoro-1-methylethylsulfinyl, 2-fluoro-1-(fluoromethyl)ethylsulfinyl, 1-(difluoromethyl)-2,2-difluoroethylsulfinyl, (R)-1-fluorobutylsulfinyl, (S)-1-fluorobutylsulfinyl, 2-fluorobutylsulfinyl, 3-fluorobutylsulfinyl, 4-fluorobutylsulfinyl, 1,1-difluorobutylsulfinyl, 2,2-difluorobutylsulfinyl, 3,3-difluorobutylsulfinyl, 4,4-difluorobutylsulfinyl, 4,4,4-trifluorobutylsulfinyl, etc.;

fluorinated C₁-C₆ alkylsulfonyl is a radical of the formula R-S(O)₂·, wherein R is a fluorinated alkyl radical having from 1 to 6 carbon atoms as defined above. Examples comprise fluoromethylsulfonyl, difluoromethylsulfonyl, trifluoromethylsulfonyl, (R)-1-fluoroethylsulfonyl, (S)-1-fluoroethylsulfonyl, 2-fluoroethylsulfonyl, 1,1-difluoroethylsulfonyl, 2,2-difluoroethylsulfonyl, 2,2,2-trifluoroethylsulfonyl, (R)-1-fluoropropylsulfonyl, (S)-1-fluoropropylsulfonyl, 2-fluoropropylsulfonyl, 3-fluoropropylsulfonyl, 1,1-difluoropropylsulfonyl, 2,2-difluoropropylsulfonyl, 3,3-difluoropropylsulfonyl, 3,3,3-trifluoropropylsulfonyl, (R)-2-fluoro-1-methylethylsulfonyl, (S)-2-fluoro-1-methylethylsulfonyl, (R)-2,2-difluoro-1-methylethylsulfonyl, (S)-2,2-difluoro-1-methylethylsulfonyl, (R)-1,2-difluoro-1-methylethylsulfonyl, (S)-1,2-difluoro-1-methylethylsulfonyl, (R)-2,2,2-trifluoro-1-methylethylsulfonyl, (S)-2,2,2-trifluoro-1-methylethylsulfonyl, 2-fluoro-1-(fluoromethyl)ethylsulfonyl, 1-(difluoromethyl)-2,2-difluoroethylsulfonyl, (R)-1-fluorobutylsulfonyl, (S)-1-fluorobutylsulfonyl, 2-fluorobutylsulfonyl, 3-fluorobutylsulfonyl, 4-fluorobutylsulfonyl, 1,1-difluorobutylsulfonyl, 2,2-difluorobutylsulfonyl, 3,3-difluorobutylsulfonyl, 4,4-difluorobutylsulfonyl, 4,4,4-trifluorobutylsulfonyl, etc.

3- to 7-membered heterocyclic radicals comprise saturated heterocyclic radicals, which generally have 3-, 4-, 5-, 6- or 7 ring forming atoms (ring members), unsaturated non-aromatic heterocyclic radicals, which generally have 5-, 6- or 7 ring forming atoms, and heteroaromatic radicals, which generally have 5-, 6- or 7 ring forming atoms. The heterocyclic radicals may be bound via a carbon atom (C-bound) or an nitrogen atom (N-bound). Preferred heterocyclic radicals comprise 1 nitrogen atom as ring member atom and optionally 1, 2 or 3 further heteroatoms as ring members, which are selected, independently of each other from O, S and N. Likewise preferred heterocyclic radicals

comprise 1 heteroatom as ring member, which is selected from O, S and N, and optionally 1, 2 or 3 further nitrogen atoms as ring members.

Examples of 3- to 7-membered, saturated heterocyclic radicals comprise 1- or 2-

5 aziridinyl, 1-, 2- or 3-azetidiny, 1-, 2- or 3-pyrrolidinyl, 1-, 2-, 3- or 4-piperidinyl, 1-, 2- or 3-morpholinyl, 1-, 2- or 3-thiomorpholinyl, 1-, 2- or 3-piperazinyl, 1-, 2- or 4-oxazolidinyl, 1-, 3- or 4-isoxazolidinyl, 2-oxiranyl, 2- or 3-oxetanyl, 2- or 3-oxolanyl, 2-, 3- or 4-oxanyl, 1,3-dioxolan-2- or 4-yl and the like, which may be unsubstituted or which may carry 1, 2 or 3 of the aforementioned radicals R^a and/or R^b.

10

Unsaturated non-aromatic heterocyclic radicals, are heterocyclic radicals which generally have 5-, 6- or 7 ring forming atoms and which have 1 or 2 doublebonds that do not form an aromatic p-electron system. Examples are 2,3-dihydropyrrolyl, 3,4-dihydropyrrolyl, 2,3-dihydrofuranyl, 3,4-dihydrofuranyl, 2,3-dihydrothiophenyl, 3,4-dihydrothiophenyl, 1,2-dihydropyridinyl, 2,3-Dihydropyridinyl, 3,4-dihydropyridinyl, 15 1,2,3,4-tetrahydropyridinyl, 2,3,4,5-tetrahydropyridinyl, and the like.

5- or 6-membered heteroaromatic radicals are heteroaromatic cyclic radicals, wherein the cyclic radical has 5 or 6 atoms which form the ring (ring members) and wherein

20 generally 1, 2, 3 or 4 ring member atoms are selected from O, S and N, the other ring member atoms being carbon atoms. The heteroaromatic radicals may be bound via a carbon atom (C-bound) or an nitrogen atom (N-bound). Preferred heteroaromatic radicals comprise 1 nitrogen atom as ring member atom and optionally 1, 2 or 3 further heteroatoms as ring members, which are selected, independently of each other from O, S and N. Likewise preferred heteroaromatic radicals comprise 1 heteroatom as ring member, which is selected from O, S and N, and optionally 1, 2 or 3 further nitrogen atoms as ring members. Examples of 5- or 6-membered heteroaromatic radicals comprise 2-, 3-, or 4-pyridyl, 2-, 4- or 5-pyrimidinyl, pyrazinyl, 3- or 4-pyridazinyl, 2- or 3-thienyl, 2- or 3-furyl, 1-, 2- or 3-pyrrolyl, 1-, 2- or 4-imidazolyl, 1-, 3- or 4-pyrazolyl, 1- or 30 3-[1,2,4]-triazolyl, 1- or 4-[1,2,3]-triazolyl, 1-, 2- or 5-tetrazolyl, 2-, 3- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 2-, 3- or 5-thiazolyl, 3-, 4- or 5-isothiazolyl, 4- or 5-[1,2,3]-oxadiazolyl, [1,2,5]-oxadiazolyl (= furazanyl), 3- or 5-[1,2,4]-oxadizolyl, [1,3,4]-oxadizolyl, 4- or 5-[1,2,3]-thiadiazolyl, [1,2,5]-thiadiazolyl, 3- or 5-[1,2,4]-thiadizolyl or [1,3,4]-thiadiazolyl, which may be unsubstituted or which may carry 1, 2 or 3 of the aforementioned radicals R^a and/or R^b.

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A skilled person will appreciate that the radical $-E-SO_2-Ar$ may be bound to any of the carbon atoms of the phenyl part of the bicyclic moiety in formula I, thereby substituting a hydrogen atom. Preferably the radical $-E-SO_2-Ar$ is not bound to a carbon atom, which is not adjacent to a bridgehead carbon atom of the bicyclic moiety.

5

Preferably, Ar is phenyl or an aromatic 5- or 6-membered C-bound heteroaromatic radical, comprising 1 nitrogen atom as ring member and 0, 1, 2 or 3 further heteroatoms, independently of each other, selected from O, S and N, as ring members which may be unsubstituted or which may carry 1, 2 or 3 of the aforementioned radicals R^a and/or R^b . Amongst these heteroaromatic radicals those are preferred, which comprise 1, 2 or 3 nitrogen atoms and no further heteroatom as ring members, or 1 or 2 nitrogen atoms and 1 atom, selected from O and S, as ring members. However, thienyl and furyl are likewise preferred. Particularly preferred radicals Ar are 2- or 3-thienyl, 2-, 3- or 4-pyridyl, 2-, 4- or 5-pyrimidinyl, 2-, 3- or 5-thiazolyl, 1,2,4-triazol-3-yl, 1,2,3-triazol-4-yl, 1,3,4-thiadiazol-2-yl, in particular 2-thienyl, 2-pyrimidinyl, 5-pyrimidinyl, 2-pyridinyl and more particularly phenyl which may be unsubstituted or which may carry 1, 2 or 3 of the aforementioned radicals R^a and/or R^b .

Preferably the aromatic radical Ar carries one radical R^a and optionally one or two further radicals R^b as mentioned above, R^b being particularly selected from methyl, fluorinated methyl, halogen, more preferably from fluorine or chlorine.

The aforementioned 5-membered heteroaromatic radicals Ar preferably one radical R^a in the 3-position (related to the position of the SO_2 -radical) and optionally one or two further radicals R^b , which are preferably selected from halogen, in particular fluorine or chlorine.

Phenyl and the aforementioned 6-membered heteroaromatic radicals Ar preferably carry one radical R^a in the 4-position (related to the position of the SO_2 -radical) and optionally one or two further radicals R^b , which are preferably selected from halogen, in particular fluorine or chlorine.

In a very preferred embodiment of the invention Ar is phenyl that carries a radical R^a in the 4-position of the phenyl ring and optionally 1 or 2 further radicals R^b , which are preferably selected from halogen, in particular from fluorine or chlorine.

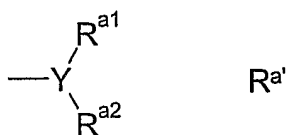
In another preferred embodiment of the invention Ar is 2-pyrimidinyl that carries a radical R^a in the 5-position of the pyrimidine ring and optionally 1 or 2 further radicals R^b , which are preferably selected from halogen, in particular from fluorine or chlorine.

- 5 In a further preferred embodiment of the invention Ar is 5-pyrimidinyl that carries a radical R^a in the 2-position of the pyrimidine ring and optionally 1 or 2 further radicals R^b , which are preferably selected from halogen, in particular from fluorine or chlorine.

- 10 In a further preferred embodiment of the invention Ar is 2-thienyl that carries a radical R^a in the 3-position of the thiophen ring and optionally 1 or 2 further radicals R^b , which are preferably selected from halogen, in particular from fluorine or chlorine.

- In a preferred embodiment Ar carries 1 radical R^a which is selected from the group consisting of C_2 - C_6 -alkyl, C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkoxy, fluorinated C_1 - C_6 -alkyl, fluorinated C_3 - C_6 -cycloalkyl, fluorinated C_1 - C_6 -alkoxy, NR^4R^5 , 1-aziridinyl, azetidin-1-yl, pyrrolidin-1-yl or piperidin-1-yl, wherein the last four mentioned radicals may be fluorinated, a phenyl group and an aromatic 5- or 6-membered C-bound heteroaromatic radical, comprising 1 nitrogen atom as ring member and 0, 1, 2 or 3 further heteroatoms, independently of each other, selected from O, S and N, wherein the last two mentioned radicals may carry 1, 2, 3 or 4 radicals selected from halogen and the radicals R^a ; and wherein Ar may carry 1 or 2 further radicals R^b , which are independently from each other selected from halogen, cyano, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, difluoromethoxy and trifluoromethoxy. In this embodiment R^4 , R^5 are, independently of each other, preferably selected from H, C_1 - C_2 -alkyl and fluorinated C_1 - C_2 -alkyl. Preferably one of the radicals R^4 or R^5 is different from hydrogen. One of the radicals R^4 or R^5 may also be C_1 - C_2 -alkoxy.
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In a very preferred embodiment, the radical Ar preferably carries one radical R^a , which has the formula $R^{a'}$



30

wherein

Y is N, CH or CF,

R^{a1} and R^{a2} are independently of each other selected from C_1 - C_2 -alkyl, C_1 - C_2 -alkoxy, fluorinated C_1 - C_2 -alkyl, provided for Y being CH or CF one of the radicals R^{a1} or R^{a2} may also be hydrogen or fluorine, or

- 5 R^{a1} and R^{a2} together form a radical $(CH_2)_m$ wherein 1 or 2 of the hydrogen atoms may be replaced by fluorine, hydroxy, oxo, C_1 - C_2 -alkyl or C_1 - C_2 -alkoxy, wherein one CH_2 moiety may be replaced by O, S, S=O, SO_2 or $N-R^c$, R^c being hydrogen or C_1 - C_2 -alkyl and wherein m is 2, 3, 4, 5 or 6;

In particular

- 10 R^{a1} or R^{a2} may also be hydrogen or fluorine R^{a1} and R^{a2} are independently of each other selected from C_1 - C_2 -alkyl, fluorinated C_1 - C_2 -alkyl, in particular fluoromethyl, difluoromethyl or trifluoromethyl, provided for Y being CH or CF one of the radicals R^{a1} or R^{a2} may also be hydrogen or fluorine, or

- 15 R^{a1} and R^{a2} form a radical $(CH_2)_k$ wherein 1 or 2 of the hydrogen atoms may be replaced by fluorine and wherein k is 2, 3 or 4, in particular CH_2-CH_2 , $CHF-CH_2$, CF_2-CH_2 , $CH_2-CH_2-CH_2$, $CHF-CH_2-CH_2$, $CF_2-CH_2-CH_2$, $CH_2-CHF-CH_2$, $CH_2-CF_2-CH_2$.

- 20 In case R^{a1} and R^{a2} are different from each other, the radical of the aforementioned formula R^a may have either (R)- or (S)-configuration with regard to the Y-moiety.

- Examples for preferred radicals R^a comprise isopropyl, (R)-1-fluoroethyl, (S)-1-fluoroethyl, 2-fluoroethyl, 1,1-difluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, (R)-1-fluoropropyl, (S)-1-fluoropropyl, 2-fluoropropyl, 3-fluoropropyl, 1,1-difluoropropyl, 2,2-difluoropropyl, 3,3-difluoropropyl, 3,3,3-trifluoropropyl, (R)-2-fluoro-1-methylethyl, (S)-2-fluoro-1-methylethyl, (R)-2,2-difluoro-1-methylethyl, (S)-2,2-difluoro-1-methylethyl, (R)-1,2-difluoro-1-methylethyl, (S)-1,2-difluoro-1-methylethyl, (R)-2,2,2-trifluoro-1-methylethyl, (S)-2,2,2-trifluoro-1-methylethyl, 2-fluoro-1-(fluoromethyl)ethyl, 1-(difluoromethyl)-2,2-difluoroethyl cyclopropyl, cyclobutyl, 1-fluorocyclopropyl, and 2-fluorocyclopropyl
- 25
- 30

- Also preferred are radicals R^a wherein one of R^{a1} or R^{a2} is C_1 - C_2 -alkoxy and the other of R^{a1} or R^{a2} is selected from H, C_1 - C_2 -alkyl, in particular methyl, fluorinated C_1 - C_2 -alkyl, in particular fluoromethyl, difluoromethyl or trifluoromethyl. Examples comprise N-methoxy-N-methylamino, N-methoxyamino and N-ethoxyamino.
- 35

Preferred radicals of the formula R^a also comprise those wherein Y is nitrogen and wherein R^{a1} and R^{a2} form a radical $(CH_2)_m$ wherein 1 or 2 of the hydrogen atoms may be replaced by fluorine, methyl, trifluoromethyl, methoxy or oxo and wherein m is 2, 3, 4 or 5. Examples comprise azetidin-1-yl, 2-methylazetidin-1-yl, (S)-2-methylazetidin-1-yl, (R)-2-methylazetidin-1-yl, 3-fluoroazetidin-1-yl, 3-methoxyazetidin-1-yl, 3-hydroxyazetidin-1-yl, pyrrolidin-1-yl, (S)-2-fluoropyrrolidin-1-yl, (R)-2-fluoropyrrolidin-1-yl, 3-fluoropyrrolidin-1-yl, (S)-3-fluoropyrrolidin-1-yl, (R)-3-fluoropyrrolidin-1-yl, 2,2-difluoropyrrolidin-1-yl, 3,3-difluoropyrrolidin-1-yl, 2-methylpyrrolidin-1-yl, (S)-2-methylpyrrolidin-1-yl, (R)-2-methylpyrrolidin-1-yl, 3-methylpyrrolidin-1-yl, (S)-3-methylpyrrolidin-1-yl, (R)-3-methylpyrrolidin-1-yl, 2,2-dimethylpyrrolidin-1-yl, 3,3-dimethylpyrrolidin-1-yl, 2-trifluoromethylpyrrolidin-1-yl, (S)-2-trifluoromethylpyrrolidin-1-yl, (R)-2-trifluoromethylpyrrolidin-1-yl, 3-trifluoromethylpyrrolidin-1-yl, (S)-3-trifluoromethylpyrrolidin-1-yl, (R)-3-trifluoromethylpyrrolidin-1-yl, 2-oxopyrrolidin-1-yl, piperidin-1-yl, 2-methylpiperidin-1-yl, (S)-2-methylpiperidin-1-yl and (R)-2-methylpiperidin-1-yl.

Likewise preferred are radicals R^a , wherein R^{a1} and R^{a2} together form a radical $(CH_2)_m$ wherein 1 or 2 of the hydrogen atoms may be replaced by fluorine, hydroxy, oxo, C_1 - C_2 -alkyl or C_1 - C_2 -alkoxy, wherein one CH_2 moiety is replaced by O, S, S=O, SO_2 or $N-R^c$, R^c being hydrogen or C_1 - C_2 -alkyl and wherein m is 2, 3, 4, 5 or 6. Examples for preferred radicals of the formula R^a also comprise 4-morpholinyl, 4-thiomorpholinyl, 4-(1,1-dioxo)thiomorpholinyl, piperazin-1-yl, 4-methylpiperazin-1-yl, 2-oxo-oxazolidin-3-yl, pyrrolidin-2-yl, (S)-pyrrolidin-2-yl, (R)-pyrrolidin-2-yl, pyrrolidin-3-yl, (S)-pyrrolidin-3-yl, (R)-pyrrolidin-3-yl, 2-fluoropyrrolidin-1-yl, 1-methylpyrrolidin-2-yl, (S)-1-methylpyrrolidin-2-yl, (R)-1-methylpyrrolidin-2-yl, 1-methylpyrrolidin-3-yl, (S)-1-methylpyrrolidin-3-yl and (R)-1-methylpyrrolidin-3-yl.

Amongst the radicals of the formula R^a those are preferred which carry 1, 2, 3 or 4, in particular 1, 2 or 3 fluorine atoms.

In a further preferred embodiment Ar carries one radical R^a , which is selected from 5- or 6-membered heteroaromatic radicals having as ring members 1 heteroatom selected from O, S and N and which may further have 1, 2 or 3 nitrogen atoms as ring members, and wherein the 5- or 6-membered heteroaromatic radical may carry 1, 2 or 3 substituents selected from halogen, NO_2 , NH_2 , OH, CN, C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkoxy, fluorinated C_1 - C_6 -alkyl, fluorinated C_3 - C_6 -cycloalkyl, fluorinated C_1 - C_6 -alkoxy, C_1 - C_6 -hydroxyalkyl, C_1 - C_4 -alkoxy- C_2 - C_4 -alkyl, C_1 - C_6 -hydroxyalkoxy, C_1 - C_4 -alkoxy- C_2 -

- C₄-alkoxy, C₁-C₆-alkylcarbonyl, C₁-C₆-alkylamino, di-C₁-C₆-alkylamino, C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, fluorinated C₁-C₆-alkylcarbonyl, C₁-C₆-alkylcarbonylamino, fluorinated C₁-C₆-alkylcarbonylamino, C₁-C₆-alkylcarbonyloxy, fluorinated C₁-C₆-alkylcarbonyloxy, C₁-C₆-alkoxycarbonyl, C₁-C₆-alkylthio, fluorinated C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, fluorinated C₁-C₆-alkylsulfinyl and fluorinated C₁-C₆-alkylsulfonyl. Amongst these radicals R^a, preference is given to radicals selected from 2-, 3-, or 4-pyridyl, 2-, 4- or 5-pyrimidinyl, pyrazinyl, 3- or 4-pyridazinyl, 2- or 3-thienyl, 2- or 3-furyl, 1-, 2- or 3-pyrrolyl, 1-, 2- or 4-imidazolyl, 1-, 3- or 4-pyrazolyl, 1- or 3-[1,2,4]-triazolyl, 1- or 4-[1,2,3]-triazolyl, 1-, 2- or 5-tetrazolyl, 2-, 3- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 2-, 3- or 5-thiazolyl, 3-, 4- or 5-isothiazolyl, 4- or 5-[1,2,3]-oxadiazolyl, [1,2,5]-oxadiazolyl (= furazanyl), 3- or 5-[1,2,4]-oxadiazolyl, [1,3,4]-oxadiazolyl, 4- or 5-[1,2,3]-thiadiazolyl, [1,2,5]-thiadiazolyl, 3- or 5-[1,2,4]-thiadiazolyl or [1,3,4]-thiadiazolyl, in particular from 2- or 3-furanyl, 2- or 3-thienyl, 1-, 2- or 3-pyrrolyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, 1,3,4-thiadiazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl and tetrazolyl, where the heteroaromatic radical may be unsubstituted or may carry 1 to 3 substituents as given above. Preferred substituents on heteroaromatic R^a are selected from halogen, C₁-C₄-alkyl, C₁-C₄-alkoxy, fluorinated C₁-C₄-alkyl and fluorinated C₁-C₄-alkoxy.
- 20 In a further preferred embodiment Ar carries 1 radical R^a which selected from the group consisting of CHF₂, CH₂F, OCHF₂ and OCH₂F, with OCHF₂ being preferred. In this embodiment Ar may also carry 1 or 2 further radicals R^b, which are independently from each other selected from halogen, cyano, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, difluoromethoxy and trifluoromethoxy. Preferably Ar carries no further radicals R^b. In this embodiment Ar is preferably phenyl which carries 1 radical R^a which selected from the group consisting of CHF₂, CH₂F, OCHF₂ and OCH₂F, with OCHF₂ being preferred. In this embodiment Ar is preferably phenyl, which carries R^a in the 4 position with respect to the SO₂-group.
- 30 In another embodiment of the invention, Ar carries 1 radical R^a which selected from the group consisting of C₂-C₆-alkenyl, fluorinated C₂-C₆-alkenyl, C₁-C₆-hydroxyalkyl, C₁-C₆-alkoxy-C₁-C₄-alkyl, C₁-C₆-hydroxyalkoxy, C₁-C₆-alkoxy-C₁-C₄-alkoxy, COOH, CH₂NR⁴R⁵, ONR⁴R⁵, NHC(O)NR⁴R⁵, C(O)NR⁴R⁵, SO₂NR⁴R⁵, C₁-C₆-alkylcarbonyl, fluorinated C₂-C₆-alkylcarbonyl, C₁-C₆-alkylcarbonylamino, fluorinated C₁-C₆-alkylcarbonylamino, C₁-C₆-alkylcarbonyloxy, fluorinated C₁-C₆-alkylcarbonyloxy, C₁-C₆-alkoxycarbonyl, C₁-C₆-alkylthio, fluorinated C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, fluorinated C₁-C₆-alkylsulfinyl, fluorinated C₁-C₆-alkylsulfonyl, phenylsul-

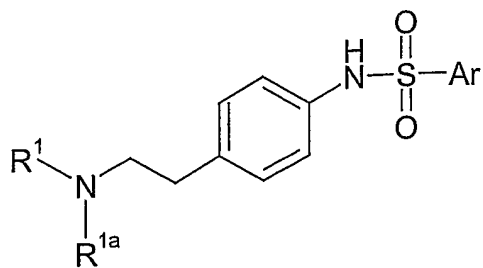
fonyl, phenoxy, benzyloxy and a 5-or 6-membered N-bound heteroaromatic radical, wherein the four last mentioned radicals may carry 1, 2, 3 or 4 radicals selected from halogen, NO₂, NH₂, OH, CN, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, fluorinated C₁-C₆-alkyl, fluorinated C₃-C₆-cycloalkyl, fluorinated C₁-C₆-alkoxy, C₁-C₆-hydroxyalkyl, C₁-C₄-alkoxy-C₂-C₄-alkyl, C₁-C₆-hydroxyalkoxy, C₁-C₄-alkoxy-C₂-C₄-alkoxy, C₁-C₆-alkylcarbonyl, C₁-C₆-alkylamino, di-C₁-C₆-alkylamino, C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, fluorinated C₁-C₆-alkylcarbonyl, C₁-C₆-alkylcarbonylamino, fluorinated C₁-C₆-alkylcarbonylamino, C₁-C₆-alkylcarbonyloxy, fluorinated C₁-C₆-alkylcarbonyloxy, C₁-C₆-alkoxycarbonyl, C₁-C₆-alkylthio, fluorinated C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, fluorinated C₁-C₆-alkylsulfinyl and fluorinated C₁-C₆-alkylsulfonyl.

In another embodiment of the invention, Ar is phenyl, which carries 1 radical R^a and at least one radical R^b and wherein R^a and one radical R^b are bound to two adjacent carbon atoms of phenyl and form a 5-or 6-membered heterocyclic or carbocyclic ring which is fused to the phenyl ring and which is unsubstituted or which may carry 1, 2 or 3 radicals as given above. Examples of a phenyl ring fused to a saturated or unsaturated 5- or 6-membered carbocyclic or heterocyclic ring comprise indenyl, indanyl, naphthyl, tetralin, benzofuranyl, 2,3-dihydrobenzofuranyl, benzothieryl, indolyl, indazolyl, benzimidazolyl, benzoxathiazolyl, benzoxadiazolyl, benzothiadiazolyl, benzoxazinyl, dihydrobenzoxazinyl, chinolyl, isochinolyl, tetrahydroisochinolyl, chromenyl, chromanyl and the like, which may be unsubstituted or which may carry 1, 2 or 3 of the aforementioned radicals. Preferred substituents for the saturated or unsaturated 5- or 6-membered carbocyclic or heterocyclic ring fused to the phenyl ring are selected from halogen, C₁-C₄-alkyl, C₁-C₄-alkoxy, fluorinated C₁-C₄-alkyl and fluorinated C₁-C₄-alkoxy.

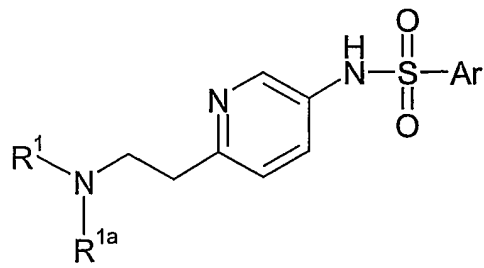
The radical R¹ is preferably C₂-C₄-alkyl, C₃-C₄-cycloalkyl, C₃-C₄-cycloalkylmethyl, C₃-C₄-alkenyl, fluorinated C₁-C₄-alkyl, fluorinated C₃-C₄-cycloalkyl, fluorinated C₃-C₄-cycloalkylmethyl, fluorinated C₃-C₄-alkenyl, formyl or C₁-C₃-alkylcarbonyl, in particular C₂-C₄-alkyl, C₃-C₄-alkenyl, fluorinated C₂-C₄-alkyl, fluorinated C₃-C₄-alkenyl, more preferably n-propyl, fluorinated C₂-C₃-alkyl or 1-propen-3-yl, in particular n-propyl.

A first preferred embodiment of the invention relates to compounds, wherein R^{1a} is hydrogen. In these compounds R¹ has the meanings given above. In particular R¹ is n-propyl. In this embodiment R^{2a} is preferably hydrogen while R² is preferably hydrogen, methyl or fluorinated methyl. In particular, both R^{2a} and R² are hydrogen or one of the radicals R^{2a} and R² is hydrogen while the other is methyl.

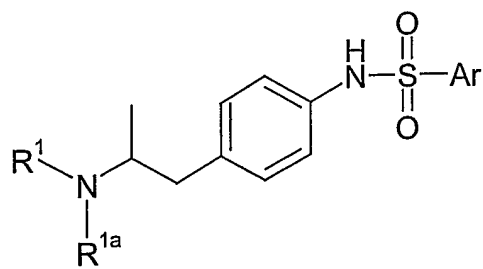
- In a second preferred embodiment, R^{1a} is different from hydrogen and preferably C_2 - C_4 -alkyl, C_3 - C_4 -alkenyl, fluorinated C_2 - C_4 -alkyl, fluorinated C_3 - C_4 -alkenyl, more preferably n-propyl, fluorinated C_2 - C_3 -alkyl or 1-propen-3-yl, in particular n-propyl. In these compounds R^1 has the meanings given above. In particular R^1 is n-propyl. In this embodiment R^{2a} is preferably hydrogen while R^2 is preferably hydrogen, methyl or fluorinated methyl. In particular both R^{2a} and R^2 are hydrogen or one of the radicals R^{2a} and R^2 is hydrogen while the other is methyl.
- 10 In a third preferred embodiment, R^{2a} and R^{1a} together are $(CH_2)_n$ with n being 3 or 4. R^2 is preferably hydrogen. In these compounds R^1 has the meanings given above. In particular R^1 is n-propyl, 1-propen-3-yl.
- One preferred embodiment of the invention, relates to compounds of the formula I, wherein X is CH. Another embodiment of the invention, relates to compounds of the formula I, wherein X is N.
- 20 Preferably the moiety E is $N-R^3$, wherein R^3 is as defined above. R^3 is in particular H or methyl and most preferred H. If E is a moiety CR^6R^7 , preferably one and in particular both of the radicals R^6 and R^7 are hydrogen.
- Preferred embodiments of the invention are compounds of the following formulae Ia, Ib, Ic, Id, Ie, If, Ig, Ih, Ii, Ik, Im, In, Io, Ip, Iq, Ir, Is, It, Iu and Iv and to the physiologically tolerated acid addition salts thereof. With regard to the carbom atom carrying the NR^{1-} group, compounds of the formulae Ic, Id, Ii, Ik, Io, Ip, Iu and Iv may exist as R-enantiomers or S-enantiomers as well as mixtures of the enantiomers such as racemic mixtures. The preferred embodiments include the R- and S-enantiomers of Ic, Id, Ii, Ik, Io, Ip, Iu and Iv and the mixtures of the enantiomers.
- 30 In the compounds of the formulae Ia, Ib, Ic, Id, Ie, If, Ig, Ih, Ii, Ik, Im, In, Io, Ip, Iq, Ir, Is, It, Iu and Iv R^1 , Ar and R^{1a} are as defined above with particular preference given to those compounds wherein R^1 , Ar and R^{1a} have one of the preferred meanings.



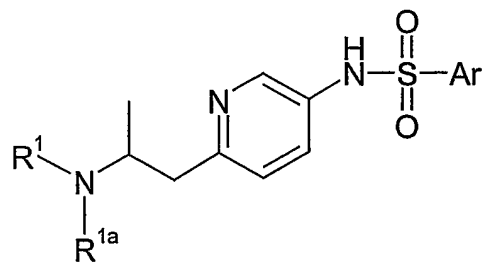
1a



1b

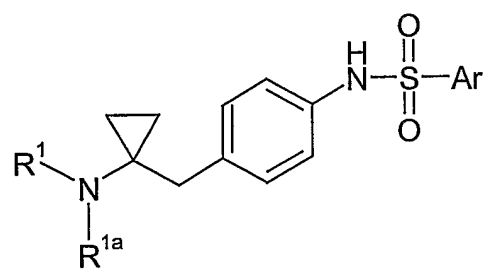


1c

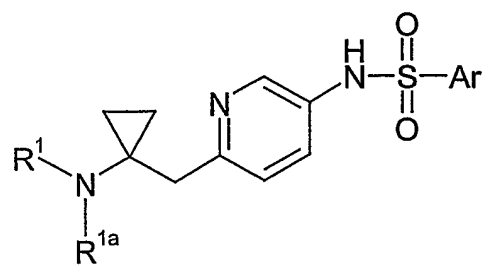


1d

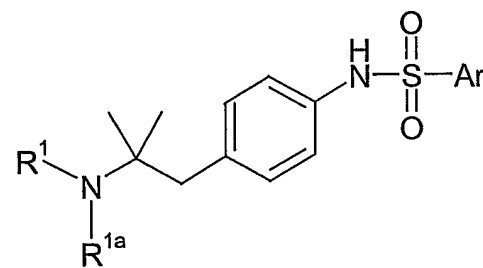
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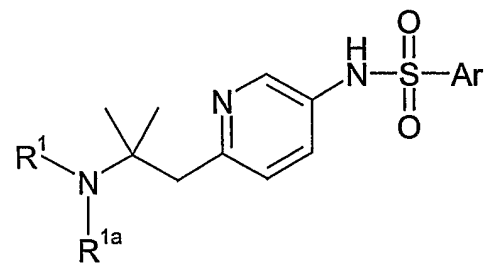
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1f

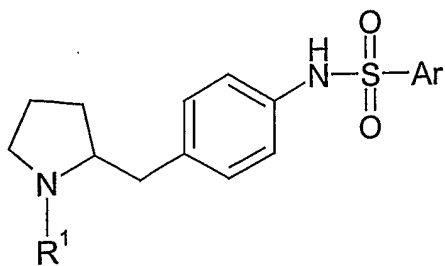


1g

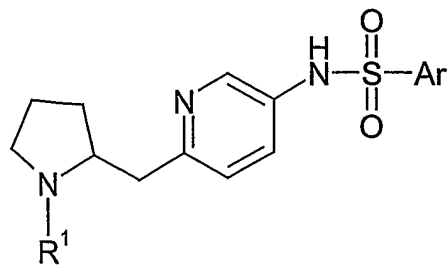


1h

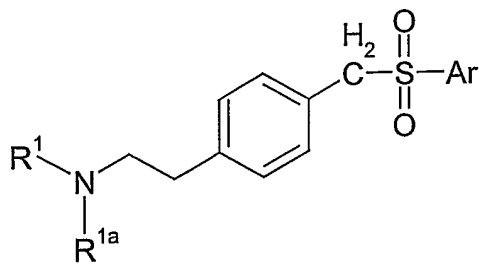
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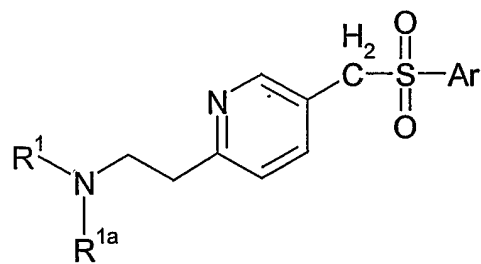
II



Ik

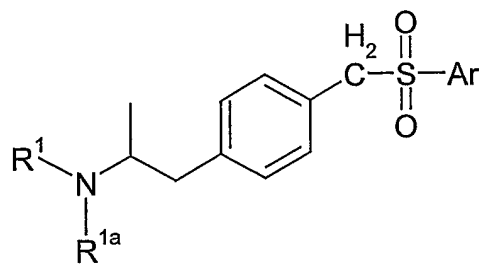


Im

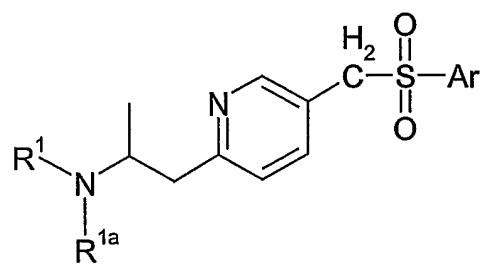


In

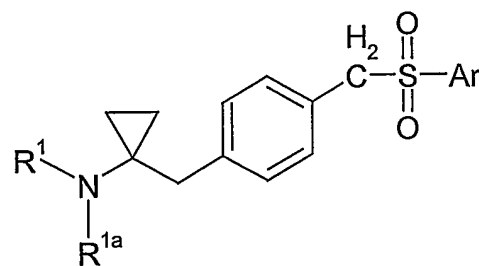
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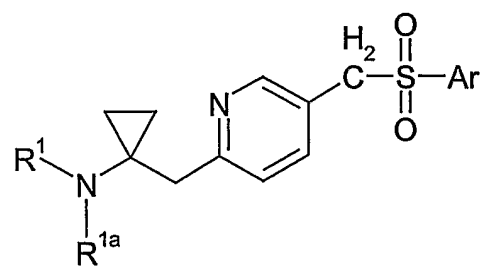
Io



Ip

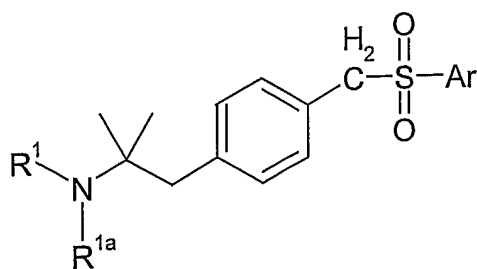


Iq

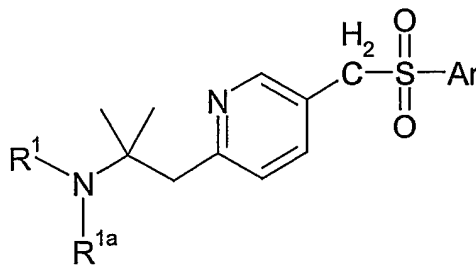


Ir

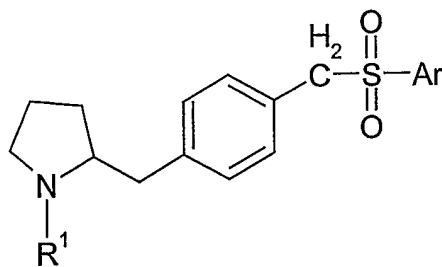
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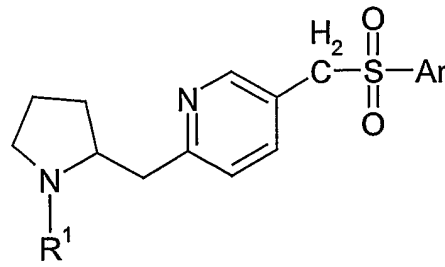
Is



It



Iu



Iv

5

Examples of preferred compounds of the general formula I are given in the following tables A-1, A-2, A-3, A-4, A-5, A-6, A-7, A-8, A-9, A-10, A-11, A-12, A-13, A-14, A-15, A-16, A-17, A-18, A-19 and A-20.

10

Table A-1: Compounds of the formula Ia, wherein R^{1a} is H and Ar and R^1 have the meaning given in one of the rows 61 to 1704 of table A.

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Table A-2: Compounds of the formula Ib, wherein R^{1a} is H and Ar and R^1 have the meaning given in one row of table A.

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Table A-3: Compounds of the formula Ic, including the pure S-isomers, the pure R-isomers and the racemic mixtures, wherein R^{1a} is H and Ar and R^1 have the meaning given in one row of table A.

25

Table A-4: Compounds of the formula Id, including the pure S-isomers, the pure R-isomers and the racemic mixtures, wherein R^{1a} is H and Ar and R^1 have the meaning given in one row of table A.

Table A-6: Compounds of the formula If, wherein R^{1a} is H and Ar and R^1 have the meaning given in one row of table A.

- 5 Table A-7: Compounds of the formula Ig, wherein R^{1a} is H and Ar and R^1 have the meaning given in one row of table A.

Table A-8: Compounds of the formula Ih, wherein R^{1a} is H and Ar and R^1 have the meaning given in one row of table A.

10

Table A-9: Compounds of the formula Ii, including the pure S-isomers, the pure R-isomers and the racemic mixtures, wherein Ar and R^1 have the meaning given in one row of table A.

- 15 Table A-10: Compounds of the formula Ik, including the pure S-isomers, the pure R-isomers and the racemic mixtures, wherein Ar and R^1 have the meaning given in one row of table A.

- 20 Table A-11: Compounds of the formula Im, wherein R^{1a} is H and Ar and R^1 have the meaning given in one of the rows of table A.

Table A-12: Compounds of the formula In, wherein R^{1a} is H and Ar and R^1 have the meaning given in one row of table A.

- 25 Table A-13: Compounds of the formula Io, including the pure S-isomers, the pure R-isomers and the racemic mixtures, wherein R^{1a} is H and Ar and R^1 have the meaning given in one row of table A.

- 30 Table A-14: Compounds of the formula Ip, including the pure S-isomers, the pure R-isomers and the racemic mixtures, wherein R^{1a} is H and Ar and R^1 have the meaning given in one row of table A.

Table A-15: Compounds of the formula Iq, wherein R^{1a} is H and Ar and R^1 have the meaning given in one row of table A.

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Table A-16: Compounds of the formula Ir, wherein R^{1a} is H and Ar and R^1 have the meaning given in one row of table A.

Table A-17: Compounds of the formula Is, wherein R^{1a} is H and Ar and R¹ have the meaning given in one row of table A.

- 5 Table A-18: Compounds of the formula It, wherein R^{1a} is H and Ar and R¹ have the meaning given in one row of table A.

- 10 Table A-19: Compounds of the formula Iu, including the pure S-isomers, the pure R-isomers and the racemic mixtures, wherein Ar and R¹ have the meaning given in one row of table A.

- 15 Table A-20: Compounds of the formula Iv, including the pure S-isomers, the pure R-isomers and the racemic mixtures, wherein Ar and R¹ have the meaning given in one row of table A.

