

HETEROCYCLIC ARYLSULPHONES SUITABLE FOR TREATING DISORDERS THAT RESPOND TO MODULATION OF THE SEROTONIN 5HT₆ RECEPTORBackground Of The Invention

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The present invention relates to novel heterocyclic compounds. The compounds possess valuable therapeutic properties and are suitable, in particular, for treating diseases that respond to modulation of the serotonin 5-HT₆ receptor.

- 10 Serotonin (5-hydroxytryptamine, 5HT), a monoamine neurotransmitter and local hormone, is formed by the hydroxylation and decarboxylation of tryptophan. The greatest concentration is found in the enterochromaffin cells of the gastrointestinal tract, the remainder being predominantly present in platelets and in the Central Nervous System (CNS). 5HT is implicated in a vast array of physiological and pathophysiological pathways.
- 15 In the periphery, it contracts a number of smooth muscles and induces endothelium-dependent vasodilation. In the CNS, it is believed to be involved in a wide range of functions, including the control of appetite, mood, anxiety, hallucinations, sleep, vomiting and pain perception.
- 20 Neurons that secrete 5HT are termed serotonergic. The function of 5HT is exerted upon its interaction with specific (serotonergic) neurons. Until now, seven types of 5HT receptors have been identified: 5HT₁ (with subtypes 5HT_{1A}, 5HT_{1B}, 5HT_{1D}, 5HT_{1E} and 5HT_{1F}), 5HT₂ (with subtypes 5HT_{2A}, 5HT_{2B} and 5HT_{2C}), 5HT₃, 5HT₄, 5HT₅ (with subtypes 5HT_{5A} and 5HT_{5B}), 5HT₆ and 5HT₇. Most of these receptors are coupled to G-
- 25 proteins that affect the activities of either adenylate cyclase or phospholipase C γ .

The human 5HT₆ receptors are positively coupled to adenylyl cyclase. They are distributed throughout the limbic, striatal and cortical regions of the brain and show a high affinity to antipsychotics.

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- The modulation of the 5HT₆ receptor by suitable substances is expected to improve certain disorders including cognitive dysfunctions, such as a deficit in memory, cognition and learning, in particular associated with Alzheimer's disease, age-related cognitive decline and mild cognitive impairment, attention deficit disorder/hyperactivity syndrome, personality disorders, such as schizophrenia, in particular cognitive deficits related with schizophrenia, affective disorders such as depression, anxiety and obsessive compulsive disorders, motion or motor disorders such as Parkinson's disease and epilepsy, migraine, sleep disorders (including disturbances of the Circadian rhythm), feeding disorders, such as anorexia and bulimia, certain gastrointestinal disorders such as
- 35 Irritable Bowel Syndrome, diseases associated with neurodegeneration, such as stroke,
- 40

spinal or head trauma and head injuries, such as hydrocephalus, drug addiction and obesity.

5 Another neurotransmitter with implications on the CNS is dopamine. Disorders in the dopaminergic transmitter system result in diseases of the central nervous system which include, for example, schizophrenia, depression and Parkinson's disease. These diseases, and others, are treated with drugs which interact with the dopamine receptors.

10 The dopamine receptors are 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 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 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)).

25 Compounds having an affinity for the dopamine D₃ receptor have been described in the prior art on various occasions, e.g. in WO 95/04713, WO 96/23760, WO 97/45503, WO 99/58499 and in the unpublished international patent application PCT/EP 2005/011106.

30 Compounds having an affinity for the 5HT₆ receptor have also been described in the prior art, e.g. in WO 2005/037830, WO 2005/026125, WO 00/05225 and WO 98/27081. However, their affinity and selectivity towards the 5HT₆ receptor or their pharmacological profile is not yet satisfactory.

35 It is an object of the present invention to provide compounds which have a high affinity and selectivity for the 5HT₆ receptor and optionally a high affinity and selectivity (in particular versus D₂) for the dopamine D₃ receptor, thus allowing the treatment of disorders related to or affected by the 5HT₆ receptor. Compounds having an affinity for both receptors are expected to be suitable for treating disorders related to or affected by both the 5HT₆ receptor and the D₃ receptor, thus allowing the treatment of more than one aspect of the respective disorder.

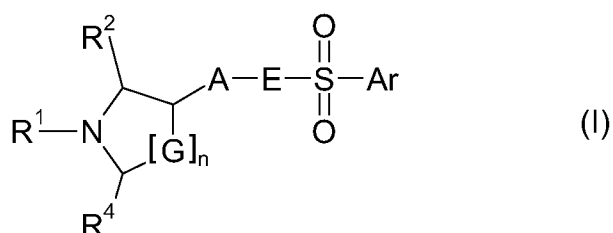
The compounds should also have good pharmacological profile, e.g. a good brain plasma ratio, a good bioavailability, good metabolic stability, or a decreased inhibition of the mitochondrial respiration.

5 Summary Of The Invention

The invention is based on the object of providing compounds which act as 5HT₆ receptor ligands. This object is surprisingly achieved by means of compounds of the formula

I

10



wherein

15 n is 0, 1 or 2;

 G is CH₂ or CHR³;

20 R¹ is H, C₁-C₆-alkyl, C₁-C₆-alkyl substituted by C₃-C₆-cycloalkyl, C₁-C₆-hydroxyalkyl, fluorinated C₁-C₆-alkyl, C₃-C₆-cycloalkyl, fluorinated C₃-C₆-cycloalkyl, C₃-C₆-alkenyl, fluorinated C₃-C₆-alkenyl, formyl, acetyl, propionyl or benzyl;

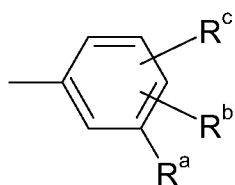
 R², R³ and R⁴ are, independently of each other, H, methyl, fluoromethyl, difluoromethyl, or trifluoromethyl;

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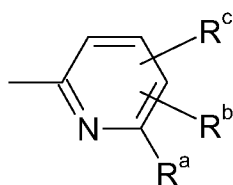
 A is 1,4-phenylene or 1,3-phenylene, which is optionally substituted by one, two, three or four substituents selected from halogen, C₁-C₄-alkyl, C₁-C₄-alkoxy, fluorinated C₁-C₄-alkyl and fluorinated C₁-C₄-alkoxy;