Table A

No.	R ¹	Ar
1.	methyl	4-(trifluoromethoxy)-phenyl
2.	methyl	3-(trifluoromethoxy)-phenyl
3.	methyl	4-cyanophenyl
4.	methyl	4-methylphenyl
5.	methyl	4-ethylphenyl
6.	methyl	4-propylphenyl
7.	methyl	4-methoxyphenyl
8.	methyl	4-fluorophenyl
9.	methyl	4-chlorophenyl
10.	methyl	4-bromophenyl
11.	methyl	3-(trifluoromethyl)phenyl
12.	methyl	4-(trifluoromethyl)phenyl
13.	methyl	2-(trifluoromethyl)phenyl
14.	methyl	3,4-difluorophenyl
15.	methyl	4-bromo-3-fluorophenyl
16.	methyl	4-bromo-2-fluorophenyl
17.	methyl	4-bromo-2,5-difluorophenyl
18.	methyl	2-fluoro-4-isopropylphenyl
19.	methyl	4-methylsulfanyl

No.	R ¹	Ar
20.	methyl	4-hydroxyphenyl
21.	ethyl	4-(trifluoromethoxy)-phenyl
22.	ethyl	3-(trifluoromethoxy)-phenyl
23.	ethyl	4-cyanophenyl
24.	ethyl	4-methylphenyl
25.	ethyl	4-ethylphenyl
26.	ethyl	4-propylphenyl
27.	ethyl	4-methoxyphenyl
28.	ethyl	4-fluorophenyl
29.	ethyl	4-chlorophenyl
30.	ethyl	4-bromophenyl
31.	ethyl	3-(trifluoromethyl)phenyl
32.	ethyl	4-(trifluoromethyl)phenyl
33.	ethyl	2-(trifluoromethyl)phenyl
34.	ethyl	3,4-difluorophenyl
35.	ethyl	4-bromo-3-fluorophenyl
36.	ethyl	4-bromo-2-fluorophenyl
37.	ethyl	4-bromo-2,5-difluorophenyl
38.	ethyl	2-fluoro-4-isopropylphenyl
39.	ethyl	4-methylsulfanyl
40.	ethyl	4-hydroxyphenyl
41.	propyl	4-(trifluoromethoxy)-phenyl
42.	propyl	3-(trifluoromethoxy)-phenyl
43.	propyl	4-cyanophenyl
44.	propyl	4-methylphenyl
45.	propyl	4-ethylphenyl
46.	propyl	4-propylphenyl
47.	propyl	4-methoxyphenyl
48.	propyl	4-fluorophenyl
49.	propyl	4-chlorophenyl
50.	propyl	4-bromophenyl
51.	propyl	3-(trifluoromethyl)phenyl
52.	propyl	4-(trifluoromethyl)phenyl
53.	propyl	2-(trifluoromethyl)phenyl

No.	R ¹	Ar
54.	propyl	3,4-difluorophenyl
55.	propyl	4-bromo-3-fluorophenyl
56.	propyl	4-bromo-2-fluorophenyl
57.	propyl	4-bromo-2,5-difluorophenyl
58.	propyl	2-fluoro-4-isopropylphenyl
59.	propyl	4-methylsulfanyl
60.	propyl	4-hydroxyphenyl
61.	propyl	4-isopropylphenyl
62.	propyl	4-sec-butylphenyl
63.	propyl	4-isobutylphenyl
64.	propyl	4-(1,1-dimethylpropyl)-phenyl
65.	propyl	4-vinylphenyl
66.	propyl	4-isopropenylphenyl
67.	propyl	4-(fluoromethyl)phenyl
68.	propyl	3-(fluoromethyl)phenyl
69.	propyl	2-(fluoromethyl)phenyl
70.	propyl	4-(difluoromethyl)phenyl
71.	propyl	3-(difluoromethyl)phenyl
72.	propyl	2-(difluoromethyl)phenyl
73.	propyl	4-(1-fluoroethyl)-phenyl
74.	propyl	4-((S)-1-fluoroethyl)-phenyl
75.	propyl	4-((R)-1-fluoroethyl)-phenyl
76.	propyl	4-(2-fluoroethyl)-phenyl
77.	propyl	4-(1,1-difluoroethyl)-phenyl
78.	propyl	4-(2,2-difluoroethyl)-phenyl
79.	propyl	4-(2,2,2-trifluoroethyl)-phenyl
80.	propyl	4-(3-fluoropropyl)-phenyl
81.	propyl	4-(2-fluoropropyl)-phenyl
82.	propyl	4-((S)-2-fluoropropyl)-phenyl
83.	propyl	4-((R)-2-fluoropropyl)-phenyl
84.	propyl	4-(3,3-difluoropropyl)-phenyl
85.	propyl	4-(3,3,3-trifluoropropyl)-phenyl
86.	propyl	4-(1-fluoro-1-methylethyl)-phenyl
87.	propyl	4-(2-fluoro-1-methylethyl)-phenyl

No.	R ¹	Ar
88.	propyl	4-((S)-2-fluoro-1-methylethyl)-phenyl
89.	propyl	4-((R)-2-fluoro-1-methylethyl)-phenyl
90.	propyl	4-(2,2-difluoro-1-methylethyl)-phenyl
91.	propyl	4-((S)-2,2-difluoro-1-methylethyl)-phenyl
92.	propyl	4-((R)-2,2-difluoro-1-methylethyl)-phenyl
93.	propyl	4-(2,2,2-trifluoro-1-methylethyl)-phenyl
94.	propyl	4-((S)-2,2,2-trifluoro-1-methylethyl)-phenyl
95.	propyl	4-((R)-2,2,2-trifluoro-1-methylethyl)-phenyl
96.	propyl	4-(2-fluoro-1-fluoromethylethyl)-phenyl
97.	propyl	4-(1-difluoromethyl-2,2-difluoroethyl)-phenyl
98.	propyl	4-(1,1-dimethyl-2-fluoroethyl)-phenyl
99.	propyl	4-ethoxyphenyl
100.	propyl	4-propoxyphenyl
101.	propyl	4-isopropoxyphenyl
102.	propyl	4-butoxyphenyl
103.	propyl	4-(fluoromethoxy)-phenyl
104.	propyl	4-(difluoromethoxy)-phenyl
105.	propyl	4-(2-fluoroethoxy)-phenyl
106.	propyl	4-(2,2-difluoroethoxy)-phenyl
107.	propyl	4-(2,2,2-trifluoroethoxy)-phenyl
108.	propyl	4-(1,1,2,2-tetrafluoroethoxy)-phenyl
109.	propyl	4-cyclopropylphenyl
110.	propyl	4-cyclobutylphenyl
111.	propyl	4-cyclopentylphenyl
112.	propyl	4-(2,2-difluorocyclopropyl)-phenyl
113.	propyl	2-fluoro-4-isopropylphenyl
114.	propyl	3-fluoro-4-isopropylphenyl
115.	propyl	4-(1-hydroxy-1-methylethyl)-phenyl
116.	propyl	4-(2-hydroxy-2-methylpropyl)-phenyl
117.	propyl	4-acetylphenyl
118.	propyl	4-carboxyphenyl
119.	propyl	4-(O-benzyl)-phenyl
120.	propyl	4-(2-methoxyethoxy)-phenyl
121.	propyl	4-(CH ₂ -N(CH ₃) ₂)-phenyl

No.	R ¹	Ar
122.	propyl	4-(NH-CO-NH ₂)-phenyl
123.	propyl	4-(fluoromethylsulfanyl)-phenyl
124.	propyl	4-(difluoromethylsulfanyl)-phenyl
125.	propyl	4-(trifluoromethylsulfanyl)-phenyl
126.	propyl	4-(methylsulfonyl)-phenyl
127.	propyl	4-(N-methoxy-N-methyl-amino)-phenyl
128.	propyl	4-(methoxyamino)-phenyl
129.	propyl	4-(ethoxyamino)-phenyl
130.	propyl	4-(N-methylaminooxy)-phenyl
131.	propyl	4-(N,N-dimethylaminooxy)-phenyl
132.	propyl	4-(azetidin-1-yl)-phenyl
133.	propyl	4-(2-methylazetidin-1-yl)-phenyl
134.	propyl	4-((S)-2-methylazetidin-1-yl)-phenyl
135.	propyl	4-((R)-2-methylazetidin-1-yl)-phenyl
136.	propyl	4-(3-fluoroazetidin-1-yl)-phenyl
137.	propyl	4-(3-methoxyazetidin-1-yl)-phenyl
138.	propyl	4-(3-hydroxyazetidin-1-yl)-phenyl
139.	propyl	4-(pyrrolidin-1-yl)-phenyl
140.	propyl	4-(pyrrolidin-2-yl)-phenyl
141.	propyl	4-((S)-pyrrolidin-2-yl)-phenyl
142.	propyl	4-((R)-pyrrolidin-2-yl)-phenyl
143.	propyl	4-(pyrrolidin-3-yl)-phenyl
144.	propyl	4-((S)-pyrrolidin-3-yl)-phenyl
145.	propyl	4-((R)-pyrrolidin-3-yl)-phenyl
146.	propyl	4-(2-fluoropyrrolidin-1-yl)-phenyl
147.	propyl	4-((S)-2-fluoropyrrolidin-1-yl)-phenyl
148.	propyl	4-((R)-2-fluoropyrrolidin-1-yl)-phenyl
149.	propyl	4-(3-fluoropyrrolidin-1-yl)-phenyl
150.	propyl	4-((S)-3-fluoropyrrolidin-1-yl)-phenyl
151.	propyl	4-((R)-3-fluoropyrrolidin-1-yl)-phenyl
152.	propyl	4-(2,2-difluoropyrrolidin-1-yl)-phenyl
153.	propyl	4-(3,3-difluoropyrrolidin-1-yl)-phenyl
154.	propyl	4-(2-methylpyrrolidin-1-yl)-phenyl
155.	propyl	4-((S)-2-methylpyrrolidin-1-yl)-phenyl

No.	R ¹	Ar
156.	propyl	4-((R)-2-methylpyrrolidin-1-yl)-phenyl
157.	propyl	4-(3-methylpyrrolidin-1-yl)-phenyl
158.	propyl	4-((S)-3-methylpyrrolidin-1-yl)-phenyl
159.	propyl	4-((R)-3-methylpyrrolidin-1-yl)-phenyl
160.	propyl	4-(1-methylpyrrolidin-2-yl)-phenyl
161.	propyl	4-((S)-1-methylpyrrolidin-2-yl)-phenyl
162.	propyl	4-((R)-1-methylpyrrolidin-2-yl)-phenyl
163.	propyl	4-(1-methylpyrrolidin-3-yl)-phenyl
164.	propyl	4-((S)-1-methylpyrrolidin-3-yl)-phenyl
165.	propyl	4-((R)-1-methylpyrrolidin-3-yl)-phenyl
166.	propyl	4-(2,2-dimethylpyrrolidin-1-yl)-phenyl
167.	propyl	4-(3,3-dimethylpyrrolidin-1-yl)-phenyl
168.	propyl	4-(2-trifluoromethylpyrrolidin-1-yl)-phenyl
169.	propyl	4-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
170.	propyl	4-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
171.	propyl	4-(3-trifluoromethylpyrrolidin-1-yl)-phenyl
172.	propyl	4-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
173.	propyl	4-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
174.	propyl	4-(2-oxopyrrolidin-1-yl)-phenyl
175.	propyl	4-(2-oxo-oxazolidin-3-yl)-phenyl
176.	propyl	4-(piperidin-1-yl)-phenyl
177.	propyl	4-(2-methylpiperidin-1-yl)-phenyl
178.	propyl	4-((S)-2-methylpiperidin-1-yl)-phenyl
179.	propyl	4-((R)-2-methylpiperidin-1-yl)-phenyl
180.	propyl	4-(piperazin-1-yl)-phenyl
181.	propyl	4-(4-methylpiperazin-1-yl)-phenyl
182.	propyl	4-(morpholin-4-yl)-phenyl
183.	propyl	4-(thiomorpholin-4-yl)-phenyl
184.	propyl	4-(1-oxo-thiomorpholin-4-yl)-phenyl
185.	propyl	4-(1,1-dioxo-thiomorpholin-4-yl)-phenyl
186.	propyl	4-(pyrrol-1-yl)-phenyl
187.	propyl	4-(pyrrol-2-yl)-phenyl
188.	propyl	4-(pyrrol-3-yl)-phenyl
189.	propyl	4-(1-methylpyrrol-2-yl)-phenyl

No.	R ¹	Ar
190.	propyl	4-(1-methylpyrrol-3-yl)-phenyl
191.	propyl	4-(furan-2-yl)-phenyl
192.	propyl	4-(furan-3-yl)-phenyl
193.	propyl	4-(thiophen-2-yl)-phenyl
194.	propyl	4-(thiophen-3-yl)-phenyl
195.	propyl	4-(5-propylthien-2-yl)-phenyl
196.	propyl	4-(pyrazol-1-yl)-phenyl
197.	propyl	4-(pyrazol-3-yl)-phenyl
198.	propyl	4-(pyrazol-4-yl)-phenyl
199.	propyl	4-(1-methyl-1H-pyrazol-4-yl)-phenyl
200.	propyl	4-(1-ethyl-1H-pyrazol-4-yl)-phenyl
201.	propyl	4-(1-methyl-1H-pyrazol-5-yl)-phenyl
202.	propyl	4-(1H-imidazol-2-yl)-phenyl
203.	propyl	4-(imidazol-1-yl)-phenyl
204.	propyl	4-(1-methylimidazol-2-yl)-phenyl
205.	propyl	4-(oxazol-2-yl)-phenyl
206.	propyl	4-(oxazol-4-yl)-phenyl
207.	propyl	4-(oxazol-5-yl)-phenyl
208.	propyl	4-(isoxazol-3-yl)-phenyl
209.	propyl	4-(isoxazol-4-yl)-phenyl
210.	propyl	4-(isoxazol-5-yl)-phenyl
211.	propyl	4-([1,2,3]-triazol-1-yl)-phenyl
212.	propyl	4-([1,2,4]-triazol-1-yl)-phenyl
213.	propyl	4-([1,2,3]-triazol-2-yl)-phenyl
214.	propyl	4-(4H-[1,2,4]-triazol-3-yl)-phenyl
215.	propyl	4-([1,2,4]-triazol-4-yl)-phenyl
216.	propyl	4-(2H-[1,2,3]-triazol-4-yl)-phenyl
217.	propyl	4-(4-methyl-4H-[1,2,4]-triazol-3-yl)-phenyl
218.	propyl	4-(2-methyl-2H-[1,2,3]-triazol-4-yl)-phenyl
219.	propyl	4-([1,3,4]-oxadiazol-2-yl)-phenyl
220.	propyl	4-([1,2,4]-oxadiazol-3-yl)-phenyl
221.	propyl	4-([1,2,4]-oxadiazol-5-yl)-phenyl
222.	propyl	4-([1,2,3]-oxadiazol-4-yl)-phenyl
223.	propyl	4-([1,2,3]-oxadiazol-5-yl)-phenyl

No.	R ¹	Ar
224.	propyl	4-([1,2,3]-thiadiazol-4-yl)-phenyl
225.	propyl	4-(1H-tetrazol-5-yl)-phenyl
226.	propyl	4-(tetrazol-1-yl)-phenyl
227.	propyl	4-(2-methyl-2H-tetrazol-5-yl)-phenyl
228.	propyl	4-(1-methyl-1H-tetrazol-5-yl)-phenyl
229.	propyl	4-furazan-3-yl-phenyl
230.	propyl	4-(pyrid-2-yl)-phenyl
231.	propyl	4-(pyrid-3-yl)-phenyl
232.	propyl	4-(pyrid-4-yl)-phenyl
233.	propyl	4-(pyrimidin-2-yl)-phenyl
234.	propyl	4-(pyrimidin-4-yl)-phenyl
235.	propyl	4-(pyrimidin-5-yl)-phenyl
236.	propyl	5-isopropylthiophen-2-yl
237.	propyl	2-chlorothiophen-5-yl
238.	propyl	2,5-dichlorothiophen-4-yl
239.	propyl	2,3-dichlorothiophen-5-yl
240.	propyl	2-chloro-3-nitrothiophen-5-yl
241.	propyl	2-(phenylsulfonyl)-thiophen-5-yl
242.	propyl	2-(pyridin-2-yl)thiophen-5-yl
243.	propyl	2-(5-(trifluoromethyl)isoxazol-3-yl)-thiophen-5-yl
244.	propyl	2-(2-methylthiazol-4-yl)-thiophen-5-yl
245.	propyl	1-methyl-1H-imidazol-4-yl
246.	propyl	1,2-dimethyl-1H-imidazol-4-yl
247.	propyl	3,5-dimethylisoxazol-4-yl
248.	propyl	thiazol-2-yl
249.	propyl	4-methylthiazol-2-yl
250.	propyl	4-isopropylthiazol-2-yl
251.	propyl	4-trifluoromethylthiazol-2-yl
252.	propyl	5-methylthiazol-2-yl
253.	propyl	5-isopropylthiazol-2-yl
254.	propyl	5-trifluoromethylthiazol-2-yl
255.	propyl	2,4-dimethylthiazol-5-yl
256.	propyl	2-acetamido-4-methylthiazol-5-yl
257.	propyl	4H-[1,2,4]triazol-3-yl

No.	R ¹	Ar
258.	propyl	5-methyl-4H-[1,2,4]triazol-3-yl
259.	propyl	4-methyl-4H-[1,2,4]triazol-3-yl
260.	propyl	5-isopropyl-4H-[1,2,4]triazol-3-yl
261.	propyl	5-trifluoromethyl-4H-[1,2,4]triazol-3-yl
262.	propyl	4,5-dimethyl-4H-[1,2,4]triazol-3-yl
263.	propyl	5-isopropyl-4-methyl-4H-[1,2,4]triazol-3-yl
264.	propyl	5-trifluoromethyl-4-methyl-4H-[1,2,4]triazol-3-yl
265.	propyl	[1,3,4]thiadiazol-2-yl
266.	propyl	5-methyl-[1,3,4]thiadiazol-2-yl
267.	propyl	5-isopropyl-[1,3,4]thiadiazol-2-yl
268.	propyl	5-trifluoromethyl-[1,3,4]thiadiazol-2-yl
269.	propyl	3-bromo-2-chloropyrid-5-yl
270.	propyl	2-(4-morpholino)-pyrid-5-yl
271.	propyl	2-phenoxy-pyrid-5-yl
272.	propyl	(2-isopropyl)-pyrimidin-5-yl
273.	propyl	(5-isopropyl)-pyrimidin-2-yl
274.	propyl	8-quinolyl
275.	propyl	5-isoquinolyl
276.	propyl	2-(trifluoroacetyl)-1,2,3,4-tetrahydroisoquinolin-7-yl
277.	propyl	5-chloro-3-methylbenzothiophen-2-yl
278.	propyl	3,4-dihydro-4-methyl-2H-benzo[b][1,4]oxazinyl
279.	propyl	benzothiazol-6-yl
280.	propyl	benzo[2,1,3]oxadiazol-4-yl
281.	propyl	5-chlorobenzo[2,1,3]oxadiazol-4-yl
282.	propyl	7-chlorobenzo[2,1,3]oxadiazol-4-yl
283.	propyl	benzo[2,1,3]thiadiazol-4-yl
284.	ethyl	4-isopropylphenyl
285.	ethyl	4-sec-butylphenyl
286.	ethyl	4-isobutylphenyl
287.	ethyl	4-(1,1-dimethylpropyl)-phenyl
288.	ethyl	4-vinylphenyl
289.	ethyl	4-isopropenylphenyl
290.	ethyl	4-(fluoromethyl)phenyl
291.	ethyl	3-(fluoromethyl)phenyl

No.	R ¹	Ar
292.	ethyl	2-(fluoromethyl)phenyl
293.	ethyl	4-(difluoromethyl)phenyl
294.	ethyl	3-(difluoromethyl)phenyl
295.	ethyl	2-(difluoromethyl)phenyl
296.	ethyl	4-(trifluoromethyl)phenyl
297.	ethyl	3-(trifluoromethyl)phenyl
298.	ethyl	2-(trifluoromethyl)phenyl
299.	ethyl	4-(1-fluoroethyl)-phenyl
300.	ethyl	4-((S)-1-fluoroethyl)-phenyl
301.	ethyl	4-((R)-1-fluoroethyl)-phenyl
302.	ethyl	4-(2-fluoroethyl)-phenyl
303.	ethyl	4-(1,1-difluoroethyl)-phenyl
304.	ethyl	4-(2,2-difluoroethyl)-phenyl
305.	ethyl	4-(2,2,2-trifluoroethyl)-phenyl
306.	ethyl	4-(3-fluoropropyl)-phenyl
307.	ethyl	4-(2-fluoropropyl)-phenyl
308.	ethyl	4-((S)-2-fluoropropyl)-phenyl
309.	ethyl	4-((R)-2-fluoropropyl)-phenyl
310.	ethyl	4-(3,3-difluoropropyl)-phenyl
311.	ethyl	4-(3,3,3-trifluoropropyl)-phenyl
312.	ethyl	4-(1-fluoro-1-methylethyl)-phenyl
313.	ethyl	4-(2-fluoro-1-methylethyl)-phenyl
314.	ethyl	4-((S)-2-fluoro-1-methylethyl)-phenyl
315.	ethyl	4-((R)-2-fluoro-1-methylethyl)-phenyl
316.	ethyl	4-(2,2-difluoro-1-methylethyl)-phenyl
317.	ethyl	4-((S)-2,2-difluoro-1-methylethyl)-phenyl
318.	ethyl	4-((R)-2,2-difluoro-1-methylethyl)-phenyl
319.	ethyl	4-(2,2,2-trifluoro-1-methylethyl)-phenyl
320.	ethyl	4-((S)-2,2,2-trifluoro-1-methylethyl)-phenyl
321.	ethyl	4-((R)-2,2,2-trifluoro-1-methylethyl)-phenyl
322.	ethyl	4-(2-fluoro-1-fluoromethylethyl)-phenyl
323.	ethyl	4-(1-difluoromethyl-2,2-difluoroethyl)-phenyl
324.	ethyl	4-(1,1-dimethyl-2-fluoroethyl)-phenyl
325.	ethyl	4-ethoxyphenyl

No.	R ¹	Ar
326.	ethyl	4-propoxyphenyl
327.	ethyl	4-isopropoxyphenyl
328.	ethyl	4-butoxyphenyl
329.	ethyl	4-(fluoromethoxy)-phenyl
330.	ethyl	4-(difluoromethoxy)-phenyl
331.	ethyl	4-(2-fluoroethoxy)-phenyl
332.	ethyl	4-(2,2-difluoroethoxy)-phenyl
333.	ethyl	4-(2,2,2-trifluoroethoxy)-phenyl
334.	ethyl	4-(1,1,2,2-tetrafluoroethoxy)-phenyl
335.	ethyl	4-cyclopropylphenyl
336.	ethyl	4-cyclobutylphenyl
337.	ethyl	4-cyclopentylphenyl
338.	ethyl	4-(2,2-difluorocyclopropyl)-phenyl
339.	ethyl	3,4-difluorophenyl
340.	ethyl	2-fluoro-4-isopropylphenyl
341.	ethyl	3-fluoro-4-isopropylphenyl
342.	ethyl	4-(1-hydroxy-1-methylethyl)-phenyl
343.	ethyl	4-(2-hydroxy-2-methylpropyl)-phenyl
344.	ethyl	4-acetylphenyl
345.	ethyl	4-carboxyphenyl
346.	ethyl	4-(O-benzyl)-phenyl
347.	ethyl	4-(2-methoxyethoxy)-phenyl
348.	ethyl	4-(CH ₂ -N(CH ₃) ₂)-phenyl
349.	ethyl	4-(NH-CO-NH ₂)-phenyl
350.	ethyl	4-(fluoromethylsulfanyl)-phenyl
351.	ethyl	4-(difluoromethylsulfanyl)-phenyl
352.	ethyl	4-(trifluoromethylsulfanyl)-phenyl
353.	ethyl	4-(methylsulfonyl)-phenyl
354.	ethyl	4-(N-methoxy-N-methyl-amino)-phenyl
355.	ethyl	4-(methoxyamino)-phenyl
356.	ethyl	4-(ethoxyamino)-phenyl
357.	ethyl	4-(N-methylaminooxy)-phenyl
358.	ethyl	4-(N,N-dimethylaminooxy)-phenyl
359.	ethyl	4-(azetidin-1-yl)-phenyl

No.	R ¹	Ar
360.	ethyl	4-(2-methylazetidin-1-yl)-phenyl
361.	ethyl	4-((S)-2-methylazetidin-1-yl)-phenyl
362.	ethyl	4-((R)-2-methylazetidin-1-yl)-phenyl
363.	ethyl	4-(3-fluoroazetidin-1-yl)-phenyl
364.	ethyl	4-(3-methoxyazetidin-1-yl)-phenyl
365.	ethyl	4-(3-hydroxyazetidin-1-yl)-phenyl
366.	ethyl	4-(pyrrolidin-1-yl)-phenyl
367.	ethyl	4-(pyrrolidin-2-yl)-phenyl
368.	ethyl	4-((S)-pyrrolidin-2-yl)-phenyl
369.	ethyl	4-((R)-pyrrolidin-2-yl)-phenyl
370.	ethyl	4-(pyrrolidin-3-yl)-phenyl
371.	ethyl	4-((S)-pyrrolidin-3-yl)-phenyl
372.	ethyl	4-((R)-pyrrolidin-3-yl)-phenyl
373.	ethyl	4-(2-fluoropyrrolidin-1-yl)-phenyl
374.	ethyl	4-((S)-2-fluoropyrrolidin-1-yl)-phenyl
375.	ethyl	4-((R)-2-fluoropyrrolidin-1-yl)-phenyl
376.	ethyl	4-(3-fluoropyrrolidin-1-yl)-phenyl
377.	ethyl	4-((S)-3-fluoropyrrolidin-1-yl)-phenyl
378.	ethyl	4-((R)-3-fluoropyrrolidin-1-yl)-phenyl
379.	ethyl	4-(2,2-difluoropyrrolidin-1-yl)-phenyl
380.	ethyl	4-(3,3-difluoropyrrolidin-1-yl)-phenyl
381.	ethyl	4-(2-methylpyrrolidin-1-yl)-phenyl
382.	ethyl	4-((S)-2-methylpyrrolidin-1-yl)-phenyl
383.	ethyl	4-((R)-2-methylpyrrolidin-1-yl)-phenyl
384.	ethyl	4-(3-methylpyrrolidin-1-yl)-phenyl
385.	ethyl	4-((S)-3-methylpyrrolidin-1-yl)-phenyl
386.	ethyl	4-((R)-3-methylpyrrolidin-1-yl)-phenyl
387.	ethyl	4-(1-methylpyrrolidin-2-yl)-phenyl
388.	ethyl	4-((S)-1-methylpyrrolidin-2-yl)-phenyl
389.	ethyl	4-((R)-1-methylpyrrolidin-2-yl)-phenyl
390.	ethyl	4-(1-methylpyrrolidin-3-yl)-phenyl
391.	ethyl	4-((S)-1-methylpyrrolidin-3-yl)-phenyl
392.	ethyl	4-((R)-1-methylpyrrolidin-3-yl)-phenyl
393.	ethyl	4-(2,2-dimethylpyrrolidin-1-yl)-phenyl

No.	R ¹	Ar
394.	ethyl	4-(3,3-dimethylpyrrolidin-1-yl)-phenyl
395.	ethyl	4-(2-trifluoromethylpyrrolidin-1-yl)-phenyl
396.	ethyl	4-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
397.	ethyl	4-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
398.	ethyl	4-(3-trifluoromethylpyrrolidin-1-yl)-phenyl
399.	ethyl	4-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
400.	ethyl	4-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
401.	ethyl	4-(2-oxopyrrolidin-1-yl)-phenyl
402.	ethyl	4-(2-oxo-oxazolidin-3-yl)-phenyl
403.	ethyl	4-(piperidin-1-yl)-phenyl
404.	ethyl	4-(2-methylpiperidin-1-yl)-phenyl
405.	ethyl	4-((S)-2-methylpiperidin-1-yl)-phenyl
406.	ethyl	4-((R)-2-methylpiperidin-1-yl)-phenyl
407.	ethyl	4-(piperazin-1-yl)-phenyl
408.	ethyl	4-(4-methylpiperazin-1-yl)-phenyl
409.	ethyl	4-(morpholin-4-yl)-phenyl
410.	ethyl	4-(thiomorpholin-4-yl)-phenyl
411.	ethyl	4-(1-oxo-thiomorpholin-4-yl)-phenyl
412.	ethyl	4-(1,1-dioxo-thiomorpholin-4-yl)-phenyl
413.	ethyl	4-(pyrrol-1-yl)-phenyl
414.	ethyl	4-(pyrrol-2-yl)-phenyl
415.	ethyl	4-(pyrrol-3-yl)-phenyl
416.	ethyl	4-(1-methylpyrrol-2-yl)-phenyl
417.	ethyl	4-(1-methylpyrrol-3-yl)-phenyl
418.	ethyl	4-(furan-2-yl)-phenyl
419.	ethyl	4-(furan-3-yl)-phenyl
420.	ethyl	4-(thiophen-2-yl)-phenyl
421.	ethyl	4-(thiophen-3-yl)-phenyl
422.	ethyl	4-(5-propylthien-2-yl)-phenyl
423.	ethyl	4-(pyrazol-1-yl)-phenyl
424.	ethyl	4-(pyrazol-3-yl)-phenyl
425.	ethyl	4-(pyrazol-4-yl)-phenyl
426.	ethyl	4-(1-methyl-1H-pyrazol-4-yl)-phenyl
427.	ethyl	4-(1-ethyl-1H-pyrazol-4-yl)-phenyl

No.	R ¹	Ar
428.	ethyl	4-(1-methyl-1H-pyrazol-5-yl)-phenyl
429.	ethyl	4-(1H-imidazol-2-yl)-phenyl
430.	ethyl	4-(imidazol-1-yl)-phenyl
431.	ethyl	4-(1-methylimidazol-2-yl)-phenyl
432.	ethyl	4-(oxazol-2-yl)-phenyl
433.	ethyl	4-(oxazol-4-yl)-phenyl
434.	ethyl	4-(oxazol-5-yl)-phenyl
435.	ethyl	4-(isoxazol-3-yl)-phenyl
436.	ethyl	4-(isoxazol-4-yl)-phenyl
437.	ethyl	4-(isoxazol-5-yl)-phenyl
438.	ethyl	4-([1,2,3]-triazol-1-yl)-phenyl
439.	ethyl	4-([1,2,4]-triazol-1-yl)-phenyl
440.	ethyl	4-([1,2,3]-triazol-2-yl)-phenyl
441.	ethyl	4-(4H-[1,2,4]-triazol-3-yl)-phenyl
442.	ethyl	4-([1,2,4]-triazol-4-yl)-phenyl
443.	ethyl	4-(2H-[1,2,3]-triazol-4-yl)-phenyl
444.	ethyl	4-(4-methyl-4H-[1,2,4]-triazol-3-yl)-phenyl
445.	ethyl	4-(2-methyl-2H-[1,2,3]-triazol-4-yl)-phenyl
446.	ethyl	4-([1,3,4]-oxadiazol-2-yl)-phenyl
447.	ethyl	4-([1,2,4]-oxadiazol-3-yl)-phenyl
448.	ethyl	4-([1,2,4]-oxadiazol-5-yl)-phenyl
449.	ethyl	4-([1,2,3]-oxadiazol-4-yl)-phenyl
450.	ethyl	4-([1,2,3]-oxadiazol-5-yl)-phenyl
451.	ethyl	4-([1,2,3]-thiadiazol-4-yl)-phenyl
452.	ethyl	4-(1H-tetrazol-5-yl)-phenyl
453.	ethyl	4-(tetrazol-1-yl)-phenyl
454.	ethyl	4-(2-methyl-2H-tetrazol-5-yl)-phenyl
455.	ethyl	4-(1-methyl-1H-tetrazol-5-yl)-phenyl
456.	ethyl	4-furazan-3-yl-phenyl
457.	ethyl	4-(pyrid-2-yl)-phenyl
458.	ethyl	4-(pyrid-3-yl)-phenyl
459.	ethyl	4-(pyrid-4-yl)-phenyl
460.	ethyl	4-(pyrimidin-2-yl)-phenyl
461.	ethyl	4-(pyrimidin-4-yl)-phenyl

No.	R ¹	Ar
462.	ethyl	4-(pyrimidin-5-yl)-phenyl
463.	ethyl	5-isopropylthiophen-2-yl
464.	ethyl	2-chlorothiophen-5-yl
465.	ethyl	2,5-dichlorothiophen-4-yl
466.	ethyl	2,3-dichlorothiophen-5-yl
467.	ethyl	2-chloro-3-nitrothiophen-5-yl
468.	ethyl	2-(phenylsulfonyl)-thiophen-5-yl
469.	ethyl	2-(pyridin-2-yl)thiophen-5-yl
470.	ethyl	2-(5-(trifluoromethyl)isoxazol-3-yl)-thiophen-5-yl
471.	ethyl	2-(2-methylthiazol-4-yl)-thiophen-5-yl
472.	ethyl	1-methyl-1H-imidazol-4-yl
473.	ethyl	1,2-dimethyl-1H-imidazol-4-yl
474.	ethyl	3,5-dimethylisoxazol-4-yl
475.	ethyl	thiazol-2-yl
476.	ethyl	4-methylthiazol-2-yl
477.	ethyl	4-isopropylthiazol-2-yl
478.	ethyl	4-trifluoromethylthiazol-2-yl
479.	ethyl	5-methylthiazol-2-yl
480.	ethyl	5-isopropylthiazol-2-yl
481.	ethyl	5-trifluoromethylthiazol-2-yl
482.	ethyl	2,4-dimethylthiazol-5-yl
483.	ethyl	2-acetamido-4-methylthiazol-5-yl
484.	ethyl	4H-[1,2,4]triazol-3-yl
485.	ethyl	5-methyl-4H-[1,2,4]triazol-3-yl
486.	ethyl	4-methyl-4H-[1,2,4]triazol-3-yl
487.	ethyl	5-isopropyl-4H-[1,2,4]triazol-3-yl
488.	ethyl	5-trifluoromethyl-4H-[1,2,4]triazol-3-yl
489.	ethyl	4,5-dimethyl-4H-[1,2,4]triazol-3-yl
490.	ethyl	5-isopropyl-4-methyl-4H-[1,2,4]triazol-3-yl
491.	ethyl	5-trifluoromethyl-4-methyl-4H-[1,2,4]triazol-3-yl
492.	ethyl	[1,3,4]thiadiazol-2-yl
493.	ethyl	5-methyl-[1,3,4]thiadiazol-2-yl
494.	ethyl	5-isopropyl-[1,3,4]thiadiazol-2-yl
495.	ethyl	5-trifluoromethyl-[1,3,4]thiadiazol-2-yl

No.	R ¹	Ar
496.	ethyl	3-bromo-2-chloropyrid-5-yl
497.	ethyl	2-(4-morpholino)-pyrid-5-yl
498.	ethyl	2-phenoxy-pyrid-5-yl
499.	ethyl	(2-isopropyl)-pyrimidin-5-yl
500.	ethyl	(5-isopropyl)-pyrimidin-2-yl
501.	ethyl	8-quinolyl
502.	ethyl	5-isoquinolyl
503.	ethyl	2-(trifluoroacetyl)-1,2,3,4-tetrahydroisoquinolin-7-yl
504.	ethyl	5-chloro-3-methylbenzothiophen-2-yl
505.	ethyl	3,4-dihydro-4-methyl-2H-benzo[b][1,4]oxazinyl
506.	ethyl	benzothiazol-6-yl
507.	ethyl	benzo[2,1,3]oxadiazol-4-yl
508.	ethyl	5-chlorobenzo[2,1,3]oxadiazol-4-yl
509.	ethyl	7-chlorobenzo[2,1,3]oxadiazol-4-yl
510.	ethyl	benzo[2,1,3]thiadiazol-4-yl
511.	methyl	4-isopropylphenyl
512.	methyl	4-sec-butylphenyl
513.	methyl	4-isobutylphenyl
514.	methyl	4-(1,1-dimethylpropyl)-phenyl
515.	methyl	4-vinylphenyl
516.	methyl	4-isopropenylphenyl
517.	methyl	4-(fluoromethyl)phenyl
518.	methyl	3-(fluoromethyl)phenyl
519.	methyl	2-(fluoromethyl)phenyl
520.	methyl	4-(difluoromethyl)phenyl
521.	methyl	3-(difluoromethyl)phenyl
522.	methyl	2-(difluoromethyl)phenyl
523.	methyl	4-(1-fluoroethyl)-phenyl
524.	methyl	4-((S)-1-fluoroethyl)-phenyl
525.	methyl	4-((R)-1-fluoroethyl)-phenyl
526.	methyl	4-(2-fluoroethyl)-phenyl
527.	methyl	4-(1,1-difluoroethyl)-phenyl
528.	methyl	4-(2,2-difluoroethyl)-phenyl
529.	methyl	4-(2,2,2-trifluoroethyl)-phenyl

No.	R ¹	Ar
530.	methyl	4-(3-fluoropropyl)-phenyl
531.	methyl	4-(2-fluoropropyl)-phenyl
532.	methyl	4-((S)-2-fluoropropyl)-phenyl
533.	methyl	4-((R)-2-fluoropropyl)-phenyl
534.	methyl	4-(3,3-difluoropropyl)-phenyl
535.	methyl	4-(3,3,3-trifluoropropyl)-phenyl
536.	methyl	4-(1-fluoro-1-methylethyl)-phenyl
537.	methyl	4-(2-fluoro-1-methylethyl)-phenyl
538.	methyl	4-((S)-2-fluoro-1-methylethyl)-phenyl
539.	methyl	4-((R)-2-fluoro-1-methylethyl)-phenyl
540.	methyl	4-(2,2-difluoro-1-methylethyl)-phenyl
541.	methyl	4-((S)-2,2-difluoro-1-methylethyl)-phenyl
542.	methyl	4-((R)-2,2-difluoro-1-methylethyl)-phenyl
543.	methyl	4-(2,2,2-trifluoro-1-methylethyl)-phenyl
544.	methyl	4-((S)-2,2,2-trifluoro-1-methylethyl)-phenyl
545.	methyl	4-((R)-2,2,2-trifluoro-1-methylethyl)-phenyl
546.	methyl	4-(2-fluoro-1-fluoromethylethyl)-phenyl
547.	methyl	4-(1-difluoromethyl-2,2-difluoroethyl)-phenyl
548.	methyl	4-(1,1-dimethyl-2-fluoroethyl)-phenyl
549.	methyl	4-ethoxyphenyl
550.	methyl	4-propoxyphenyl
551.	methyl	4-isopropoxyphenyl
552.	methyl	4-butoxyphenyl
553.	methyl	4-(fluoromethoxy)-phenyl
554.	methyl	4-(difluoromethoxy)-phenyl
555.	methyl	4-(2-fluoroethoxy)-phenyl
556.	methyl	4-(2,2-difluoroethoxy)-phenyl
557.	methyl	4-(2,2,2-trifluoroethoxy)-phenyl
558.	methyl	4-(1,1,2,2-tetrafluoroethoxy)-phenyl
559.	methyl	4-cyclopropylphenyl
560.	methyl	4-cyclobutylphenyl
561.	methyl	4-cyclopentylphenyl
562.	methyl	4-(2,2-difluorocyclopropyl)-phenyl
563.	methyl	3-fluoro-4-isopropylphenyl

No.	R ¹	Ar
564.	methyl	4-(1-hydroxy-1-methylethyl)-phenyl
565.	methyl	4-(2-hydroxy-2-methylpropyl)-phenyl
566.	methyl	4-acetylphenyl
567.	methyl	4-carboxyphenyl
568.	methyl	4-cyanophenyl
569.	methyl	4-hydroxyphenyl
570.	methyl	4-(O-benzyl)-phenyl
571.	methyl	4-(2-methoxyethoxy)-phenyl
572.	methyl	4-(CH ₂ -N(CH ₃) ₂)-phenyl
573.	methyl	4-(NH-CO-NH ₂)-phenyl
574.	methyl	4-(methylsulfanyl)-phenyl
575.	methyl	4-(fluoromethylsulfanyl)-phenyl
576.	methyl	4-(difluoromethylsulfanyl)-phenyl
577.	methyl	4-(trifluoromethylsulfanyl)-phenyl
578.	methyl	4-(methylsulfonyl)-phenyl
579.	methyl	4-(N-methoxy-N-methyl-amino)-phenyl
580.	methyl	4-(methoxyamino)-phenyl
581.	methyl	4-(ethoxyamino)-phenyl
582.	methyl	4-(N-methylaminooxy)-phenyl
583.	methyl	4-(N,N-dimethylaminooxy)-phenyl
584.	methyl	4-(azetidin-1-yl)-phenyl
585.	methyl	4-(2-methylazetidin-1-yl)-phenyl
586.	methyl	4-((S)-2-methylazetidin-1-yl)-phenyl
587.	methyl	4-((R)-2-methylazetidin-1-yl)-phenyl
588.	methyl	4-(3-fluoroazetidin-1-yl)-phenyl
589.	methyl	4-(3-methoxyazetidin-1-yl)-phenyl
590.	methyl	4-(3-hydroxyazetidin-1-yl)-phenyl
591.	methyl	4-(pyrrolidin-1-yl)-phenyl
592.	methyl	4-(pyrrolidin-2-yl)-phenyl
593.	methyl	4-((S)-pyrrolidin-2-yl)-phenyl
594.	methyl	4-((R)-pyrrolidin-2-yl)-phenyl
595.	methyl	4-(pyrrolidin-3-yl)-phenyl
596.	methyl	4-((S)-pyrrolidin-3-yl)-phenyl
597.	methyl	4-((R)-pyrrolidin-3-yl)-phenyl

No.	R ¹	Ar
598.	methyl	4-(2-fluoropyrrolidin-1-yl)-phenyl
599.	methyl	4-((S)-2-fluoropyrrolidin-1-yl)-phenyl
600.	methyl	4-((R)-2-fluoropyrrolidin-1-yl)-phenyl
601.	methyl	4-(3-fluoropyrrolidin-1-yl)-phenyl
602.	methyl	4-((S)-3-fluoropyrrolidin-1-yl)-phenyl
603.	methyl	4-((R)-3-fluoropyrrolidin-1-yl)-phenyl
604.	methyl	4-(2,2-difluoropyrrolidin-1-yl)-phenyl
605.	methyl	4-(3,3-difluoropyrrolidin-1-yl)-phenyl
606.	methyl	4-(2-methylpyrrolidin-1-yl)-phenyl
607.	methyl	4-((S)-2-methylpyrrolidin-1-yl)-phenyl
608.	methyl	4-((R)-2-methylpyrrolidin-1-yl)-phenyl
609.	methyl	4-(3-methylpyrrolidin-1-yl)-phenyl
610.	methyl	4-((S)-3-methylpyrrolidin-1-yl)-phenyl
611.	methyl	4-((R)-3-methylpyrrolidin-1-yl)-phenyl
612.	methyl	4-(1-methylpyrrolidin-2-yl)-phenyl
613.	methyl	4-((S)-1-methylpyrrolidin-2-yl)-phenyl
614.	methyl	4-((R)-1-methylpyrrolidin-2-yl)-phenyl
615.	methyl	4-(1-methylpyrrolidin-3-yl)-phenyl
616.	methyl	4-((S)-1-methylpyrrolidin-3-yl)-phenyl
617.	methyl	4-((R)-1-methylpyrrolidin-3-yl)-phenyl
618.	methyl	4-(2,2-dimethylpyrrolidin-1-yl)-phenyl
619.	methyl	4-(3,3-dimethylpyrrolidin-1-yl)-phenyl
620.	methyl	4-(2-trifluoromethylpyrrolidin-1-yl)-phenyl
621.	methyl	4-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
622.	methyl	4-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
623.	methyl	4-(3-trifluoromethylpyrrolidin-1-yl)-phenyl
624.	methyl	4-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
625.	methyl	4-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
626.	methyl	4-(2-oxopyrrolidin-1-yl)-phenyl
627.	methyl	4-(2-oxo-oxazolidin-3-yl)-phenyl
628.	methyl	4-(piperidin-1-yl)-phenyl
629.	methyl	4-(2-methylpiperidin-1-yl)-phenyl
630.	methyl	4-((S)-2-methylpiperidin-1-yl)-phenyl
631.	methyl	4-((R)-2-methylpiperidin-1-yl)-phenyl

No.	R ¹	Ar
632.	methyl	4-(piperazin-1-yl)-phenyl
633.	methyl	4-(4-methylpiperazin-1-yl)-phenyl
634.	methyl	4-(morpholin-4-yl)-phenyl
635.	methyl	4-(thiomorpholin-4-yl)-phenyl
636.	methyl	4-(1-oxo-thiomorpholin-4-yl)-phenyl
637.	methyl	4-(1,1-dioxo-thiomorpholin-4-yl)-phenyl
638.	methyl	4-(pyrrol-1-yl)-phenyl
639.	methyl	4-(pyrrol-2-yl)-phenyl
640.	methyl	4-(pyrrol-3-yl)-phenyl
641.	methyl	4-(1-methylpyrrol-2-yl)-phenyl
642.	methyl	4-(1-methylpyrrol-3-yl)-phenyl
643.	methyl	4-(furan-2-yl)-phenyl
644.	methyl	4-(furan-3-yl)-phenyl
645.	methyl	4-(thiophen-2-yl)-phenyl
646.	methyl	4-(thiophen-3-yl)-phenyl
647.	methyl	4-(5-propylthien-2-yl)-phenyl
648.	methyl	4-(pyrazol-1-yl)-phenyl
649.	methyl	4-(pyrazol-3-yl)-phenyl
650.	methyl	4-(pyrazol-4-yl)-phenyl
651.	methyl	4-(1-methyl-1H-pyrazol-4-yl)-phenyl
652.	methyl	4-(1-ethyl-1H-pyrazol-4-yl)-phenyl
653.	methyl	4-(1-methyl-1H-pyrazol-5-yl)-phenyl
654.	methyl	4-(1H-imidazol-2-yl)-phenyl
655.	methyl	4-(imidazol-1-yl)-phenyl
656.	methyl	4-(1-methylimidazol-2-yl)-phenyl
657.	methyl	4-(oxazol-2-yl)-phenyl
658.	methyl	4-(oxazol-4-yl)-phenyl
659.	methyl	4-(oxazol-5-yl)-phenyl
660.	methyl	4-(isoxazol-3-yl)-phenyl
661.	methyl	4-(isoxazol-4-yl)-phenyl
662.	methyl	4-(isoxazol-5-yl)-phenyl
663.	methyl	4-([1,2,3]-triazol-1-yl)-phenyl
664.	methyl	4-([1,2,4]-triazol-1-yl)-phenyl
665.	methyl	4-([1,2,3]-triazol-2-yl)-phenyl

No.	R ¹	Ar
666.	methyl	4-(4H-[1,2,4]-triazol-3-yl)-phenyl
667.	methyl	4-([1,2,4]-triazol-4-yl)-phenyl
668.	methyl	4-(2H-[1,2,3]-triazol-4-yl)-phenyl
669.	methyl	4-(4-methyl-4H-[1,2,4]-triazol-3-yl)-phenyl
670.	methyl	4-(2-methyl-2H-[1,2,3]-triazol-4-yl)-phenyl
671.	methyl	4-([1,3,4]-oxadiazol-2-yl)-phenyl
672.	methyl	4-([1,2,4]-oxadiazol-3-yl)-phenyl
673.	methyl	4-([1,2,4]-oxadiazol-5-yl)-phenyl
674.	methyl	4-([1,2,3]-oxadiazol-4-yl)-phenyl
675.	methyl	4-([1,2,3]-oxadiazol-5-yl)-phenyl
676.	methyl	4-([1,2,3]-thiadiazol-4-yl)-phenyl
677.	methyl	4-(1H-tetrazol-5-yl)-phenyl
678.	methyl	4-(tetrazol-1-yl)-phenyl
679.	methyl	4-(2-methyl-2H-tetrazol-5-yl)-phenyl
680.	methyl	4-(1-methyl-1H-tetrazol-5-yl)-phenyl
681.	methyl	4-furazan-3-yl-phenyl
682.	methyl	4-(pyrid-2-yl)-phenyl
683.	methyl	4-(pyrid-3-yl)-phenyl
684.	methyl	4-(pyrid-4-yl)-phenyl
685.	methyl	4-(pyrimidin-2-yl)-phenyl
686.	methyl	4-(pyrimidin-4-yl)-phenyl
687.	methyl	4-(pyrimidin-5-yl)-phenyl
688.	methyl	5-isopropylthiophen-2-yl
689.	methyl	2-chlorothiophen-5-yl
690.	methyl	2,5-dichlorothiophen-4-yl
691.	methyl	2,3-dichlorothiophen-5-yl
692.	methyl	2-chloro-3-nitrothiophen-5-yl
693.	methyl	2-(phenylsulfonyl)-thiophen-5-yl
694.	methyl	2-(pyridin-2-yl)thiophen-5-yl
695.	methyl	2-(5-(trifluoromethyl)isoxazol-3-yl)-thiophen-5-yl
696.	methyl	2-(2-methylthiazol-4-yl)-thiophen-5-yl
697.	methyl	1-methyl-1H-imidazol-4-yl
698.	methyl	1,2-dimethyl-1H-imidazol-4-yl
699.	methyl	3,5-dimethylisoxazol-4-yl

No.	R ¹	Ar
700.	methyl	thiazol-2-yl
701.	methyl	4-methylthiazol-2-yl
702.	methyl	4-isopropylthiazol-2-yl
703.	methyl	4-trifluoromethylthiazol-2-yl
704.	methyl	5-methylthiazol-2-yl
705.	methyl	5-isopropylthiazol-2-yl
706.	methyl	5-trifluoromethylthiazol-2-yl
707.	methyl	2,4-dimethylthiazol-5-yl
708.	methyl	2-acetamido-4-methylthiazol-5-yl
709.	methyl	4H-[1,2,4]triazol-3-yl
710.	methyl	5-methyl-4H-[1,2,4]triazol-3-yl
711.	methyl	4-methyl-4H-[1,2,4]triazol-3-yl
712.	methyl	5-isopropyl-4H-[1,2,4]triazol-3-yl
713.	methyl	5-trifluoromethyl-4H-[1,2,4]triazol-3-yl
714.	methyl	4,5-dimethyl-4H-[1,2,4]triazol-3-yl
715.	methyl	5-isopropyl-4-methyl-4H-[1,2,4]triazol-3-yl
716.	methyl	5-trifluoromethyl-4-methyl-4H-[1,2,4]triazol-3-yl
717.	methyl	[1,3,4]thiadiazol-2-yl
718.	methyl	5-methyl-[1,3,4]thiadiazol-2-yl
719.	methyl	5-isopropyl-[1,3,4]thiadiazol-2-yl
720.	methyl	5-trifluoromethyl-[1,3,4]thiadiazol-2-yl
721.	methyl	3-bromo-2-chloropyrid-5-yl
722.	methyl	2-(4-morpholino)-pyrid-5-yl
723.	methyl	2-phenoxy-pyrid-5-yl
724.	methyl	(2-isopropyl)-pyrimidin-5-yl
725.	methyl	(5-isopropyl)-pyrimidin-2-yl
726.	methyl	8-quinolyl
727.	methyl	5-isoquinolyl
728.	methyl	2-(trifluoroacetyl)-1,2,3,4-tetrahydroisoquinolin-7-yl
729.	methyl	5-chloro-3-methylbenzothiophen-2-yl
730.	methyl	3,4-dihydro-4-methyl-2H-benzo[b][1,4]oxazinyl
731.	methyl	benzothiazol-6-yl
732.	methyl	benzo[2,1,3]oxadiazol-4-yl
733.	methyl	5-chlorobenzo[2,1,3]oxadiazol-4-yl

No.	R ¹	Ar
734.	methyl	7-chlorobenzo[2,1,3]oxadiazol-4-yl
735.	methyl	benzo[2,1,3]thiadiazol-4-yl
736.	3-fluoropropyl	4-methylphenyl
737.	3-fluoropropyl	4-ethylphenyl
738.	3-fluoropropyl	4-propylphenyl
739.	3-fluoropropyl	4-isopropylphenyl
740.	3-fluoropropyl	4-sec-butylphenyl
741.	3-fluoropropyl	4-isobutylphenyl
742.	3-fluoropropyl	4-(1,1-dimethylpropyl)-phenyl
743.	3-fluoropropyl	4-vinylphenyl
744.	3-fluoropropyl	4-isopropenylphenyl
745.	3-fluoropropyl	4-fluorophenyl
746.	3-fluoropropyl	4-chlorophenyl
747.	3-fluoropropyl	4-bromophenyl
748.	3-fluoropropyl	4-(fluoromethyl)phenyl
749.	3-fluoropropyl	3-(fluoromethyl)phenyl
750.	3-fluoropropyl	2-(fluoromethyl)phenyl
751.	3-fluoropropyl	4-(difluoromethyl)phenyl
752.	3-fluoropropyl	3-(difluoromethyl)phenyl
753.	3-fluoropropyl	2-(difluoromethyl)phenyl
754.	3-fluoropropyl	4-(trifluoromethyl)phenyl
755.	3-fluoropropyl	3-(trifluoromethyl)phenyl
756.	3-fluoropropyl	2-(trifluoromethyl)phenyl
757.	3-fluoropropyl	4-(1-fluoroethyl)-phenyl
758.	3-fluoropropyl	4-((S)-1-fluoroethyl)-phenyl
759.	3-fluoropropyl	4-((R)-1-fluoroethyl)-phenyl
760.	3-fluoropropyl	4-(2-fluoroethyl)-phenyl
761.	3-fluoropropyl	4-(1,1-difluoroethyl)-phenyl
762.	3-fluoropropyl	4-(2,2-difluoroethyl)-phenyl
763.	3-fluoropropyl	4-(2,2,2-trifluoroethyl)-phenyl
764.	3-fluoropropyl	4-(3-fluoropropyl)-phenyl
765.	3-fluoropropyl	4-(2-fluoropropyl)-phenyl
766.	3-fluoropropyl	4-((S)-2-fluoropropyl)-phenyl
767.	3-fluoropropyl	4-((R)-2-fluoropropyl)-phenyl

No.	R ¹	Ar
768.	3-fluoropropyl	4-(3,3-difluoropropyl)-phenyl
769.	3-fluoropropyl	4-(3,3,3-trifluoropropyl)-phenyl
770.	3-fluoropropyl	4-(1-fluoro-1-methylethyl)-phenyl
771.	3-fluoropropyl	4-(2-fluoro-1-methylethyl)-phenyl
772.	3-fluoropropyl	4-((S)-2-fluoro-1-methylethyl)-phenyl
773.	3-fluoropropyl	4-((R)-2-fluoro-1-methylethyl)-phenyl
774.	3-fluoropropyl	4-(2,2-difluoro-1-methylethyl)-phenyl
775.	3-fluoropropyl	4-((S)-2,2-difluoro-1-methylethyl)-phenyl
776.	3-fluoropropyl	4-((R)-2,2-difluoro-1-methylethyl)-phenyl
777.	3-fluoropropyl	4-(2,2,2-trifluoro-1-methylethyl)-phenyl
778.	3-fluoropropyl	4-((S)-2,2,2-trifluoro-1-methylethyl)-phenyl
779.	3-fluoropropyl	4-((R)-2,2,2-trifluoro-1-methylethyl)-phenyl
780.	3-fluoropropyl	4-(2-fluoro-1-fluoromethylethyl)-phenyl
781.	3-fluoropropyl	4-(1-difluoromethyl-2,2-difluoroethyl)-phenyl
782.	3-fluoropropyl	4-(1,1-dimethyl-2-fluoroethyl)-phenyl
783.	3-fluoropropyl	4-methoxyphenyl
784.	3-fluoropropyl	4-ethoxyphenyl
785.	3-fluoropropyl	4-propoxyphenyl
786.	3-fluoropropyl	4-isopropoxyphenyl
787.	3-fluoropropyl	4-butoxyphenyl
788.	3-fluoropropyl	4-(fluoromethoxy)-phenyl
789.	3-fluoropropyl	4-(difluoromethoxy)-phenyl
790.	3-fluoropropyl	4-(trifluoromethoxy)-phenyl
791.	3-fluoropropyl	3-(trifluoromethoxy)-phenyl
792.	3-fluoropropyl	4-(2-fluoroethoxy)-phenyl
793.	3-fluoropropyl	4-(2,2-difluoroethoxy)-phenyl
794.	3-fluoropropyl	4-(2,2,2-trifluoroethoxy)-phenyl
795.	3-fluoropropyl	4-(1,1,2,2-tetrafluoroethoxy)-phenyl
796.	3-fluoropropyl	4-cyclopropylphenyl
797.	3-fluoropropyl	4-cyclobutylphenyl
798.	3-fluoropropyl	4-cyclopentylphenyl
799.	3-fluoropropyl	4-(2,2-difluorocyclopropyl)-phenyl
800.	3-fluoropropyl	3,4-difluorophenyl
801.	3-fluoropropyl	4-bromo-3-fluorophenyl

No.	R ¹	Ar
802.	3-fluoropropyl	4-bromo-2-fluorophenyl
803.	3-fluoropropyl	4-bromo-2,5-difluorophenyl
804.	3-fluoropropyl	2-fluoro-4-isopropylphenyl
805.	3-fluoropropyl	3-fluoro-4-isopropylphenyl
806.	3-fluoropropyl	4-(1-hydroxy-1-methylethyl)-phenyl
807.	3-fluoropropyl	4-(2-hydroxy-2-methylpropyl)-phenyl
808.	3-fluoropropyl	4-acetylphenyl
809.	3-fluoropropyl	4-carboxyphenyl
810.	3-fluoropropyl	4-cyanophenyl
811.	3-fluoropropyl	4-hydroxyphenyl
812.	3-fluoropropyl	4-(O-benzyl)-phenyl
813.	3-fluoropropyl	4-(2-methoxyethoxy)-phenyl
814.	3-fluoropropyl	4-(CH ₂ -N(CH ₃) ₂)-phenyl
815.	3-fluoropropyl	4-(NH-CO-NH ₂)-phenyl
816.	3-fluoropropyl	4-(methylsulfanyl)-phenyl
817.	3-fluoropropyl	4-(fluoromethylsulfanyl)-phenyl
818.	3-fluoropropyl	4-(difluoromethylsulfanyl)-phenyl
819.	3-fluoropropyl	4-(trifluoromethylsulfanyl)-phenyl
820.	3-fluoropropyl	4-(methylsulfonyl)-phenyl
821.	3-fluoropropyl	4-(N-methoxy-N-methyl-amino)-phenyl
822.	3-fluoropropyl	4-(methoxyamino)-phenyl
823.	3-fluoropropyl	4-(ethoxyamino)-phenyl
824.	3-fluoropropyl	4-(N-methylaminooxy)-phenyl
825.	3-fluoropropyl	4-(N,N-dimethylaminooxy)-phenyl
826.	3-fluoropropyl	4-(azetidin-1-yl)-phenyl
827.	3-fluoropropyl	4-(2-methylazetidin-1-yl)-phenyl
828.	3-fluoropropyl	4-((S)-2-methylazetidin-1-yl)-phenyl
829.	3-fluoropropyl	4-((R)-2-methylazetidin-1-yl)-phenyl
830.	3-fluoropropyl	4-(3-fluoroazetidin-1-yl)-phenyl
831.	3-fluoropropyl	4-(3-methoxyazetidin-1-yl)-phenyl
832.	3-fluoropropyl	4-(3-hydroxyazetidin-1-yl)-phenyl
833.	3-fluoropropyl	4-(pyrrolidin-1-yl)-phenyl
834.	3-fluoropropyl	4-(pyrrolidin-2-yl)-phenyl
835.	3-fluoropropyl	4-((S)-pyrrolidin-2-yl)-phenyl

No.	R ¹	Ar
836.	3-fluoropropyl	4-((R)-pyrrolidin-2-yl)-phenyl
837.	3-fluoropropyl	4-(pyrrolidin-3-yl)-phenyl
838.	3-fluoropropyl	4-((S)-pyrrolidin-3-yl)-phenyl
839.	3-fluoropropyl	4-((R)-pyrrolidin-3-yl)-phenyl
840.	3-fluoropropyl	4-(2-fluoropyrrolidin-1-yl)-phenyl
841.	3-fluoropropyl	4-((S)-2-fluoropyrrolidin-1-yl)-phenyl
842.	3-fluoropropyl	4-((R)-2-fluoropyrrolidin-1-yl)-phenyl
843.	3-fluoropropyl	4-(3-fluoropyrrolidin-1-yl)-phenyl
844.	3-fluoropropyl	4-((S)-3-fluoropyrrolidin-1-yl)-phenyl
845.	3-fluoropropyl	4-((R)-3-fluoropyrrolidin-1-yl)-phenyl
846.	3-fluoropropyl	4-(2,2-difluoropyrrolidin-1-yl)-phenyl
847.	3-fluoropropyl	4-(3,3-difluoropyrrolidin-1-yl)-phenyl
848.	3-fluoropropyl	4-(2-methylpyrrolidin-1-yl)-phenyl
849.	3-fluoropropyl	4-((S)-2-methylpyrrolidin-1-yl)-phenyl
850.	3-fluoropropyl	4-((R)-2-methylpyrrolidin-1-yl)-phenyl
851.	3-fluoropropyl	4-(3-methylpyrrolidin-1-yl)-phenyl
852.	3-fluoropropyl	4-((S)-3-methylpyrrolidin-1-yl)-phenyl
853.	3-fluoropropyl	4-((R)-3-methylpyrrolidin-1-yl)-phenyl
854.	3-fluoropropyl	4-(1-methylpyrrolidin-2-yl)-phenyl
855.	3-fluoropropyl	4-((S)-1-methylpyrrolidin-2-yl)-phenyl
856.	3-fluoropropyl	4-((R)-1-methylpyrrolidin-2-yl)-phenyl
857.	3-fluoropropyl	4-(1-methylpyrrolidin-3-yl)-phenyl
858.	3-fluoropropyl	4-((S)-1-methylpyrrolidin-3-yl)-phenyl
859.	3-fluoropropyl	4-((R)-1-methylpyrrolidin-3-yl)-phenyl
860.	3-fluoropropyl	4-(2,2-dimethylpyrrolidin-1-yl)-phenyl
861.	3-fluoropropyl	4-(3,3-dimethylpyrrolidin-1-yl)-phenyl
862.	3-fluoropropyl	4-(2-trifluoromethylpyrrolidin-1-yl)-phenyl
863.	3-fluoropropyl	4-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
864.	3-fluoropropyl	4-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
865.	3-fluoropropyl	4-(3-trifluoromethylpyrrolidin-1-yl)-phenyl
866.	3-fluoropropyl	4-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
867.	3-fluoropropyl	4-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
868.	3-fluoropropyl	4-(2-oxopyrrolidin-1-yl)-phenyl
869.	3-fluoropropyl	4-(2-oxo-oxazolidin-3-yl)-phenyl

No.	R ¹	Ar
870.	3-fluoropropyl	4-(piperidin-1-yl)-phenyl
871.	3-fluoropropyl	4-(2-methylpiperidin-1-yl)-phenyl
872.	3-fluoropropyl	4-((S)-2-methylpiperidin-1-yl)-phenyl
873.	3-fluoropropyl	4-((R)-2-methylpiperidin-1-yl)-phenyl
874.	3-fluoropropyl	4-(piperazin-1-yl)-phenyl
875.	3-fluoropropyl	4-(4-methylpiperazin-1-yl)-phenyl
876.	3-fluoropropyl	4-(morpholin-4-yl)-phenyl
877.	3-fluoropropyl	4-(thiomorpholin-4-yl)-phenyl
878.	3-fluoropropyl	4-(1-oxo-thiomorpholin-4-yl)-phenyl
879.	3-fluoropropyl	4-(1,1-dioxo-thiomorpholin-4-yl)-phenyl
880.	3-fluoropropyl	4-(pyrrol-1-yl)-phenyl
881.	3-fluoropropyl	4-(pyrrol-2-yl)-phenyl
882.	3-fluoropropyl	4-(pyrrol-3-yl)-phenyl
883.	3-fluoropropyl	4-(1-methylpyrrol-2-yl)-phenyl
884.	3-fluoropropyl	4-(1-methylpyrrol-3-yl)-phenyl
885.	3-fluoropropyl	4-(furan-2-yl)-phenyl
886.	3-fluoropropyl	4-(furan-3-yl)-phenyl
887.	3-fluoropropyl	4-(thiophen-2-yl)-phenyl
888.	3-fluoropropyl	4-(thiophen-3-yl)-phenyl
889.	3-fluoropropyl	4-(5-propylthien-2-yl)-phenyl
890.	3-fluoropropyl	4-(pyrazol-1-yl)-phenyl
891.	3-fluoropropyl	4-(pyrazol-3-yl)-phenyl
892.	3-fluoropropyl	4-(pyrazol-4-yl)-phenyl
893.	3-fluoropropyl	4-(1-methyl-1H-pyrazol-4-yl)-phenyl
894.	3-fluoropropyl	4-(1-ethyl-1H-pyrazol-4-yl)-phenyl
895.	3-fluoropropyl	4-(1-methyl-1H-pyrazol-5-yl)-phenyl
896.	3-fluoropropyl	4-(1H-imidazol-2-yl)-phenyl
897.	3-fluoropropyl	4-(imidazol-1-yl)-phenyl
898.	3-fluoropropyl	4-(1-methylimidazol-2-yl)-phenyl
899.	3-fluoropropyl	4-(oxazol-2-yl)-phenyl
900.	3-fluoropropyl	4-(oxazol-4-yl)-phenyl
901.	3-fluoropropyl	4-(oxazol-5-yl)-phenyl
902.	3-fluoropropyl	4-(isoxazol-3-yl)-phenyl
903.	3-fluoropropyl	4-(isoxazol-4-yl)-phenyl

No.	R ¹	Ar
904.	3-fluoropropyl	4-(isoxazol-5-yl)-phenyl
905.	3-fluoropropyl	4-([1,2,3]-triazol-1-yl)-phenyl
906.	3-fluoropropyl	4-([1,2,4]-triazol-1-yl)-phenyl
907.	3-fluoropropyl	4-([1,2,3]-triazol-2-yl)-phenyl
908.	3-fluoropropyl	4-(4H-[1,2,4]-triazol-3-yl)-phenyl
909.	3-fluoropropyl	4-([1,2,4]-triazol-4-yl)-phenyl
910.	3-fluoropropyl	4-(2H-[1,2,3]-triazol-4-yl)-phenyl
911.	3-fluoropropyl	4-(4-methyl-4H-[1,2,4]-triazol-3-yl)-phenyl
912.	3-fluoropropyl	4-(2-methyl-2H-[1,2,3]-triazol-4-yl)-phenyl
913.	3-fluoropropyl	4-([1,3,4]-oxadiazol-2-yl)-phenyl
914.	3-fluoropropyl	4-([1,2,4]-oxadiazol-3-yl)-phenyl
915.	3-fluoropropyl	4-([1,2,4]-oxadiazol-5-yl)-phenyl
916.	3-fluoropropyl	4-([1,2,3]-oxadiazol-4-yl)-phenyl
917.	3-fluoropropyl	4-([1,2,3]-oxadiazol-5-yl)-phenyl
918.	3-fluoropropyl	4-([1,2,3]-thiadiazol-4-yl)-phenyl
919.	3-fluoropropyl	4-(1H-tetrazol-5-yl)-phenyl
920.	3-fluoropropyl	4-(tetrazol-1-yl)-phenyl
921.	3-fluoropropyl	4-(2-methyl-2H-tetrazol-5-yl)-phenyl
922.	3-fluoropropyl	4-(1-methyl-1H-tetrazol-5-yl)-phenyl
923.	3-fluoropropyl	4-furazan-3-yl-phenyl
924.	3-fluoropropyl	4-(pyrid-2-yl)-phenyl
925.	3-fluoropropyl	4-(pyrid-3-yl)-phenyl
926.	3-fluoropropyl	4-(pyrid-4-yl)-phenyl
927.	3-fluoropropyl	4-(pyrimidin-2-yl)-phenyl
928.	3-fluoropropyl	4-(pyrimidin-4-yl)-phenyl
929.	3-fluoropropyl	4-(pyrimidin-5-yl)-phenyl
930.	3-fluoropropyl	5-isopropylthiophen-2-yl
931.	3-fluoropropyl	2-chlorothiophen-5-yl
932.	3-fluoropropyl	2,5-dichlorothiophen-4-yl
933.	3-fluoropropyl	2,3-dichlorothiophen-5-yl
934.	3-fluoropropyl	2-chloro-3-nitrothiophen-5-yl
935.	3-fluoropropyl	2-(phenylsulfonyl)-thiophen-5-yl
936.	3-fluoropropyl	2-(pyridin-2-yl)thiophen-5-yl
937.	3-fluoropropyl	2-(5-(trifluoromethyl)isoxazol-3-yl)-thiophen-5-yl

No.	R ¹	Ar
938.	3-fluoropropyl	2-(2-methylthiazol-4-yl)-thiophen-5-yl
939.	3-fluoropropyl	1-methyl-1H-imidazol-4-yl
940.	3-fluoropropyl	1,2-dimethyl-1H-imidazol-4-yl
941.	3-fluoropropyl	3,5-dimethylisoxazol-4-yl
942.	3-fluoropropyl	thiazol-2-yl
943.	3-fluoropropyl	4-methylthiazol-2-yl
944.	3-fluoropropyl	4-isopropylthiazol-2-yl
945.	3-fluoropropyl	4-trifluoromethylthiazol-2-yl
946.	3-fluoropropyl	5-methylthiazol-2-yl
947.	3-fluoropropyl	5-isopropylthiazol-2-yl
948.	3-fluoropropyl	5-trifluoromethylthiazol-2-yl
949.	3-fluoropropyl	2,4-dimethylthiazol-5-yl
950.	3-fluoropropyl	2-acetamido-4-methylthiazol-5-yl
951.	3-fluoropropyl	4H-[1,2,4]triazol-3-yl
952.	3-fluoropropyl	5-methyl-4H-[1,2,4]triazol-3-yl
953.	3-fluoropropyl	4-methyl-4H-[1,2,4]triazol-3-yl
954.	3-fluoropropyl	5-isopropyl-4H-[1,2,4]triazol-3-yl
955.	3-fluoropropyl	5-trifluoromethyl-4H-[1,2,4]triazol-3-yl
956.	3-fluoropropyl	4,5-dimethyl-4H-[1,2,4]triazol-3-yl
957.	3-fluoropropyl	5-isopropyl-4-methyl-4H-[1,2,4]triazol-3-yl
958.	3-fluoropropyl	5-trifluoromethyl-4-methyl-4H-[1,2,4]triazol-3-yl
959.	3-fluoropropyl	[1,3,4]thiadiazol-2-yl
960.	3-fluoropropyl	5-methyl-[1,3,4]thiadiazol-2-yl
961.	3-fluoropropyl	5-isopropyl-[1,3,4]thiadiazol-2-yl
962.	3-fluoropropyl	5-trifluoromethyl-[1,3,4]thiadiazol-2-yl
963.	3-fluoropropyl	3-bromo-2-chloropyrid-5-yl
964.	3-fluoropropyl	2-(4-morpholino)-pyrid-5-yl
965.	3-fluoropropyl	2-phenoxy-pyrid-5-yl
966.	3-fluoropropyl	(2-isopropyl)-pyrimidin-5-yl
967.	3-fluoropropyl	(5-isopropyl)-pyrimidin-2-yl
968.	3-fluoropropyl	8-quinolyl
969.	3-fluoropropyl	5-isoquinolyl
970.	3-fluoropropyl	2-(trifluoroacetyl)-1,2,3,4-tetrahydroisoquinolin-7-yl
971.	3-fluoropropyl	5-chloro-3-methylbenzothiophen-2-yl

No.	R ¹	Ar
972.	3-fluoropropyl	3,4-dihydro-4-methyl-2H-benzo[b][1,4]oxazinyl
973.	3-fluoropropyl	benzothiazol-6-yl
974.	3-fluoropropyl	benzo[2,1,3]oxadiazol-4-yl
975.	3-fluoropropyl	5-chlorobenzo[2,1,3]oxadiazol-4-yl
976.	3-fluoropropyl	7-chlorobenzo[2,1,3]oxadiazol-4-yl
977.	3-fluoropropyl	benzo[2,1,3]thiadiazol-4-yl
978.	2-fluoroethyl	4-methylphenyl
979.	2-fluoroethyl	4-ethylphenyl
980.	2-fluoroethyl	4-propylphenyl
981.	2-fluoroethyl	4-isopropylphenyl
982.	2-fluoroethyl	4-sec-butylphenyl
983.	2-fluoroethyl	4-isobutylphenyl
984.	2-fluoroethyl	4-(1,1-dimethylpropyl)-phenyl
985.	2-fluoroethyl	4-vinylphenyl
986.	2-fluoroethyl	4-isopropenylphenyl
987.	2-fluoroethyl	4-fluorophenyl
988.	2-fluoroethyl	4-chlorophenyl
989.	2-fluoroethyl	4-bromophenyl
990.	2-fluoroethyl	4-(fluoromethyl)phenyl
991.	2-fluoroethyl	3-(fluoromethyl)phenyl
992.	2-fluoroethyl	2-(fluoromethyl)phenyl
993.	2-fluoroethyl	4-(difluoromethyl)phenyl
994.	2-fluoroethyl	3-(difluoromethyl)phenyl
995.	2-fluoroethyl	2-(difluoromethyl)phenyl
996.	2-fluoroethyl	4-(trifluoromethyl)phenyl
997.	2-fluoroethyl	3-(trifluoromethyl)phenyl
998.	2-fluoroethyl	2-(trifluoromethyl)phenyl
999.	2-fluoroethyl	4-(1-fluoroethyl)-phenyl
1000.	2-fluoroethyl	4-((S)-1-fluoroethyl)-phenyl
1001.	2-fluoroethyl	4-((R)-1-fluoroethyl)-phenyl
1002.	2-fluoroethyl	4-(2-fluoroethyl)-phenyl
1003.	2-fluoroethyl	4-(1,1-difluoroethyl)-phenyl
1004.	2-fluoroethyl	4-(2,2-difluoroethyl)-phenyl
1005.	2-fluoroethyl	4-(2,2,2-trifluoroethyl)-phenyl

No.	R ¹	Ar
1006.	2-fluoroethyl	4-(3-fluoropropyl)-phenyl
1007.	2-fluoroethyl	4-(2-fluoropropyl)-phenyl
1008.	2-fluoroethyl	4-((S)-2-fluoropropyl)-phenyl
1009.	2-fluoroethyl	4-((R)-2-fluoropropyl)-phenyl
1010.	2-fluoroethyl	4-(3,3-difluoropropyl)-phenyl
1011.	2-fluoroethyl	4-(3,3,3-trifluoropropyl)-phenyl
1012.	2-fluoroethyl	4-(1-fluoro-1-methylethyl)-phenyl
1013.	2-fluoroethyl	4-(2-fluoro-1-methylethyl)-phenyl
1014.	2-fluoroethyl	4-((S)-2-fluoro-1-methylethyl)-phenyl
1015.	2-fluoroethyl	4-((R)-2-fluoro-1-methylethyl)-phenyl
1016.	2-fluoroethyl	4-(2,2-difluoro-1-methylethyl)-phenyl
1017.	2-fluoroethyl	4-((S)-2,2-difluoro-1-methylethyl)-phenyl
1018.	2-fluoroethyl	4-((R)-2,2-difluoro-1-methylethyl)-phenyl
1019.	2-fluoroethyl	4-(2,2,2-trifluoro-1-methylethyl)-phenyl
1020.	2-fluoroethyl	4-((S)-2,2,2-trifluoro-1-methylethyl)-phenyl
1021.	2-fluoroethyl	4-((R)-2,2,2-trifluoro-1-methylethyl)-phenyl
1022.	2-fluoroethyl	4-(2-fluoro-1-fluoromethylethyl)-phenyl
1023.	2-fluoroethyl	4-(1-difluoromethyl-2,2-difluoroethyl)-phenyl
1024.	2-fluoroethyl	4-(1,1-dimethyl-2-fluoroethyl)-phenyl
1025.	2-fluoroethyl	4-methoxyphenyl
1026.	2-fluoroethyl	4-ethoxyphenyl
1027.	2-fluoroethyl	4-propoxyphenyl
1028.	2-fluoroethyl	4-isopropoxyphenyl
1029.	2-fluoroethyl	4-butoxyphenyl
1030.	2-fluoroethyl	4-(fluoromethoxy)-phenyl
1031.	2-fluoroethyl	4-(difluoromethoxy)-phenyl
1032.	2-fluoroethyl	4-(trifluoromethoxy)-phenyl
1033.	2-fluoroethyl	3-(trifluoromethoxy)-phenyl
1034.	2-fluoroethyl	4-(2-fluoroethoxy)-phenyl
1035.	2-fluoroethyl	4-(2,2-difluoroethoxy)-phenyl
1036.	2-fluoroethyl	4-(2,2,2-trifluoroethoxy)-phenyl
1037.	2-fluoroethyl	4-(1,1,2,2-tetrafluoroethoxy)-phenyl
1038.	2-fluoroethyl	4-cyclopropylphenyl
1039.	2-fluoroethyl	4-cyclobutylphenyl

No.	R ¹	Ar
1040.	2-fluoroethyl	4-cyclopentylphenyl
1041.	2-fluoroethyl	4-(2,2-difluorocyclopropyl)-phenyl
1042.	2-fluoroethyl	3,4-difluorophenyl
1043.	2-fluoroethyl	4-bromo-3-fluorophenyl
1044.	2-fluoroethyl	4-bromo-2-fluorophenyl
1045.	2-fluoroethyl	4-bromo-2,5-difluorophenyl
1046.	2-fluoroethyl	2-fluoro-4-isopropylphenyl
1047.	2-fluoroethyl	3-fluoro-4-isopropylphenyl
1048.	2-fluoroethyl	4-(1-hydroxy-1-methylethyl)-phenyl
1049.	2-fluoroethyl	4-(2-hydroxy-2-methylpropyl)-phenyl
1050.	2-fluoroethyl	4-acetylphenyl
1051.	2-fluoroethyl	4-carboxyphenyl
1052.	2-fluoroethyl	4-cyanophenyl
1053.	2-fluoroethyl	4-hydroxyphenyl
1054.	2-fluoroethyl	4-(O-benzyl)-phenyl
1055.	2-fluoroethyl	4-(2-methoxyethoxy)-phenyl
1056.	2-fluoroethyl	4-(CH ₂ -N(CH ₃) ₂)-phenyl
1057.	2-fluoroethyl	4-(NH-CO-NH ₂)-phenyl
1058.	2-fluoroethyl	4-(methylsulfanyl)-phenyl
1059.	2-fluoroethyl	4-(fluoromethylsulfanyl)-phenyl
1060.	2-fluoroethyl	4-(difluoromethylsulfanyl)-phenyl
1061.	2-fluoroethyl	4-(trifluoromethylsulfanyl)-phenyl
1062.	2-fluoroethyl	4-(methylsulfonyl)-phenyl
1063.	2-fluoroethyl	4-(N-methoxy-N-methyl-amino)-phenyl
1064.	2-fluoroethyl	4-(methoxyamino)-phenyl
1065.	2-fluoroethyl	4-(ethoxyamino)-phenyl
1066.	2-fluoroethyl	4-(N-methylaminooxy)-phenyl
1067.	2-fluoroethyl	4-(N,N-dimethylaminoxy)-phenyl
1068.	2-fluoroethyl	4-(azetidin-1-yl)-phenyl
1069.	2-fluoroethyl	4-(2-methylazetidin-1-yl)-phenyl
1070.	2-fluoroethyl	4-((S)-2-methylazetidin-1-yl)-phenyl
1071.	2-fluoroethyl	4-((R)-2-methylazetidin-1-yl)-phenyl
1072.	2-fluoroethyl	4-(3-fluoroazetidin-1-yl)-phenyl
1073.	2-fluoroethyl	4-(3-methoxyazetidin-1-yl)-phenyl

No.	R ¹	Ar
1074.	2-fluoroethyl	4-(3-hydroxyazetidin-1-yl)-phenyl
1075.	2-fluoroethyl	4-(pyrrolidin-1-yl)-phenyl
1076.	2-fluoroethyl	4-(pyrrolidin-2-yl)-phenyl
1077.	2-fluoroethyl	4-((S)-pyrrolidin-2-yl)-phenyl
1078.	2-fluoroethyl	4-((R)-pyrrolidin-2-yl)-phenyl
1079.	2-fluoroethyl	4-(pyrrolidin-3-yl)-phenyl
1080.	2-fluoroethyl	4-((S)-pyrrolidin-3-yl)-phenyl
1081.	2-fluoroethyl	4-((R)-pyrrolidin-3-yl)-phenyl
1082.	2-fluoroethyl	4-(2-fluoropyrrolidin-1-yl)-phenyl
1083.	2-fluoroethyl	4-((S)-2-fluoropyrrolidin-1-yl)-phenyl
1084.	2-fluoroethyl	4-((R)-2-fluoropyrrolidin-1-yl)-phenyl
1085.	2-fluoroethyl	4-(3-fluoropyrrolidin-1-yl)-phenyl
1086.	2-fluoroethyl	4-((S)-3-fluoropyrrolidin-1-yl)-phenyl
1087.	2-fluoroethyl	4-((R)-3-fluoropyrrolidin-1-yl)-phenyl
1088.	2-fluoroethyl	4-(2,2-difluoropyrrolidin-1-yl)-phenyl
1089.	2-fluoroethyl	4-(3,3-difluoropyrrolidin-1-yl)-phenyl
1090.	2-fluoroethyl	4-(2-methylpyrrolidin-1-yl)-phenyl
1091.	2-fluoroethyl	4-((S)-2-methylpyrrolidin-1-yl)-phenyl
1092.	2-fluoroethyl	4-((R)-2-methylpyrrolidin-1-yl)-phenyl
1093.	2-fluoroethyl	4-(3-methylpyrrolidin-1-yl)-phenyl
1094.	2-fluoroethyl	4-((S)-3-methylpyrrolidin-1-yl)-phenyl
1095.	2-fluoroethyl	4-((R)-3-methylpyrrolidin-1-yl)-phenyl
1096.	2-fluoroethyl	4-(1-methylpyrrolidin-2-yl)-phenyl
1097.	2-fluoroethyl	4-((S)-1-methylpyrrolidin-2-yl)-phenyl
1098.	2-fluoroethyl	4-((R)-1-methylpyrrolidin-2-yl)-phenyl
1099.	2-fluoroethyl	4-(1-methylpyrrolidin-3-yl)-phenyl
1100.	2-fluoroethyl	4-((S)-1-methylpyrrolidin-3-yl)-phenyl
1101.	2-fluoroethyl	4-((R)-1-methylpyrrolidin-3-yl)-phenyl
1102.	2-fluoroethyl	4-(2,2-dimethylpyrrolidin-1-yl)-phenyl
1103.	2-fluoroethyl	4-(3,3-dimethylpyrrolidin-1-yl)-phenyl
1104.	2-fluoroethyl	4-(2-trifluoromethylpyrrolidin-1-yl)-phenyl
1105.	2-fluoroethyl	4-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
1106.	2-fluoroethyl	4-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
1107.	2-fluoroethyl	4-(3-trifluoromethylpyrrolidin-1-yl)-phenyl