30 E is NR⁵ or CH₂, wherein R⁵ is H or C₁-C₃-alkyl;

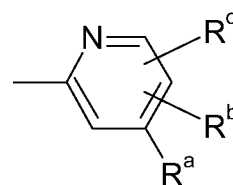
 Ar is a radical of the formula A, B, C, D, E, F or G



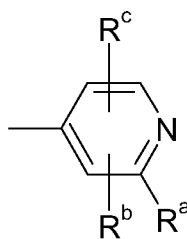
(A)



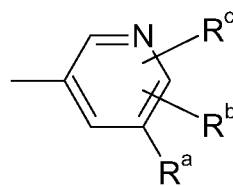
(B)



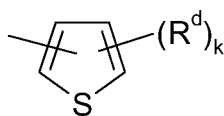
(C)



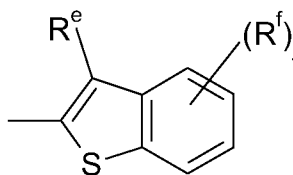
(D)



(E)



(F)



(G)

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wherein

R^a is halogen, hydroxyl, C_1 - C_6 -alkyl, fluorinated C_1 - C_6 -alkyl, C_1 - C_6 -hydroxyalkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, fluorinated C_2 - C_6 -alkenyl, C_3 - C_6 -cycloalkyl, fluorinated C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkoxy, C_1 - C_6 -hydroxyalkoxy, C_1 - C_6 -alkoxy- C_1 - C_6 -alkoxy, fluorinated C_1 - C_6 -alkoxy, C_1 - C_6 -alkylthio, fluorinated C_1 - C_6 -alkylthio, C_1 - C_6 -alkylsulfinyl, fluorinated C_1 - C_6 -alkylsulfinyl, C_1 - C_6 -alkylsulfonyl, fluorinated C_1 - C_6 -alkylsulfonyl, phenylsulfonyl, pyridylsulfonyl, benzyloxy, phenoxy, phenyl, where the phenyl and the pyridyl radical in the 5 last-mentioned radicals may be unsubstituted or may carry 1 to 3 substituents selected from C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl and halogen, CN, nitro, C_1 - C_6 -alkylcarbonyl, fluorinated C_1 - C_6 -alkylcarbonyl, C_1 - C_6 -alkylcarbonylamino, fluorinated C_1 - C_6 -alkylcarbonylamino, carboxy, $NH-C(O)-NR^6R^7$, NR^6R^7 , $NR^6R^7-C_1$ - C_6 -alkylene, $O-NR^6R^7$, where R^6 and R^7 are, independently of each other, H, C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl or C_1 - C_4 -alkoxy or may form, together with N, a 4-, 5- or 6-membered saturated or unsaturated ring, $R^9-CO-NR^6-C_1$ - C_6 -alkylene, where R^6 is as defined above and R^9

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- is C₁-C₄-alkyl or phenyl, where the phenyl radical may be unsubstituted or may carry 1 to 3 substituents selected from C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl and halogen, CH₂-pyridyl, where the pyridyl radical may be unsubstituted or may carry 1 to 3 substituents selected from C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl and halogen, or is a saturated or unsaturated aromatic or non-aromatic 3- to 7-membered heterocyclic ring comprising as ring members 1, 2, 3 or 4 heteroatoms selected from N, O and S and/or 1, 2 or 3 heteroatom-containing groups selected from NR⁸, where R⁸ is H, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl, C₁-C₄-alkylcarbonyl or fluorinated C₁-C₄-alkylcarbonyl, SO, SO₂ and CO, and where the heterocyclic ring may carry 1, 2 or 3 substituents selected from hydroxy, halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl, C₁-C₆-alkoxy, fluorinated C₁-C₆-alkoxy, C₁-C₆-alkylthio, fluorinated C₁-C₆-alkylthio, NR⁶R⁷-C₁-C₆-alkylene, where R⁶ and R⁷ are as defined above, carboxyl and C₁-C₄-alkyoxycarbonyl;
- 15 R^b and R^c, independently of each other, are H, halogen, CH₃, OCH₃, CH₂F, OCH₂F, CHF₂, OCHF₂, CF₃, OCF₃, CH₂CH₂F, OCH₂CH₂F, CH₂CHF₂, OCH₂CHF₂, CH₂CF₃ or OCH₂CF₃;
- R^d is defined like R^a;
- 20 R^e is H or is defined like R^a;
- R^f is defined like R^a;
- 25 k is 0, 1, 2 or 3; and
- j is 0, 1, 2, 3 or 4;
- with the proviso that R^a is not F, CH₂F, CHF₂, CF₃ or OCF₃ if A is 1,4-phenylene, Ar is a radical of the formula (A) and R^b and R^c are H or halogen;
- 30 except compounds, where R¹ is propyl, G is CH₂, n is 1, A is 1,4-phenylene, E is NH, Ar is a radical of formula (F) and R^d is halogen, C₁-C₆-alkyl, C₂-C₆-alkenyl or a 5-membered heteroaromatic ring;
- 35 and physiologically tolerated acid addition salts thereof.

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

In a specific embodiment of compounds I, Ar is a radical of the formula (A), (B), (C), (D) or (E), where the substituents have the following meanings:

5 R^a is halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl, C₁-C₆-hydroxyalkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₂-C₆-alkenyl, fluorinated C₂-C₆-alkenyl, C₃-C₆-cycloalkyl, fluorinated C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₁-C₆-hydroxyalkoxy, C₁-C₆-alkoxy-C₁-C₆-alkoxy, fluorinated C₁-C₆-alkoxy, C₁-C₆-alkylthio, fluorinated C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, fluorinated C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, fluorinated C₁-C₆-alkylsulfonyl, phenylsulfonyl, benzyloxy, phenoxy, where the phenyl radical in the
10 3 last-mentioned radicals may be unsubstituted or may carry 1 to 3 substituents selected from C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl and halogen, CN, nitro, C₁-C₆-alkylcarbonyl, fluorinated C₁-C₆-alkylcarbonyl, C₁-C₆-alkylcarbonylamino, fluorinated C₁-C₆-alkylcarbonylamino, carboxy, NH-C(O)-NR⁶R⁷, NR⁶R⁷, NR⁶R⁷-C₁-C₆-alkylene, O-NR⁶R⁷, where R⁶ and R⁷ are, independently of each other, H, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl or C₁-C₄-alkoxy or may form, together with N, a 4-, 5-
15 or 6-membered saturated or unsaturated ring, or is a saturated or unsaturated 3- to 7-membered heterocyclic ring comprising as ring members 1, 2, 3 or 4 heteroatoms selected from N, O and S and/or 1, 2 or 3 heteroatom-containing groups selected from NR⁸, where R⁸ is H, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl, C₁-C₄-alkylcarbonyl or fluorinated C₁-C₄-alkylcarbonyl, SO, SO₂ and CO, and
20 where the heterocyclic ring may carry 1, 2 or 3 substituents selected from hydroxy, halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl and C₁-C₆-alkoxy; and