No.	R ¹	Ar
1108.	2-fluoroethyl	4-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
1109.	2-fluoroethyl	4-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
1110.	2-fluoroethyl	4-(2-oxopyrrolidin-1-yl)-phenyl
1111.	2-fluoroethyl	4-(2-oxo-oxazolidin-3-yl)-phenyl
1112.	2-fluoroethyl	4-(piperidin-1-yl)-phenyl
1113.	2-fluoroethyl	4-(2-methylpiperidin-1-yl)-phenyl
1114.	2-fluoroethyl	4-((S)-2-methylpiperidin-1-yl)-phenyl
1115.	2-fluoroethyl	4-((R)-2-methylpiperidin-1-yl)-phenyl
1116.	2-fluoroethyl	4-(piperazin-1-yl)-phenyl
1117.	2-fluoroethyl	4-(4-methylpiperazin-1-yl)-phenyl
1118.	2-fluoroethyl	4-(morpholin-4-yl)-phenyl
1119.	2-fluoroethyl	4-(thiomorpholin-4-yl)-phenyl
1120.	2-fluoroethyl	4-(1-oxo-thiomorpholin-4-yl)-phenyl
1121.	2-fluoroethyl	4-(1,1-dioxo-thiomorpholin-4-yl)-phenyl
1122.	2-fluoroethyl	4-(pyrrol-1-yl)-phenyl
1123.	2-fluoroethyl	4-(pyrrol-2-yl)-phenyl
1124.	2-fluoroethyl	4-(pyrrol-3-yl)-phenyl
1125.	2-fluoroethyl	4-(1-methylpyrrol-2-yl)-phenyl
1126.	2-fluoroethyl	4-(1-methylpyrrol-3-yl)-phenyl
1127.	2-fluoroethyl	4-(furan-2-yl)-phenyl
1128.	2-fluoroethyl	4-(furan-3-yl)-phenyl
1129.	2-fluoroethyl	4-(thiophen-2-yl)-phenyl
1130.	2-fluoroethyl	4-(thiophen-3-yl)-phenyl
1131.	2-fluoroethyl	4-(5-propylthien-2-yl)-phenyl
1132.	2-fluoroethyl	4-(pyrazol-1-yl)-phenyl
1133.	2-fluoroethyl	4-(pyrazol-3-yl)-phenyl
1134.	2-fluoroethyl	4-(pyrazol-4-yl)-phenyl
1135.	2-fluoroethyl	4-(1-methyl-1H-pyrazol-4-yl)-phenyl
1136.	2-fluoroethyl	4-(1-ethyl-1H-pyrazol-4-yl)-phenyl
1137.	2-fluoroethyl	4-(1-methyl-1H-pyrazol-5-yl)-phenyl
1138.	2-fluoroethyl	4-(1H-imidazol-2-yl)-phenyl
1139.	2-fluoroethyl	4-(imidazol-1-yl)-phenyl
1140.	2-fluoroethyl	4-(1-methylimidazol-2-yl)-phenyl
1141.	2-fluoroethyl	4-(oxazol-2-yl)-phenyl

No.	R ¹	Ar
1142.	2-fluoroethyl	4-(oxazol-4-yl)-phenyl
1143.	2-fluoroethyl	4-(oxazol-5-yl)-phenyl
1144.	2-fluoroethyl	4-(isoxazol-3-yl)-phenyl
1145.	2-fluoroethyl	4-(isoxazol-4-yl)-phenyl
1146.	2-fluoroethyl	4-(isoxazol-5-yl)-phenyl
1147.	2-fluoroethyl	4-([1,2,3]-triazol-1-yl)-phenyl
1148.	2-fluoroethyl	4-([1,2,4]-triazol-1-yl)-phenyl
1149.	2-fluoroethyl	4-([1,2,3]-triazol-2-yl)-phenyl
1150.	2-fluoroethyl	4-(4H-[1,2,4]-triazol-3-yl)-phenyl
1151.	2-fluoroethyl	4-([1,2,4]-triazol-4-yl)-phenyl
1152.	2-fluoroethyl	4-(2H-[1,2,3]-triazol-4-yl)-phenyl
1153.	2-fluoroethyl	4-(4-methyl-4H-[1,2,4]-triazol-3-yl)-phenyl
1154.	2-fluoroethyl	4-(2-methyl-2H-[1,2,3]-triazol-4-yl)-phenyl
1155.	2-fluoroethyl	4-([1,3,4]-oxadiazol-2-yl)-phenyl
1156.	2-fluoroethyl	4-([1,2,4]-oxadiazol-3-yl)-phenyl
1157.	2-fluoroethyl	4-([1,2,4]-oxadiazol-5-yl)-phenyl
1158.	2-fluoroethyl	4-([1,2,3]-oxadiazol-4-yl)-phenyl
1159.	2-fluoroethyl	4-([1,2,3]-oxadiazol-5-yl)-phenyl
1160.	2-fluoroethyl	4-([1,2,3]-thiadiazol-4-yl)-phenyl
1161.	2-fluoroethyl	4-(1H-tetrazol-5-yl)-phenyl
1162.	2-fluoroethyl	4-(tetrazol-1-yl)-phenyl
1163.	2-fluoroethyl	4-(2-methyl-2H-tetrazol-5-yl)-phenyl
1164.	2-fluoroethyl	4-(1-methyl-1H-tetrazol-5-yl)-phenyl
1165.	2-fluoroethyl	4-furazan-3-yl-phenyl
1166.	2-fluoroethyl	4-(pyrid-2-yl)-phenyl
1167.	2-fluoroethyl	4-(pyrid-3-yl)-phenyl
1168.	2-fluoroethyl	4-(pyrid-4-yl)-phenyl
1169.	2-fluoroethyl	4-(pyrimidin-2-yl)-phenyl
1170.	2-fluoroethyl	4-(pyrimidin-4-yl)-phenyl
1171.	2-fluoroethyl	4-(pyrimidin-5-yl)-phenyl
1172.	2-fluoroethyl	5-isopropylthiophen-2-yl
1173.	2-fluoroethyl	2-chlorothiophen-5-yl
1174.	2-fluoroethyl	2,5-dichlorothiophen-4-yl
1175.	2-fluoroethyl	2,3-dichlorothiophen-5-yl

No.	R ¹	Ar
1176.	2-fluoroethyl	2-chloro-3-nitrothiophen-5-yl
1177.	2-fluoroethyl	2-(phenylsulfonyl)-thiophen-5-yl
1178.	2-fluoroethyl	2-(pyridin-2-yl)thiophen-5-yl
1179.	2-fluoroethyl	2-(5-(trifluoromethyl)isoxazol-3-yl)-thiophen-5-yl
1180.	2-fluoroethyl	2-(2-methylthiazol-4-yl)-thiophen-5-yl
1181.	2-fluoroethyl	1-methyl-1H-imidazol-4-yl
1182.	2-fluoroethyl	1,2-dimethyl-1H-imidazol-4-yl
1183.	2-fluoroethyl	3,5-dimethylisoxazol-4-yl
1184.	2-fluoroethyl	thiazol-2-yl
1185.	2-fluoroethyl	4-methylthiazol-2-yl
1186.	2-fluoroethyl	4-isopropylthiazol-2-yl
1187.	2-fluoroethyl	4-trifluoromethylthiazol-2-yl
1188.	2-fluoroethyl	5-methylthiazol-2-yl
1189.	2-fluoroethyl	5-isopropylthiazol-2-yl
1190.	2-fluoroethyl	5-trifluoromethylthiazol-2-yl
1191.	2-fluoroethyl	2,4-dimethylthiazol-5-yl
1192.	2-fluoroethyl	2-acetamido-4-methylthiazol-5-yl
1193.	2-fluoroethyl	4H-[1,2,4]triazol-3-yl
1194.	2-fluoroethyl	5-methyl-4H-[1,2,4]triazol-3-yl
1195.	2-fluoroethyl	4-methyl-4H-[1,2,4]triazol-3-yl
1196.	2-fluoroethyl	5-isopropyl-4H-[1,2,4]triazol-3-yl
1197.	2-fluoroethyl	5-trifluoromethyl-4H-[1,2,4]triazol-3-yl
1198.	2-fluoroethyl	4,5-dimethyl-4H-[1,2,4]triazol-3-yl
1199.	2-fluoroethyl	5-isopropyl-4-methyl-4H-[1,2,4]triazol-3-yl
1200.	2-fluoroethyl	5-trifluoromethyl-4-methyl-4H-[1,2,4]triazol-3-yl
1201.	2-fluoroethyl	[1,3,4]thiadiazol-2-yl
1202.	2-fluoroethyl	5-methyl-[1,3,4]thiadiazol-2-yl
1203.	2-fluoroethyl	5-isopropyl-[1,3,4]thiadiazol-2-yl
1204.	2-fluoroethyl	5-trifluoromethyl-[1,3,4]thiadiazol-2-yl
1205.	2-fluoroethyl	3-bromo-2-chloropyrid-5-yl
1206.	2-fluoroethyl	2-(4-morpholino)-pyrid-5-yl
1207.	2-fluoroethyl	2-phenoxy-pyrid-5-yl
1208.	2-fluoroethyl	(2-isopropyl)-pyrimidin-5-yl
1209.	2-fluoroethyl	(5-isopropyl)-pyrimidin-2-yl

No.	R ¹	Ar
1210.	2-fluoroethyl	8-quinolyl
1211.	2-fluoroethyl	5-isoquinolyl
1212.	2-fluoroethyl	2-(trifluoroacetyl)-1,2,3,4-tetrahydroisoquinolin-7-yl
1213.	2-fluoroethyl	5-chloro-3-methylbenzothiophen-2-yl
1214.	2-fluoroethyl	3,4-dihydro-4-methyl-2H-benzo[b][1,4]oxazinyl
1215.	2-fluoroethyl	benzothiazol-6-yl
1216.	2-fluoroethyl	benzo[2,1,3]oxadiazol-4-yl
1217.	2-fluoroethyl	5-chlorobenzo[2,1,3]oxadiazol-4-yl
1218.	2-fluoroethyl	7-chlorobenzo[2,1,3]oxadiazol-4-yl
1219.	2-fluoroethyl	benzo[2,1,3]thiadiazol-4-yl
1220.	cyclopropylmethyl	4-methylphenyl
1221.	cyclopropylmethyl	4-ethylphenyl
1222.	cyclopropylmethyl	4-propylphenyl
1223.	cyclopropylmethyl	4-isopropylphenyl
1224.	cyclopropylmethyl	4-sec-butylphenyl
1225.	cyclopropylmethyl	4-isobutylphenyl
1226.	cyclopropylmethyl	4-(1,1-dimethylpropyl)-phenyl
1227.	cyclopropylmethyl	4-vinylphenyl
1228.	cyclopropylmethyl	4-isopropenylphenyl
1229.	cyclopropylmethyl	4-fluorophenyl
1230.	cyclopropylmethyl	4-chlorophenyl
1231.	cyclopropylmethyl	4-bromophenyl
1232.	cyclopropylmethyl	4-(fluoromethyl)phenyl
1233.	cyclopropylmethyl	3-(fluoromethyl)phenyl
1234.	cyclopropylmethyl	2-(fluoromethyl)phenyl
1235.	cyclopropylmethyl	4-(difluoromethyl)phenyl
1236.	cyclopropylmethyl	3-(difluoromethyl)phenyl
1237.	cyclopropylmethyl	2-(difluoromethyl)phenyl
1238.	cyclopropylmethyl	4-(trifluoromethyl)phenyl
1239.	cyclopropylmethyl	3-(trifluoromethyl)phenyl
1240.	cyclopropylmethyl	2-(trifluoromethyl)phenyl
1241.	cyclopropylmethyl	4-(1-fluoroethyl)-phenyl
1242.	cyclopropylmethyl	4-((S)-1-fluoroethyl)-phenyl
1243.	cyclopropylmethyl	4-((R)-1-fluoroethyl)-phenyl

No.	R ¹	Ar
1244.	cyclopropylmethyl	4-(2-fluoroethyl)-phenyl
1245.	cyclopropylmethyl	4-(1,1-difluoroethyl)-phenyl
1246.	cyclopropylmethyl	4-(2,2-difluoroethyl)-phenyl
1247.	cyclopropylmethyl	4-(2,2,2-trifluoroethyl)-phenyl
1248.	cyclopropylmethyl	4-(3-fluoropropyl)-phenyl
1249.	cyclopropylmethyl	4-(2-fluoropropyl)-phenyl
1250.	cyclopropylmethyl	4-((S)-2-fluoropropyl)-phenyl
1251.	cyclopropylmethyl	4-((R)-2-fluoropropyl)-phenyl
1252.	cyclopropylmethyl	4-(3,3-difluoropropyl)-phenyl
1253.	cyclopropylmethyl	4-(3,3,3-trifluoropropyl)-phenyl
1254.	cyclopropylmethyl	4-(1-fluoro-1-methylethyl)-phenyl
1255.	cyclopropylmethyl	4-(2-fluoro-1-methylethyl)-phenyl
1256.	cyclopropylmethyl	4-((S)-2-fluoro-1-methylethyl)-phenyl
1257.	cyclopropylmethyl	4-((R)-2-fluoro-1-methylethyl)-phenyl
1258.	cyclopropylmethyl	4-(2,2-difluoro-1-methylethyl)-phenyl
1259.	cyclopropylmethyl	4-((S)-2,2-difluoro-1-methylethyl)-phenyl
1260.	cyclopropylmethyl	4-((R)-2,2-difluoro-1-methylethyl)-phenyl
1261.	cyclopropylmethyl	4-(2,2,2-trifluoro-1-methylethyl)-phenyl
1262.	cyclopropylmethyl	4-((S)-2,2,2-trifluoro-1-methylethyl)-phenyl
1263.	cyclopropylmethyl	4-((R)-2,2,2-trifluoro-1-methylethyl)-phenyl
1264.	cyclopropylmethyl	4-(2-fluoro-1-fluoromethylethyl)-phenyl
1265.	cyclopropylmethyl	4-(1-difluoromethyl-2,2-difluoroethyl)-phenyl
1266.	cyclopropylmethyl	4-(1,1-dimethyl-2-fluoroethyl)-phenyl
1267.	cyclopropylmethyl	4-methoxyphenyl
1268.	cyclopropylmethyl	4-ethoxyphenyl
1269.	cyclopropylmethyl	4-propoxyphenyl
1270.	cyclopropylmethyl	4-isopropoxyphenyl
1271.	cyclopropylmethyl	4-butoxyphenyl
1272.	cyclopropylmethyl	4-(fluoromethoxy)-phenyl
1273.	cyclopropylmethyl	4-(difluoromethoxy)-phenyl
1274.	cyclopropylmethyl	4-(trifluoromethoxy)-phenyl
1275.	cyclopropylmethyl	3-(trifluoromethoxy)-phenyl
1276.	cyclopropylmethyl	4-(2-fluoroethoxy)-phenyl
1277.	cyclopropylmethyl	4-(2,2-difluoroethoxy)-phenyl

No.	R ¹	Ar
1278.	cyclopropylmethyl	4-(2,2,2-trifluoroethoxy)-phenyl
1279.	cyclopropylmethyl	4-(1,1,2,2-tetrafluoroethoxy)-phenyl
1280.	cyclopropylmethyl	4-cyclopropylphenyl
1281.	cyclopropylmethyl	4-cyclobutylphenyl
1282.	cyclopropylmethyl	4-cyclopentylphenyl
1283.	cyclopropylmethyl	4-(2,2-difluorocyclopropyl)-phenyl
1284.	cyclopropylmethyl	3,4-difluorophenyl
1285.	cyclopropylmethyl	4-bromo-3-fluorophenyl
1286.	cyclopropylmethyl	4-bromo-2-fluorophenyl
1287.	cyclopropylmethyl	4-bromo-2,5-difluorophenyl
1288.	cyclopropylmethyl	2-fluoro-4-isopropylphenyl
1289.	cyclopropylmethyl	3-fluoro-4-isopropylphenyl
1290.	cyclopropylmethyl	4-(1-hydroxy-1-methylethyl)-phenyl
1291.	cyclopropylmethyl	4-(2-hydroxy-2-methylpropyl)-phenyl
1292.	cyclopropylmethyl	4-acetylphenyl
1293.	cyclopropylmethyl	4-carboxyphenyl
1294.	cyclopropylmethyl	4-cyanophenyl
1295.	cyclopropylmethyl	4-hydroxyphenyl
1296.	cyclopropylmethyl	4-(O-benzyl)-phenyl
1297.	cyclopropylmethyl	4-(2-methoxyethoxy)-phenyl
1298.	cyclopropylmethyl	4-(CH ₂ -N(CH ₃) ₂)-phenyl
1299.	cyclopropylmethyl	4-(NH-CO-NH ₂)-phenyl
1300.	cyclopropylmethyl	4-(methylsulfanyl)-phenyl
1301.	cyclopropylmethyl	4-(fluoromethylsulfanyl)-phenyl
1302.	cyclopropylmethyl	4-(difluoromethylsulfanyl)-phenyl
1303.	cyclopropylmethyl	4-(trifluoromethylsulfanyl)-phenyl
1304.	cyclopropylmethyl	4-(methylsulfonyl)-phenyl
1305.	cyclopropylmethyl	4-(N-methoxy-N-methyl-amino)-phenyl
1306.	cyclopropylmethyl	4-(methoxyamino)-phenyl
1307.	cyclopropylmethyl	4-(ethoxyamino)-phenyl
1308.	cyclopropylmethyl	4-(N-methylaminooxy)-phenyl
1309.	cyclopropylmethyl	4-(N,N-dimethylaminooxy)-phenyl
1310.	cyclopropylmethyl	4-(azetidin-1-yl)-phenyl
1311.	cyclopropylmethyl	4-(2-methylazetidin-1-yl)-phenyl

No.	R ¹	Ar
1312.	cyclopropylmethyl	4-((S)-2-methylazetidin-1-yl)-phenyl
1313.	cyclopropylmethyl	4-((R)-2-methylazetidin-1-yl)-phenyl
1314.	cyclopropylmethyl	4-(3-fluoroazetidin-1-yl)-phenyl
1315.	cyclopropylmethyl	4-(3-methoxyazetidin-1-yl)-phenyl
1316.	cyclopropylmethyl	4-(3-hydroxyazetidin-1-yl)-phenyl
1317.	cyclopropylmethyl	4-(pyrrolidin-1-yl)-phenyl
1318.	cyclopropylmethyl	4-(pyrrolidin-2-yl)-phenyl
1319.	cyclopropylmethyl	4-((S)-pyrrolidin-2-yl)-phenyl
1320.	cyclopropylmethyl	4-((R)-pyrrolidin-2-yl)-phenyl
1321.	cyclopropylmethyl	4-(pyrrolidin-3-yl)-phenyl
1322.	cyclopropylmethyl	4-((S)-pyrrolidin-3-yl)-phenyl
1323.	cyclopropylmethyl	4-((R)-pyrrolidin-3-yl)-phenyl
1324.	cyclopropylmethyl	4-(2-fluoropyrrolidin-1-yl)-phenyl
1325.	cyclopropylmethyl	4-((S)-2-fluoropyrrolidin-1-yl)-phenyl
1326.	cyclopropylmethyl	4-((R)-2-fluoropyrrolidin-1-yl)-phenyl
1327.	cyclopropylmethyl	4-(3-fluoropyrrolidin-1-yl)-phenyl
1328.	cyclopropylmethyl	4-((S)-3-fluoropyrrolidin-1-yl)-phenyl
1329.	cyclopropylmethyl	4-((R)-3-fluoropyrrolidin-1-yl)-phenyl
1330.	cyclopropylmethyl	4-(2,2-difluoropyrrolidin-1-yl)-phenyl
1331.	cyclopropylmethyl	4-(3,3-difluoropyrrolidin-1-yl)-phenyl
1332.	cyclopropylmethyl	4-(2-methylpyrrolidin-1-yl)-phenyl
1333.	cyclopropylmethyl	4-((S)-2-methylpyrrolidin-1-yl)-phenyl
1334.	cyclopropylmethyl	4-((R)-2-methylpyrrolidin-1-yl)-phenyl
1335.	cyclopropylmethyl	4-(3-methylpyrrolidin-1-yl)-phenyl
1336.	cyclopropylmethyl	4-((S)-3-methylpyrrolidin-1-yl)-phenyl
1337.	cyclopropylmethyl	4-((R)-3-methylpyrrolidin-1-yl)-phenyl
1338.	cyclopropylmethyl	4-(1-methylpyrrolidin-2-yl)-phenyl
1339.	cyclopropylmethyl	4-((S)-1-methylpyrrolidin-2-yl)-phenyl
1340.	cyclopropylmethyl	4-((R)-1-methylpyrrolidin-2-yl)-phenyl
1341.	cyclopropylmethyl	4-(1-methylpyrrolidin-3-yl)-phenyl
1342.	cyclopropylmethyl	4-((S)-1-methylpyrrolidin-3-yl)-phenyl
1343.	cyclopropylmethyl	4-((R)-1-methylpyrrolidin-3-yl)-phenyl
1344.	cyclopropylmethyl	4-(2,2-dimethylpyrrolidin-1-yl)-phenyl
1345.	cyclopropylmethyl	4-(3,3-dimethylpyrrolidin-1-yl)-phenyl

No.	R ¹	Ar
1346.	cyclopropylmethyl	4-(2-trifluoromethylpyrrolidin-1-yl)-phenyl
1347.	cyclopropylmethyl	4-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
1348.	cyclopropylmethyl	4-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
1349.	cyclopropylmethyl	4-(3-trifluoromethylpyrrolidin-1-yl)-phenyl
1350.	cyclopropylmethyl	4-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
1351.	cyclopropylmethyl	4-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
1352.	cyclopropylmethyl	4-(2-oxopyrrolidin-1-yl)-phenyl
1353.	cyclopropylmethyl	4-(2-oxo-oxazolidin-3-yl)-phenyl
1354.	cyclopropylmethyl	4-(piperidin-1-yl)-phenyl
1355.	cyclopropylmethyl	4-(2-methylpiperidin-1-yl)-phenyl
1356.	cyclopropylmethyl	4-((S)-2-methylpiperidin-1-yl)-phenyl
1357.	cyclopropylmethyl	4-((R)-2-methylpiperidin-1-yl)-phenyl
1358.	cyclopropylmethyl	4-(piperazin-1-yl)-phenyl
1359.	cyclopropylmethyl	4-(4-methylpiperazin-1-yl)-phenyl
1360.	cyclopropylmethyl	4-(morpholin-4-yl)-phenyl
1361.	cyclopropylmethyl	4-(thiomorpholin-4-yl)-phenyl
1362.	cyclopropylmethyl	4-(1-oxo-thiomorpholin-4-yl)-phenyl
1363.	cyclopropylmethyl	4-(1,1-dioxo-thiomorpholin-4-yl)-phenyl
1364.	cyclopropylmethyl	4-(pyrrol-1-yl)-phenyl
1365.	cyclopropylmethyl	4-(pyrrol-2-yl)-phenyl
1366.	cyclopropylmethyl	4-(pyrrol-3-yl)-phenyl
1367.	cyclopropylmethyl	4-(1-methylpyrrol-2-yl)-phenyl
1368.	cyclopropylmethyl	4-(1-methylpyrrol-3-yl)-phenyl
1369.	cyclopropylmethyl	4-(furan-2-yl)-phenyl
1370.	cyclopropylmethyl	4-(furan-3-yl)-phenyl
1371.	cyclopropylmethyl	4-(thiophen-2-yl)-phenyl
1372.	cyclopropylmethyl	4-(thiophen-3-yl)-phenyl
1373.	cyclopropylmethyl	4-(5-propylthien-2-yl)-phenyl
1374.	cyclopropylmethyl	4-(pyrazol-1-yl)-phenyl
1375.	cyclopropylmethyl	4-(pyrazol-3-yl)-phenyl
1376.	cyclopropylmethyl	4-(pyrazol-4-yl)-phenyl
1377.	cyclopropylmethyl	4-(1-methyl-1H-pyrazol-4-yl)-phenyl
1378.	cyclopropylmethyl	4-(1-ethyl-1H-pyrazol-4-yl)-phenyl
1379.	cyclopropylmethyl	4-(1-methyl-1H-pyrazol-5-yl)-phenyl

No.	R ¹	Ar
1380.	cyclopropylmethyl	4-(1H-imidazol-2-yl)-phenyl
1381.	cyclopropylmethyl	4-(imidazol-1-yl)-phenyl
1382.	cyclopropylmethyl	4-(1-methylimidazol-2-yl)-phenyl
1383.	cyclopropylmethyl	4-(oxazol-2-yl)-phenyl
1384.	cyclopropylmethyl	4-(oxazol-4-yl)-phenyl
1385.	cyclopropylmethyl	4-(oxazol-5-yl)-phenyl
1386.	cyclopropylmethyl	4-(isoxazol-3-yl)-phenyl
1387.	cyclopropylmethyl	4-(isoxazol-4-yl)-phenyl
1388.	cyclopropylmethyl	4-(isoxazol-5-yl)-phenyl
1389.	cyclopropylmethyl	4-([1,2,3]-triazol-1-yl)-phenyl
1390.	cyclopropylmethyl	4-([1,2,4]-triazol-1-yl)-phenyl
1391.	cyclopropylmethyl	4-([1,2,3]-triazol-2-yl)-phenyl
1392.	cyclopropylmethyl	4-(4H-[1,2,4]-triazol-3-yl)-phenyl
1393.	cyclopropylmethyl	4-([1,2,4]-triazol-4-yl)-phenyl
1394.	cyclopropylmethyl	4-(2H-[1,2,3]-triazol-4-yl)-phenyl
1395.	cyclopropylmethyl	4-(4-methyl-4H-[1,2,4]-triazol-3-yl)-phenyl
1396.	cyclopropylmethyl	4-(2-methyl-2H-[1,2,3]-triazol-4-yl)-phenyl
1397.	cyclopropylmethyl	4-([1,3,4]-oxadiazol-2-yl)-phenyl
1398.	cyclopropylmethyl	4-([1,2,4]-oxadiazol-3-yl)-phenyl
1399.	cyclopropylmethyl	4-([1,2,4]-oxadiazol-5-yl)-phenyl
1400.	cyclopropylmethyl	4-([1,2,3]-oxadiazol-4-yl)-phenyl
1401.	cyclopropylmethyl	4-([1,2,3]-oxadiazol-5-yl)-phenyl
1402.	cyclopropylmethyl	4-([1,2,3]-thiadiazol-4-yl)-phenyl
1403.	cyclopropylmethyl	4-(1H-tetrazol-5-yl)-phenyl
1404.	cyclopropylmethyl	4-(tetrazol-1-yl)-phenyl
1405.	cyclopropylmethyl	4-(2-methyl-2H-tetrazol-5-yl)-phenyl
1406.	cyclopropylmethyl	4-(1-methyl-1H-tetrazol-5-yl)-phenyl
1407.	cyclopropylmethyl	4-furazan-3-yl-phenyl
1408.	cyclopropylmethyl	4-(pyrid-2-yl)-phenyl
1409.	cyclopropylmethyl	4-(pyrid-3-yl)-phenyl
1410.	cyclopropylmethyl	4-(pyrid-4-yl)-phenyl
1411.	cyclopropylmethyl	4-(pyrimidin-2-yl)-phenyl
1412.	cyclopropylmethyl	4-(pyrimidin-4-yl)-phenyl
1413.	cyclopropylmethyl	4-(pyrimidin-5-yl)-phenyl

No.	R ¹	Ar
1414.	cyclopropylmethyl	5-isopropylthiophen-2-yl
1415.	cyclopropylmethyl	2-chlorothiophen-5-yl
1416.	cyclopropylmethyl	2,5-dichlorothiophen-4-yl
1417.	cyclopropylmethyl	2,3-dichlorothiophen-5-yl
1418.	cyclopropylmethyl	2-chloro-3-nitrothiophen-5-yl
1419.	cyclopropylmethyl	2-(phenylsulfonyl)-thiophen-5-yl
1420.	cyclopropylmethyl	2-(pyridin-2-yl)thiophen-5-yl
1421.	cyclopropylmethyl	2-(5-(trifluoromethyl)isoxazol-3-yl)-thiophen-5-yl
1422.	cyclopropylmethyl	2-(2-methylthiazol-4-yl)-thiophen-5-yl
1423.	cyclopropylmethyl	1-methyl-1H-imidazol-4-yl
1424.	cyclopropylmethyl	1,2-dimethyl-1H-imidazol-4-yl
1425.	cyclopropylmethyl	3,5-dimethylisoxazol-4-yl
1426.	cyclopropylmethyl	thiazol-2-yl
1427.	cyclopropylmethyl	4-methylthiazol-2-yl
1428.	cyclopropylmethyl	4-isopropylthiazol-2-yl
1429.	cyclopropylmethyl	4-trifluoromethylthiazol-2-yl
1430.	cyclopropylmethyl	5-methylthiazol-2-yl
1431.	cyclopropylmethyl	5-isopropylthiazol-2-yl
1432.	cyclopropylmethyl	5-trifluoromethylthiazol-2-yl
1433.	cyclopropylmethyl	2,4-dimethylthiazol-5-yl
1434.	cyclopropylmethyl	2-acetamido-4-methylthiazol-5-yl
1435.	cyclopropylmethyl	4H-[1,2,4]triazol-3-yl
1436.	cyclopropylmethyl	5-methyl-4H-[1,2,4]triazol-3-yl
1437.	cyclopropylmethyl	4-methyl-4H-[1,2,4]triazol-3-yl
1438.	cyclopropylmethyl	5-isopropyl-4H-[1,2,4]triazol-3-yl
1439.	cyclopropylmethyl	5-trifluoromethyl-4H-[1,2,4]triazol-3-yl
1440.	cyclopropylmethyl	4,5-dimethyl-4H-[1,2,4]triazol-3-yl
1441.	cyclopropylmethyl	5-isopropyl-4-methyl-4H-[1,2,4]triazol-3-yl
1442.	cyclopropylmethyl	5-trifluoromethyl-4-methyl-4H-[1,2,4]triazol-3-yl
1443.	cyclopropylmethyl	[1,3,4]thiadiazol-2-yl
1444.	cyclopropylmethyl	5-methyl-[1,3,4]thiadiazol-2-yl
1445.	cyclopropylmethyl	5-isopropyl-[1,3,4]thiadiazol-2-yl
1446.	cyclopropylmethyl	5-trifluoromethyl-[1,3,4]thiadiazol-2-yl
1447.	cyclopropylmethyl	3-bromo-2-chloropyrid-5-yl

No.	R ¹	Ar
1448.	cyclopropylmethyl	2-(4-morpholino)-pyrid-5-yl
1449.	cyclopropylmethyl	2-phenoxy-pyrid-5-yl
1450.	cyclopropylmethyl	(2-isopropyl)-pyrimidin-5-yl
1451.	cyclopropylmethyl	(5-isopropyl)-pyrimidin-2-yl
1452.	cyclopropylmethyl	8-quinolyl
1453.	cyclopropylmethyl	5-isoquinolyl
1454.	cyclopropylmethyl	2-(trifluoroacetyl)-1,2,3,4-tetrahydroisoquinolin-7-yl
1455.	cyclopropylmethyl	5-chloro-3-methylbenzothiophen-2-yl
1456.	cyclopropylmethyl	3,4-dihydro-4-methyl-2H-benzo[b][1,4]oxazinyl
1457.	cyclopropylmethyl	benzothiazol-6-yl
1458.	cyclopropylmethyl	benzo[2,1,3]oxadiazol-4-yl
1459.	cyclopropylmethyl	5-chlorobenzo[2,1,3]oxadiazol-4-yl
1460.	cyclopropylmethyl	7-chlorobenzo[2,1,3]oxadiazol-4-yl
1461.	cyclopropylmethyl	benzo[2,1,3]thiadiazol-4-yl
1462.	allyl	4-methylphenyl
1463.	allyl	4-ethylphenyl
1464.	allyl	4-propylphenyl
1465.	allyl	4-isopropylphenyl
1466.	allyl	4-sec-butylphenyl
1467.	allyl	4-isobutylphenyl
1468.	allyl	4-(1,1-dimethylpropyl)-phenyl
1469.	allyl	4-vinylphenyl
1470.	allyl	4-isopropenylphenyl
1471.	allyl	4-fluorophenyl
1472.	allyl	4-chlorophenyl
1473.	allyl	4-bromophenyl
1474.	allyl	4-(fluoromethyl)phenyl
1475.	allyl	3-(fluoromethyl)phenyl
1476.	allyl	2-(fluoromethyl)phenyl
1477.	allyl	4-(difluoromethyl)phenyl
1478.	allyl	3-(difluoromethyl)phenyl
1479.	allyl	2-(difluoromethyl)phenyl
1480.	allyl	4-(trifluoromethyl)phenyl
1481.	allyl	3-(trifluoromethyl)phenyl

No.	R ¹	Ar
1482.	allyl	2-(trifluoromethyl)phenyl
1483.	allyl	4-(1-fluoroethyl)-phenyl
1484.	allyl	4-((S)-1-fluoroethyl)-phenyl
1485.	allyl	4-((R)-1-fluoroethyl)-phenyl
1486.	allyl	4-(2-fluoroethyl)-phenyl
1487.	allyl	4-(1,1-difluoroethyl)-phenyl
1488.	allyl	4-(2,2-difluoroethyl)-phenyl
1489.	allyl	4-(2,2,2-trifluoroethyl)-phenyl
1490.	allyl	4-(3-fluoropropyl)-phenyl
1491.	allyl	4-(2-fluoropropyl)-phenyl
1492.	allyl	4-((S)-2-fluoropropyl)-phenyl
1493.	allyl	4-((R)-2-fluoropropyl)-phenyl
1494.	allyl	4-(3,3-difluoropropyl)-phenyl
1495.	allyl	4-(3,3,3-trifluoropropyl)-phenyl
1496.	allyl	4-(1-fluoro-1-methylethyl)-phenyl
1497.	allyl	4-(2-fluoro-1-methylethyl)-phenyl
1498.	allyl	4-((S)-2-fluoro-1-methylethyl)-phenyl
1499.	allyl	4-((R)-2-fluoro-1-methylethyl)-phenyl
1500.	allyl	4-(2,2-difluoro-1-methylethyl)-phenyl
1501.	allyl	4-((S)-2,2-difluoro-1-methylethyl)-phenyl
1502.	allyl	4-((R)-2,2-difluoro-1-methylethyl)-phenyl
1503.	allyl	4-(2,2,2-trifluoro-1-methylethyl)-phenyl
1504.	allyl	4-((S)-2,2,2-trifluoro-1-methylethyl)-phenyl
1505.	allyl	4-((R)-2,2,2-trifluoro-1-methylethyl)-phenyl
1506.	allyl	4-(2-fluoro-1-fluoromethylethyl)-phenyl
1507.	allyl	4-(1-difluoromethyl-2,2-difluoroethyl)-phenyl
1508.	allyl	4-(1,1-dimethyl-2-fluoroethyl)-phenyl
1509.	allyl	4-methoxyphenyl
1510.	allyl	4-ethoxyphenyl
1511.	allyl	4-propoxyphenyl
1512.	allyl	4-isopropoxyphenyl
1513.	allyl	4-butoxyphenyl
1514.	allyl	4-(fluoromethoxy)-phenyl
1515.	allyl	4-(difluoromethoxy)-phenyl

No.	R ¹	Ar
1516.	allyl	4-(trifluoromethoxy)-phenyl
1517.	allyl	3-(trifluoromethoxy)-phenyl
1518.	allyl	4-(2-fluoroethoxy)-phenyl
1519.	allyl	4-(2,2-difluoroethoxy)-phenyl
1520.	allyl	4-(2,2,2-trifluoroethoxy)-phenyl
1521.	allyl	4-(1,1,2,2-tetrafluoroethoxy)-phenyl
1522.	allyl	4-cyclopropylphenyl
1523.	allyl	4-cyclobutylphenyl
1524.	allyl	4-cyclopentylphenyl
1525.	allyl	4-(2,2-difluorocyclopropyl)-phenyl
1526.	allyl	3,4-difluorophenyl
1527.	allyl	4-bromo-3-fluorophenyl
1528.	allyl	4-bromo-2-fluorophenyl
1529.	allyl	4-bromo-2,5-difluorophenyl
1530.	allyl	2-fluoro-4-isopropylphenyl
1531.	allyl	3-fluoro-4-isopropylphenyl
1532.	allyl	4-(1-hydroxy-1-methylethyl)-phenyl
1533.	allyl	4-(2-hydroxy-2-methylpropyl)-phenyl
1534.	allyl	4-acetylphenyl
1535.	allyl	4-carboxyphenyl
1536.	allyl	4-cyanophenyl
1537.	allyl	4-hydroxyphenyl
1538.	allyl	4-(O-benzyl)-phenyl
1539.	allyl	4-(2-methoxyethoxy)-phenyl
1540.	allyl	4-(CH ₂ -N(CH ₃) ₂)-phenyl
1541.	allyl	4-(NH-CO-NH ₂)-phenyl
1542.	allyl	4-(methylsulfanyl)-phenyl
1543.	allyl	4-(fluoromethylsulfanyl)-phenyl
1544.	allyl	4-(difluoromethylsulfanyl)-phenyl
1545.	allyl	4-(trifluoromethylsulfanyl)-phenyl
1546.	allyl	4-(methylsulfonyl)-phenyl
1547.	allyl	4-(N-methoxy-N-methyl-amino)-phenyl
1548.	allyl	4-(methoxyamino)-phenyl
1549.	allyl	4-(ethoxyamino)-phenyl

No.	R ¹	Ar
1550.	allyl	4-(N-methylaminoxy)-phenyl
1551.	allyl	4-(N,N-dimethylaminoxy)-phenyl
1552.	allyl	4-(azetidin-1-yl)-phenyl
1553.	allyl	4-(2-methylazetidin-1-yl)-phenyl
1554.	allyl	4-((S)-2-methylazetidin-1-yl)-phenyl
1555.	allyl	4-((R)-2-methylazetidin-1-yl)-phenyl
1556.	allyl	4-(3-fluoroazetidin-1-yl)-phenyl
1557.	allyl	4-(3-methoxyazetidin-1-yl)-phenyl
1558.	allyl	4-(3-hydroxyazetidin-1-yl)-phenyl
1559.	allyl	4-(pyrrolidin-1-yl)-phenyl
1560.	allyl	4-(pyrrolidin-2-yl)-phenyl
1561.	allyl	4-((S)-pyrrolidin-2-yl)-phenyl
1562.	allyl	4-((R)-pyrrolidin-2-yl)-phenyl
1563.	allyl	4-(pyrrolidin-3-yl)-phenyl
1564.	allyl	4-((S)-pyrrolidin-3-yl)-phenyl
1565.	allyl	4-((R)-pyrrolidin-3-yl)-phenyl
1566.	allyl	4-(2-fluoropyrrolidin-1-yl)-phenyl
1567.	allyl	4-((S)-2-fluoropyrrolidin-1-yl)-phenyl
1568.	allyl	4-((R)-2-fluoropyrrolidin-1-yl)-phenyl
1569.	allyl	4-(3-fluoropyrrolidin-1-yl)-phenyl
1570.	allyl	4-((S)-3-fluoropyrrolidin-1-yl)-phenyl
1571.	allyl	4-((R)-3-fluoropyrrolidin-1-yl)-phenyl
1572.	allyl	4-(2,2-difluoropyrrolidin-1-yl)-phenyl
1573.	allyl	4-(3,3-difluoropyrrolidin-1-yl)-phenyl
1574.	allyl	4-(2-methylpyrrolidin-1-yl)-phenyl
1575.	allyl	4-((S)-2-methylpyrrolidin-1-yl)-phenyl
1576.	allyl	4-((R)-2-methylpyrrolidin-1-yl)-phenyl
1577.	allyl	4-(3-methylpyrrolidin-1-yl)-phenyl
1578.	allyl	4-((S)-3-methylpyrrolidin-1-yl)-phenyl
1579.	allyl	4-((R)-3-methylpyrrolidin-1-yl)-phenyl
1580.	allyl	4-(1-methylpyrrolidin-2-yl)-phenyl
1581.	allyl	4-((S)-1-methylpyrrolidin-2-yl)-phenyl
1582.	allyl	4-((R)-1-methylpyrrolidin-2-yl)-phenyl
1583.	allyl	4-(1-methylpyrrolidin-3-yl)-phenyl

No.	R ¹	Ar
1584.	allyl	4-((S)-1-methylpyrrolidin-3-yl)-phenyl
1585.	allyl	4-((R)-1-methylpyrrolidin-3-yl)-phenyl
1586.	allyl	4-(2,2-dimethylpyrrolidin-1-yl)-phenyl
1587.	allyl	4-(3,3-dimethylpyrrolidin-1-yl)-phenyl
1588.	allyl	4-(2-trifluoromethylpyrrolidin-1-yl)-phenyl
1589.	allyl	4-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
1590.	allyl	4-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
1591.	allyl	4-(3-trifluoromethylpyrrolidin-1-yl)-phenyl
1592.	allyl	4-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
1593.	allyl	4-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
1594.	allyl	4-(2-oxopyrrolidin-1-yl)-phenyl
1595.	allyl	4-(2-oxo-oxazolidin-3-yl)-phenyl
1596.	allyl	4-(piperidin-1-yl)-phenyl
1597.	allyl	4-(2-methylpiperidin-1-yl)-phenyl
1598.	allyl	4-((S)-2-methylpiperidin-1-yl)-phenyl
1599.	allyl	4-((R)-2-methylpiperidin-1-yl)-phenyl
1600.	allyl	4-(piperazin-1-yl)-phenyl
1601.	allyl	4-(4-methylpiperazin-1-yl)-phenyl
1602.	allyl	4-(morpholin-4-yl)-phenyl
1603.	allyl	4-(thiomorpholin-4-yl)-phenyl
1604.	allyl	4-(1-oxo-thiomorpholin-4-yl)-phenyl
1605.	allyl	4-(1,1-dioxo-thiomorpholin-4-yl)-phenyl
1606.	allyl	4-(pyrrol-1-yl)-phenyl
1607.	allyl	4-(pyrrol-2-yl)-phenyl
1608.	allyl	4-(pyrrol-3-yl)-phenyl
1609.	allyl	4-(1-methylpyrrol-2-yl)-phenyl
1610.	allyl	4-(1-methylpyrrol-3-yl)-phenyl
1611.	allyl	4-(furan-2-yl)-phenyl
1612.	allyl	4-(furan-3-yl)-phenyl
1613.	allyl	4-(thiophen-2-yl)-phenyl
1614.	allyl	4-(thiophen-3-yl)-phenyl
1615.	allyl	4-(5-propylthien-2-yl)-phenyl
1616.	allyl	4-(pyrazol-1-yl)-phenyl
1617.	allyl	4-(pyrazol-3-yl)-phenyl

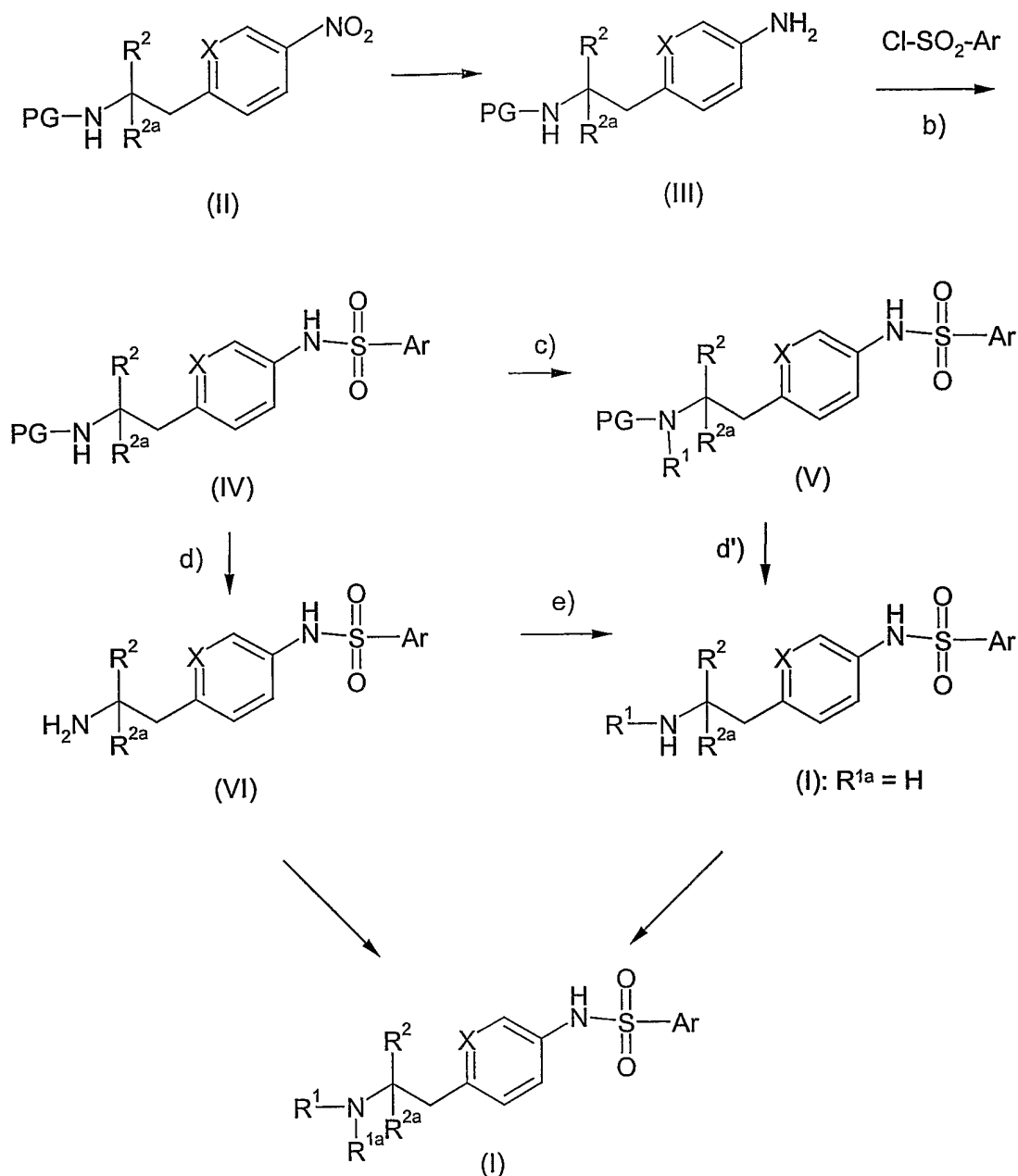
No.	R ¹	Ar
1618.	allyl	4-(pyrazol-4-yl)-phenyl
1619.	allyl	4-(1-methyl-1H-pyrazol-4-yl)-phenyl
1620.	allyl	4-(1-ethyl-1H-pyrazol-4-yl)-phenyl
1621.	allyl	4-(1-methyl-1H-pyrazol-5-yl)-phenyl
1622.	allyl	4-(1H-imidazol-2-yl)-phenyl
1623.	allyl	4-(imidazol-1-yl)-phenyl
1624.	allyl	4-(1-methylimidazol-2-yl)-phenyl
1625.	allyl	4-(oxazol-2-yl)-phenyl
1626.	allyl	4-(oxazol-4-yl)-phenyl
1627.	allyl	4-(oxazol-5-yl)-phenyl
1628.	allyl	4-(isoxazol-3-yl)-phenyl
1629.	allyl	4-(isoxazol-4-yl)-phenyl
1630.	allyl	4-(isoxazol-5-yl)-phenyl
1631.	allyl	4-([1,2,3]-triazol-1-yl)-phenyl
1632.	allyl	4-([1,2,4]-triazol-1-yl)-phenyl
1633.	allyl	4-([1,2,3]-triazol-2-yl)-phenyl
1634.	allyl	4-(4H-[1,2,4]-triazol-3-yl)-phenyl
1635.	allyl	4-([1,2,4]-triazol-4-yl)-phenyl
1636.	allyl	4-(2H-[1,2,3]-triazol-4-yl)-phenyl
1637.	allyl	4-(4-methyl-4H-[1,2,4]-triazol-3-yl)-phenyl
1638.	allyl	4-(2-methyl-2H-[1,2,3]-triazol-4-yl)-phenyl
1639.	allyl	4-([1,3,4]-oxadiazol-2-yl)-phenyl
1640.	allyl	4-([1,2,4]-oxadiazol-3-yl)-phenyl
1641.	allyl	4-([1,2,4]-oxadiazol-5-yl)-phenyl
1642.	allyl	4-([1,2,3]-oxadiazol-4-yl)-phenyl
1643.	allyl	4-([1,2,3]-oxadiazol-5-yl)-phenyl
1644.	allyl	4-([1,2,3]-thiadiazol-4-yl)-phenyl
1645.	allyl	4-(1H-tetrazol-5-yl)-phenyl
1646.	allyl	4-(tetrazol-1-yl)-phenyl
1647.	allyl	4-(2-methyl-2H-tetrazol-5-yl)-phenyl
1648.	allyl	4-(1-methyl-1H-tetrazol-5-yl)-phenyl
1649.	allyl	4-furazan-3-yl-phenyl
1650.	allyl	4-(pyrid-2-yl)-phenyl
1651.	allyl	4-(pyrid-3-yl)-phenyl

No.	R ¹	Ar
1652.	allyl	4-(pyrid-4-yl)-phenyl
1653.	allyl	4-(pyrimidin-2-yl)-phenyl
1654.	allyl	4-(pyrimidin-4-yl)-phenyl
1655.	allyl	4-(pyrimidin-5-yl)-phenyl
1656.	allyl	5-isopropylthiophen-2-yl
1657.	allyl	2-chlorothiophen-5-yl
1658.	allyl	2,5-dichlorothiophen-4-yl
1659.	allyl	2,3-dichlorothiophen-5-yl
1660.	allyl	2-chloro-3-nitrothiophen-5-yl
1661.	allyl	2-(phenylsulfonyl)-thiophen-5-yl
1662.	allyl	2-(pyridin-2-yl)thiophen-5-yl
1663.	allyl	2-(5-(trifluoromethyl)isoxazol-3-yl)-thiophen-5-yl
1664.	allyl	2-(2-methylthiazol-4-yl)-thiophen-5-yl
1665.	allyl	1-methyl-1H-imidazol-4-yl
1666.	allyl	1,2-dimethyl-1H-imidazol-4-yl
1667.	allyl	3,5-dimethylisoxazol-4-yl
1668.	allyl	thiazol-2-yl
1669.	allyl	4-methylthiazol-2-yl
1670.	allyl	4-isopropylthiazol-2-yl
1671.	allyl	4-trifluoromethylthiazol-2-yl
1672.	allyl	5-methylthiazol-2-yl
1673.	allyl	5-isopropylthiazol-2-yl
1674.	allyl	5-trifluoromethylthiazol-2-yl
1675.	allyl	2,4-dimethylthiazol-5-yl
1676.	allyl	2-acetamido-4-methylthiazol-5-yl
1677.	allyl	4H-[1,2,4]triazol-3-yl
1678.	allyl	5-methyl-4H-[1,2,4]triazol-3-yl
1679.	allyl	4-methyl-4H-[1,2,4]triazol-3-yl
1680.	allyl	5-isopropyl-4H-[1,2,4]triazol-3-yl
1681.	allyl	5-trifluoromethyl-4H-[1,2,4]triazol-3-yl
1682.	allyl	4,5-dimethyl-4H-[1,2,4]triazol-3-yl
1683.	allyl	5-isopropyl-4-methyl-4H-[1,2,4]triazol-3-yl
1684.	allyl	5-trifluoromethyl-4-methyl-4H-[1,2,4]triazol-3-yl
1685.	allyl	[1,3,4]thiadiazol-2-yl

No.	R ¹	Ar
1686.	allyl	5-methyl-[1,3,4]thiadiazol-2-yl
1687.	allyl	5-isopropyl-[1,3,4]thiadiazol-2-yl
1688.	allyl	5-trifluoromethyl-[1,3,4]thiadiazol-2-yl
1689.	allyl	3-bromo-2-chloropyrid-5-yl
1690.	allyl	2-(4-morpholino)-pyrid-5-yl
1691.	allyl	2-phenoxy-pyrid-5-yl
1692.	allyl	(2-isopropyl)-pyrimidin-5-yl
1693.	allyl	(5-isopropyl)-pyrimidin-2-yl
1694.	allyl	8-quinolyl
1695.	allyl	5-isoquinolyl
1696.	allyl	2-(trifluoroacetyl)-1,2,3,4-tetrahydroisoquinolin-7-yl
1697.	allyl	5-chloro-3-methylbenzothiophen-2-yl
1698.	allyl	3,4-dihydro-4-methyl-2H-benzo[b][1,4]oxazinyl
1699.	allyl	benzothiazol-6-yl
1700.	allyl	benzo[2,1,3]oxadiazol-4-yl
1701.	allyl	5-chlorobenzo[2,1,3]oxadiazol-4-yl
1702.	allyl	7-chlorobenzo[2,1,3]oxadiazol-4-yl
1703.	allyl	benzo[2,1,3]thiadiazol-4-yl
1704.	allyl	6-chloroimidazo[2,1-b]thiazolyl

The compounds of the formula I where E is NH and R^{1a} is hydrogen can be prepared by analogy to methods which are well known in the art, e.g. from the international patent applications cited in the introductory part. A preferred method for the preparation of compounds I is outlined in scheme 1:

Scheme 1



In scheme 1, R^1 , R^2 , R^{2a} , X and Ar have the meanings as given above. PG is an amino-protecting group such as tert.-butoxycarbonyl. Suitable protecting groups are disclosed, for example, in P. Kocienski, *Protecting Groups*, Thieme-Verlag, Stuttgart 2000, Chapter 6.

In step a) the protected nitrophenethylamine II is reduced by conventional means into the corresponding amino compound III. The required reaction conditions correspond to the customary conditions for reducing aromatic nitro groups which have been de-

- scribed extensively in the literature (see, for example, J. March, *Advanced Organic Chemistry*, 3rd ed., J. Wiley & Sons, New-York, 1985, p. 1183 and the literature cited in this reference). The reduction is achieved, for example, by reacting the nitro compound VII with a metal such as iron, zinc or tin under acidic reaction conditions, i.e. using nascent hydrogen, or using a complex hydride such as lithium aluminum hydride or sodium borohydride, preferably in the presence of transition metal compounds of nickel or cobalt such as $\text{NiCl}_2(\text{P}(\text{phenyl})_3)_2$, or CoCl_2 , (see Ono et al. *Chem. Ind. (London)*, 1983 p.480), or using NaBH_2S_3 (see Lalancette et al. *Can. J. Chem.* 49, 1971, p. 2990), with it being possible to carry out these reductions, depending on the given reagent, in substance or in a solvent or diluent. Alternatively, the reduction of II to III can be carried out with hydrogen in the presence of a transition metal catalyst, e.g. using hydrogen in the presence of catalysts based on platinum, palladium, nickel, ruthenium or rhodium. The catalysts can contain the transition metal in elemental form or in the form of a complex compound, of a salt or of an oxide of the transition metal, with it being possible, for the purpose of modifying the activity, to use customary coligands, e.g. organic phosphine compounds, such as triphenylphosphine, tricyclohexylphosphine or tri-n-butylphosphines or phosphites. The catalyst is customarily employed in quantities of from 0.001 to 1 mol per mol of compound II, calculated as catalyst metal. In a preferred variant, the reduction is effected using tin(II) chloride in analogy with the methods described in *Bioorganic and Medicinal Chemistry Letters*, 2002, 12(15), pp. 1917-1919 and *J. Med. Chem.* 2002, 45(21), pp. 4679-4688. The reaction of II with tin(II) chloride is preferably carried out in an inert organic solvent, preferably an alcohol such as methanol, ethanol, isopropanol or butanol.
- 25 The thus obtained compound III is reacted with an arylchlorosulfonylchloride $\text{Cl-SO}_2\text{-Ar}$, preferably in the presence of a base, according to standard procedures in the art to obtain compound IV. The reaction depicted in scheme 1 step b) takes place under the reaction conditions which are customary for preparing arylsulfonamide compounds or arylsulfonic esters, respectively, and which are described, for example, in J. March, *Advanced Organic Chemistry*, 3rd edition, John Wiley & Sons, New York, 1985 p 444 and the literature cited therein, *European J. Org. Chem.* 2002 (13), pp. 2094-2108, *Tetrahedron* 2001, 57 (27) pp. 5885-5895, *Bioorganic and Medicinal Chemistry Letters*, 2000, 10(8), pp. 835-838 and *Synthesis* 2000 (1), pp. 103-108. The reaction customarily takes place in an inert solvent, for example in an ether, such as diethyl ether, diisopropyl ether, methyl tert-butyl ether or tetrahydrofuran, a halohydrocarbon, such as dichloromethane, an aliphatic or cycloaliphatic hydrocarbon, such as pentane, hexane or cyclohexane, or an aromatic hydrocarbon, such as toluene, xylene, cumene and the

- like, or in a mixture of the abovementioned solvents. The reaction of III with $\text{Cl-SO}_2\text{-Ar}$ is customarily carried out in the presence of an auxiliary base. Suitable bases are inorganic bases, such as sodium carbonate or potassium carbonate, or sodium hydrogen-carbonate or potassium hydrogencarbonate, and organic bases, for example trialkylamines, such as triethylamine, or pyridine compounds, such as pyridine, lutidine and the like. The latter compounds can at the same time serve as solvents. The auxiliary base is customarily employed in at least equimolar quantities, based on the amine compound III.
- 10 The thus obtained compound can be alkylated or acylated in step c with a compound $\text{R}^1\text{-L}$, wherein R^1 has the meanings given above and L is a leaving group that can be replaced by the nucleophilic amino group. Leaving groups L comprise e.g. halogen, , trifluoroacetate, arylsulfonyloxy such as tosylate, phenylsulfonyloxy, $\text{C}_1\text{-C}_4\text{-alkylsulfonyloxy}$, trifluoromethylsulfonyloxy, $\text{C}_1\text{-C}_4\text{-alkoxysulfonyloxy}$, etc. The reaction
- 15 conditions which are required for the alkylation have been adequately disclosed, e.g. in Bioorganic and Medicinal Chemistry Lett. 2002, 12(7), pp. 2443-2446 and also 2002, 12(5), pp. 1917-1919.
- In step d') the protecting group PG is cleaved by conventional means (see e.g. P. Kocienski, Protecting Groups, Thieme-Verlag, Stuttgart 2000, Chapter 6) thereby obtaining a compound I, wherein R^{1a} is hydrogen. This compound can be further reacted by alkylation or acylation with $\text{R}^{1a}\text{-L}$, wherein L has the meanings given above and R^{1a} is as defined above but different from hydrogen.
- 25 It is also possible to first cleave the protecting group in IV (step d), thereby obtaining the compound VI and then to introduce the radical R^1 and optionally R^{1a} (step e). The introduction of the radical R^1 into compound VI can also be achieved, in the sense of a reductive amination, by reacting VI with a suitable ketone or aldehyde in the presence of a reducing agent, e.g. in the presence of a borohydride such as sodium borohydride, sodium cyanoborohydride or sodium triacetoxyborohydride. The skilled person is familiar with the reaction conditions which are required for a reductive amination, e.g. from Bioorganic and Medicinal Chemistry Lett. 2002, 12(5), pp. 795-798 and 12(7) pp. 1269-1273. The introduction of the radical R^1 into compound VI can also be achieved by reacting VI with a suitable acyl halide to obtain a compound of the formula I wherein R^1 is
- 35 $\text{C}_1\text{-C}_3\text{-alkylcarbonyl}$. The carbonyl group in these compounds can be reduced with diborane to obtain compounds of the general formula I, wherein R is $\text{C}_2\text{-C}_4\text{-alkyl}$. The carbonyl group can also be reacted with a fluorinating agent to obtain a compound I

wherein R^1 is 1,1-difluoroalkyl. Acylation and reduction can be achieved by standard methods, which are discussed in J. March, Advanced Organic Chemistry, 3rd ed. J. Wiley & Sons, New York 1985, p.370 and 373 (acylation) and p. 1099 f. and in the literature cited in this publication (with regard to acylation, see also Synth. Commun. 1986, 16, p. 267, and with regard to reduction, see also J. Heterocycl. Chem. 1979, 16, p. 1525).

The starting materials of the formula II can be simply obtained from commercially available phenethylamines by selectively protecting the aliphatic amino group of these compounds according to standard methods (see e.g. P. Kocienski, Protecting Groups, loc. cit.).

A skilled person will also appreciate that the reactions of step b) and c) as well as steps b) and d) can be exchanged, e.g. by performing the reaction of step c) first and then the reaction of step b).

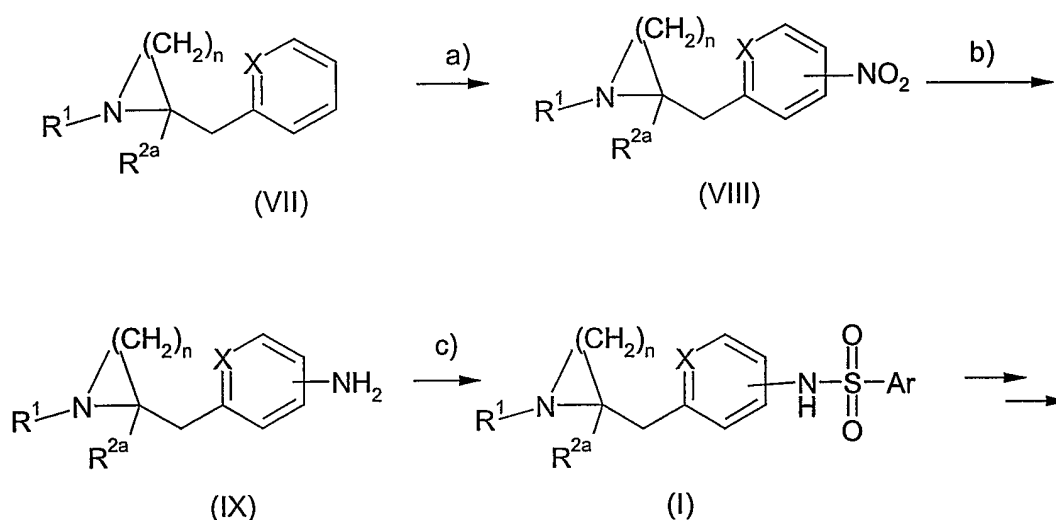
A skilled person will also appreciate that compounds of the formula I with $E = N-R^3$, wherein R^3 is different from hydrogen, can be obtained by selective alkylation of the sulfonamide group in the compounds of the formulae V, VI or I.

If R^1 or R^{1a} in compound I is (are) allyl the allyl group(s) can be cleaved to obtain a compound I' or I'' wherein R is hydrogen. The cleavage of the allyl group is achieved, for example, by reacting I [$R^1 = \text{allyl}$] with an allyl trapping agent, such as mercaptobenzoic acid or 1,3-dimethylbarbituric acid, in the presence of catalytic quantities of palladium (0) compounds or palladium compounds which are able to form a palladium(0) compound under reaction conditions, e.g. palladium dichloride, tetrakis(triphenylphosphine)palladium(0) or tris(dibenzylideneacetone)dipalladium(0), advantageously in combination with phosphine ligands, e.g. triarylphosphines, such as triphenylphosphine, trialkylphosphines, such as tributylphosphine, and cycloalkylphosphines, such as tricyclohexylphosphine, and especially with phosphine chelate ligands, such as 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl or 1,4-bis(diphenylphosphino)butane, using methods known from the literature (with regard to eliminating N-allyl in the presence of mercaptobenzoic acid, see WO 94/24088; with regard to eliminating in the presence of 1,3-dimethylbarbituric acid, see J. Am. Chem. Soc. 2001, 123 (28), pp. 6801-6808 and J. Org. Chem 2002, 67(11) pp. 3718-3723). Alternatively, the cleavage of N-allyl can also be effected by reacting in the presence of rhodium compounds, such as tris(triphenylphosphine)chlororhodium(I), using methods

known from the literature (see J. Chem. Soc., Perkin Transaction I: Organic and Bio-Organic Chemistry 1999 (21) pp. 3089-3104 and Tetrahedron Asymmetry 1997, 8(20), pp. 3387 - 3391). If R¹ or R^{1a} in compound I is (are) allyl the allyl group can be also converted into a n-propyl group by hydrogenation in the presence of Pd-C as a catalyst.

Compounds of the formula I, wherein R^{1a} and R² or R^{1a} and R^{2a} together are (CH₂)_n with n being 2, 3 or 4 can be prepared in a manner similar to the method outlined in scheme 1 starting from a compound of the formula VII, by the method outlined in
10 scheme 2 (showing the sequence for R^{1a} and R² together are (CH₂)_n).

Scheme 2:



In scheme 2, R^1 , R^{2a} , n and Ar have the meanings given above.

The reaction depicted in step a) in scheme 2 takes place under the reaction conditions which are customary for a nitration of an aromatic radical and which are described, for example, in J. March, *Advanced Organic Chemistry*, 3rd ed., John Wiley & Sons, New York 1985, pp 468-470 and the literature cited therein). In step b), the nitro group in VIII is reduced to the NH₂ group according to the method of step b) in scheme 1. Step c) in scheme 2 corresponds to step b) in scheme 1, which can be performed in analogous manner. Thereby a compound of the general formula VIII is obtained.

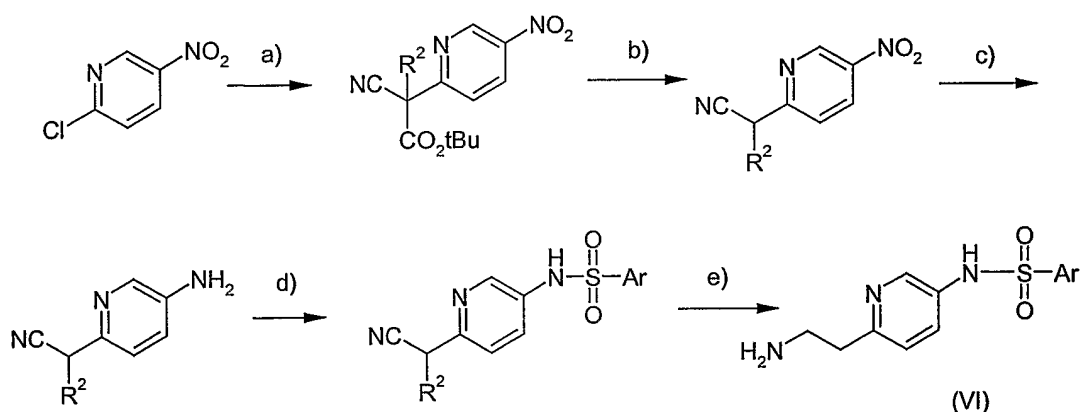
The radical R in the thus obtained compounds VIII can be transformed into other radicals by the methods outlined in connection with scheme 1.

Compounds of the formula VII are known in the art or can be prepared according to standard procedures.

Compounds of the formula I, where R^{2a} is H, X is N and E is NH can be also obtained by the synthetic approach outlined in scheme 3. In scheme 3, R^2 and Ar have the meanings given above.

10

Scheme 3:



- 15 step a: K₂CO₃ in tetrahydrofuran
 step b: p-toluene sulfonic acid, toluene
 step c: reduction (see step a of scheme 1)
 step d: reaction with Ar-SO₂-Cl (see step b of scheme 1)
 step e: reduction, e.g. by H₂/Raney nickel, NH₃

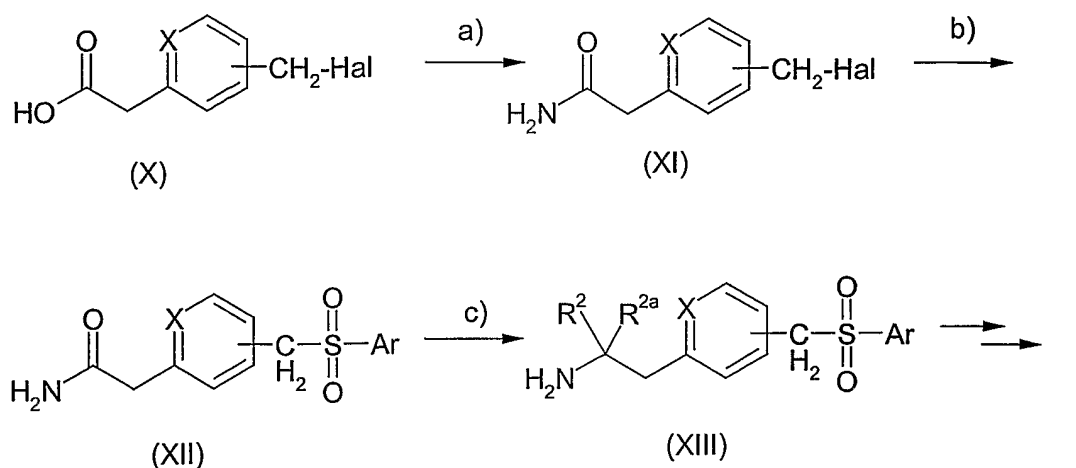
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The obtained compound VI can be further reacted as outlined in scheme 1 to obtain compound I.

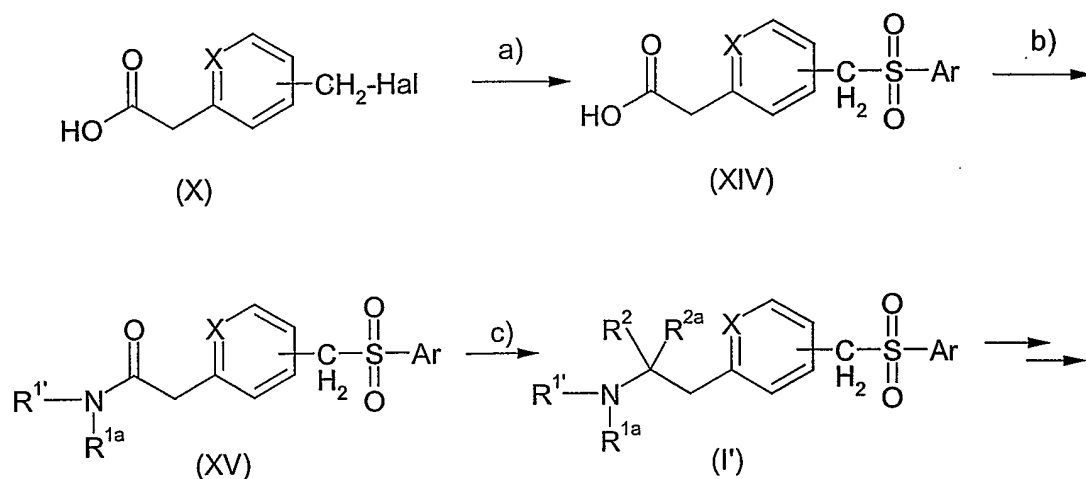
The compounds of the formula I where E is CH₂ as outlined in schemes 4a and 4b:

25

Scheme 4a:



Scheme 4b:



In schemes 4a and 4b, X, R^{1a}, R², R^{2a}, and Ar have the meanings given above. R^{1'} is a radical R¹ that is different from hydrogen, formyl or alkylcarbonyl. Hal is halogen, in particular bromine.

10

According to scheme 4a, the carboxyl group in compound X is transformed into the carboxamide group by standard methods, e.g. by successively reacting compound X with thionyl chloride and then with aqueous ammonia. The amide XI is then reacted in step b) with a mercapto compound HS-Ar in the presence of a base, such as sodium hydride or sodium alkoxide or with an alkali metal salt of HS-Ar, thereby yielding thioether compound. The thioether moiety is oxidized to a sulfone moiety, e.g. by oxone to obtain compound XII. Compound XII can be either reduced, e.g. by BH₃-Dimethylsulfide, to obtain compound XIII with R² = R^{2a} = H, or reacted with a suitable

15

organometal compound or successively with a reducing agent and an organometal compound to obtain a compound XIII, where R^2 and/or R^{2a} is (are) different from hydrogen. Compound XIII can be further converted into compound I as outlined for scheme 1.

5

According to scheme 4b, compound X is reacted in step a) with a mercapto compound HS-Ar in the presence of a base, such as sodium hydride or sodium alkoxide or with an alkali metal salt of HS-Ar, thereby yielding thioether compound. The thioether moiety is oxidized to a sulfone moiety, e.g. by oxone to obtain compound XIV. Compound XIV is
10 reacted in step b) with an amine R^1R^1aNH in the presence of a dehydrating agent such as cyclohexylcarbodiimide (CDI). Compound XV can be either reduced, e.g. by BH_3 -dimethylsulfide, to obtain compound I' with $R^2 = R^{2a} = H$, or reacted with a suitable organometal compound or successively with a reducing agent and an organometal compound to obtain a compound I', where R^2 and/or R^{2a} is (are) different from hydrogen.
15 Compound I' can be further converted into other compounds I as outlined for scheme 1.

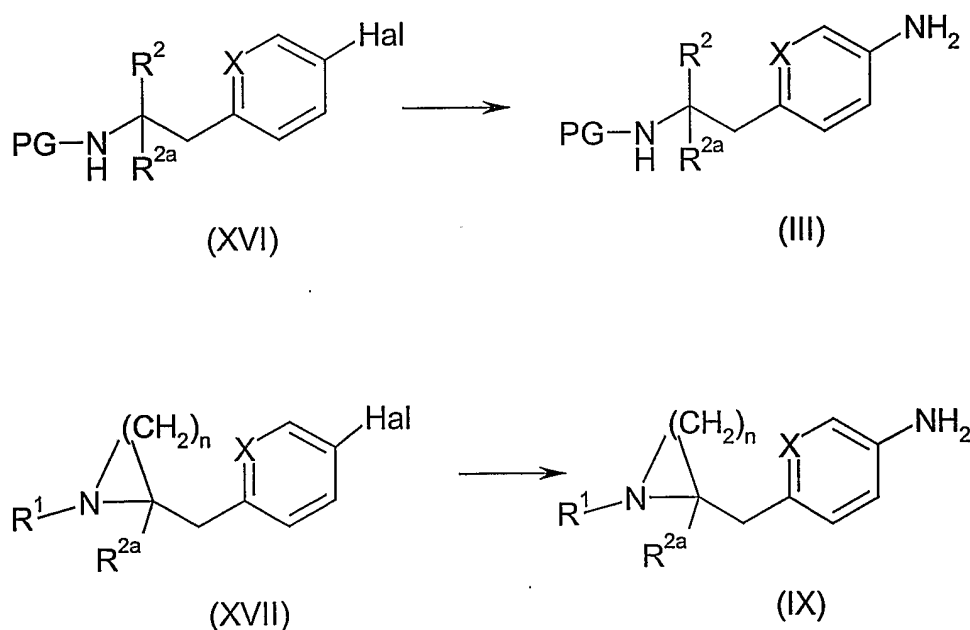
If not indicated otherwise, the above-described reactions are generally carried out in a solvent at temperatures between room temperature and the boiling temperature of the
20 solvent employed. Alternatively, the activation energy which is required for the reaction can be introduced into the reaction mixture using microwaves, something which has proved to be of value, in particular, in the case of the reactions catalyzed by transition metals (with regard to reactions using microwaves, see Tetrahedron 2001, 57, p. 9199 ff. p. 9225 ff. and also, in a general manner, "Microwaves in Organic Synthesis", André
25 Loupy (Ed.), Wiley-VCH 2002.

The sulfonylchlorides $Cl-SO_2-Ar$ are either commercially available or can be prepared according to standard synthetic methods. Sulfonylchlorides containing a fluorinated radical R^a may be prepared by different synthetic routes, e.g. by reacting suitable hydroxy or oxo precursor (e.g. a compound $Cl-SO_2-Ar$, carrying a hydroxy or oxo substituted radical) with fluorinating reagents like DAST (diethylaminosulfurtrifluoride), morpholine-DAST, deoxo-fluor (bis(2-methoxyethyl)aminosulfur trifluoride), Ishikawa's reagent (N,N-diethyl-(1,1,2,3,3,3-hexafluoropropyl)amine; Journal of Fluorine Chemistry, 1989, 43, 371-377). More conventionally, the hydroxy group of an aromatic compound
30 which carries a hydroxy substituted radical but not a chlorosulfonyl group, is transformed into a leaving group which is then replaced by a fluoride ion (J. Org. Chem., 1994, 59, 2898-22901; Tetrahedron Letters, 1998, 7305-6; J. Org. Chem., 1998, 63,

9587-9589, Synthesis, 1987, 920-21)). Subsequent direct chlorosulfonylation with chlorosulfonic acid (Heterocycles, 2001, 55, 9, 1789-1803; J. Org. Chem., 2000, 65, 1399-1406) or a two step process preparing first the sulfonic acid derivatives which are then transformed to the sulfonylchlorides with e.g. chlorosulfonic acid, phosphorus pentachloride (Eur. J. Med. Chem., 2002, 36, 809-828) and the like, yields the desired sulfonylchloride (Tetrahedron Letters, 1991, 33, 50 7787-7788)) Sulfonylchlorides may also be prepared by diazotation of suitable amine precursor Ar-NH₂ with sodium nitrite under acidic conditions and reaction with sulfur dioxide in acetic acid (scheme (iii); J. Org. Chem., 1960, 25, 1824-26;); by oxidation of suitable heteroaryl-thiols HS-Ar or heteroaryl-benzyl-thioethers C₆H₅-CH₂-S-Ar with chlorine (Synthesis, 1998, 36-38; J. Am. Chem. Soc., 1950, 74, 4890-92;) directly to the corresponding sulfonyl chlorides. The further are known in the art or may be prepared by standard methods. E.g. mercapto-pyrimidines or pyrimidinyl-benzylthioether precursors can e.g. be prepared according to literature (Chemische Berichte, 1960, 1208-11; Chemische Berichte, 1960, 95, 230-235; Collection Czechoslow. Chem. Comm., 1959, 24, 1667-1671; Austr. J. Chem., 1966, 19, 2321-30; Chemiker-Zeitung, 101, 6, 1977, 305-7; Tetrahedron, 2002, 58, 887-890; Synthesis, 1983, 641-645.

The aminocompounds of the formulae III or IX may also be prepared from the corresponding halogen compound XVI or XVII according to the method as described in scheme 5:

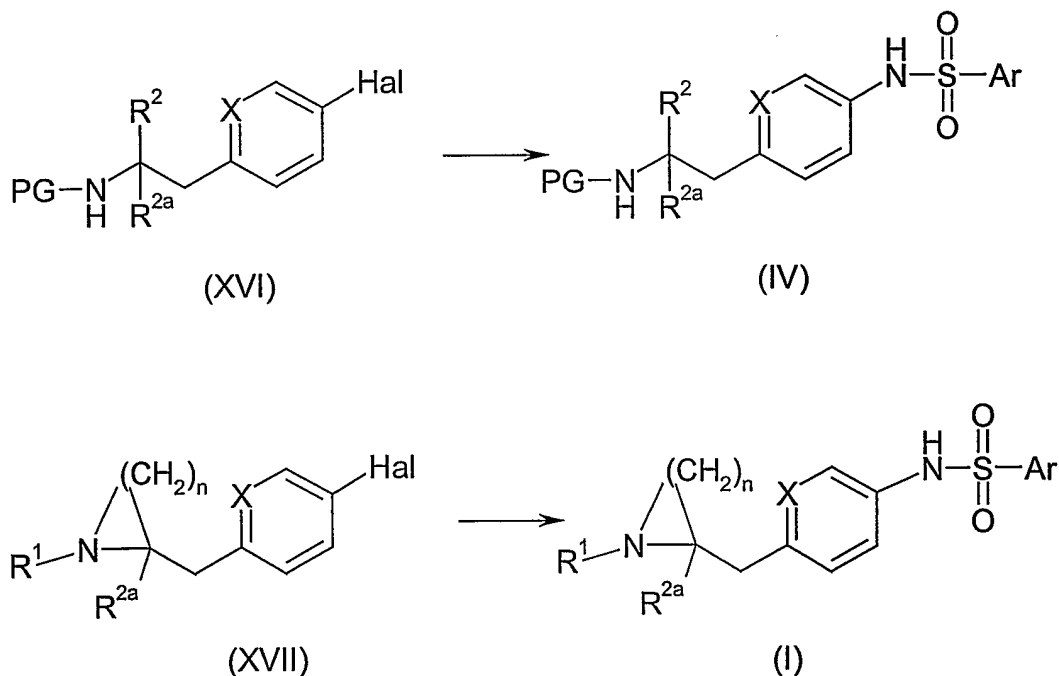
Scheme 5



In scheme 5, R^1 , R^2 , R^{2a} , n and X are as defined above. Hal is halogen, in particular bromine, and PG is a protecting group. The reaction can be performed by reacting XVI or XVII, respectively, with an alkalimetal salt of a bis(trialkylsilyl)amine such as lithium bis(trimethylsilyl)amide in the presence of a palladium catalyst and subsequent hydrolysis. An example for a suitable palladium catalyst is tris(dibenzylideneacetone)-dipalladium(0), optionally in the presence of a tri(substituted)phosphine, e.g. a triarylphosphine such as triphenylphosphine or tritolylphosphine, tri(cyclo)alkylphosphine such as tris-*n*-butylphosphine, tris(tert.-butyl)phosphine or tris(cyclohexyl)phosphine, or $PdCl_2(dppf)$. The reaction of VIIa with the alkalimetal-bis(trialkylsilyl)amide can be performed by analogy to a Buchwald-Hartig coupling. the alkalimetal-bis(trialkylsilyl)amide can be generated in-situ from the corresponding amine by a strong base such an alkalimetal alkoxide, e.g. potassium tert.-butylat or an alkalimetal hydride such as lithium hydride, sodium hydride and the like. Hydrolysis is simply achieved by aqueous work-up.

Compounds of the formulae XVI or XVII may also serve as a starting material in the synthetic route depicted in scheme 6.

Scheme 6:



In scheme 6, R^1 , R^2 , R^{2a} , n , Ar and X are as defined above. Hal is halogen, in particular bromine, and PG is a protecting group. According to scheme 6, a compound of the formulae XVI or VXVII is reacted with an arylsulfonylamide $Ar-SO_2-NH_2$ or the lithium salt thereof in the presence of a palladium(0) compound such as

5 tris(dibenzylideneacetone)dipalladium(0) in the presence of a tri(substituted)phosphine, e.g. a triarylphosphine such as triphenylphosphine or tritolylphosphine, tri(cyclo)alkylphosphine such as tris-*n*-butylphosphine, tris(tert.-butyl)phosphine or tris(cyclohexylphosphine), preferably in the presence of a base such as sodium hydride according to the method described in J. Org. Chem., 68 (1993) pp 8274-8276, and out-

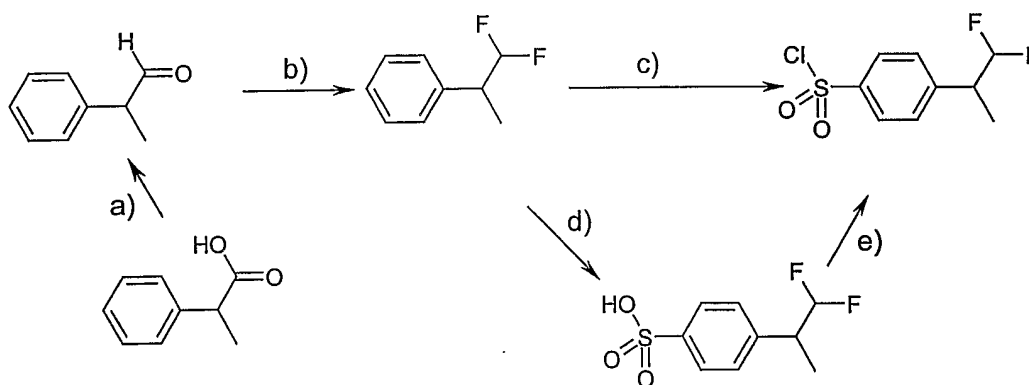
10 lined below.

A skilled person will readily appreciate that compounds of the formula I can also be obtained from structurally similar compounds by functional group interconversion. In particular N-bound radicals R^a can be introduced into compounds of the formula I by

15 reacting the corresponding halogen compound, i.e. a compound of the formula I, which instead of R^a carries a halogen atom, in particular a bromine or iodine atom, with a primary or secondary amine in the presence of a base, preferably also in the presence of a palladium catalyst in terms of a Buchwald-Hartwig reaction.

20 In the following schemes 7 to 9 several routes are shown which are suitable to prepare benzenesulfonyl chlorides carrying a fluorinated propyl radical.