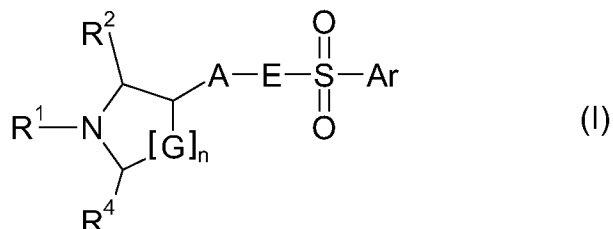
25 R^b and R^c , independently of each other, are H, halogen, CH₃, OCH₃, CHF₂, OCHF₂, CF₃ or OCF₃;

with the proviso that R^a is not F, CH₂F, CHF₂, CF₃ or OCF₃ if A is 1,4-phenylene and R^b and R^c are H or halogen;

30 and physiologically tolerated acid addition salts thereof.

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

The present invention also relates to a method for treating disorders which respond to influencing by 5HT₆ receptor antagonists or 5HT₆ agonists, said method comprising administering an effective amount of at least one compound of the formula I



wherein

n is 0, 1 or 2;

G is CH₂ or CHR³;

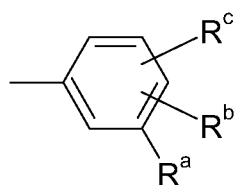
R¹ is H, C₁-C₆-alkyl, C₁-C₆-alkyl substituted by C₃-C₆-cycloalkyl, C₁-C₆-hydroxyalkyl, fluorinated C₁-C₆-alkyl, C₃-C₆-cycloalkyl, fluorinated C₃-C₆-cycloalkyl, C₃-C₆-alkenyl, fluorinated C₃-C₆-alkenyl, formyl, acetyl, propionyl or benzyl;

R², R³ and R⁴ are, independently of each other, H, methyl, fluoromethyl, difluoromethyl, or trifluoromethyl;

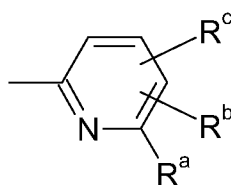
A is 1,4-phenylene or 1,3-phenylene, which is optionally substituted by one, two, three or four substituents selected from halogen, C₁-C₄-alkyl, C₁-C₄-alkoxy, fluorinated C₁-C₄-alkyl and fluorinated C₁-C₄-alkoxy;

E is NR⁵ or CH₂, wherein R⁵ is H or C₁-C₃-alkyl;

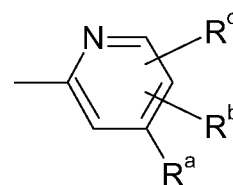
Ar is a radical of the formula A, B, C, D, E, F or G



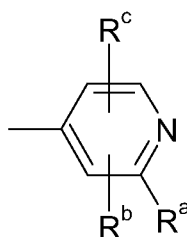
(A)



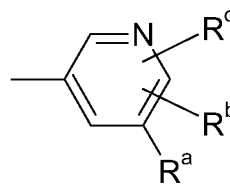
(B)



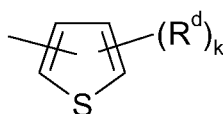
(C)



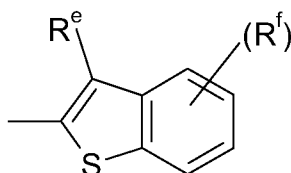
(D)



(E)



(F)



(G)

5 wherein

R^a is halogen, hydroxy, C_1 - C_6 -alkyl, fluorinated C_1 - C_6 -alkyl, C_1 - C_6 -hydroxyalkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, fluorinated C_2 - C_6 -alkenyl, C_3 - C_6 -cycloalkyl, fluorinated C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkoxy, C_1 - C_6 -hydroxyalkoxy, C_1 - C_6 -alkoxy- C_1 - C_6 -alkoxy, fluorinated C_1 - C_6 -alkoxy, C_1 - C_6 -alkylthio, fluorinated C_1 - C_6 -alkylthio, C_1 - C_6 -alkylsulfinyl, fluorinated C_1 - C_6 -alkylsulfinyl, C_1 - C_6 -alkylsulfonyl, fluorinated C_1 - C_6 -alkylsulfonyl, phenylsulfonyl, pyridylsulfonyl, benzyloxy, phenoxy, phenyl, where the phenyl and the pyridyl radical in the 5 last-mentioned radicals may be unsubstituted or may carry 1 to 3 substituents selected from C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl and halogen, CN, nitro, C_1 - C_6 -alkylcarbonyl, fluorinated C_1 - C_6 -alkylcarbonyl, C_1 - C_6 -alkylcarbonylamino, fluorinated C_1 - C_6 -alkylcarbonylamino, carboxy, $NH-C(O)-NR^6R^7$, NR^6R^7 , $NR^6R^7-C_1$ - C_6 -alkylene, $O-NR^6R^7$, where R^6 and R^7 are, independently of each other, H, C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl or C_1 - C_4 -alkoxy or may form, together with N, a 4-, 5- or 6-membered saturated or unsaturated ring, $R^9-CO-NR^6-C_1$ - C_6 -alkylene, where R^6 is as defined above and R^9 is C_1 - C_4 -alkyl or phenyl, where the phenyl radical may be unsubstituted or may carry 1 to 3 substituents selected from C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl and halogen, CH_2 -pyridyl, where the pyridyl radical may be unsubstituted or may carry 1 to 3 substituents selected from C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl and halogen, or is a saturated or unsaturated aromatic or non-aromatic 3- to 7-membered heterocyclic ring comprising as ring members 1, 2, 3 or 4 heteroatoms selected from N, O and S and/or 1, 2 or 3 heteroatom-containing groups selected