Scheme 7:



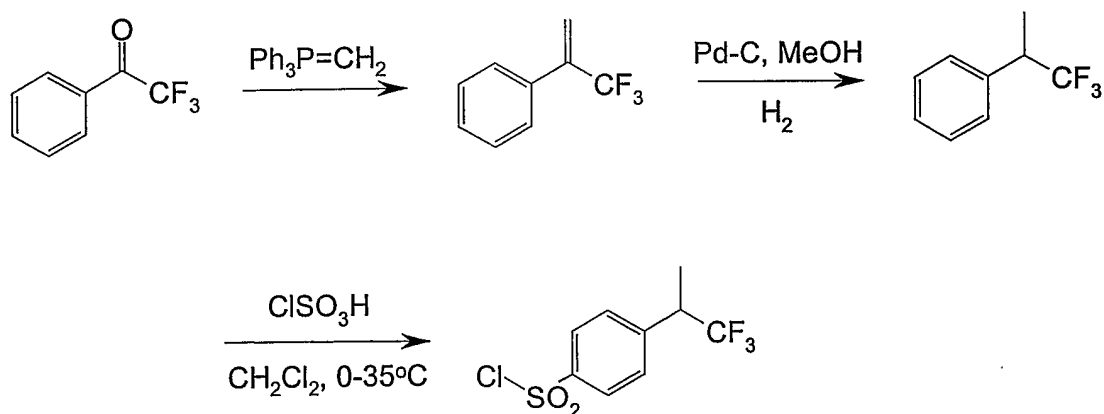
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The 4-(1,1-difluoropropan-2-yl)benzene-1-sulfonyl chloride intermediate can be prepared from the commercially available 2-phenylpropanoic acid. In the first step a) the 2-phenylpropanoic acid is converted to the alkyl ester by esterification with an alcohol (e.g. methanol or ethanol) under acid catalysis (e.g. HCl, SO_2Cl_2). The ester can be re-

duced to the corresponding 2-phenyl propanal by a reducing agent such as DIBAL (diisobutylaluminium hydride). The aldehyde is converted to the 1,1-difluoro-2-propyl derivative by reaction with a suitable fluorinating reagent like DAST (diethylaminosulfur trifluoride), morpholine-DAST, deoxo-fluor (bis(2-methoxyethyl)aminosulfur trifluoride), Ishikawa's reagent (N,N-diethyl-(1,1,2,3,3,3-hexafluoropropyl)amine; Journal of Fluorine Chemistry, 1989, 43, 371-377) (step b). The thus obtained 1,1-difluoro-2-phenylpropane can be converted into 4-(1,1-difluoro-2-propyl)benzenesulfonyl chloride by either direct chlorosulfonylation with chlorosulfonic acid (Heterocycles, 2001, 55, 9, 1789-1803; J. Org. Chem., 2000, 65, 1399-1406) (step c) or by a two step process preparing first the sulfonic acid derivatives (step d) which are then transformed to the sulfonylchlorides (step e) by reaction with e.g. chlorosulfonic acid, phosphorous pentachloride (Eur. J. Med. Chem., 2002, 36, 809-828); through diazotisation of suitable amine precursors with sodium nitrite under acidic conditions and reaction with sulfur dioxide in acetic acid (J. Org. Chem., 1960, 25, 1824-26); oxidation of suitable heteroaryl-thiols or heteroaryl-benzyl-thioethers with chlorine (Synthesis, 1998, 36-38; J. Am. Chem. Soc., 1950, 74, 4890-92) directly to the corresponding sulfonyl chlorides.

The synthesis shown in scheme 7 can also be performed using (R)-2-phenylpropanic acid and (S)-2-phenylpropanic acid respectively to give the corresponding chiral 4-(1,1-difluoropropan-2-yl)benzene-1-sulfonyl chlorides.

Scheme 8:

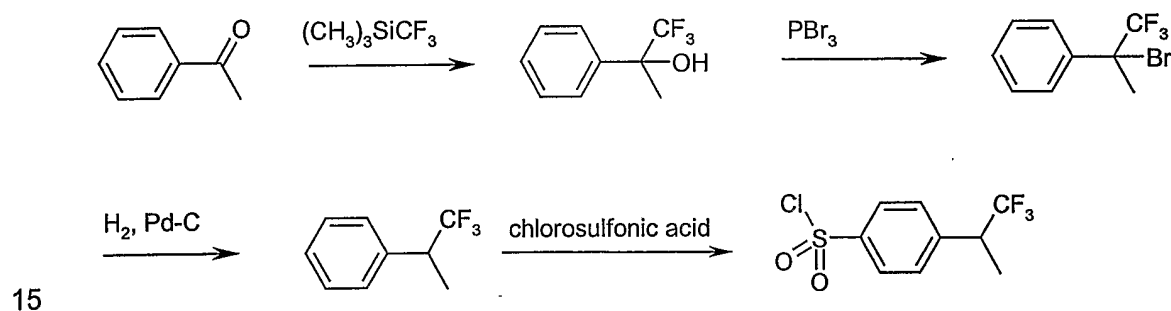


4-(1,1,1-Trifluoropropan-2-yl)benzene-1-sulfonyl chloride intermediate can be prepared from the commercially available 2,2,2-trifluoro-1-phenylethanone by a synthetic route shown in scheme 6. The ketone can be converted to the 3,3,3-trifluoro-2-phenylpropene by a Wittig reaction with a suitable ylide such as methylene-

triphenylphosphane (prepared by reaction of methyltriphenylphosphonium halide and a suitable base such as lithium diisopropylamide or potassium *tert*-butoxide) or according to a Horner-Emmons reaction by reacting the ketone with a suitable phosphonate such as diethyl methylphosphonate and a suitable suitable base such as lithium diisopropylamide or potassium *tert*-butoxide. The thus obtained 3,3,3-trifluoro-2-phenylpropene can then be reduced to the saturated alkane by catalytic hydrogenation (eg Pd-C) followed by conversion to the sulfonyl chloride by the methods described in scheme 5.

The synthesis of scheme 8 can also be performed using a chiral catalyst for the alkene hydrogenation to allow the preparation of the corresponding chiral 4-(1,1,1-triisopropylpropan-2-yl)benzene-1-sulfonyl chlorides.

Scheme 9:



The 4-(1,1,1-trifluoropropan-2-yl)benzene-1-sulfonyl chloride can be also prepared from the commercially available 1-phenyl-ethanone by a four step procedure as shown in scheme 9. The ketone can be converted to the trifluoromethyl hydroxyl intermediate by reaction with trimethyl-trifluoromethyl-silane (Journal of Organic Chemistry, 2000, 65, 8848-8856; Journal of Fluorine Chemistry, 2003, 122, 243-246) which can then be converted to the trifluoromethyl bromide (Journal of the American Chemical Society, 1987, 109, 2435-4). Dehalogenation by catalytic hydrogenation (eg Pd-C) can then be followed by conversion to the sulfonyl chloride by the methods discussed above.

Examples of solvents which can be used are ethers, such as diethyl ether, diisopropyl ether, methyl *tert*-butyl ether or tetrahydrofuran, aprotic polar solvent, such as dimethylformamide, dimethyl sulfoxide, dimethoxyethane, and acetonitrile, aromatic hydrocarbons, such as toluene and xylene, ketones, such as acetone or methyl ethyl ketone, halohydrocarbons, such as dichloromethane, trichloromethane and dichloroethane, esters, such as ethyl acetate and methyl butyrate, carboxylic acids, such as acetic acid

or propionic acid, and alcohols, such as methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, 2-butanol and tert.-butanol.

If desired, it is possible for a base to be present in order to neutralize protons which are released in the reactions. Suitable bases include inorganic bases, such as sodium carbonate, potassium carbonate, sodium hydrogen carbonate or potassium hydrogen carbonate, and, in addition, alkoxides, such as sodium methoxide or sodium ethoxide, alkali metal hydrides, such as sodium hydride, and also organometallic compounds, such as butyllithium compounds or alkylmagnesium compounds, or organic nitrogen bases, such as triethylamine or pyridine. The latter compounds can at the same time serve as solvents.

The crude product is isolated in a customary manner, for example by filtering, distilling off the solvent or extracting from the reaction mixture, etc. The resulting compounds can be purified in a customary manner, for example by means of recrystallizing from a solvent, by means of chromatography or by means of converting into an acid addition salt.

The acid addition salts are prepared in a customary manner by mixing the free base with a corresponding acid, where appropriate in solution in an organic solvent, for example a lower alcohol, such as methanol, ethanol or propanol, an ether, such as methyl *tert*-butyl ether or diisopropyl ether, a ketone, such as acetone or methyl ethyl ketone, or an ester, such as ethyl acetate.

The compounds according to the invention of the formula I are surprisingly highly selective dopamine D₃ receptor ligands which, because of their low affinity for other receptors such as D₁ receptors, D₄ receptors, α 1-adrenergic and/or α 2-adrenergic receptors, muscarinergic receptors, histamine receptors, opiate receptors and, in particular, dopamine D₂ receptors, give rise to fewer side-effects than do the classic neuroleptics, which are D₂ receptor antagonists. A compound of the invention can be a dopamine D₃ receptor agonist, including partial agonistic activity, or a dopamine D₃ receptor antagonist, including partial antagonistic activity.

The high affinity of the compounds according to the invention for D₃ receptors is reflected in very low in-vitro receptor binding constants ($K_i(D_3)$ values) of as a rule less than 50 nM (nmol/l), preferably of less than 10 nM and, in particular of less than 5 nM.

The displacement of [^{125} I]-iodosulpride can, for example, be used in receptor binding studies for determining binding affinities for D₃ receptors.

5 The selectivity of the compounds according to the invention, i.e. the ratio $K_i(D_2)/K_i(D_3)$ of the receptor binding constants, is as a rule at least 50, preferably at least 100, even better at least 150. The displacement of [^{3} H]SCH23390, [^{125} I] idosulpride or [^{125} I] spiperone can be used, for example, for carrying out receptor binding studies on D₁, D₂ and D₄ receptors.

10 Because of their binding profile, the compounds can be used for treating diseases which respond to dopamine D₃ receptor ligands (or which are susceptible to treatment with a dopamine D₃ receptor ligand, respectively), i.e. they are effective for treating those medical disorders or diseases in which exerting an influence on (modulating) the dopamine D₃ receptors leads to an improvement in the clinical picture or to the disease
15 being cured. Examples of these diseases are disorders or diseases of the central nervous system.

Disorders or diseases of the central nervous system are understood as meaning disorders which affect the spinal chord and, in particular, the brain. Within the meaning of
20 the invention, the term "disorder" denotes disturbances and/or anomalies which are as a rule regarded as being pathological conditions or functions and which can manifest themselves in the form of particular signs, symptoms and/or malfunctions. While the treatment according to the invention can be directed toward individual disorders, i.e. anomalies or pathological conditions, it is also possible for several anomalies, which
25 may be causatively linked to each other, to be combined into patterns, i.e. syndromes, which can be treated in accordance with the invention.

The disorders which can be treated in accordance with the invention are, in particular, psychiatric and neurological disturbances. These disturbances include, in particular,
30 organic disturbances, including symptomatic disturbances, such as psychoses of the acute exogenous reaction type or attendant psychoses of organic or exogenous cause, e.g., in association with metabolic disturbances, infections and endocrinopathologies; endogenous psychoses, such as schizophrenia and schizotypic and delusional disturbances; affective disturbances, such as depressions, mania and/or manic-depressive
35 conditions; and also mixed forms of the above-described disturbances; neurotic and somatoform disturbances and also disturbances in association with stress; dissociative disturbances, e.g. loss of consciousness, clouding of consciousness, double con-

- sciousness and personality disturbances; disturbances in attention and waking/sleeping behavior, such as behavioral disturbances and emotional disturbances whose onset lies in childhood and youth, e.g. hyperactivity in children, intellectual deficits, in particular attention disturbances (attention deficit disorders), memory disturbances and cognitive disturbances, e.g. impaired learning and memory (impaired cognitive function), dementia, narcolepsy and sleep disturbances, e.g. restless legs syndrome; development disturbances; anxiety states, delirium; sexlife disturbances, e.g. impotence in men; eating disturbances, e.g. anorexia or bulimia; addiction; and other unspecified psychiatric disturbances.
- 10 The disorders which can be treated in accordance with the invention also include Parkinson's disease and epilepsy and, in particular, the affective disturbances connected thereto.
- 15 The addiction diseases include psychic disorders and behavioral disturbances which are caused by the abuse of psychotropic substances, such as pharmaceuticals or narcotics, and also other addiction diseases, such as addiction to gaming (impulse control disorders not elsewhere classified). Examples of addictive substances are: opioids (e.g. morphine, heroin and codeine), cocaine; nicotine; alcohol; substances which interact with the GABA chloride channel complex, sedatives, hypnotics and tranquilizers, for example benzodiazepines; LSD; cannabinoids; psychomotor stimulants, such as 3,4-methylenedioxy-N-methylamphetamine (ecstasy); amphetamine and amphetamine-like substances such as methylphenidate and other stimulants including caffeine. Addictive substances which come particularly into consideration are opioids, cocaine, amphetamine or amphetamine-like substances, nicotine and alcohol.
- 20
- 25

- With regard to the treatment of addiction diseases, particular preference is given to those compounds according to the invention of the formula I which themselves do not possess any psychotropic effect. This can also be observed in a test using rats, which, after having been administered compounds which can be used in accordance with the invention, reduce their self administration of psychotropic substances, for example cocaine.
- 30

- According to another aspect of the present invention, the compounds according to the invention are suitable for treating disorders whose causes can at least partially be attributed to an anomalous activity of dopamine D₃ receptors.
- 35

According to another aspect of the present invention, the treatment is directed, in particular, toward those disorders which can be influenced, within the sense of an expedient medicinal treatment, by the binding of preferably exogeneously administered binding partners (ligands) to dopamine D₃ receptors.

5

The diseases which can be treated with the compounds according to the invention are frequently characterized by progressive development, i.e. the above-described conditions change over the course of time; as a rule, the severity increases and conditions may possibly merge into each other or other conditions may appear in addition to those which already exist.

10

The compounds according to the invention can be used to treat a large number of signs, symptoms and/or malfunctions which are connected with the disorders of the central nervous system and, in particular, the abovementioned conditions. These signs, symptoms and/or malfunctions include, for example, a disturbed relationship to reality, lack of insight and ability to meet customary social norms or the demands made by life, changes in temperament, changes in individual drives, such as hunger, sleep, thirst, etc., and in mood, disturbances in the ability to observe and combine, changes in personality, in particular emotional lability, hallucinations, ego-disturbances, distractedness, ambivalence, autism, depersonalization and false perceptions, delusional ideas, chanting speech, lack of synkinesia, short-step gait, flexed posture of trunk and limbs, tremor, poverty of facial expression, monotonous speech, depressions, apathy, impeded spontaneity and decisiveness, impoverished association ability, anxiety, nervous agitation, stammering, social phobia, panic disturbances, withdrawal symptoms in association with dependency, manifold syndromes, states of excitation and confusion, dysphoria, dyskinetic syndromes and tic disorders, e.g. Huntington's chorea and Gilles-de-la-Tourette's syndrome, vertigo syndromes, e.g. peripheral positional, rotational and oscillatory vertigo, melancholia, hysteria, hypochondria and the like.

Within the meaning of the invention, a treatment also includes a preventive treatment (prophylaxis), in particular as relapse prophylaxis or phase prophylaxis, as well as the treatment of acute or chronic signs, symptoms and/or malfunctions. The treatment can be orientated symptomatically, for example as the suppression of symptoms. It can be effected over a short period, be orientated over the medium term or can be a long-term treatment, for example within the context of a maintenance therapy.

35

Therefore the compounds according to the invention are preferentially suitable for treating diseases of the central nervous system, in particular for treating affective disorders; neurotic disturbances, stress disturbances and somatoform disturbances and psychoses, and, in particular, for treating schizophrenia and depression. Because of their high selectivity with regard to the D₃ receptor, the compounds I according to the invention are also suitable for treating disturbances of kidney function, in particular disturbances of kidney function which are caused by diabetes mellitus (see WO 00/67847) and, especially, diabetic nephropathy.

Within the context of the treatment, the use according to the invention of the described compounds involves a method. In this method, an effective quantity of one or more compounds, as a rule formulated in accordance with pharmaceutical and veterinary practice, is administered to the individual to be treated, preferably a mammal, in particular a human being, productive animal or domestic animal. Whether such a treatment is indicated, and in which form it is to take place, depends on the individual case and is subject to medical assessment (diagnosis) which takes into consideration signs, symptoms and/or malfunctions which are present, the risks of developing particular signs, symptoms and/or malfunctions, and other factors.

As a rule, the treatment is effected by means of single or repeated daily administration, where appropriate together, or alternating, with other active compounds or active compound-containing preparations such that a daily dose of preferably from about 0.1 to 1000 mg/kg of bodyweight, in the case of oral administration, or of from about 0.1 to 100 mg/kg of bodyweight, in the case of parenteral administration, is supplied to an individual to be treated.

The invention also relates to the production of pharmaceutical compositions for treating an individual, preferably a mammal, in particular a human being, productive animal or domestic animal. Thus, the ligands are customarily administered in the form of pharmaceutical compositions which comprise a pharmaceutically acceptable excipient together with at least one compound according to the invention and, where appropriate, other active compounds. These compositions can, for example, be administered orally, rectally, transdermally, subcutaneously, intravenously, intramuscularly or intranasally.

Examples of suitable pharmaceutical formulations are solid medicinal forms, such as powders, granules, tablets, in particular film tablets, lozenges, sachets, cachets, sugar-coated tablets, capsules, such as hard gelatin capsules and soft gelatin capsules, sup-

positories or vaginal medicinal forms, semisolid medicinal forms, such as ointments, creams, hydrogels, pastes or plasters, and also liquid medicinal forms, such as solutions, emulsions, in particular oil-in-water emulsions, suspensions, for example lotions, injection preparations and infusion preparations, and eyedrops and eardrops. Im-
5 planted release devices can also be used for administering inhibitors according to the invention. In addition, it is also possible to use liposomes or microspheres.

When producing the compositions, the compounds according to the invention are optionally mixed or diluted with one or more excipients. Excipients can be solid, semisolid
10 or liquid materials which serve as vehicles, carriers or medium for the active compound.

Suitable excipients are listed in the specialist medicinal monographs. In addition, the formulations can comprise pharmaceutically acceptable carriers or customary auxiliary
15 substances, such as glidants; wetting agents; emulsifying and suspending agents; preservatives; antioxidants; antiirritants; chelating agents; coating auxiliaries; emulsion stabilizers; film formers; gel formers; odor masking agents; taste corrigents; resin; hydrocolloids; solvents; solubilizers; neutralizing agents; diffusion accelerators; pigments; quaternary ammonium compounds; refatting and overfatting agents; raw materials for
20 ointments, creams or oils; silicone derivatives; spreading auxiliaries; stabilizers; sterilants; suppository bases; tablet auxiliaries, such as binders, fillers, glidants, disintegrants or coatings; propellants; drying agents; opacifiers; thickeners; waxes; plasticizers and white mineral oils. A formulation in this regard is based on specialist knowledge as described, for example, in Fiedler, H.P., Lexikon der Hilfsstoffe für Pharmazie, Kos-
25 metik und angrenzende Gebiete [Encyclopedia of auxiliary substances for pharmacy, cosmetics and related fields], 4th edition, Aulendorf: ECV-Editio-Kantor-Verlag, 1996.

The following examples serve to explain the invention without limiting it.

- 30 The compounds were either characterized via proton-NMR in d₆-dimethylsulfoxid or d-chloroform, if not stated otherwise, on a 400 MHz or 500 MHz NMR instrument (Bruker AVANCE), or by mass spectrometry, generally recorded via HPLC-MS in a fast gradient on C18-material (electrospray-ionisation (ESI) mode), or melting point.
- 35 The magnetic nuclear resonance spectral properties (NMR) refer to the chemical shifts (δ) expressed in parts per million (ppm). The relative area of the shifts in the ¹H NMR

spectrum corresponds to the number of hydrogen atoms for a particular functional type in the molecule. The nature of the shift, as regards multiplicity, is indicated as singlet (s), broad singlet (s. br.), doublet (d), broad doublet (d br.), triplet (t), broad triplet (t br.), quartet (q), quintet (quint.) and multiplet (m).

5

Preparation Examples:

I. Preparation of intermediates

10 a. Preparation of 2-Aminopropylphenylamines

a.1 4-((S)-2-Amino-propyl)-phenylamine x HCl

15 A mixture of 4-nitrophenylacetone (5g, 27.91 mmol), (S)-(-)- α -phenylethylamine (3.4 g, 28.06 mmol), and platinum(IV)oxide (100 mg) in methanol (MeOH) (50 ml) was hydrogenated at atmospheric pressure for a period of 8 h. After filtration and evaporation of the solvent under reduced pressure 4-[(S)-2-((S)-1-phenyl-ethylamino)-propyl]-phenylamine was obtained as a yellow oil 6.7 g, 94%). Without further purification a solution of this oil in methanol (100 ml) together with
20 ammonium formate (16.4 g, 260.1 mmol), and 10% palladium on charcoal (200 mg) were heated to reflux for 30 h. The mixture was evaporated under reduced pressure and the residue was partitioned between ethyl acetate and water. The organic layer was dried over MgSO_4 and evaporated under reduced pressure. To a solution of the obtained residue in isopropanol HCl in isopropanol was added.
25 The hydrochloride salt was collected and dried in a vacuum oven at 50°C to give orange crystals (900 mg, 17%).

a.2 4-((R)-2-Amino-propyl)-phenylamine x HCl

30 Starting from 4-nitrophenylacetone (5g, 27.91 mmol) and (R)-(-)- α -phenylethylamine (3.4 g, 28.06 mmol) following the same synthetic procedure as described for 4-((S)-2-amino-propyl)-phenylamine x HCl the product was obtained as a yellow powder (3 g, 57%).

b. Preparation of N-substituted propionamides

35

b.1 N-[1,1-Dimethyl-2-(4-nitro-phenyl)-ethyl]-propionamide

b.1.1: N-(1,1-Dimethyl-2-phenyl-ethyl)-propionamide

5 To a solution of (2-methyl-propenyl)-benzene (2.6 g, 19.67 mmol) in propionitrile (20 g, 363 mmol) H₂SO₄ (39.33. mmol) was added at 10°C. The mixture was stirred at room temperature for 16 h. Then the mixture was poured into water and adjusted to an alkaline pH with NaOH. The aqueous layer was extracted three times with ethyl acetate, the organic layers combined, washed with water and brine, dried over MgSO₄, filtered, and the solvent evaporated under reduced pressure to give the product as a yellow oil (1.6 g, 40%).

b.1.2: N-[1,1-Dimethyl-2-(4-nitro-phenyl)-ethyl]-propionamide

15 To H₂SO₄ (20 ml) at 0-10°C N-(1,1-dimethyl-2-phenyl-ethyl)-propionamide was slowly added. The mixture was stirred until a clear solution was obtained. Then KNO₃ (750 mg, 7.42 mmol) was added in portions at 0-5°C. The mixture was stirred at room temperature for 16 h after which it was poured into ice water. The aqueous layer was extracted three times with ethyl acetate. The combined organic layers were washed with NaOH, water and brine, dried over MgSO₄, filtered, and the solvent evaporated under reduced pressure to give the product as a brown oil (1 g, 55%).

b.2 N-[1-(4-Nitro-benzyl)-cyclopropyl]-propionamide

25 b.2.1: 1-Benzylcyclopropylamine

30 To a solution of phenylacetonitrile (3g, 25.61 mmol) and tetraisopropylorthotitanate (8 ml, 27.15 mmol) in diethyl ether (Et₂O)/ tetrahydrofuran (THF) (1/1, 100 ml) ethylmagnesiumbromide (49.33 mmol) was added at room temperature. The exothermic mixture was stirred for 1 h at room temperature. Then BF₃·xEt₂O (49.34 mmol) was added and the mixture was stirred for 1 h. The mixture was poured into a cold aqueous solution of NaOH (10%) and diluted with ethyl acetate. The mixture was filtered, and the organic layer was washed with water and brine, dried over MgSO₄, filtered, and the solvent evaporated under reduced pressure to give the product as a yellow oil (3.6 g, 96%).

35 MS (ESI) m/z: 148.15 [M+H]⁺

b.2.2: *N*-(1-Benzyl-cyclopropyl)-propionamide

5 To a solution of 1-benzylcyclopropylamine (3.6 g, 24.45 mmol) and triethylamine (4.9 g, 48.85 mmol) in dichloromethane (100 ml) propionyl chloride (2.5 g, 27.02 mmol) was added at 10°C. The mixture was stirred at room temperature for 16 h. The mixture was partitioned between water and dichloromethane. The organic layer was washed with water, dried over MgSO₄ and the solvent evaporated under reduced pressure. The residue was triturated with diethylether, the precipitate
10 filtered and dried in vacuo to give the product as a brown powder (2 g, 40%).

MS (ESI) *m/z*: 204.10 [M+H]⁺

b.2.3: *N*-[1-(4-Nitro-benzyl)-cyclopropyl]-propionamide

15 To H₂SO₄ (20 ml) at 0-10°C *N*-(1-benzyl-cyclopropyl)-propionamide (2 g, 9.84 mmol) was slowly added. The mixture was stirred until a clear solution was obtained. Then KNO₃ (1 g, 9.89 mmol) was added in portions at 0-5°C. The mixture was stirred at room temperature for 16 h after which it was poured into ice water, and 50% NaOH was added. The aqueous layer was extracted three times with
20 ethyl acetate. The combined organic layers were washed with water and brine, dried over MgSO₄, filtered, and the solvent evaporated under reduced pressure. The residue was triturated with isopropylether and the precipitate filtered and dried in vacuo to give the product as a brown powder (900 mg, 37%).

25 MS (ESI) *m/z*: 249.25 [M+H]⁺

c. Preparation of [2-(aminophenyl)ethyl]-carbamic acid *tert*-butyl ester30 c.1 [2-(4-Amino-phenyl)-ethyl]-carbamic acid *tert*-butyl esterc.1.1: [2-(4-Nitro-phenyl)-ethyl]-carbamic acid *tert*-butyl ester

35 To a solution of 2-(4-nitrophenyl)ethylamine (25.2 g, 124.31 mmol) in Tetrahydrofuran (THF) (100 ml) at 0°C di-*tert*-butyl dicarbonate (38.5 g, 176.33 mmol) was added slowly. The mixture was stirred at room temperature for 16 h. After filtra-

tion the mixture was concentrated in vacuo and the residue partitioned between ethyl acetate and saturated aqueous NaHCO₃. The organic layer was washed with citric acid (5%), dried over MgSO₄, filtered and the solvent evaporated under reduced pressure to give the product as a yellow powder (18.8 g, 57%).

5

c.1.2: [2-(4-Amino-phenyl)-ethyl]-carbamicacid *tert*-butyl ester

To a solution of [2-(4-nitro-phenyl)-ethyl]-carbamicacid *tert*-butyl ester (18.7 g, 70.30 mmol) in ethanol (200 ml) a slurry of 10% palladium on charcoal (2 g) in water (10 ml) was added. At 80°C ammonium formate (44.3 g, 703 mmol) in water (90 ml) was added slowly. After complete addition the mixture was stirred at 80°C for 1 h. The mixture was allowed to come to room temperature, filtered and concentrated in vacuo. The residue was diluted with water and extracted twice with dichloromethane. The combined organic layers were washed with water, dried over MgSO₄, filtered and the solvent evaporated under reduced pressure to give the product as a yellow oil (13.5 g, 81%).

10

15

c.2 Allyl-[2-(4-amino-phenyl)-ethyl]-carbamic acid *tert*-butyl ester

To a solution of [2-(4-amino-phenyl)-ethyl]-carbamicacid *tert*-butyl ester (2.32 g, 9.82 mmol) in N,N-dimethylformamide (DMF) (50 ml) 18-crown-6 (50 mg) was added. At 0°C potassium *tert*-butoxide (1.10 g, 9.82 mmol) was added and the mixture stirred for 30 min. After the addition of allylbromide (1.19 g, 9.82 mmol) the mixture was stirred at room temperature for 16 h. After concentration in vacuo the residue was partitioned between ethyl acetate and saturated aqueous NaHCO₃. The organic layer was washed with water, dried over MgSO₄, filtered and the solvent evaporated under reduced pressure to give the product as a red oil (2.50 g, 92%).

20

25

30 c.3 [2-(3-Amino-phenyl)-ethyl]-carbamicacid *tert*-butyl ester

c.3.1: 2-(3-Nitrophenyl)ethylamine

35

A solution of (3-nitro-phenyl)-acetonitrile (11.4 g, 70.4 mmol) in THF (100 ml) was heated to reflux and borane dimethylsulfide (2M in THF, 77.34 mmol) was added. The mixture was stirred for 2 h under reflux. After complete conversion the mixture was allowed to come to room temperature and a solution of HCl in ethanol

(1M) was added. After stirring the mixture for 30 min it was concentrated under reduced pressure. The residue was triturated with diethylether, filtered, washed with diethylether and dried in vacuo to give the product as a yellow powder (13.1 g, 92%).

5

c.3.2: [2-(3-Amino-phenyl)-ethyl]-carbamic acid *tert*-butyl ester

The desired product was obtained as a brown oil following the synthetic procedure described for allyl-[2-(4-amino-phenyl)-ethyl]-carbamic acid *tert*-butyl ester starting from 2-(3-Nitrophenyl)ethylamine.

10

c.4 Allyl-[2-(3-amino-phenyl)-ethyl]-carbamic acid *tert*-butyl ester

The desired product was obtained as an orange oil following the synthetic procedure described for Allyl-[2-(4-amino-phenyl)-ethyl]-carbamic acid *tert*-butyl ester starting from [2-(3-Amino-phenyl)-ethyl]-carbamic acid *tert*-butyl ester and allyl-bromide.

15

d. Preparation of 2-(4-Aminobenzyl)-1-propylpyrrolidine

20

d.1.1: 2-(4-Nitrobenzyl)-1-propylpyrrolidine

25

2-Benzyl-1-propylpyrrolidine (0.90 g, 3.75 mmol) was dissolved in nitromethane (10 mL) and added to a mixture of concentrated H₂SO₄ (3.7 mL), concentrated nitric acid (0.3 mL) and water (0.6 mL) cooled to 5°C. After stirring for 2 h, the reaction solution was poured into water, extracted with ethyl acetate and the organic phase separated and dried over MgSO₄. The filtered solution was concentrated to give a brown oil (0.95 g, 100%).

30

MS (ESI) *m/z*: 249.3 [M+H]⁺

d.1.2: 2-(4-Aminobenzyl)-1-propylpyrrolidine

35

The mixture of nitro compounds from d.1.1 (0.94 g, 3.79 mmol) was dissolved in methanol (60 mL) and tin chloride (4.30 g, 19.1 mmol) added. The solution was heated to reflux for 3 h, the solution was concentrated and the residue partitioned

between ethyl acetate and NaOH (2M), and the organic phase separated and dried over MgSO₄. The filtered solution was concentrated and the residue separated by preparative HPLC (10-90% methanol) to give the 2 amino isomers. The *p*-amino product was obtained as a yellow oil (0.30 g, 37 %). The *m*-amino product was obtained as a yellow oil (38 mg, 5 %).

MS (ESI) *m/z*: 219.4 [M+H]⁺

¹H-NMR (DMSO-d₆): δ [ppm] 6.85 (d, 2H), 6.43 (d, 1H), 3.08 (m, 1H), 2.75 (m, 1H), 2.45 (m, 1H), 2.18 (m, 3H), 1.62-1.35 (m, 6H), 0.82 (t, 3H).

¹³C-NMR (DMSO-d₆): δ [ppm] 146.5 (s), 129.4 (d), 126.5 (s), 113.8 (d), 66.2 (d), 55.8 (t), 53.3 (t), 29.7 (t), 21.6 (t), 11.9 (q).

e. Preparation of sulfonyl chlorides

e.1 4-((S)-2-Fluoro-1-methyl-ethyl)-benzenesulfonyl chloride

e.1.1 Toluene-4-sulfonic acid (S)-2-phenyl-propyl ester

To a solution of 20 g of (S)-(-)-2-phenyl-1-propanol in 240 ml of dichloromethane was added in portions 28 g of *p*-toluenesulfonyl chloride (146.8 mmol). After stirring for 18 h at room temperature, the organic phase was washed with 100 ml of water, dried over magnesium sulfate, filtered, and the solvent evaporated under reduced pressure to yield 43 g of the title compound.

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 7.65 (d, 2H), 7.15-7.3 (m, 5H), 7.1 (d, 2H), 4.0-4.1 (m, 2H), 3.1 (m, 1H), 2.4 (s, 3H), 1.3 (d, 3H).

e.1.2 ((S)-2-Fluoro-1-methyl-ethyl)-benzene

9.62 g of toluene-4-sulfonic acid (S)-2-phenyl-propyl ester (33.13 mmol) were dissolved in 80 ml of polyethylenglycol 400. 9.62 g of potassium fluoride (165.6 mmol) were added and the reaction mixture was stirred at 50°C for 3 days and another 2 days at 55-70°C. The reaction was treated with 150 ml of saturated aqueous sodium chloride solution, extracted three times with diethyl ether, and the combined organic layers were dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure. The crude product was purified

via silica gel chromatography using cyclohexane/ethyl acetate 15% as eluent. 2.85 g of the desired product were isolated, containing ~ 25% of the elimination side product.

5 $^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ [ppm] 7.2-7.4 (m, 5H), 4.3-4.6 (several m, 2H), 3.15 (m, 1H), 1.3 (m, 3H).

e.1.3 4-((S)-2-Fluoro-1-methyl-ethyl)-benzenesulfonyl chloride

10 3.5 g of ((S)-2-fluoro-1-methyl-ethyl)-benzene (25.32 mmol) were dissolved in 80 ml of dichloromethane. At 0-5°C, 11.81 g of chlorosulfonic acid (101.31 mmol), dissolved in 20 ml of dichloromethane, were added dropwise. The reaction mixture was stirred for 30 min at room temperature and 2 h at 30°C. The solvent was evaporated. 150 ml of diethyl ether were added to the residue, washed once with
15 150 ml of water, and the organic layer was dried over magnesium sulfate, filtered, and the solvent evaporated under reduced pressure. The crude product was purified via silica gel chromatography with n-heptane-dichloromethane (6:4) as eluent to give 1.5 g of the title compound.

20 $^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ [ppm] 8.0 (d, 2H), 7.5 (d, 2H), 4.5 (dd, 2H), 3.25 (m, 1H), 1.4 (d, 3H).

e.2 4-((R)-2-Fluoro-1-methyl-ethyl)-benzenesulfonyl chloride

25 e.2.1 Toluene-4-sulfonic acid (R)-2-phenyl-propyl ester

Following the procedure analogous to that used for the synthesis of toluene-4-sulfonic acid (S)-2-phenyl-propyl ester, but using (R)-2-phenyl-1-propanol, the title compound was prepared.

30 e.2.2 ((R)-2-Fluoro-1-methyl-ethyl)-benzene

The title compound was prepared as described above for the synthesis of ((S)-2-fluoro-1-methyl-ethyl)-benzene, but using toluene-4-sulfonic acid (R)-2-phenyl-propyl ester instead of toluene-4-sulfonic acid (S)-2-phenyl-propyl ester.
35

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 7.2-7.4 (m, 5H), 4.3-4.6 (several m, 2H), 3.15 (m, 1H), 1.3 (m, 3H).

e.2.3 4-((R)-2-Fluoro-1-methyl-ethyl)-benzenesulfonyl chloride

5

1.3 g of ((R)-2-fluoro-1-methyl-ethyl)-benzene (9.4 mmol) were dissolved in 50 ml of dichloromethane. At 0-5°C, 1.1 g of chlorosulfonic acid (9.4 mmol), dissolved in 10 ml of dichloromethane, were added dropwise. The reaction mixture was stirred for 20 min at 0-5°C and then added to a solution of 2.15 g of phosphorous pentachloride dissolved in 40 ml of dichloromethane. The reaction mixture was stirred for 30 min at 0-5°C and 1 h at room temperature. The solvent was evaporated, 100 ml of diethyl ether were added, the mixture was washed once with 150 ml of water, and the organic layer dried over magnesium sulfate, filtered, and the solvent evaporated under reduced pressure. The crude product was purified via silica gel chromatography with n-heptane-dichloromethane (1:1) as eluent to give 0.261 g of the title compound.

15

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 8.0 (d, 2H), 7.5 (d, 2H), 4.5 (dd, 2H), 3.25 (m, 1H), 1.4 (d, 3H).

20

e.3 4-(2-Fluoro-1-methyl-ethyl)-benzenesulfonyl chloride

25

Following the procedures analogous to that used for the preparation of 4-((S)-2-fluoro-1-methyl-ethyl)-benzenesulfonyl chloride, but starting with 2-phenyl-1-propanol in step a.3.1, the title compound was prepared.

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 8.0 (d, 2H), 7.5 (d, 2H), 4.5 (dd, 2H), 3.25 (m, 1H), 1.4 (d, 3H).

30

e.4 4-(2-Fluoro-1-fluoromethyl-ethyl)-benzenesulfonyl chloride

e.4.1 (2-Fluoro-1-fluoromethyl-ethyl)-benzene

35

4 g of 3-phenylglutaric acid (19.21 mmol) were suspended in 350 ml of dichloromethane. At room temperature, 6.5 g of xenon difluoride (38.42 mmol) were added and the reaction mixture was stirred at room temperature for 18 h. The organic phase was washed once with 975 ml of 6% aqueous sodium hydrogencar-

bonate, dried over magnesium sulfate, filtered, and the solvent evaporated. The remaining residue was distilled at a bath temperature of 123°C at 21 mm to yield 0.78 g of the title compound that contained ~ 50% of 4-(2-Fluoro-1-methyl-ethyl)-benzene.

5

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 7.2-7.4 (m, 5H), 4.6-4.8 (dd, 4H), 3.3 (m, 1H).

e.4.2 4-(2-Fluoro-1-fluoromethyl-ethyl)-benzenesulfonyl chloride

10

Following the procedures analogous to that used for the preparation of 4-((S)-2-fluoro-1-methyl-ethyl)-benzenesulfonyl chloride, but using 5 equivalents. of chlorosulfonic acid, 0,12 g of the title compound were obtained.

15

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 8.05 (d, 2H), 7.55 (d, 2H), 4.75 (dd, 4H), 3.4 (m, 1H).

e.5 4-(3,3,3-Trifluoropropyl)-benzenesulfonyl chloride

20

2.9 g were obtained from commercially available (3,3,3-trifluoropropyl)-benzene following the procedure used for the synthesis of 4-((S)-2-fluoro-1-methyl-ethyl)-benzenesulfonyl chloride described above.

25

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 8.0 (d, 2H), 7.45 (d, 2H), 3.0 (t, 2H), 2.45 (m, 2H).

e.6 4-(2,2,2-Trifluoroethyl)-benzenesulfonyl chloride

30

The product was obtained from commercially available (2,2,2-trifluoroethyl)-benzene following the procedure as described in J. Org. Chem., 1960, 25, 1824-26.

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 8.05 (d, 2H), 7.55 (d, 2H), 3.5 (q, 2H).

35

e.7 4-(3-Fluoropropyl)-benzenesulfonyl chloride

e.7.1 (3-Fluoropropyl)-benzene

15.6 g of diethylaminosulfurtrifluoride (DAST, 96.91 mmol) were dissolved in 18 ml of dichloromethane. At 0-5°C, 12 g of 3-phenyl-1-propanol (88.1 mmol) dissolved in 30 ml of dichloromethane, were added dropwise. The reaction mixture was stirred for 18 h, and, after addition of 30 ml of dichloromethane, poured onto 100 ml of ice water. The organic layer was separated, dried over magnesium sulfate, filtered, and the solvent evaporated. The crude product was purified by distillation at a bath temperature of 106°C at 20 mm to yield 7.4 g of the title compound.

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 7.1-7.3 (m, 5H), 4.4 (dt, 2H), 2.7 (m, 2H). 2.0 (m, 2H).

e.7.2 4-(3-Fluoropropyl)-benzenesulfonyl chloride

4.1 g of (3-fluoro-propyl)-benzene (29.67 mmol) were dissolved in 40 ml of dichloromethane. At 0-5°C, 6.91 g of chlorosulfonic acid (59.34 mmol), dissolved in 10 ml of dichloromethane, were added dropwise. The reaction mixture was stirred for 45 min at 0-5°C and then added to a solution of 6.8 g of phosphorous pentachloride (32.63 mmol) dissolved in 50 ml of dichloromethane. The reaction mixture was stirred for 1 h at 5-10°C. The solvent was evaporated, 150 ml of diethyl ether added, washed once with 150 ml of ice water, and the organic layer dried over magnesium sulfate, filtered, and the solvent evaporated under reduced pressure. The crude product was purified via silica gel chromatography with n-heptane-dichloromethane (11:9) as eluent to give 5.5 g of the title compound.

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 7.95 (d, 2H), 7.45 (d, 2H), 4.5 (dt, 2H), 2.9 (t, 2H), 2.05 (m, 2H).

e.8 4-(2,2-Difluoro-cyclopropyl)-benzenesulfonyl chloride

2.07 g of were obtained from commercially available (2,2-difluorocyclopropyl)-benzene following the procedure used for the synthesis of (3-fluoropropyl)-benzenesulfonyl chloride with the exception that only 1.1 equivalents of phosphorous pentachloride were used.

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 8.0 (d, 2H), 7.45 (d, 2H), 2.85 (m, 1H), 2.0 (m, 1H), 1.75 (m, 1H).

e.9 3-Bromo-4-trifluoromethoxy-benzenesulfonyl chloride

5

2.0 g of 1-bromo-2-(trifluoro-methoxy)benzene (8.3 mmol) were dissolved in 30 ml of dichloromethane. At 0-5°C, 1.06 g of chlorosulfonic acid (9.13 mmol), dissolved in 3 ml of dichloromethane, were added dropwise. The reaction mixture was stirred for 30 min at room temperature. Additional 5.5 equivalents of chlorosulfonic in dichloromethane were added to drive the reaction to completion. Standard work-up was followed and silica gel chromatography with n-heptane-dichloromethane (6:4) as eluent gave 2.19 g of the title compound.