from NR^8 , where R^8 is H, $\text{C}_1\text{-C}_4\text{-alkyl}$, fluorinated $\text{C}_1\text{-C}_4\text{-alkyl}$, $\text{C}_1\text{-C}_4\text{-alkylcarbonyl}$ or fluorinated $\text{C}_1\text{-C}_4\text{-alkylcarbonyl}$, SO, SO_2 and CO, and where the heterocyclic ring may carry 1, 2 or 3 substituents selected from hydroxy, halogen, $\text{C}_1\text{-C}_6\text{-alkyl}$, fluorinated $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_1\text{-C}_6\text{-alkoxy}$, fluorinated $\text{C}_1\text{-C}_6\text{-alkoxy}$, $\text{C}_1\text{-C}_6\text{-alkylthio}$, fluorinated $\text{C}_1\text{-C}_6\text{-alkylthio}$, $\text{NR}^6\text{R}^7\text{-C}_1\text{-C}_6\text{-alkylene}$, where R^6 and R^7 are as defined above, carboxyl and $\text{C}_1\text{-C}_4\text{-alkyoxycarbonyl}$;

R^b and R^c , independently of each other, are H, halogen, CH_3 , OCH_3 , CH_2F , OCH_2F , CHF_2 , OCHF_2 , CF_3 , OCF_3 , $\text{CH}_2\text{CH}_2\text{F}$, $\text{OCH}_2\text{CH}_2\text{F}$, CH_2CHF_2 , OCH_2CHF_2 , CH_2CF_3 or OCH_2CF_3 ;

R^d is defined like R^a ;

R^e is H or is defined like R^a ;

R^f is defined like R^a ;

k is 0, 1, 2 or 3; and

j is 0, 1, 2, 3 or 4;

and/or at least one physiologically tolerated acid addition salt of I to a subject in need thereof.

The present invention further relates to the use of a compound as defined for the above method and/or physiologically tolerated acid addition salts thereof, for preparing a pharmaceutical composition for the treatment of a medical disorder susceptible to treatment with a 5-HT_6 receptor ligand.

In a specific embodiment, the compound used according to the invention or in the method of the invention is as defined above, however with the above provisos.

In a specific embodiment of the use and the method of the invention, in compounds I, Ar is a radical of the formula (A), (B), (C), (D) or (E), where the substituents have the following meanings:

R^1 is H, $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_1\text{-C}_6\text{-alkyl}$ substituted by $\text{C}_3\text{-C}_6\text{-cycloalkyl}$, $\text{C}_1\text{-C}_6\text{-hydroxyalkyl}$, fluorinated $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_3\text{-C}_6\text{-cycloalkyl}$, fluorinated $\text{C}_3\text{-C}_6\text{-cycloalkyl}$, $\text{C}_3\text{-C}_6\text{-alkenyl}$, fluorinated $\text{C}_3\text{-C}_6\text{-alkenyl}$, formyl, acetyl or propionyl;

R^a is halogen, C_1 - C_6 -alkyl, fluorinated C_1 - C_6 -alkyl, C_1 - C_6 -hydroxyalkyl, C_1 - C_6 -alkoxy-
 C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, fluorinated C_2 - C_6 -alkenyl, C_3 - C_6 -cycloalkyl, fluorinated
 C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkoxy, C_1 - C_6 -hydroxyalkoxy, C_1 - C_6 -alkoxy- C_1 - C_6 -alkoxy,
 5 fluorinated C_1 - C_6 -alkoxy, C_1 - C_6 -alkylthio, fluorinated C_1 - C_6 -alkylthio, C_1 - C_6 -
 alkylsulfinyl, fluorinated C_1 - C_6 -alkylsulfinyl, C_1 - C_6 -alkylsulfonyl, fluorinated C_1 - C_6 -
 alkylsulfonyl, phenylsulfonyl, benzyloxy, phenoxy, where the phenyl radical in the
 3 last-mentioned radicals may be unsubstituted or may carry 1 to 3 substituents
 selected from C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl and halogen, CN, nitro, C_1 - C_6 -
 10 alkylcarbonyl, fluorinated C_1 - C_6 -alkylcarbonyl, C_1 - C_6 -alkylcarbonylamino, fluori-
 nated C_1 - C_6 -alkylcarbonylamino, carboxy, $NH-C(O)-NR^6R^7$, NR^6R^7 , $NR^6R^7-C_1-C_6$ -
 alkylene, $O-NR^6R^7$, where R^6 and R^7 are, independently of each other, H, C_1 - C_4 -
 alkyl, fluorinated C_1 - C_4 -alkyl or C_1 - C_4 -alkoxy or may form, together with N, a 4-, 5-
 or 6-membered saturated or unsaturated ring, or is a saturated or unsaturated 3-
 15 to 7-membered heterocyclic ring comprising as ring members 1, 2, 3 or 4 het-
 eroatoms selected from N, O and S and/or 1, 2 or 3 heteroatom-containing
 groups selected from NR^8 , where R^8 is H, C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl,
 C_1 - C_4 -alkylcarbonyl or fluorinated C_1 - C_4 -alkylcarbonyl, SO, SO_2 and CO, and
 where the heterocyclic ring may carry 1, 2 or 3 substituents selected from hy-
 20 droxy, halogen, C_1 - C_6 -alkyl, fluorinated C_1 - C_6 -alkyl and C_1 - C_6 -alkoxy; and

R^b and R^c , independently of each other, are H, halogen, CH_3 , OCH_3 , CHF_2 , $OCHF_2$,
 CF_3 or OCF_3 ;

25 with the proviso that R^a is not F, CH_2F , CHF_2 , CF_3 or OCF_3 if A is 1,4-phenylene and R^b
 and R^c are H or halogen.

Detailed Description Of The Invention

30 The remarks made in the following with respect to preferred aspects of the invention,
 e.g. to preferred meanings of the variables of compound I, to preferred compounds I
 and to preferred embodiments of the method or the use according to the invention,
 apply in each case on their own or to combinations thereof.

35 The diseases which respond to the influence of 5HT₆ receptor antagonists or agonists
 include, in particular, disorders and diseases of the central nervous system, in particu-
 lar cognitive dysfunctions, such as a deficit in memory, cognition and learning, in par-
 ticular associated with Alzheimer's disease, age-related cognitive decline and mild

cognitive impairment, attention deficit disorder/hyperactivity syndrome, personality disorders, such as schizophrenia, in particular cognitive deficits related with schizophrenia, affective disorders such as depression, bipolar disorder, anxiety and obsessive compulsive disorders, motion or motor disorders such as Parkinson's disease and epilepsy, migraine, sleep disorders (including disturbances of the Circadian rhythm), feeding disorders, such as anorexia and bulimia, certain gastrointestinal disorders such as Irritable Bowl Syndrome, diseases associated with neurodegeneration, such as stroke, spinal or head trauma and head injuries, such as hydrocephalus, drug addiction and obesity.

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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.

15

Particularly, the carbon atom of the nitrogen-containing ring carrying the group A may have (S) or (R) configuration. However, the (S) configuration is preferred.

20

Moreover, the radical A may be in a cis or trans position to either of the substituents R^2 , R^3 or R^4 (if at least one of those is not hydrogen). However, the trans position is preferred.

25

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, hydrobromic acid, phosphoric acid, sulfuric acid, C_1 - C_4 -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.

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35

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. 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, chlorine or bromine.

5

C₁-C₄ Alkyl 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, isobutyl or *tert*-butyl. C₁-C₂ Alkyl is methyl or ethyl, C₁-C₃ alkyl is additionally n-propyl or isopropyl.

10

C₁-C₆ Alkyl 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.

15

20 Fluorinated C₁-C₆ alkyl is a straight-chain or branched alkyl group having from 1 to 6, especially 1 to 4 carbon atoms (= fluorinated C₁-C₄ alkyl), in particular 1 to 3 carbon atoms (= fluorinated C₁-C₃ alkyl), wherein at least one, e.g. 1, 2, 3, 4 or all of the hydrogen atoms are replaced by a fluorine atom such as in fluoromethyl, difluoromethyl, trifluoromethyl, (R)-1-fluoroethyl, (S)-1-fluoroethyl, 2-fluoroethyl, 1,1-difluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, 1,1,2,2-tetrafluoroethyl, (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, 1-(trifluoromethyl)-2,2,2-trifluoroethyl, 1-(trifluoromethyl)-1,2,2,2-tetrafluoroethyl, (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, and the like.

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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.

40

Fluorinated branched C₃-C₆ alkyl is alkyl having 3 to 6 carbon atoms at least one being a secondary or tertiary carbon atom wherein at least one, e.g. 1, 2, 3, 4 or all of the hydrogen atoms are replaced by a fluorine atom.

- 5 C₁-C₆ Alkoxy is a straight-chain or branched alkyl group having from 1 to 6, in particular 1 to 4 carbon atoms (= C₁-C₄ alkoxy), 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, 10 1,2-dimethylpropoxy, 1-methylpentyloxy, 2-methylpentyloxy, 3-methylpentyloxy, 4-methylpentyloxy, 1,1-dimethylbutoxy, 1,2-dimethylbutoxy, 1,3-dimethylbutoxy, 2,2-dimethylbutoxy, 2,3-dimethylbutoxy, 3,3-dimethylbutoxy, 1-ethylbutoxy, 2-ethylbutoxy, 1,1,2-trimethylpropoxy, 1,2,2-trimethylpropoxy, 1-ethyl-1-methylpropoxy and 1-ethyl-2-methylpropoxy.

- 15 Fluorinated C₁-C₆ alkoxy is a straight-chain or branched alkoxy group having from 1 to 6, in particular 1 to 4 carbon atoms (= fluorinated C₁-C₄ alkoxy), 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, 20 2-fluoroethoxy, 1,1-difluoroethoxy, 2,2-difluoroethoxy, 2,2,2-trifluoroethoxy, 1,1,2,2-tetrafluoroethoxy, (R)-1-fluoropropoxy, (S)-1-fluoropropoxy, (R)-2-fluoropropoxy, (S)-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, and the 30 like.

- C₁-C₆ Hydroxyalkyl is a straight-chain or branched alkyl group having from 1 to 6, especially 1 to 4 carbon atoms (= C₁-C₄ hydroxyalkyl), in particular 1 to 3 carbon atoms (= C₁-C₃ hydroxyalkyl), wherein one of the hydrogen atoms is replaced by a hydroxy 35 group, such as in 2-hydroxyethyl or 3-hydroxypropyl.

- C₁-C₆-Alkoxy-C₁-C₆-alkyl is a straight-chain or branched alkyl group having from 1 to 6, especially 1 to 4 carbon atoms, in particular 1 to 3 carbon atoms, wherein one of the hydrogen atoms is replaced by a C₁-C₆-alkoxy group, such as in methoxymethyl, 2-methoxyethyl, ethoxymethyl, 3-methoxypropyl, 3-ethoxypropyl and the like. 40

C₁-C₆-Alkoxy-C₁-C₆-alkoxy is a straight-chain or branched alkyl group having from 1 to 6, especially 1 to 4 carbon atoms, in particular 1 to 3 carbon atoms, wherein one of the hydrogen atoms is replaced by a C₁-C₆-alkoxy group, such as in 2-methoxyethoxy,
5 ethoxymethoxy, 2-ethoxyethoxy, 3-methoxypropoxy, 3-ethoxypropoxy and the like.

C₁-C₆-Alkylcarbonyl is a straight-chain or branched alkyl group having from 1 to 6, especially 1 to 4 carbon atoms (= C₁-C₄ alkylcarbonyl), in particular 1 to 3 carbon atoms (= fluorinated C₁-C₃ alkylcarbonyl), wherein one of the hydrogen atoms is replaced by a
10 carbonyl group (CO), such as in acetyl and propionyl.

Fluorinated C₁-C₆-alkylcarbonyl is a straight-chain or branched alkyl group having from 1 to 6, especially 1 to 4 carbon atoms (= fluorinated C₁-C₄ alkylcarbonyl), in particular 1 to 3 carbon atoms (= fluorinated C₁-C₃ alkylcarbonyl), wherein one of the hydrogen
15 atoms is replaced by a carbonyl group (CO) and wherein at least one of the remaining hydrogen atoms, e.g. 1, 2, 3, or 4 of the hydrogen atoms are replaced by a fluorine atom, such as in trifluoroacetyl and 3,3,3-trifluoropropionyl.