10

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 8.3 (d, 1H), 8.05 (dd, 1H), 7.5 (dd, 1H).

15

e.10 4-(2-Fluoroethyl)-benzenesulfonyl chloride

e.10.1 (2-Fluoroethyl)-benzene

20

6.8 g of the title compound were obtained from commercially available 2-phenylethanol following the procedure used for the synthesis of (3-fluoropropyl)-benzene.

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 7.1-7.3 (m, 5H), 4.6 (m, 1H), 4.45 (m, 1H), 2.95 (m, 1H), 2.9 (m, 1H).

25

e.10.2 4-(2-Fluoroethyl)-benzenesulfonyl chloride

30

3.55 g were obtained following the procedure used for the synthesis of 4-((R)-2-fluoro-1-methyl-ethyl)-benzenesulfonyl chloride.

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 8.0 (d, 2H), 7.5 (d, 2H), 4.7 (dt, 2H), 3.05-3.2 (dt, 2H).

35

e.11 5-Propylthiophene-2-sulfonyl chloride

Following the procedures analogous to that used for the preparation of (3-fluoropropyl)-benzenesulfonyl chloride, but using only 1 equivalent of phosphorous pentachloride, the title compound was prepared.

5 $^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ [ppm] 7.7 (d, 1H), 6.85 (d, 1H), 2.9 (t, 2H), 1.75 (m, 2H), 1.0 (t, 3H).

e.12 4-(1-Methyl-1H-pyrazol-4-yl)-benzenesulfonyl chloride

10 e.12.1 1-Methyl-4-phenyl-1H-pyrazole

1 g of 2-phenylmalonaldehyde (6.75 mmol) were dissolved in 25 ml of ethanol. 0.36 ml of N-methyl-hydrazine (6.75 mmol) were added, the reaction mixture was stirred under reflux for 4 h, the solvent evaporated under reduced pressure to
15 yield 1.09 g of the product.

ESI-MS: 159.1 $[\text{M}+\text{H}]^+$

20 $^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ [ppm] 7.75 (s, 1H), 7.6 (s, 1H), 7.45 (d, 2H), 7.35 (t, 2H), 7.2 (t, 1H), 3.9 (s, 3H)

e.12.2 4-(1-Methyl-1H-pyrazol-4-yl)-benzenesulfonyl chloride

0.5 g of 1-methyl-4-phenyl-1H-pyrazole (3.16 mmol) were dissolved in 20ml of dichloromethane. At 0°C, 0.232 ml of chlorosulfonic acid were added and the reaction mixture was stirred for 1 h under ice cooling. Additional 0.7 ml of chlorosulfonic acid were added, the mixture was stirred at 0°C for 30 minutes and then 90
25 minutes at 50°C. The two phases were separated and the lower layer put on ice, extracted twice with diethyl ether, dried over magnesium sulfate, filtered, and the
30 solvent evaporated under reduced pressure to yield 0.496 g of the product.

$^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ [ppm] 8.0 (d, 2H), 7.85 (s, 1H), 7.75 (s, 1H), 7.65 (d, 2H), 4.0 (s, 3H).

35 e.13 4-(1,1,1-Trifluoropropan-2-yl)benzenesulfonyl chloride and
2-(1,1,1-trifluoropropan-2-yl)benzenesulfonyl chloride

Prepared on a 14 g scale following the procedure outlined in Scheme 7. 2-(1,1,1-Trifluoropropan-2-yl)benzenesulfonyl chloride is a by-product of the reaction.

4-(1,1,1-Trifluoropropan-2-yl)benzenesulfonyl chloride:

5 MS (ESI) m/z : 273.1 $[M+H]^+$

$^1\text{H-NMR}$ (DMSO-d_6): δ [ppm] 7.62 (d, 2H), 7.33 (d, 2H), 3.81 (m, 1H), 1.42 (d, 3H).

2-(1,1,1-Trifluoropropan-2-yl)benzenesulfonyl chloride:

10 MS (ESI) m/z : 273.1 $[M+H]^+$

e.14 4-(1,1-Difluoropropan-2-yl)benzenesulfonyl chloride and
2-(1,1-Difluoropropan-2-yl)benzene-1-sulfonyl chloride

15 Prepared on an 11 g scale following the procedure outlined in Scheme 6. 2-(1,1-Difluoropropan-2-yl)benzene-1-sulfonyl chloride is a by-product of the reaction.

4-(1,1-Difluoropropan-2-yl)benzenesulfonyl chloride:

20 MS (ESI) m/z : 255.0 $[M+H]^+$

$^1\text{H-NMR}$ (DMSO-d_6): δ [ppm] 8.03 (d, 2H), 7.55 (d, 2H), 5.88 (dt, 1H), 3.34 (m, 1H), 1.47 (d, 3H).

$^{13}\text{C-NMR}$ (DMSO-d_6): δ [ppm] 146.43, 143.54, 129.77, 127.28, 117.06 (t), 43.76, 13.78.

25 2-(1,1-difluoropropan-2-yl)benzene-1-sulfonyl chloride:

Isolated by chromatography on 110 mg scale.

MS (ESI) m/z : 255.0 $[M+H]^+$

$^1\text{H-NMR}$ (DMSO-d_6): δ [ppm] 8.15 (d, 1H), 7.77 (t, 1H), 7.70 (d, 1H), 7.54 (t, 1H), 5.99 (dt, 1H), 4.43 (m, 1H), 1.51 (d, 3H).

30 $^{13}\text{C-NMR}$ (DMSO-d_6): δ [ppm] 143.45, 138.63, 135.53, 130.93, 129.04, 128.17, 116.61 (t), 38.38, 13.68.

II. Preparation of compounds I

35 EXAMPLE 1:

N-[4-((S)-2-Propylamino-propyl)-phenyl]-4-trifluoromethoxy-benzenesulfonamide

1.1 N-[(S)-2-(4-Amino-phenyl)-1-methyl-ethyl]-propionamide

To a solution of 4-((S)-2-amino-propyl)-phenylamine x HCl (1.24 g, 6.66 mmol) and triethylamine (1.4 g, 13.83 mmol) in dichloromethane (20 ml) propionyl chloride (620 mg, 6.66 mmol) was added at $-5-0^{\circ}\text{C}$. The mixture was stirred at room temperature for 4 h. The mixture was partitioned between water and dichloromethane and to the organic layer was added HCl (1M). At pH=8 the aqueous layer was extracted three times with ethyl acetate. The combined organic layers were washed with water, dried over MgSO_4 and the solvent evaporated under reduced pressure to give the product as an orange oil (300 mg, 22%).

1.2 N-[(S)-1-Methyl-2-[4-(4-trifluoromethoxy-benzenesulfonylamino)-phenyl]-ethyl]-propionamide

To a solution of N-[(S)-2-(4-amino-phenyl)-1-methyl-ethyl]-propionamide (300 mg, 1.45 mmol) and triethylamine (300 mg, 2.96 mmol) in tetrahydrofuran (THF) (30 ml) 4-trifluoromethoxy-benzenesulfonyl chloride (380 mg, 1.45 mmol) was added at $-5-0^{\circ}\text{C}$. The mixture was stirred at room temperature for 2 h. The mixture was partitioned between water and ethyl acetate. The organic layer was washed with 5% citric acid, saturated aqueous NaHCO_3 , water, and brine, dried over MgSO_4 and the solvent evaporated under reduced pressure to give the product as a brown oil (500 mg, 80%).

1.3 N-[4-((S)-2-Propylamino-propyl)-phenyl]-4-trifluoromethoxy-benzenesulfonamide

To a solution of N-[(S)-1-methyl-2-[4-(4-trifluoromethoxy-benzenesulfonylamino)-phenyl]-ethyl]-propionamide (500 mg, 1.16 mmol) in THF (20 ml) borane-dimethylsulfid complex (2M in THF, 2.63 mmol) was added at room temperature. The mixture was heated to reflux for 2 h. The mixture was allowed to come to room temperature and HCl (2M) was added. This mixture was stirred for 16 h at room temperature. After extracting the mixture three times with dichloromethane the combined organic layers were washed with saturated aqueous NaHCO_3 , water, and brine, dried over MgSO_4 and the solvent evaporated under reduced pressure to give the product as a yellow oil. Column chromatography (CH_2Cl_2 , 2%/methanol, 5%, 10%) gave the product as a yellow oil (300 mg, 62%).

MS (ESI) m/z : 417.15 $[M+H]^+$

$^1\text{H-NMR}$ (CDCl_3): δ [ppm] 7.80 (d, 2H), 7.20 (d, 2H), 7.06 (d, 2H), 7.00 (d, 2H), 2.90-3.00 (m, 1H), 2.80-2.90 (m, 1H), 2.65-2.75 (m, 1H), 2.52-2.60 (m, 2H), 1.45-1.60 (m, 2H), 1.05-1.10 (m, 3H), 0.85 (t, 3H).

5

EXAMPLE 2

N-[4-((R)-2-Propylamino-propyl)-phenyl]-4-trifluoromethoxy-benzenesulfonamide

10 The desired product was obtained as a yellow powder following the same synthetic procedure as described for N-[4-((S)-2-propylamino-propyl)-phenyl]-4-trifluoromethoxy-benzenesulfonamide starting from 4-((R)-2-amino-propyl)-phenylamine x HCl.

MS (ESI) m/z : 417.15 $[M+H]^+$

15 $^1\text{H-NMR}$ (CDCl_3): δ [ppm] 7.80 (d, 2H), 7.20 (d, 2H), 7.06 (d, 2H), 7.00 (d, 2H), 2.90-3.00 (m, 1H), 2.80-2.90 (m, 1H), 2.65-2.75 (m, 1H), 2.52-2.60 (m, 2H), 1.45-1.60 (m, 2H), 1.05-1.10 (m, 3H), 0.85 (t, 3H).

EXAMPLE 3

4-Isopropyl-N-[4-(2-propylamino-propyl)-phenyl]-benzenesulfonamide x HCl

20

Starting from racemic 4-(2-amino-propyl)-phenylamine and propionyl chloride the desired product was obtained as a yellow powder following the synthetic protocol of example 1 using 4-Isopropyl-benzenesulfonyl chloride.

25 MS (ESI) m/z : 375.25 $[M+H]^+$

$^1\text{H-NMR}$ (CDCl_3): δ [ppm] 7.69 (d, 2H), 7.25 (d, 2H), 7.06 (d, 2H), 7.00 (d, 2H), 2.88-2.98 (m, 1H), 2.78-2.87 (m, 1H), 2.42-2.70 (several m, 4H), 1.36-1.49 (m, 2H), 1.19-1.22 (m, 6H), 0.99-1.01 (m, 3H), 0.82 (t, 3H).

30 EXAMPLE 4

N-[4-(2-Methyl-2-propylamino-propyl)-phenyl]-4-trifluoromethoxy-benzenesulfonamide

4.1 N-[2-(4-Amino-phenyl)-1,1-dimethyl-ethyl]-propionamide

35 A mixture of N-[1,1-dimethyl-2-(4-nitro-phenyl)-ethyl]-propionamide (1g, 4 mmol) and 10% palladium on charcoal (100 mg) in methanol (50 ml) was hydrogenated at atmos-

pheric pressure. After filtration the solvent was evaporated and the residue dissolved in ethyl acetate. The solution was dried over MgSO_4 , filtered, and the solvent evaporated under reduced pressure to give the product as a yellow oil (800 mg, 91%).

5 4.2 N-{1,1-Dimethyl-2-[4-(4-trifluoromethoxy-benzenesulfonylamino)-phenyl]-ethyl}-propionamide

To a solution of N-[2-(4-amino-phenyl)-1,1-dimethyl-ethyl]-propionamide (800 mg, 3.63 mmol) and triethylamine (800 mg, 7.91 mmol) in THF (30 ml) 4-Trifluoromethoxy-benzenesulfonyl chloride (950 mg, 3.63 mmol) was added at $-5-0^\circ\text{C}$. The mixture was
10 stirred at room temperature for 2 h. The mixture was partitioned between water and ethyl acetate. The organic layer was washed with 5% citric acid, saturated aqueous NaHCO_3 , water, and brine, dried over MgSO_4 and the solvent evaporated under reduced pressure. The residue was triturated with diethylether and the precipitate filtered
15 and dried in vacuo to give the product as a brown powder (700 mg, 43%).

MS (ESI) m/z : 445.35 $[\text{M}+\text{H}]^+$

20 4.3 N-[4-(2-Methyl-2-propylamino-propyl)-phenyl]-4-trifluoromethoxy-benzene-sulfonamide

To a solution of N-{1,1-dimethyl-2-[4-(4-trifluoromethoxy-benzenesulfonylamino)-phenyl]-ethyl}-propionamide (700 mg, 1.57 mmol) in THF (20 ml) borane-dimethylsulfid complex (2M in THF, 6.32 mmol) was added at room temperature. The mixture was
25 heated to reflux for 2 h. The mixture was allowed to come to room temperature and HCl (2M) was added. This mixture was stirred for 16 h at room temperature. After extracting the mixture three times with dichloromethane the combined organic layers were washed with saturated aqueous NaHCO_3 , water, brine, dried over MgSO_4 , filtered, and the solvent evaporated under reduced pressure to give the product as a yellow oil. Col-
30 umn chromatography (CH_2Cl_2 , 2%/methanol, 5%, 10%) gave the product as a yellow foam (500 mg, 74%).

MS (ESI) m/z : 431.35 $[\text{M}+\text{H}]^+$

$^1\text{H-NMR}$ (CDCl_3): δ [ppm] 7.82 (d, 2H), 7.21 (d, 2H), 7.03 (d, 2H), 6.99 (d, 2H), 2.78 (s,
35 2H), 2.64-2.70 (m, 2H), 1.55-1.65 (m, 2H), 1.08 (s, 6H), 0.91 (t, 3H).

EXAMPLE 5N-[4-((1-Propylamino-cyclopropyl)methyl)-phenyl]-4-trifluoromethoxy-benzene-sulfonamide

- 5 Starting from N-[1-(4-nitro-benzyl)-cyclopropyl]-propionamide the desired product was obtained as a yellow oil following the synthetic protocol of example 4.

MS (ESI) m/z: 429.15 [M+H]⁺

- 10 ¹H-NMR (CDCl₃): δ [ppm] 7.81 (d, 2H), 7.24 (d, 2H), 7.12 (d, 2H), 7.02 (d, 2H), 2.70 (s, 2H), 2.58-2.63 (m, 2H), 1.30-1.40 (m, 2H), 0.81 (t, 3H), 0.64 (m, 2H), 0.50 (m, 2H).

EXAMPLE 64-Isopropyl-N-[4-(2-propylamino-ethyl)-phenyl]-benzenesulfonamide x HCl

- 15 Starting from commercially available 2-(4-aminophenyl)ethylamine and propionyl chloride the desired product was obtained as a colorless powder following the synthetic protocol of example 1 using 4-isopropyl-benzenesulfonyl chloride.

MS (ESI) m/z: 361.15 [M+H]⁺

- 20 ¹H-NMR (DMSO-d₆): δ [ppm] 10.25 (s, 1H); 8.93 (bs, 2H), 7.7 (d, 2H), 7.41 (d, 2H), 7.04-7.15 (m, 4H), 3.47-3.65 (m, 2H), 2.77-3.10 (m, 5H), 1.58-1.69 (m, 2H), 1.18 (d, 6H), 0.90 (t, 3H).

EXAMPLE 7

- 25 N-{4-[2-(Cyclopropylmethyl-amino)-ethyl]-phenyl}-4-isopropyl-benzenesulfonamide x HCl

- 30 Starting from commercially available 2-(4-aminophenyl)ethylamine and cyclopropane-carbonyl chloride the desired product was obtained as a colorless powder following the synthetic protocol of example 1 using 4-isopropyl-benzenesulfonyl chloride.

MS (ESI) m/z: 373.15 [M+H]⁺

- 35 ¹H-NMR (DMSO-d₆): δ [ppm] 10.28 (s, 1H); 9.02 (bs, 2H), 7.70 (d, 2H), 7.41 (d, 2H), 7.04-7.15 (m, 4H), 2.75-3.10 (several m, 7H), 1.15-1.22 (m, 2H), 1.01-1.12 (m, 1H), 0.52-0.61 (m, 2H), 0.30-0.41 (m, 2H).

EXAMPLE 8N-[4-(2-Dipropylamino-ethyl)-phenyl]-4-isopropyl-benzenesulfonamide x HCl

- 5 8.1 {2-[4-(4-Isopropyl-benzenesulfonylamino)-phenyl]-ethyl}-carbamic acid *tert*-butyl ester

To a solution of [2-(4-amino-phenyl)-ethyl]-carbamic acid *tert*-butyl ester (10.75 g, 45.49 mmol) in pyridine (125 ml) at 0°C 4-isopropyl-benzenesulfonyl chloride (10.45 g, 47.76 mmol) was added. The mixture was stirred at 0°C for 1 h and 16 h at room temperature. After concentration in vacuo the residue was partitioned between dichloromethane and saturated aqueous NaHCO₃. The organic layer was washed with water, dried over MgSO₄, filtered and the solvent evaporated under reduced pressure to give the product as a brown oil (20.82 g, 50%).

- 15 8.2 N-[4-(2-Amino-ethyl)-phenyl]-4-isopropyl-benzenesulfonamide x HCl

To a solution of {2-[4-(4-isopropyl-benzenesulfonylamino)-phenyl]-ethyl}-carbamic acid *tert*-butyl ester (20.42 g, 48.79 mmol) in diethylether (200 ml) and THF (80 ml) at 0°C HCl in diethylether (100 ml) was added slowly. The mixture was stirred at room temperature for 16 h. After concentration in vacuo the product was obtained as a yellow foam (17.3 g, 99.9%).

- 8.3 N-[4-(2-Dipropylamino-ethyl)-phenyl]-4-isopropyl-benzenesulfonamide x HCl

25 A solution of N-[4-(2-amino-ethyl)-phenyl]-4-isopropyl-benzenesulfonamide x HCl (740 mg, 2.09 mmol), 4Å molecular sieves (750 mg) and cesium hydroxide (1.09 g, 6.27 mmol) in DMF was stirred at room temperature for 1 h before 1-bromo-propane (516 mg, 4.2 mmol) was added. The mixture was stirred at room temperature for 16 h. After concentrating the mixture in vacuo the residue was purified by column chromatography (toluene/THF/methanol, 4/1/1 + 2.5% triethylamine). The obtained yellow oil was dissolved in diethylether, and HCl in diethylether (1M) was added. The precipitate was collected and dried in vacuo to give the product as a colorless powder (210 mg, 23%).

MS (ESI) m/z: 403.25 [M+H]⁺

¹H-NMR (DMSO-d₆): δ [ppm] 10.30 (s, 1H), 7.69 (d, 2H), 7.4 (d, 2H), 7.17 (d, 2H), 7.06 (d, 2H), 3.12-3.22 (m, 2H), 2.87-3.08 (m, 7H), 1.61-1.75 (m, 4H), 1.19 (d, 6H), 0.88 (t, 6H).

5 EXAMPLE 9

N-[4-(2-Dipropylamino-ethyl)-phenyl]-4-isopropyl-N-methyl-benzenesulfonamide x HCl

To a solution of N-[4-(2-dipropylamino-ethyl)-phenyl]-4-isopropyl-benzenesulfonamide x HCl (80 mg, 0.17 mmol) in N,N-dimethylformamide (DMF) (2.5 ml) 15-crown-5, and sodium hydride (10 mg, 0.36 mmol) were added, and the mixture was stirred at room temperature for 30 min. At 0°C methyl iodide (10 ml, 0.17 mmol) was added and the mixture was kept at 0°C for 1 h. Then it was stirred for 16 h at room temperature. After concentration in vacuo the residue was partitioned between ethyl acetate and saturated aqueous NaHCO₃. The organic layer was washed with water, dried over MgSO₄, filtered and the solvent evaporated under reduced pressure. The residue was dissolved in THF/diethyl ether and HCl in diethyl ether (1M) was added. The precipitate was collected and dried in vacuo to give the product as a yellow powder (50 mg, 59%).

MS (ESI) m/z: 417.25 [M+H]⁺

¹H-NMR (DMSO-d₆): δ [ppm] 9.76 (bs, 1H), 7.45 (s, 4H), 7.29 (d, 2H), 7.09 (d, 2H), 3.21-3.4 (m, 2H), 2.95-3.15 (m, 10H), 1.60-1.76 (m, 4H), 1.23 (d, 6H), 0.90 (t, 6H).

EXAMPLE 10

4-Isopropyl-N-[6-(2-propylamino-ethyl)-pyridin-3-yl]-benzenesulfonamide x 2HCl

25

10.1 (5-Nitro-pyridin-2-yl)-acetonitrile

To a solution of 5-nitro-2-chloropyridine (18 g, 113.5 mmol) in THF (100 ml) at room temperature K₂CO₃ (39.2 g, 283.8 mmol), cyanoacetic acid tert-butyl ester (24 g, 170.30 mmol) and 4Å molecular sieves were added. The mixture was heated to reflux and stirred for 20 h. After concentrating the mixture under reduced pressure the residue was partitioned between ethyl acetate and saturated aqueous NaHCO₃. The organic layer was washed with brine, dried over MgSO₄, filtered and the solvent evaporated under reduced pressure. The obtained oil was dissolved in toluene (300 ml), toluene-4-sulfonic acid (2g, 11.6 mmol) was added, and the mixture was heated to reflux for 2 h. The mixture then was stirred at room temperature for 16 h. After which the mix-

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ture was concentrated under reduced pressure. The residue was partitioned between ethyl acetate and water. The aqueous layer was extracted with ethyl acetate and the combined organic layers were washed with brine, dried over MgSO_4 , filtered, and the solvent evaporated under reduced pressure. Column chromatography (cyclohexane/dichloromethane, 4/1) gave the product as a colorless oil (10.3 g, 66%).

10.2 (5-Amino-pyridin-2-yl)-acetonitrile

To a mixture of (5-nitro-pyridin-2-yl)-acetonitrile (500 mg, 3.06 mmol) in concentrated aqueous HCl (3.1 ml) and ethanol (3.1 ml) at 0°C SnCl_2 (2.3 g, 10.11 mmol) was added. The mixture was allowed to come to room temperature and was stirred for 2h. The mixture was partitioned between ethyl acetate and saturated aqueous NaHCO_3 . The aqueous layer was extracted three times with ethyl acetate and the combined organic layers were washed with brine, dried over MgSO_4 , filtered, and the solvent evaporated under reduced pressure to give the product as a brown oil (300 mg, 74%).

MS (ESI) m/z : 134.05 $[\text{M}+\text{H}]^+$

10.3 N-(6-Cyanomethyl-pyridin-3-yl)-4-isopropyl-benzenesulfonamide

To a solution of (5-amino-pyridin-2-yl)-acetonitrile (1 g, 7.5 mmol) in pyridine (10 ml) 4-Isopropyl-benzenesulfonyl chloride (1.64 g, 7.5 mmol) was added at $-5-0^\circ\text{C}$. The mixture was stirred at 0°C for 2 h and at room temperature for 16 h. The mixture was concentrated under reduced pressure, and the residue partitioned between ethyl acetate and saturated aqueous NaHCO_3 . The aqueous layer was extracted three times with ethyl acetate and the combined organic layers were washed with water, and brine, dried over MgSO_4 , filtered, and the solvent evaporated under reduced pressure to give the product as a brown oil which was purified by column chromatography using methyl-*tert*-butylether as an eluent to give a colorless oil (1.7 g, 72%).

MS (ESI) m/z : 316.10 $[\text{M}+\text{H}]^+$

10.4 N-[6-(2-Amino-ethyl)-pyridin-3-yl]-4-isopropyl-benzenesulfonamide

A mixture of N-(6-cyanomethyl-pyridin-3-yl)-4-isopropyl-benzenesulfonamide (1.7 g, 5.4 mmol) aqueous ammonia (45 ml) and raney-nickel (2.7 mmol) in ethanol (50 ml) was hydrogenated at atmospheric pressure. After filtration the mixture was concentrated

under reduced pressure. The residue was partitioned between ethyl acetate and saturated aqueous NaHCO_3 and the aqueous layer extracted five times with ethyl acetate. The combined organic layers were dried over MgSO_4 , filtered, and the solvent evaporated under reduced pressure to give the product as a yellow powder after recrystallisation from methanol/ethyl acetate (1.3 g, 73%).

MS (ESI) m/z : 320.00 $[\text{M}+\text{H}]^+$

10.5 N-{2-[5-(4-Isopropyl-benzenesulfonylamino)-pyridin-2-yl]-ethyl}-propionamide

10

To a solution of N-[6-(2-Amino-ethyl)-pyridin-3-yl]-4-isopropyl-benzenesulfonamide (50 mg, 0.16 mmol) in pyridine (3 ml) propionyl chloride (10 mg, 0.16 mmol) was added at $-5-0^\circ\text{C}$. The mixture was stirred at 0°C for 2 h and 3 h at room temperature. The mixture was partitioned between water and ethyl acetate and HCl (1M) was added. At pH=8 the aqueous layer was extracted three times with ethyl acetate. The combined organic layers were washed with water, dried over MgSO_4 , filtered, and the solvent evaporated under reduced pressure to give the product as a yellow oil (40 mg, 68%).

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MS (ESI) m/z : 376.15 $[\text{M}+\text{H}]^+$

20

10.6 4-Isopropyl-N-[6-(2-propylamino-ethyl)-pyridin-3-yl]-benzenesulfonamide x 2HCl

To a solution of N-{2-[5-(4-Isopropyl-benzenesulfonylamino)-pyridin-2-yl]-ethyl}-propionamide (40 mg, 0.11 mmol) in THF (3 ml) borane-dimethylsulfid complex (2M in THF, 1.49 mmol) was added at room temperature. The mixture was heated to reflux for 2 h. The mixture was allowed to come to room temperature and HCl (2M) was added. This mixture was stirred for 16 h at room temperature. After extracting the mixture three times with dichloromethane the combined organic layers were washed with saturated aqueous NaHCO_3 , water, and brine, dried over MgSO_4 and the solvent evaporated under reduced pressure to give the product as a yellow oil which was dissolved in diethylether, and HCl in diethylether (1M) was added. The precipitate was collected and dried in vacuo to give the product as a colorless powder (6 mg, 15%).

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MS (ESI) m/z : 362.15 $[\text{M}+\text{H}]^+$

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$^1\text{H-NMR}$ (MeOD): δ [ppm] 8.39 (s, 1H), 7.98 (bs, 1H), 7.62-7.80 (m, 3H), 7.35 (d, 2H), 3.18-3.40 (m, 4H), 2.82-3.00 (m, 3H), 1.58-1.75 (m, 2H), 1.28 (d, 6H), 0.95 (t, 3H).

EXAMPLE 11**4-Isopropyl-N-[4-(1-propyl-pyrrolidin-2-ylmethyl)-phenyl]-benzenesulfonamide**

- 5 2-(4-Aminobenzyl)-1-propylpyrrolidine (300 mg, 1.37 mmol) was dissolved in pyridine-dichloromethane (1:2, 9 mL) and cooled to 5°C. 4-Isopropylbenzenesulfonyl chloride (300 mg, 0.24 mmol) was added and the solution stirred at 5°C for 18 h. The solution was evaporated, partitioned between ethyl acetate and water, and the organic phase separated and dried over MgSO₄. The filtered solution was concentrated and separated by column chromatography (dichloromethane-2% methanol) to give an oil. The oil was dissolved in ethyl acetate and HCl (4M, dioxane) was added to give the product as a white solid (180 mg, 30%).

MS (ESI) m/z: 401.5 [M+H]⁺

- 15 ¹H-NMR (DMSO-d₆): δ [ppm] 10.52 (s, 1H), 7.67 (d, 2H), 7.38 (d, 2H), 7.18 (d, 2H), 7.04 (d, 1H), 3.52 (m, 1H), 3.43 (m, 1H), 3.24 (m, 1H), 3.10-2.75 (m, 5H), 1.82 (m, 3H), 1.62 (m, 3H), 1.15 (d, 6H), 0.82 (t, 3H).
¹³C-NMR (DMSO-d₆): δ [ppm] 153.5 (s), 137.2 (s), 136.5 (s), 132.6 (s), 129.7 (d), 127.1 (d), 126.7 (d), 119.9 (d), 68.1 (d), 54.5 (t), 52.8 (t), 35.2 (t), 33.2 (d), 29.1 (t), 26.8 (t),
20 23.3 (q), 21.1 (t), 18.2 (t), 11.0 (q).

EXAMPLE 12 (reference)**4-Isopropyl-N-[3-(1-propyl-pyrrolidin-2-ylmethyl)-phenyl]-benzenesulfonamide**

- 25 2-(3-Aminobenzyl)-1-propylpyrrolidine (30 mg, 0.14 mmol) was converted to the target sulfonamide by a procedure identical to that described in example 11. The product was obtained as a white solid (18 mg, 26%).

MS (ESI) m/z: 401.5 [M+H]⁺

- 30 ¹H-NMR (DMSO-d₆): δ [ppm] 10.81 (s, 1H), 10.32 (s, 1H), 7.70 (d, 2H), 7.47 (d, 2H), 7.18 (m, 1H), 6.97 (m, 2H), 3.42 (m, 2H), 3.30 (m, 1H), 3.13 (m, 1H), 3.02 (m, 1H), 2.85 (m, 2H), 1.88 (m, 2H), 1.62 (m, 4H), 1.15 (d, 6H), 0.82 (t, 3H).
¹³C-NMR (DMSO-d₆): δ [ppm] 153.6 (s), 138.1 (s), 136.9 (s), 129.4 (d), 127.1 (d), 126.9 (d), 124.5 (d), 120.2 (d), 118.4 (d), 67.8 (d), 54.2 (t), 52.6 (t), 35.7 (t), 33.2 (d),
35 28.9 (t), 26.8 (d), 23.3 (q), 20.9 (t), 18.2 (t), 11.0 (q).

EXAMPLE 13N-[4-(2-Allylamino-ethyl)-phenyl]-4-isopropyl-benzenesulfonamide x HCl

- 5 13.1 Allyl-{2-[4-(4-isopropyl-benzenesulfonylamino)-phenyl]-ethyl}-carbamic acid *tert*-butyl ester

To a solution of allyl-[2-(4-amino-phenyl)-ethyl]-carbamic acid *tert*-butyl ester (1.86 g, 6.74 mmol) in pyridine (25 ml) at 0°C was added 4-isopropyl-benzenesulfonyl chloride (1.47 g, 6.74 mmol) and the mixture was stirred at 0°C for 1h. After concentration in
10 vacuo the residue was partitioned between ethyl acetate and saturated aqueous NaHCO₃. The organic layer was washed with water, dried over MgSO₄, filtered and the solvent evaporated under reduced pressure. The residue was purified by column chromatography (n-heptane/ethyl acetate, 2/1) to give the product as a yellow resin (1.35 g, 43.6 mmol).

15

MS (ESI) m/z: 459.2 [M+H]⁺

13.2 N-[4-(2-Allylamino-ethyl)-phenyl]-4-isopropyl-benzenesulfonamide x HCl

- 20 To a solution of allyl-{2-[4-(4-isopropyl-benzenesulfonylamino)-phenyl]-ethyl}-carbamic acid *tert*-butyl ester (1.35 g, 2.94 mmol) in diethylether (25 ml) was added HCl in diethylether (1M, 10 ml), and the mixture was stirred for 2 h at room temperature. After concentration in vacuo the obtained residue was triturated with diethylether, filtered, washed with diethylether, and dried in vacuo to give the product as a yellow powder
25 (1.16 g, 99.8%).

MS (ESI) m/z: 359.15 [M+H]⁺

- ¹H-NMR (DMSO-d₆): δ [ppm] 10.29 (s, 1H), 9.15 (bs, 2H), 7.69 (d, 2H), 7.42 (d, 2H), 7.05-7.12 (m, 4H), 5.85-5.96 (m, 1H), 5.35-5.48 (m, 2H), 3.50-3.59 (m, 2H), 2.8-3.09
30 (m, 5H), 1.19 (d, 6H).

EXAMPLE 14N-[4-(2-Allylamino-ethyl)-phenyl]-4-isopropyl-N-methyl-benzenesulfonamide x HCl

- 35 14.1 Allyl-(2-{4-[(4-isopropyl-benzenesulfonyl)-methyl-amino]-phenyl}-ethyl)-carbamic acid *tert*-butyl ester

To a solution of allyl-(2-[4-(4-isopropyl-benzenesulfonylamino)-phenyl]-ethyl)-carbamic acid *tert*-butyl ester (200 mg, 0.44 mmol) in DMF (5 ml), 15-crown-5, and sodium hydride (20 mg, 0.48 mmol) were added, and the mixture was stirred at room temperature for 30 min. Methyl iodide (60 mg, 0.44 mmol) was added and the mixture was stirred for 3 h at room temperature. After concentration in vacuo the residue was partitioned between dichloromethane and saturated aqueous NaHCO₃. The organic layer was washed with water, dried over MgSO₄, filtered and the solvent evaporated under reduced pressure to give the product as a yellow oil (200 mg, 97%).

10

MS (ESI) *m/z*: 417.1 [M+H]⁺

14.2 N-[4-(2-Allylamino-ethyl)-phenyl]-4-isopropyl-N-methyl-benzenesulfonamide x HCl

15

To a solution of allyl-(2-[4-[(4-isopropyl-benzenesulfonyl)-methyl-amino]-phenyl]-ethyl)-carbamic acid *tert*-butyl ester (180 mg, 0.39 mmol) in diethylether (10 ml) was added HCl in diethylether (1M, 10 ml), and the mixture was stirred for 3 h at room temperature. After concentration in vacuo the obtained residue was dissolved in THF and with addition of *n*-pentane a precipitate was formed which was collected, washed with *n*-pentane and dried in vacuo to give the product as a yellow powder (110 mg, 68%).

20

MS (ESI) *m/z*: 373.15 [M+H]⁺

¹H-NMR (CDCl₃): δ [ppm] 9.93 (bs, 1H), 7.49 (d, 2H), 7.30 (d, 2H), 7.19 (m, 2H), 7.05 (d, 2H), 6.02-6.18 (m, 1H), 5.45-5.54 (m, 2H), 3.58-3.69 (m, 2H), 3.05-3.30 (m, 7H), 2.90-3.03 (m, 1H), 1.28 (d, 6H).

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EXAMPLE 15

N-[4-(2-Allylamino-ethyl)-phenyl]-4-isopropyl-N-propyl-benzenesulfonamide x HCl

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The desired product was obtained as a colorless powder following the synthetic procedure described for N-[4-(2-allylamino-ethyl)-phenyl]-4-isopropyl-N-methyl-benzenesulfonamide x HCl starting from Allyl-(2-[4-(4-isopropyl-benzenesulfonylamino)-phenyl]-ethyl)-carbamic acid *tert*-butyl ester and 1-bromopropane.

35

MS (ESI) m/z : 401.25 $[M+H]^+$

$^1\text{H-NMR}$ (DMSO- d_6): δ [ppm] 9.19 (bs, 2H), 7.50 (d, 2H), 7.45 (d, 2H), 7.25 (d, 2H), 7.02 (d, 2H), 5.88-6.00 (m, 1H), 5.38-5.51 (m, 2H), 3.55-3.65 (m, 2H), 3.42-3.51 (m, 2H), 3.07-3.17 (m, 2H), 2.90-3.05 (m, 3H), 1.18-1.45 (m, 8H), 0.81 (t, 3H).

5

EXAMPLE 16

N-[4-(2-Allylamino-ethyl)-phenyl]-4-trifluoromethoxy-benzenesulfonamide x HCl

The desired product was obtained as a yellow powder following the synthetic procedure described for N-[4-(2-allylamino-ethyl)-phenyl]-4-isopropyl-benzenesulfonamide x HCl starting from allyl-[2-(4-amino-phenyl)-ethyl]-carbamic acid *tert*-butyl ester and 4-trifluoromethoxy-benzenesulfonyl chloride.

MS (ESI) m/z : 401.05 $[M+H]^+$

$^1\text{H-NMR}$ (DMSO- d_6): δ [ppm] 10.45 (bs, 1H), 9.01 (bs, 2H), 7.89 (d, 2H), 7.56 (d, 2H), 7.15 (d, 2H), 7.06 (d, 2H), 5.81-5.98 (m, 1H), 5.35-5.49 (m, 2H), 3.52-3.60 (m, 2H), 3.0-3.08 (m, 2H), 2.8-2.9 (m, 2H).

EXAMPLE 17

N-[4-(2-Allylamino-ethyl)-phenyl]-N-methyl-4-trifluoromethoxy-benzenesulfonamide x HCl

The desired product was obtained as a yellow powder following the synthetic procedure described for N-[4-(2-allylamino-ethyl)-phenyl]-4-isopropyl-N-methyl-benzenesulfonamide x HCl starting from Allyl-{2-[4-(4-trifluoromethoxy-benzenesulfonylamino)-phenyl]-ethyl}-carbamic acid *tert*-butyl ester and methyl iodide.

MS (ESI) m/z : 415.15 $[M+H]^+$

$^1\text{H-NMR}$ (DMSO- d_6): δ [ppm] 9.12 (bs, 2H), 7.68 (d, 2H), 7.49 (d, 2H), 7.25 (d, 2H), 7.09 (d, 2H), 5.86-5.98 (m, 1H), 5.38-5.52 (m, 2H), 3.55-3.65 (m, 2H), 3.05-3.19 (m, 5H), 2.90-3.00 (m, 2H).

EXAMPLE 18

N-[4-(2-Allylamino-ethyl)-phenyl]-N-propyl-4-trifluoromethoxy-benzenesulfonamide x HCl

The desired product was obtained as a colorless powder following the synthetic procedure described for N-[4-(2-Allylamino-ethyl)-phenyl]-4-isopropyl-N-methyl-benzenesulfonamide x HCl starting from Allyl-{2-[4-(4-trifluoromethoxy-benzenesulfonylamino)-phenyl]-ethyl}-carbamic acid *tert*-butyl ester and 1-bromopropane.

MS (ESI) m/z : 443.15 $[M+H]^+$

$^1\text{H-NMR}$ (DMSO- d_6): δ [ppm] 9.18 (bs, 2H), 7.70 (d, 2H), 7.59 (d, 2H), 7.26 (d, 2H), 7.05 (d, 2H), 5.87-6.00 (m, 1H), 5.38-5.50 (m, 2H), 3.48-3.65 (m, 4H), 3.08-3.18 (m, 2H), 2.92-3.01 (m, 2H), 1.26-1.35 (m, 2H), 0.82 (t, 3H).

EXAMPLE 19

N-[4-(2-Diallylamino-ethyl)-phenyl]-4-isopropyl-benzenesulfonamide x HCl

19.1 {2-[4-(4-Isopropyl-benzenesulfonylamino)-phenyl]-ethyl}-carbamic acid *tert*-butyl ester

To a solution of [2-(4-amino-phenyl)-ethyl]-carbamic acid *tert*-butyl ester (10.75 g, 45.49 mmol) in pyridine (125 ml) at 0°C 4-Isopropyl-benzenesulfonyl chloride (10.45 g, 47.76 mmol) was added. The mixture was stirred at 0°C for 1 h and 16 h at room temperature. After concentration in vacuo the residue was partitioned between dichloromethane and saturated aqueous NaHCO_3 . The organic layer was washed with water, dried over MgSO_4 , filtered and the solvent evaporated under reduced pressure to give the product as a brown oil (20.82 g, 50%).

19.2 N-[4-(2-Amino-ethyl)-phenyl]-4-isopropyl-benzenesulfonamide x HCl

To a solution of {2-[4-(4-isopropyl-benzenesulfonylamino)-phenyl]-ethyl}-carbamic acid *tert*-butyl ester (20.42 g, 48.79 mmol) in diethylether (200 ml) and THF (80 ml) at 0°C HCl in diethylether (100 ml) was added slowly. The mixture was stirred at room temperature for 16 h. After concentration in vacuo the product was obtained as a yellow foam (17.3 g, 99.9%)

19.3 N-[4-(2-Diallylamino-ethyl)-phenyl]-4-isopropyl-benzenesulfonamide x HCl

A solution of N-[4-(2-Amino-ethyl)-phenyl]-4-isopropyl-benzenesulfonamide x HCl (740 mg, 2.09 mmol), 4Å molecular sieves (750 mg) and cesium hydroxide (1.09 g, 6.27 mmol) in DMF was stirred at room temperature for 1 h before allylbromide (508 mg, 4.2 mmol) was added. The mixture was stirred at room temperature for 16 h. After concentrating the mixture in vacuo the residue was purified by column chromatography (toluene/THF/methanol, 4/1/1 + 2.5% triethylamine). The obtained yellow oil was dissolved in diethylether, and HCl in diethylether (1M) was added. The precipitate was collected and dried in vacuo to give the product as a colorless powder (210 mg, 23%).

MS (ESI) m/z : 399.15 $[M+H]^+$

$^1\text{H-NMR}$ (DMSO- d_6): δ [ppm] 10.39 (s, 1H), 7.69 (d, 2H), 7.41 (d, 2H), 7.04-7.13 (m, 4H), 5.96-6.08 (m, 2H), 5.47-5.59 (m, 4H), 3.71-3.80 (m, 4H), 3.04-3.15 (m, 2H), 2.89-2.99 (m, 3H), 1.19 (d, 6H).

EXAMPLE 20

N-[4-(2-Diallylamino-ethyl)-phenyl]-4-trifluoromethoxy-benzenesulfonamide x HCl

The desired product was obtained as a yellow foam following the synthetic procedure described for N-[4-(2-diallylamino-ethyl)-phenyl]-4-isopropyl-benzenesulfonamide x HCl starting from [2-(4-amino-phenyl)-ethyl]-carbamic acid *tert*-butyl ester and 4-trifluoromethoxy-benzenesulfonyl chloride.

MS (ESI) m/z : 441.15 $[M+H]^+$

$^1\text{H-NMR}$ (DMSO- d_6): δ [ppm] 10.93 (bs, 1H), 10.45 (s, 1H), 7.89 (d, 2H), 7.55 (d, 2H), 7.14 (d, 2H), 7.06 (d, 2H), 5.93-6.09 (m, 2H), 5.46-5.59 (m, 4H), 3.68-3.84 (m, 4H), 3.04-3.17 (m, 2H), 2.90-3.01 (m, 2H).

EXAMPLE 21 (reference)

N-[3-(2-Allylamino-ethyl)-phenyl]-4-isopropyl-benzenesulfonamide

The desired product was obtained as a pink powder following the synthetic procedure described for N-[4-(2-Allylamino-ethyl)-phenyl]-4-isopropyl-benzenesulfonamide x HCl starting from allyl-[2-(3-amino-phenyl)-ethyl]-carbamic acid *tert*-butyl ester and 4-Isopropyl-benzenesulfonyl chloride.

MS (ESI) m/z : 359.15 $[M+H]^+$

¹H-NMR (DMSO-d₆): δ [ppm] 10.30 (s, 1H), 9.09 (bs, 2H), 7.69 (d, 2H), 7.42 (d, 2H), 7.19 (t, 1H), 6.95-7.03 (m, 2H), 6.90 (d, 1H), 5.85-5.98 (m, 1H), 5.38-5.50 (m, 2H), 2.80-3.05 (several m, 5H), 1.19 (d, 6H).

5 EXAMPLE 22

N-[3-(2-Allylamino-ethyl)-phenyl]-4-trifluoromethoxy-benzenesulfonamide

The desired product was obtained as a pink powder following the synthetic procedure described for N-[4-(2-allylamino-ethyl)-phenyl]-4-isopropyl-benzenesulfonamide x HCl
10 starting from allyl-[2-(3-amino-phenyl)-ethyl]-carbamic acid *tert*-butyl ester and 4-trifluoromethoxy-benzenesulfonyl chloride.

MS (ESI) m/z: 401.05 [M+H]⁺

¹H-NMR (DMSO-d₆): δ [ppm] 10.48 (s, 1H), 9.05 (bs, 2H), 7.89 (d, 2H), 7.55 (d, 2H),
15 7.20 (t, 1H), 6.91-7.03 (m, 3H), 5.85-5.98 (m, 1H), 5.38-5.50 (m, 2H), 3.52-3.62 (m, 2H), 2.95-3.05 (m, 2H), 2.82-2.90 (m, 2H).

EXAMPLE 23

Diallyl-{2-[4-(4-isopropyl-benzenesulfonylmethyl)-phenyl]-ethyl}-amine x HCl

20

23.1 2-(4-Bromomethyl-phenyl)-acetamide

To a solution of (4-bromomethyl-phenyl)-acetic acid (9.23 g, 40.30 mmol) and N,N-dimethylformamide (0,5 ml, 6.47 mmol) in toluene (100 ml) thionyl chloride (3.1 ml,
25 42.31 mmol) was added. The mixture was heated at 80°C for 1 h. At 0°C, this mixture was added to a solution of ammonia in water (25%, 200 ml). After stirring for 30 min the precipitate was collected, washed with water and pentane, and dried in a vacuum oven at 50°C to give the product as white crystals (5.8 g, 63%).

30 23.2 2-[4-(4-Isopropyl-benzenesulfonylmethyl)-phenyl]-acetamide

To a solution of 4-(isopropyl)thiophenol (1.91 g, 12.54 mmol) in N,N-dimethylformamide (50 ml) sodium hydride (530 mg, 13.17 mmol) was added. The exothermic reaction was allowed to cool down to room temperature. At 15°C, a solution of 2-(4-
35 bromomethyl-phenyl)-acetamide (2.86 g, 12.54 mmol) in N,N-dimethylformamide (25 ml) was added. After stirring the reaction mixture at room temperature for 16 h, the

mixture was poured into ice-water. The precipitate was collected, washed with water and pentane, and dried in a vacuum oven at 50°C to give the title compound as a white powder (3.46 g, 92%). This powder was used without further purification in the next step.

5

The powder obtained above was dissolved in methanol (100 ml). At 0-5°C a solution of oxone (20.6 g, 33.5 mmol) in water (75 ml) was added. The mixture was stirred at 0°C for 1 h and at room temperature for 16 h. On diluting the mixture with water a white solid was formed, which was collected, washed with water and pentane, and dried in a vacuum oven at 50°C to give 2-[4-(4-isopropyl-benzenesulfonylmethyl)-phenyl]-acetamide as a white powder (3.39 g, 92%).

10

23.3 2-[4-(4-Isopropyl-benzenesulfonylmethyl)-phenyl]-ethylamine x HCl

A solution of 2-[4-(4-isopropyl-benzenesulfonylmethyl)-phenyl]-acetamide (1.37 g, 4.13 mmol) in tetrahydrofuran (30 ml) was refluxed and then a solution of borane-dimethylsulfid complex (2M in tetrahydrofuran, 10.33 mmol) was added. The mixture was refluxed for 2 h. The mixture was allowed to cool down to room temperature and adjusted to pH = 1 with a solution of HCl in ethanol (2M). After stirring the mixture for 15 min the solvents were evaporated under reduce pressure. Diethyl ether was added to residue. A slurry of the resulting white powder in diethyl ether was stirred for 15 min. The remaining solid was collected, washed with diethyl ether, and dried in a vacuum oven to give white crystals of 2-[4-(4-isopropyl-benzenesulfonylmethyl)-phenyl]-ethylamine x HCl (1.36 g, 92.6%).

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MS (ESI) m/z: 318.15 [M+H]⁺

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23.4 Diallyl-{2-[4-(4-isopropyl-benzenesulfonylmethyl)-phenyl]-ethyl}-amine x HCl

To a solution of 2-[4-(4-isopropyl-benzenesulfonylmethyl)-phenyl]-ethylamine x HCl (0.81 g, 2.27 mmol) in N,N-dimethylformamide (30 ml) cesium hydroxide (1.2 g, 6.9 mmol) was added. After the mixture was stirred for 1 h, allylbromide (0.83 g, 6.8 mmol) was added. The mixture was stirred for 16 h. The solvents were evaporated under reduced pressure and the residue was purified by column chromatography (toluene:tetrahydrofuran:methanol, 4:1:1, + 2.5% triethylamine). A solution of HCl in isopropanol (1M) was added to the resulting oil. The precipitate was collected, washed with pentane, and dried in vacuo to give a white powder (0.5 g, 50%).

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MS (ESI) m/z: 398.20 [M+H]⁺

¹H-NMR (DMSO-d₆): δ [ppm] 11.10 (bs, 1H), 7.68 (d, 2H), 7.49 (d, 2H), 7.29 (d, 2H), 7.15 (d, 2H), 5.95-6.12 (m, 2H), 5.47-5.65 (m, 4H), 4.61 (m, 2H), 3.68-3.88 (m, 4H),
5 2.92-3.25 (m, 3H), 1.22 (d, 6H).

EXAMPLE 24

Diallyl-{2-[4-(4-trifluoromethoxy-benzenesulfonylmethyl)-phenyl]-ethyl}-amine x HCl

10 24.1 2-[4-(4-Trifluoromethoxy-benzenesulfonylmethyl)-phenyl]-acetamide

To a solution of 4-(trifluoromethoxy)thiophenol (2.86 g, 12.54 mmol) in N,N-dimethylformamide (50 ml) sodium hydride (530 mg, 13.17 mmol) was added. The exo-
thermic reaction was allowed to cool down to room temperature. At 15°C a solution of
15 2-(4-bromomethyl-phenyl)-acetamide (2.86 g, 12.54 mmol) in N,N-dimethylformamide (25 ml) was added. After stirring the reaction mixture at room temperature for 16 h the mixture was added to ice-water. The precipitate was collected, washed with water and pentane, and dried in a vacuum oven at 50°C to give the product as a yellow powder (3.56 g, 83%).

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The thus obtained powder, which was used without further purification, was dissolved in methanol (200 ml). At room temperature a solution of oxone (18.4 g, 29.9 mmol) in water (75 ml) was added. The mixture was stirred at room temperature for 16 h and additional 3 h at 50°C. Upon diluting the mixture with water a white solid was formed,
25 which was collected, washed with water and pentane, and dried in a vacuum oven at 50°C to give 2-[4-(4-trifluoromethoxy-benzenesulfonylmethyl)-phenyl]-acetamide as a white powder (2.66 g, 71%).

30

24.2 2-[4-(4-Trifluoromethoxy-benzenesulfonylmethyl)-phenyl]-ethylamine x HCl

A solution of 2-[4-(4-trifluoromethoxy-benzenesulfonylmethyl)-phenyl]-acetamide (1.36 g, 3.64 mmol) in tetrahydrofuran (30 ml) was refluxed and a solution of borane-dimethylsulfid complex (2M in tetrahydrofuran, 9.11 mmol) was added. The mixture was refluxed for 2 h. The mixture was allowed to come to room temperature and was
35 adjusted to pH = 1 using a solution of HCl in ethanol (2M). After stirring the mixture for 15 min the solvents were evaporated under reduced pressure. A slurry of the resulting

white powder in diethyl ether was stirred for 15 min. The remaining solid was collected, washed with diethyl ether, and dried in a vacuum oven to give white crystals of 2-[4-(4-trifluoromethoxy-benzenesulfonylmethyl)-phenyl]-ethylamine x HCl (1.22 g, 84.7%).

5 MS (ESI) m/z : 360.05 $[M+H]^+$

24.3 Diallyl-{2-[4-(4-trifluoromethoxy-benzenesulfonylmethyl)-phenyl]-ethyl}-amine x HCl

10 To a solution of 2-[4-(4-trifluoromethoxy-benzenesulfonylmethyl)-phenyl]-ethylamine x HCl (1.14 g, 2.89 mmol) in N,N-dimethylformamide (30 ml) cesium hydroxide (1.5 g, 8.7 mmol) was added. After the mixture was stirred for 1 h, allylbromide (1.05 g, 8.7 mmol) was added. The mixture was stirred for 16 h. The solvents were evaporated in vacuo and the residue was purified by column chromatography (toluene: tetrahydrofuran:methanol, 4:1:1, + 2.5% triethylamine). To the resulting oil a solution of HCl in isopropanol (1M) was added. The precipitate was collected, washed with pentane and dried in vacuo to give a white powder (0.78 g, 56%).

MS (ESI) m/z : 440.15 $[M+H]^+$

20 $^1\text{H-NMR}$ (DMSO- d_6): δ [ppm] 11.40 (bs, 1H), 7.88 (d, 2H), 7.60 (d, 2H), 7.20 (d, 2H), 7.15 (d, 2H), 5.98-6.11 (m, 2H), 5.49-5.65 (m, 4H), 4.71 (m, 2H), 3.70-3.85 (m, 4H), 3.30-3.40 (m, 2H), 3.00-3.22 (m, 4H).

EXAMPLE 25

25 Dipropyl-{2-[4-(4-isopropyl-benzenesulfonylmethyl)-phenyl]-ethyl}-amine x HCl

To a solution of diallyl-{2-[4-(4-isopropyl-benzenesulfonylmethyl)-phenyl]-ethyl}-amine x HCl (90 mg, 0.21 mmol) in ethanol (25 ml) a suspension of palladium on charcoal (10%, 100 mg) in ethanol was added. The mixture was hydrogenated at atmospheric pressure. After filtration and removal of the solvents in vacuo the resulting oil was triturated with diethyl ether. The precipitate was collected, washed with diethyl ether and dried in vacuo to give the product as a yellow foam (30 mg, 36.2%).

MS (ESI) m/z : 402.25 $[M+H]^+$

¹H-NMR (DMSO-d₆): δ [ppm] 10.30 (bs, 1H), 7.67 (d, 2H), 7.49 (d, 2H), 7.25 (d, 2H), 7.15 (d, 2H), 4.61 (m, 2H), 3.15-3.29 (m, 2H), 2.92-3.15 (m, 7H), 1.6-1.8 (m, 4H), 1.23 (d, 6H), 0.92 (t, 6H).

5 EXAMPLE 26

Dipropyl-{2-[4-(4-trifluoromethoxy-benzenesulfonylmethyl)-phenyl]-ethyl}-dipropyl-amine x HCl

To a solution of diallyl-{2-[4-(4-trifluoromethoxy-benzenesulfonylmethyl)-phenyl]-ethyl}-amine x HCl (160 mg, 0.34 mmol) in ethanol (25 ml) a suspension of palladium on charcoal (10%, 150 mg) in ethanol was added. The mixture was hydrogenated at atmospheric pressure. After filtration and removal of the solvents in vacuo the resulting oil was triturated with diethyl ether. The precipitate was collected, washed with diethyl ether and dried in vacuo to give the product as a colourless powder (120 mg, 70%).

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MS (ESI) m/z:444.15 [M+H]⁺

¹H-NMR (DMSO-d₆): δ [ppm] 10.30 (bs, 1H), 7.89 (d, 2H), 7.59 (d, 2H), 7.25 (d, 2H), 7.13 (d, 2H), 4.71 (m, 2H), 3.15-3.29 (m, 2H), 2.98-3.15 (m, 6H), 1.61-1.78 (m, 4H), 0.92 (t, 6H).

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EXAMPLE 27

Allyl-{2-[4-(4-isopropyl-benzenesulfonylmethyl)-phenyl]-ethyl}-amine x HCl

2-[4-(4-Isopropyl-benzenesulfonylmethyl)-phenyl]-ethylamine x HCl (0.81 g, 2.27 mmol) was dissolved in a solution of sodium hydroxide in methanol (1M, 2.27 mmol), the methanol was removed and N,N-dimethylformamide (20 ml) was added. To a solution of the resulting 2-[4-(4-isopropyl-benzenesulfonylmethyl)-phenyl]-ethylamine in N,N-dimethylformamide activated 4Å molecular sieves (700 mg) and cesium hydroxide (40 mg, 0.228 mmol) were added. The mixture was stirred at room temperature for 1 h. After addition of allylbromide (0.82 g, 6.81 mmol) the mixture was stirred at room temperature for 16 h. The solvents were evaporated in vacuo and the residue was purified by column chromatography (toluene:tetrahydrofuran:methanol, 4:1:1, + 2.5% triethylamine). To the resulting oil a solution of HCl in isopropanol (1M) was added. The precipitate was collected, washed with pentane, and dried in vacuo to give a white powder (0.14 g, 15%).

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MS (ESI) m/z : 358.15 $[M+H]^+$

$^1\text{H-NMR}$ (DMSO-d_6): δ [ppm] 9.01-9.20 (m, 1H), 7.68 (d, 2H), 7.49 (d, 2H), 7.19 (d, 2H), 7.12 (d, 2H), 5.85-5.99 (m, 1H), 5.39-5.52 (m, 2H), 4.60 (s, 2H), 3.55-3.65 (m, 2H), 2.90-3.15 (m, 5H), 1.22 (d, 6H).

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EXAMPLE 28

{2-[4-(4-Isopropyl-benzenesulfonylmethyl)-phenyl]-ethyl}-propyl-amine x HCl

28.1 [4-(4-Isopropyl-phenylsulfanylmethyl)-phenyl]-acetic acid

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To a solution of 4-(isopropyl)thiophenol (10 g, 65.68 mmol) in N,N-dimethylformamide (200 ml) sodium hydride (3.15 g, 131.35 mmol) was added. The exothermic reaction was allowed to cool down to room temperature. At 15°C a solution of (4-bromomethyl-phenyl)-acetic acid (15.04 g, 65.68 mmol) in N,N-dimethylformamide (100 ml) was added. After stirring the reaction mixture at room temperature for 16 h the mixture was concentrated, diluted with water, and adjusted to pH = 2 by adding HCl (2N). The aqueous phase was extracted three times with ethyl acetate. The combined organic layers were dried over MgSO_4 , filtered, and the solvent evaporated under reduced pressure to give the product as a yellow oil (19.5 g, 99%).

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MS (ESI) m/z : 301.15 $[M+H]^+$

28.2 [4-(4-Isopropyl-benzenesulfonylmethyl)-phenyl]-acetic acid

A solution of [4-(4-isopropyl-phenylsulfanylmethyl)-phenyl]-acetic acid (20.3 g, 67.57 mmol) in acetic acid (100 ml) was heated to 70°C and hydrogen peroxide (24.5 g, 216.23 mmol) was added over a period of 10 min. The mixture was stirred at 70°C for 2 h. The mixture was poured into ice-water and the precipitate was filtered, washed with diisopropyl ether and dried in vacuo to give the product as a colorless powder (19.9 g, 89%).

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28.3 2-[4-(4-Isopropyl-benzenesulfonylmethyl)-phenyl]-N-propyl-acetamide

To a solution of [4-(4-isopropyl-benzenesulfonylmethyl)-phenyl]-acetic acid (1 g, 3.00 mmol) in pyridine (15 ml)/N,N-dimethylformamide (15 ml) N,N'-carbonyldiimidazole (0.54 g, 3.31 mmol) was added and the mixture heated to 50°C for 1 h. At 0°C pro-

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pylamine was added. The mixture was stirred at room temperature for 16 h. Then, the mixture was poured into water. The precipitate was collected and dried in a vacuum oven at 70°C to give the product as a yellow powder (0.89 g, 2.39 mmol).

5 MS (ESI) m/z : 374.15 $[M+H]^+$

28.4 {2-[4-(4-Isopropyl-benzenesulfonylmethyl)-phenyl]-ethyl}-propyl-amine

To a solution of 2-[4-(4-isopropyl-benzenesulfonylmethyl)-phenyl]-N-propylacetamide
 10 (500 mg, 1.34 mmol) in tetrahydrofuran (30 ml) borane-tetrahydrofuran complex (2M in tetrahydrofuran, 6.70 mmol) was added at 0°C. The mixture was stirred at room temperature for 16 h after which a solution of HCl in ethanol (1M) was added and the mixture was stirred for 2 h. The mixture was concentrated in vacuo, diluted with water, and
 15 adjusted to pH = 10 by adding aqueous NaOH. The aqueous phase was extracted three times with ethyl acetate. The combined organic layers were dried over $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure. The residue was purified by preparative HPLC (water/methanol/0.1% acetic acid) to give the product as a colorless powder (130 mg, 27%).

20 MS (ESI) m/z : 360.25 $[M+H]^+$

^1H -NMR ($DMSO-d_6$): δ [ppm] 7.68 (d, 2H), 7.49 (d, 2H), 7.19 (d, 2H), 7.12 (d, 2H), 4.59 (m, 2H), 2.83-3.10 (m, 5H), 2.68-2.82 (m, 2H), 1.52-1.68 (m, 2H), 1.22 (d, 6H), 0.90 (t, 6H).

III. Examples of galenic administration forms

30 A) Tablets

Tablets of the following composition are pressed on a tablet press in the customary manner:

35	40 mg	of substance from Example 8
	120 mg	of corn starch
	13.5 mg	of gelatin
	45 mg	of lactose

M/45293

2.25 mg of Aerosil® (chemically pure silicic acid in submicroscopically fine dispersion)
6.75 mg of potato starch (as a 6% paste)

B) Sugar-coated tablets

5

20 mg of substance from Example 8
60 mg of core composition
70 mg of saccharification composition

- 10 The core composition consists of 9 parts of corn starch, 3 parts of lactose and 1 part of 60:40 vinylpyrrolidone/vinyl acetate copolymer. The saccharification composition consists of 5 parts of cane sugar, 2 parts of corn starch, 2 parts of calcium carbonate and 1 part of talc. The sugar-coated tablets which had been prepared in this way are subsequently provided with a gastric juice-resistant coating.

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IV. Biological investigations

Receptor binding studies:

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The substance to be tested was either dissolved in methanol/Chremophor® (BASF-AG) or in dimethyl sulfoxide and then diluted with water to the desired concentration.

Dopamine D₃ receptor:

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The assay mixture (0.250 ml) was composed of membranes derived from ~ 10⁶ HEK-293 cells possessing stably expressed human dopamine D₃ receptors, 0.1 nM [¹²⁵I]-iodosulpride and incubation buffer (total binding) or, in addition, test substance (inhibition curve) or 1 μM spiperone (nonspecific binding). Each assay mixture was run in triplicate.

30

The incubation buffer contained 50 mM tris, 120 mM NaCl, 5 mM KCl, 2 mM CaCl₂, 2 mM MgCl₂ and 0.1% bovine serum albumin, 10 μM quinolone and 0.1% ascorbic acid (prepared fresh daily). The buffer was adjusted to pH 7.4 with HCl.

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Dopamine D_{2L} receptor:

The assay mixture (1 ml) was composed of membranes from $\sim 10^6$ HEK-293 cells possessing stably expressed human dopamine D_{2L} receptors (long isoform) and 0.01 nM [^{125} I] idospiperone and incubation buffer (total binding) or, in addition, test substance (inhibition curve) or 1 μ M haloperidol (nonspecific binding). Each assay mixture was run in triplicate.

The incubation buffer contained 50 mM tris, 120 mM NaCl, 5 mM KCl, 2 mM $CaCl_2$, 2 mM $MgCl_2$ and 0.1% bovine serum albumin. The buffer was adjusted to pH 7.4 with HCl.

Measurement and analysis:

After having been incubated at 25°C for 60 minutes, the assay mixtures were filtered through a Whatman GF/B glass fiber filter under vacuum using a cell collecting device. The filters were transferred to scintillation vials using a filter transfer system. After 4 ml of Ultima Gold[®] (Packard) have been added, the samples were shaken for one hour and the radioactivity was then counted in a Beta-Counter (Packard, Tricarb 2000 or 2200CA). The cpm values were converted into dpm using a standard quench series and the program belonging to the instrument.

The inhibition curves were analyzed by means of iterative nonlinear regression analysis using the Statistical Analysis System (SAS) which is similar to the "LIGAND" program described by Munson and Rodbard.

The results of the receptro binding studies are expressed as receptor binding constants $K_i(D_2)$ and $K_i(D_3)$, respectively, as herein before described, and given in table 3.

In these tests, the compounds according to the invention exhibit very good affinities for the D_3 receptor (< 10 nM, frequently < 5 nM) and bind selectively to the D_3 receptor.

The results of the binding tests are given in table 3.

Table 3:

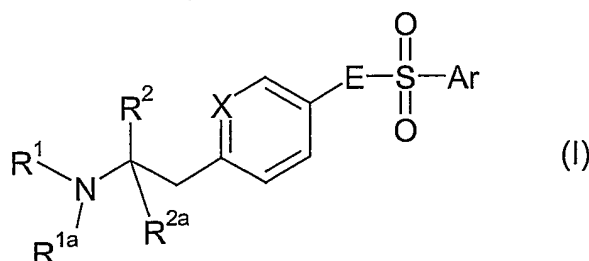
M/45293

Example	$K_i(\text{D3})^*$ [nM]	$K_i(\text{D2})^*/K_i(\text{D3})^*$
1	43	41
2	21	57
3	2.8	33
6	2.2	22
7	18	23
8	0.2	54
9	2	40
10	42	53
11	0.58	16
13	1.7	74
14	27	40
15	22	22
16	31	79
17	34	75
18	37	24
19	2.7	42
20	64	65
21 ref.	22	62
23	8.4	59
25	0.5	175
26	3.9	170
28	4.8	130

* Receptor binding constants obtained according to the assays described herein before

We claim:

1. An aminoethylaromatic compound of the formula I



wherein

Ar is phenyl or an aromatic 5- or 6-membered C-bound heteroaromatic radical, wherein Ar may carry 1 radical R^a and wherein Ar may also carry 1 or 2 radicals R^b;

R^a being selected from the group consisting of C₁-C₆-alkyl, C₂-C₆-alkenyl, fluorinated C₂-C₆-alkenyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, fluorinated C₁-C₆-alkyl, fluorinated C₃-C₆-cycloalkyl, fluorinated C₁-C₆-alkoxy, C₁-C₆-hydroxyalkyl, C₁-C₆-alkoxy-C₁-C₄-alkyl, C₁-C₆-hydroxyalkoxy, C₁-C₆-alkoxy-C₁-C₄-alkoxy, COOH, NR⁴R⁵, CH₂NR⁴R⁵, ONR⁴R⁵, NHC(O)NR⁴R⁵, C(O)NR⁴R⁵, SO₂NR⁴R⁵, C₁-C₆-alkylcarbonyl, fluorinated C₁-C₆-alkylcarbonyl, C₁-C₆-alkylcarbonylamino, fluorinated C₁-C₆-alkylcarbonylamino, C₁-C₆-alkylcarbonyloxy, fluorinated C₁-C₆-alkylcarbonyloxy, C₁-C₆-alkoxycarbonyl, C₁-C₆-alkylthio, fluorinated C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, fluorinated C₁-C₆-alkylsulfinyl, fluorinated C₁-C₆-alkylsulfonyl, phenylsulfonyl, phenyl, phenoxy, benzyloxy and a 3- to 7-membered heterocyclic radical, wherein the five last mentioned radicals may carry 1, 2, 3 or 4 radicals selected from halogen, cyano, OH, oxo, CN, and the radicals R^a,

R^b being, independently from each other, selected from halogen, cyano, nitro, OH, methyl, methoxy, fluoromethyl, difluoromethyl, trifluoromethyl, fluormethoxy, difluoromethoxy and trifluoromethoxy,

the radical R^a and one radical R^b, if present and bound to two adjacent carbon atoms of phenyl, may form a 5- or 6-membered heterocyclic or carbocyclic ring which is fused to the phenyl ring and which is unsubstituted or which may carry 1, 2 or 3 radicals selected from halogen, NO₂, NH₂, OH, CN, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, fluorinated C₁-C₆-alkyl, fluorinated C₃-C₆-cycloalkyl, fluorinated C₁-C₆-alkoxy, C₁-C₆-hydroxyalkyl, C₁-C₄-alkoxy-C₂-C₄-alkyl, C₁-C₆-hydroxyalkoxy, C₁-C₄-alkoxy-C₂-C₄-alkoxy, C₁-C₆-alkylcarbonyl, C₁-C₆-alkylamino, di-C₁-C₆-alkylamino, C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, fluorinated C₁-C₆-

alkylcarbonyl, C₁-C₆-alkylcarbonylamino, fluorinated C₁-C₆-alkylcarbonylamino, C₁-C₆-alkylcarbonyloxy, fluorinated C₁-C₆-alkylcarbonyloxy, C₁-C₆-alkoxycarbonyl, C₁-C₆-alkylthio, fluorinated C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, fluorinated C₁-C₆-alkylsulfinyl and fluorinated C₁-C₆-alkylsulfonyl,

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X is N or CH;

E is CR⁶R⁷ or NR³;

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R¹ is C₁-C₄-alkyl, C₃-C₄-cycloalkyl, C₃-C₄-cycloalkylmethyl, C₃-C₄-alkenyl, fluorinated C₁-C₄-alkyl, fluorinated C₃-C₄-cycloalkyl, fluorinated C₃-C₄-cycloalkylmethyl, fluorinated C₃-C₄-alkenyl, formyl or C₁-C₃-alkylcarbonyl;

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R^{1a} is H, C₁-C₄-alkyl, C₃-C₄-cycloalkyl, C₃-C₄-cycloalkylmethyl, C₃-C₄-alkenyl, fluorinated C₁-C₄-alkyl, fluorinated C₃-C₄-cycloalkyl, fluorinated C₃-C₄-cycloalkylmethyl, fluorinated C₃-C₄-alkenyl, or R^{1a} and R² together are (CH₂)_n with n being 2, 3 or 4, or R^{1a} and R^{2a} together are (CH₂)_n with n being 2, 3 or 4;

20

R², R^{2a} are independently of each other H, C₁-C₄-alkyl or fluorinated C₁-C₄-alkyl or R^{2a} and R² together are (CH₂)_m with m being 1, 2, 3, 4 or 5;

R³ is H or C₁-C₄-alkyl;

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R⁴, R⁵ independently of each other are selected from H, C₁-C₃-alkyl, C₁-C₃-alkoxy and fluorinated C₁-C₃-alkyl;

R⁶, R⁷ independently of each other are selected from H, fluorine, C₁-C₄-alkyl and fluorinated C₁-C₄-alkyl or together form a moiety (CH₂)_p with p being 2, 3, 4 or 5;

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provided that for R¹ being C₁-C₄-alkyl, R² = R^{2a} being H, E being NH, X being CH and Ar = substituted phenyl Ar carries at least one substituent R^a which is different from linear C₁-C₃-alkyl, OCH₃, OCF₃, CF₃, SCH₃ or NHC(O)CH₃.

and the physiologically tolerated acid addition salts of these compounds.

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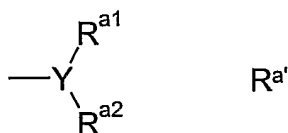
2. The compounds as claimed in claim 1, wherein Ar is phenyl or an aromatic 5- or 6-membered C-bound heteroaromatic radical, comprising 1 nitrogen atom as ring member and 0, 1, 2 or 3 further heteroatoms, independently of each other, selected from O, S and N, as ring members, wherein Ar carries one radical R^a which is selected from the group consisting of C₂-C₆-alkyl, C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, fluorinated C₁-C₆-alkyl, fluorinated C₃-C₆-cycloalkyl, fluorinated C₁-C₆-alkoxy, NR⁴R⁵, 1-aziridinyl, azetidin-1-yl, pyrrolidin-1-yl or piperidin-1-yl, wherein the last four mentioned radicals may be fluorinated,

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a phenyl group and an aromatic 5- or 6-membered C-bound heteroaromatic radical, comprising 1 nitrogen atom as ring member and 0, 1, 2 or 3 further heteroatoms, independently of each other, selected from O, S and N, wherein the last two mentioned radicals may carry 1, 2, 3 or 4 radicals selected from halogen and the radicals R^a ; and wherein Ar may carry 1 or 2 further radicals R^b , which are independently from each other selected from halogen, cyano, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, difluoromethoxy and trifluoromethoxy; and wherein R^4 , R^5 , independently of each other are selected from H, C_1 - C_3 -alkyl and fluorinated C_1 - C_3 -alkyl,

provided that for $R^2 = R^{2a} = H$, $E = NH$, $X = CH$ and Ar = substituted phenyl Ar carries at least one substituent R^a which is selected from secondary C_3 - C_6 -alkyl, fluorinated C_2 - C_6 -alkyl, fluorinated C_3 - C_6 -cycloalkyl, fluorinated C_2 - C_6 -alkoxy, NR^4R^5 , 1-aziridinyl, azetidin-1-yl, pyrrolidin-1-yl or piperidin-1-yl, wherein the last for mentioned radicals may be fluorinated, a phenyl group and an aromatic 5- or 6-membered C-bound heteroaromatic radical, comprising 1 nitrogen atom as ring member and 0, 1, 2 or 3 further heteroatoms, independently of each other, selected from O, S and N, wherein the last two mentioned radicals may carry 1, 2, 3 or 4 radicals selected from Halogen and the the radicals R^a ;

3. The compounds as claimed in claim 1 or 2, wherein Ar carries one radical R^a of the formula R^a



wherein

Y is N, CH or CF,

R^{a1} and R^{a2} are independently of each other selected from C_1 - C_2 -alkyl, C_1 - C_2 -alkoxy, fluorinated C_1 - C_2 -alkyl, provided for Y being CH or CF one of the radicals R^{a1} or R^{a2} may also be hydrogen or fluorine, or

R^{a1} and R^{a2} together form a radical $(CH_2)_m$ wherein 1 or 2 of the hydrogen atoms may be replaced by fluorine, hydroxy, oxo, C_1 - C_2 -alkyl or C_1 - C_2 -alkoxy, wherein one CH_2 moiety may be replaced by O, S, S=O, SO_2 or $N-R^c$, R^c being hydrogen or C_1 - C_2 -alkyl and wherein m is 2, 3, 4, 5 or 6;

4. The compounds as claimed in claim 3, wherein the radical R^a is selected from isopropyl, (R)-1-fluoroethyl, (S)-1-fluoroethyl, 2-fluoroethyl, 1,1-difluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, (R)-1-fluoropropyl, (S)-1-fluoropropyl, 2-fluoropropyl, 3-fluoropropyl, 1,1-difluoropropyl, 2,2-difluoropropyl, 3,3-difluoropropyl, 3,3,3-trifluoropropyl, (R)-2-fluoro-1-methylethyl, (S)-2-fluoro-1-methylethyl, (R)-2,2-difluoro-1-methylethyl, (S)-2,2-difluoro-1-methylethyl, (R)-1,2-difluoro-1-methylethyl, (S)-1,2-difluoro-1-methylethyl, (R)-2,2,2-trifluoro-1-methylethyl, (S)-2,2,2-trifluoro-1-methylethyl, 2-fluoro-1-(fluoromethyl)ethyl, 1-

(difluoromethyl)-2,2-difluoroethyl, cyclopropyl, cyclobutyl, 1-fluorocyclopropyl, and 2-fluorocyclopropyl.

5. The compounds as claimed in claim 3, wherein the radical R^a is selected from 4-morpholinyl, 4-thiomorpholinyl, 4-(1,1-dioxo)thiomorpholinyl, piperazin-1-yl, 4-methylpiperazin-1-yl, azetidin-1-yl, 2-methylazetidin-1-yl, (S)-2-methylazetidin-1-yl, (R)-2-methylazetidin-1-yl, 3-fluoroazetidin-1-yl, 3-methoxyazetidin-1-yl, 3-hydroxyazetidin-1-yl, pyrrolidin-1-yl, pyrrolidin-2-yl, (S)-pyrrolidin-2-yl, (R)-pyrrolidin-2-yl, pyrrolidin-3-yl, (S)-pyrrolidin-3-yl, (R)-pyrrolidin-3-yl, 2-fluoropyrrolidin-1-yl, (S)-2-fluoropyrrolidin-1-yl, (R)-2-fluoropyrrolidin-1-yl, 3-fluoropyrrolidin-1-yl, (S)-3-fluoropyrrolidin-1-yl, (R)-3-fluoropyrrolidin-1-yl, 2,2-difluoropyrrolidin-1-yl, 3,3-difluoropyrrolidin-1-yl, 2-methylpyrrolidin-1-yl, (S)-2-methylpyrrolidin-1-yl, (R)-2-methylpyrrolidin-1-yl, 3-methylpyrrolidin-1-yl, (S)-3-methylpyrrolidin-1-yl, (R)-3-methylpyrrolidin-1-yl, 1-methylpyrrolidin-2-yl, (S)-1-methylpyrrolidin-2-yl, (R)-1-methylpyrrolidin-2-yl, 1-methylpyrrolidin-3-yl, (S)-1-methylpyrrolidin-3-yl, (R)-1-methylpyrrolidin-3-yl, 2,2-dimethylpyrrolidin-1-yl, 3,3-dimethylpyrrolidin-1-yl, 2-trifluoromethylpyrrolidin-1-yl, (S)-2-trifluoromethylpyrrolidin-1-yl, (R)-2-trifluoromethylpyrrolidin-1-yl, 3-trifluoromethylpyrrolidin-1-yl, (S)-3-trifluoromethylpyrrolidin-1-yl, (R)-3-trifluoromethylpyrrolidin-1-yl, 2-oxopyrrolidin-1-yl, 2-oxo-oxazolidin-3-yl, piperidin-1-yl, 2-methylpiperidin-1-yl, (S)-2-methylpiperidin-1-yl and (R)-2-methylpiperidin-1-yl.
6. The compounds as claimed in any of the claims 2 or 3, wherein the radical R^a carries 1, 2, 3 or 4 fluorine atoms.
7. The compounds as claimed in claim 1, wherein Ar carries one radical R^a , which is selected from CHF_2 , CH_2F , OCHF_2 and OCH_2F .
8. The compounds as claimed in claim 1, wherein Ar carries one radical R^a , which is selected from 5- or 6-membered heteroaromatic radicals having as ring members 1 heteroatom selected from O, S and N and which may further have 1, 2 or 3 nitrogen atoms as ring members, and wherein the 5- or 6-membered heteroaromatic radical may carry 1, 2 or 3 substituents selected from halogen, NO_2 , NH_2 , OH, CN, $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_3\text{-C}_6\text{-cycloalkyl}$, $\text{C}_1\text{-C}_6\text{-alkoxy}$, fluorinated $\text{C}_1\text{-C}_6\text{-alkyl}$, fluorinated $\text{C}_3\text{-C}_6\text{-cycloalkyl}$, fluorinated $\text{C}_1\text{-C}_6\text{-alkoxy}$, $\text{C}_1\text{-C}_6\text{-hydroxyalkyl}$, $\text{C}_1\text{-C}_4\text{-alkoxy-C}_2\text{-C}_4\text{-alkyl}$, $\text{C}_1\text{-C}_6\text{-hydroxyalkoxy}$, $\text{C}_1\text{-C}_4\text{-alkoxy-C}_2\text{-C}_4\text{-alkoxy}$, $\text{C}_1\text{-C}_6\text{-alkylcarbonyl}$, $\text{C}_1\text{-C}_6\text{-alkylamino}$, di- $\text{C}_1\text{-C}_6\text{-alkylamino}$, $\text{C}_1\text{-C}_6\text{-alkylaminocarbonyl}$, di- $\text{C}_1\text{-C}_6\text{-alkylaminocarbonyl}$, fluorinated $\text{C}_1\text{-C}_6\text{-alkylcarbonyl}$, $\text{C}_1\text{-C}_6\text{-alkylcarbonylamino}$, fluorinated $\text{C}_1\text{-C}_6\text{-alkylcarbonylamino}$, $\text{C}_1\text{-C}_6\text{-alkylcarbonyloxy}$, fluorinated $\text{C}_1\text{-C}_6\text{-alkylcarbonyloxy}$, $\text{C}_1\text{-C}_6\text{-alkoxycarbonyl}$, $\text{C}_1\text{-C}_6\text{-alkylthio}$, fluorinated $\text{C}_1\text{-C}_6\text{-alkylthio}$, $\text{C}_1\text{-C}_6\text{-alkylsulfinyl}$, $\text{C}_1\text{-C}_6\text{-alkylsulfonyl}$, fluorinated $\text{C}_1\text{-C}_6\text{-alkylsulfinyl}$ and fluorinated $\text{C}_1\text{-C}_6\text{-alkylsulfonyl}$.

9. The compounds as claimed in claim 8, wherein Ar carries one heteroaromatic radical R^a, which is selected from furanyl, thienyl, pyrrolyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, 1,3,4-thiadiazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl and tetrazolyl, where the heteroaromatic radical may be unsubstituted or may carry 1 to 3 substituents selected from halogen, C₁-C₄-alkyl, C₁-C₄-alkoxy, fluorinated C₁-C₄-alkyl and fluorinated C₁-C₄-alkoxy.
10. The compounds as claimed in any of the preceding claims, wherein Ar is phenyl.
11. The compounds as claimed in any of the preceding claims, wherein Ar is phenyl that carries a radical R^a in the 4-position of the phenyl ring.
12. The compound as claimed in any of the preceding claims, wherein X is CH.
13. The compound as claimed in any of claims 1 to 11, wherein X is N.
14. The compound as claimed in any of the preceding claims, wherein R¹ is n-propyl, fluorinated C₂-C₃-alkyl or 1-propen-3-yl
15. The compound as claimed in any of the preceding claims, wherein R^{1a} is hydrogen.
16. The compound as claimed in any of the preceding claims, wherein R^{2a} is hydrogen.
17. The compound as claimed in claim 16, wherein both R^{2a} and R² are hydrogen.
18. The compound as claimed in any of claims 1 to 15, wherein one of the radicals R^{2a} and R² is hydrogen while the other is methyl.
19. The compound as claimed in any of claims 1 to 8, wherein R^{1a} is n-propyl or 1-propen-3-yl.
20. The compound as claimed in any of claims 1 to 14, wherein R² is hydrogen and R^{2a} and R^{1a} together are (CH₂)_n with n being 3 or 4.
21. A pharmaceutical composition comprising at least one compound of the formula I or a pharmaceutically acceptable salt thereof as claimed in any of the preceding claims, optionally together with at least one physiologically acceptable carrier or auxiliary substance.
22. A method for treating a medical disorder susceptible to treatment with a dopamine D3 receptor ligand, said method comprising administering an effective amount of at least one compound of the formula I or a pharmaceutically acceptable salt thereof as claimed

in any of the preceding claims to a subject in need thereof.

23. The method as claimed in claim 22, wherein the medical disorder is a disease of the central nervous system.

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24. The use of a compound of the formula I or a pharmaceutically acceptable salt thereof as claimed in any of the preceding claims for preparing a pharmaceutical composition for the treatment of a medical disorder susceptible to treatment with a dopamine D3 receptor ligand.

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25. The use as claimed in claim 24, wherein the medical disorder is a disease of the central nervous system.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2005/011092

A. CLASSIFICATION OF SUBJECT MATTER

C07C311/29 C07C311/21 C07D213/76 C07D207/09 C07C317/22
C07C317/14 A61K31/18 A61K31/44 A61P25/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07C C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99/58499 A (PHARMACIA & UPJOHN COMPANY; ROMERO, ARTHUR, GLENN; LEIBY, JEFFREY, A) 18 November 1999 (1999-11-18) cited in the application page 1, line 31 - page 2, line 2; claims 1,8; compounds 3,6-11,14,15 page 2, line 25 - line 27 -----	1-4,6,7, 10-12, 14-19, 21-25
A	WO 03/095428 A (GLAXO GROUP LIMITED; GRIBBLE, ANDREW, DERRICK; FORBES, IAN, THOMSON; L) 20 November 2003 (2003-11-20) page 18, line 6 - line 7; claim 1 -----	1-25



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

4 January 2006

Date of mailing of the international search report

17/01/2006

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Johnson, C

INTERNATIONAL SEARCH REPORT

national application No.
PCT/EP2005/011092

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 22-23 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2005/011092

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