C₁-C₆-Alkylcarbonylamino is a straight-chain or branched alkyl group having from 1 to
20 6, especially 1 to 4 carbon atoms (= C₁-C₄ alkylcarbonylamino), in particular 1 to 3 carbon atoms (= C₁-C₄ alkylcarbonylamino), wherein one of the hydrogen atoms is replaced by a carbonylamino group (CO-NH-), such as in acetamido (acetylamino) (CH₃CONH-) and propionamido (CH₃CH₂CONH-).

25 Fluorinated C₁-C₆-alkylcarbonylamino is a straight-chain or branched alkyl group having from 1 to 6, especially 1 to 4 carbon atoms (= fluorinated C₁-C₄ alkylcarbonylamino), in particular 1 to 3 carbon atoms (= fluorinated C₁-C₄ alkylcarbonylamino), wherein one of the hydrogen atoms is replaced by a carbonylamino group (CO-NH-) and wherein at least one of the remaining hydrogen atoms, e.g. 1, 2, 3, or 4 of the hy-
30 drogen atoms are replaced by a fluorine atom, such as in trifluoroacetylamino and 3,3,3-trifluoropropionylamino.

C₁-C₆ Alkylthio (also termed as C₁-C₆-alkylsulfanyl) (or C₁-C₆-alkylsulfinyl or C₁-C₆-alkylsulfonyl, respectively) refer to straight-chain or branched alkyl groups having 1 to 6
35 carbon atoms, e.g. 1 to 4 carbon atoms, which are bound to the remainder of the molecule via a sulfur atom (or S(O)O in case of alkylsulfinyl or S(O)₂O in case of alkylsulfonyl, respectively), at any bond in the alkyl group. Examples for C₁-C₄-alkylthio include methylthio, ethylthio, propylthio, isopropylthio, and n-butylthio. Examples for C₁-C₄-alkylsulfinyl include methylsulfinyl, ethylsulfinyl, propylsulfinyl, isopropylsulfinyl, and n-

butylsulfinyl. Examples for C₁-C₄-alkylsulfonyl include methylsulfonyl, ethylsulfonyl, propylsulfonyl, isopropylsulfonyl, and n-butylsulfonyl.

5 Fluorinated C₁-C₆ alkylthio (also termed fluorinated C₁-C₆-alkylsulfanyl) is a straight-chain or branched alkylthio 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 fluorine atoms. Fluorinated C₁-C₆ alkylsulfinyl is a straight-chain or branched alkylsulfinyl 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 fluorine atoms. Fluorinated C₁-C₆ alkylsulfonyl is a straight-chain or branched alkylsulfonyl 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 fluorine atoms.

15 C₃-C₆ Cycloalkyl is a cycloaliphatic radical having from 3 to 6 C atoms, such as cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl. The cycloalkyl radical may be unsubstituted or may carry 1, 2, 3 or 4 C₁-C₄ 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.

20 Fluorinated C₃-C₆ cycloalkyl is a cycloaliphatic radical having from 3 to 6 C atoms, such as cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl, 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, (S)- and (R)-2,2-difluorocyclopropyl, 1,2-difluorocyclopropyl, 2,3-difluorocyclopropyl, pentafluorocyclopropyl, 1-fluorocyclobutyl, 25 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.

30 C₂-C₆-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. C₃-C₆-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.

35 Fluorinated C₂-C₆-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 replaced 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.

C₁-C₆-Alkylene is a hydrocarbon bridging group having 1, 2, 3, 4, 5 or 6 carbon atoms, like methylene, ethylene, 1,2- and 1,3-propylene, 1,4-butylene and the like.

5 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, 2- or 3-pyrrolyl, 2-, 3- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 2-, 3- or 5-thiazolyl, 3-, 4- or 5-isothiazolyl, 3-, 4- or 5-pyrazolyl, 2-, 4- or 5-imidazolyl, 2- or 5-[1,3,4]oxadiazolyl, 4- or 5-[1,2,3]oxadiazolyl, 3- or 5-[1,2,4]oxadiazolyl, 2- or 5-[1,3,4]thiadiazolyl, 2- or 5-[1,3,4]thiadiazolyl, 4- or 5-[1,2,3]thiadiazolyl, 3- or 5-[1,2,4]thiadiazolyl 1*H*-, 2*H*- or 3*H*-
10 1,2,3-triazol-4-yl, 2*H*-triazol-3-yl, 1*H*-, 2*H*-, or 4*H*-1,2,4-triazolyl and 1*H*- or 2*H*-tetrazolyl, which may be unsubstituted or which may carry 1, 2 or 3 of the aforementioned radicals R^a.

15 Examples of a phenyl ring fused to a saturated or unsaturated 5- or 6-membered carbocyclic or heterocyclic ring comprise indenyl, indanyl, naphthyl, 1,2- or 2,3-dihydronaphthyl, tetralin, benzofuranyl, 2,3-dihydrobenzofuranyl, benzothienyl, indolyl, indazolyl, benzimidazolyl, benzoxathiazolyl, benzoxadiazolyl, benzothiadiazolyl, benzoxazinyl, dihydrobenzoxazinyl, chinoliny, isochinoliny, tetrahydroisochinoliny, chromenyl, chromanyl and the like, which may be unsubstituted or which may carry 1,
20 2 or 3 of the aforementioned radicals R^a. This fused system may be bonded to the remainder of the molecule (more precisely to the sulfonyl group) via carbon atoms of the phenyl moiety or via ring atoms (C- or N-atoms) of the ring fused to phenyl.

25 Examples for saturated or unsaturated 3- to 7-membered heterocyclic rings (as radicals R^a) comprise saturated or unsaturated, aromatic or non-aromatic heterocyclic rings. Examples therefore include, apart from the above-defined 5- or 6-membered heteroaromatic radicals, aziridyl, diaziridinyl, oxiranyl, azetidiny, azetiny, di- and tetrahydrofuranyl, pyrroliny, pyrrolidinyl, oxopyrrolidinyl, pyrazoliny, pyrazolidiny, imidazoliny, imidazolidiny, oxazoliny, oxazolidiny, oxo-oxazolidiny, isoxazoliny, isoxazolidiny,
30 piperidiny, piperaziny, morpholiny, thiomorpholiny, oxothiomorpholiny, dioxothiomorpholiny and the like.

If R⁶ and R⁷ form together with N a 4-, 5- or 6-membered ring, examples for this type of radical comprise, apart from the above-defined 5- or 6-membered heteroaromatic radicals containig at least one N atom as ring member, azetidiny, azetiny, pyrroliny, pyrrolidinyl, pyrazoliny, pyrazolidiny, imidazoliny, imidazolidiny, oxazoliny, oxazolidiny, piperidiny, piperaziny, morpholiny and the like.

In compounds of formula I, n preferably is 0 or 1; i.e. the nitrogen-containing ring is an azetidiny group or a pyrrolidinyl group; and particularly, n is 1, which means that in a particularly preferred embodiment, the nitrogen-containing ring is a pyrrolidinyl ring.

- 5 Preferably, the radical R^1 is selected from H, C_1 - C_4 -alkyl, C_1 - C_4 -alkyl which is substituted by C_3 - C_6 -cycloalkyl or hydroxy, fluorinated C_1 - C_4 -alkyl, C_2 - C_4 -alkenyl and benzyl. More preference is given to H, propyl, cyclopropylmethylene, fluorinated ethyl, e.g. 2-fluoroethyl, fluorinated propyl, e.g. 3-fluoropropyl, hydroxypropyl, e.g. 3-hydroxypropyl, propionyl, allyl and benzyl. More preferably, R^1 is selected from H, propyl, ethyl, methyl, 10 cyclopropylmethylene, 2-fluoroethyl, 3-fluoropropyl, 3-hydroxypropyl, allyl and benzyl. Even more preferably, R^1 is selected from H, propyl, cyclopropylmethylene, 2-fluoroethyl, 3-fluoropropyl, 3-hydroxypropyl, allyl or benzyl. In a particularly preferred embodiment, R^1 is H, n-propyl or allyl, in particular H or n-propyl and especially H.
- 15 Preferably, R^2 , R^3 and R^4 are H, CH_3 or CH_2F and more preferably H.

- If the group A is substituted, preferred substituents are selected from halogen, in particular fluorine, methyl, difluoromethyl, trifluoromethyl, methoxy, difluoromethoxy and trifluoromethoxy. More preferred substituents are selected from halogen, in particular 20 fluorine, and methoxy. Specifically, the substituent is methoxy. Examples include 2-fluoro-1,4-phenylene, 3-fluoro-1,4-phenylene, 2-fluoro-1,3-phenylene, 4-fluoro-1,3-phenylene, 2-methoxy-1,4-phenylene, 3-methoxy-1,4-phenylene, 2-methoxy-1,3-phenylene and 3-methoxy-1,3-phenylene. In a specific embodiment, A is unsubstituted 1,4-phenylene or unsubstituted 1,3-phenylene. More specifically, A is 1,3-pyridylene, 25 particular unsubstituted 1,3-pyridylene.

The group E is preferably NR^5 , more preferably NH or NCH_3 and in particular NH.

- In one preferred embodiment of the invention, Ar is a radical of the formula (A), (B), 30 (C), (D) or (E). Particular preference is given to the radical (A). Among the pyridyl radicals (B) to (E), preference is given to radicals (C) and (E).

- In these Ar radicals (A) to (E), R^a is preferably selected from the group consisting of halogen, C_1 - C_6 -alkyl, fluorinated C_1 - C_6 -alkyl, C_1 - C_6 -hydroxyalkyl, C_1 - C_6 -alkoxy- C_1 - C_6 - 35 alkyl, C_2 - C_6 -alkenyl, C_3 - C_6 -cycloalkyl, fluorinated C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkoxy, C_1 - C_6 -alkoxy- C_1 - C_6 -alkoxy, fluorinated C_1 - C_6 -alkoxy, fluorinated C_1 - C_6 -alkylthio, C_1 - C_6 -alkylsulfonyl, phenylsulfonyl, benzyloxy, phenoxy, CN, nitro, acetyl, trifluoroacetyl, acetamido, carboxy, $NH-C(O)-NH_2$, NR^6R^7 , $NR^6R^7-C_1-C_6$ -alkylene, $O-NR^6R^7$, where R^6 and R^7 are, independently of each other, H, C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl or C_1 - 40 C_4 -alkoxy, and a saturated or unsaturated aromatic or non-aromatic 3- to 7-membered

heterocyclic ring comprising as ring members 1, 2, 3 or 4 heteroatoms selected from N, O and S and/or 1, 2 or 3 heteroatom-containing groups selected from NR⁸, where R⁸ is as defined above and is preferably H or C₁-C₄-alkyl such as methyl, SO, SO₂ and CO, and where the 3- to 7-membered heterocyclic ring may carry 1, 2 or 3 substituents selected from hydroxy, halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl and C₁-C₆-alkoxy.

Preferably, the saturated or unsaturated 3- to 7-membered heterocyclic ring is selected from azetidin-1-yl, 2-methylazetidiny, 3-methoxyazetidiny, 3-hydroxyazetidiny, 3-fluoroazetidiny, 2,2-difluoroazetidin-1-yl, pyrrolidin-1-yl, pyrrolidin-2-yl, pyrrolidin-3-yl, 2- and 3-fluoropyrrolidin-1-yl, 2,2-difluoropyrrolidin-1-yl, 3,3-difluoropyrrolidin-1-yl, 2- and 3-methylpyrrolidin-1-yl, 1-methylpyrrolidin-2-yl, 2,2-dimethylpyrrolidin-1-yl, 3,3-dimethylpyrrolidin-1-yl, 2-oxo-pyrrolidin-1-yl, 2- and 3-trifluoromethylpyrrolidin-1-yl, 2-oxo-oxazolidin-1-yl, piperidin-1-yl, 2-methylpiperidin-1-yl, 2-fluoropiperidin-1-yl, 2,2-difluoropiperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, 1-oxothiomorpholin-4-yl, 1,1-dioxothiomorpholin-4-yl, pyrrol-1-yl, pyrrol-2-yl, pyrrol-3-yl, 1-methylpyrrol-2-yl, 1-methylpyrrol-3-yl, furan-2-yl, furan-3-yl, thiophen-2-yl, thiophen-3-yl, 5-propylthiophen-2-yl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, 1-methylpyrazol-4-yl, 4-fluoropyrazol-1-yl, imidazol-1-yl, imidazol-2-yl, 1-methylimidazol-2-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, isoxazol-3-yl, isoxazol-4-yl, isoxazol-5-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, 2-methylthiazol-4-yl, 2-methylthiazol-5-yl, [1,2,3]triazol-1-yl, [1,2,4]triazol-1-yl, [1,2,3]triazol-2-yl, [1,2,4]triazol-3-yl, [1,2,4]triazol-4-yl, 4-methyl-[1,2,4]triazol-3-yl, 2-methyl-[1,2,3]triazol-4-yl, [1,3,4]-oxadiazol-2-yl, [1,2,4]-oxadiazol-3-yl, [1,2,4]-oxadiazol-5-yl, [1,2,3]-oxadiazol-5-yl, [1,3,4]-oxadiazol-2-yl, 5-methyl-[1,3,4]-oxadiazol-2-yl, 5-methyl-[1,2,4]-oxadiazol-3-yl, [1,2,3]thiadiazol-4-yl, tetrazol-1-yl, tetrazol-5-yl, 2-methyltetrazol-5-yl, 1-methyltetrazol-5-yl, furazan-3-yl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl and 2-methylpyrimidin-4-yl.

More preferably, the saturated or unsaturated 3- to 7-membered heterocyclic ring is selected from nitrogen containing rings such as azetidin-1-yl, 2-methylazetidiny, 3-methoxyazetidiny, 3-hydroxyazetidiny, 3-fluoroazetidiny, 2,2-difluoroazetidin-1-yl, pyrrolidin-1-yl, pyrrolidin-2-yl, pyrrolidin-3-yl, 2- and 3-fluoropyrrolidin-1-yl, 2,2-difluoropyrrolidin-1-yl, 3,3-difluoropyrrolidin-1-yl, 2- and 3-methylpyrrolidin-1-yl, 1-methylpyrrolidin-2-yl, 2,2-dimethylpyrrolidin-1-yl, 3,3-dimethylpyrrolidin-1-yl, 2-oxo-pyrrolidin-1-yl, 2- and 3-trifluoromethylpyrrolidin-1-yl, 2-oxo-oxazolidin-1-yl, piperidin-1-yl, 2-methylpiperidin-1-yl, 2-fluoropiperidin-1-yl, 2,2-difluoropiperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, 1-oxothiomorpholin-4-yl, 1,1-dioxothiomorpholin-4-yl, pyrrol-1-yl, pyrrol-2-yl, pyrrol-3-yl, 1-methylpyrrol-2-yl, 1-methylpyrrol-3-yl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, 1-methylpyrazol-4-yl, 4-fluoropyrazol-1-yl, imidazol-1-yl, imidazol-2-yl, 1-methylimidazol-2-yl, oxazol-2-yl, oxa-

- zol-4-yl, oxazol-5-yl, isoxazol-3-yl, isoxazol-4-yl, isoxazol-5-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, 2-methylthiazol-4-yl, 2-methylthiazol-5-yl, [1,2,3]triazol-1-yl, [1,2,4]triazol-1-yl, [1,2,3]triazol-2-yl, [1,2,4]triazol-3-yl, [1,2,4]triazol-4-yl, 4-methyl-[1,2,4]triazol-3-yl, 2-methyl-[1,2,3]triazol-4-yl, [1,3,4]-oxadiazol-2-yl, [1,2,4]-oxadiazol-3-yl, [1,2,4]-oxadiazol-5-yl, [1,2,3]-oxadiazol-5-yl, [1,3,4]-oxadiazol-2-yl, 5-methyl-[1,3,4]-oxadiazol-2-yl, 5-methyl-[1,2,4]-oxadiazol-3-yl, [1,2,3]thiadiazol-4-yl, tetrazol-1-yl, tetrazol-5-yl, 2-methyltetrazol-5-yl, 1-methyltetrazol-5-yl, furazan-3-yl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl and 2-methylpyrimidin-4-yl.
- 10 Even more preferably, the saturated or unsaturated 3- to 7-membered heterocyclic ring is selected from nitrogen containing rings which are bound to the phenyl or pyridyl ring of the group Ar via their nitrogen atom, such as azetidin-1-yl, 2-methylazetidin-1-yl, 3-methoxyazetidin-1-yl, 3-hydroxyazetidin-1-yl, 3-fluoroazetidin-1-yl, 2,2-difluoroazetidin-1-yl, pyrrolidin-1-yl, 2- and 3-fluoropyrrolidin-1-yl, 2,2-difluoropyrrolidin-1-yl, 3,3-difluoropyrrolidin-1-yl, 2- and 3-methylpyrrolidin-1-yl, 2,2-dimethylpyrrolidin-1-yl, 3,3-dimethylpyrrolidin-1-yl, 2-oxo-pyrrolidin-1-yl, 2- and 3-trifluoromethylpyrrolidin-1-yl, 2-oxo-oxazolidin-1-yl, piperidin-1-yl, 2-methylpiperidin-1-yl, 2-fluoropiperidin-1-yl, 2,2-difluoropiperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, 1-oxothiomorpholin-4-yl, 1,1-dioxothiomorpholin-4-yl, pyrrol-1-yl, pyrazol-1-yl, 4-fluoropyrazol-1-yl, imidazol-1-yl, [1,2,3]triazol-1-yl, [1,2,4]triazol-1-yl, [1,2,3]triazol-2-yl, [1,2,4]triazol-3-yl, [1,2,4]triazol-4-yl, 4-methyl-[1,2,4]triazol-3-yl, 2-methyl-[1,2,3]triazol-4-yl, tetrazol-1-yl and tetrazol-2-yl.
- In an alternative even more preferable embodiment, the saturated or unsaturated 3- to 7-membered heterocyclic ring is selected from 5- or 6-membered, preferably 5-membered, nitrogen containing heteroaromatic rings bound via a carbon atom, such as pyrrol-2-yl, pyrrol-3-yl, 1-methylpyrrol-2-yl, 1-methylpyrrol-3-yl, pyrazol-3-yl, pyrazol-4-yl, 1-methylpyrazol-4-yl, imidazol-2-yl, 1-methylimidazol-2-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, isoxazol-3-yl, isoxazol-4-yl, isoxazol-5-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, 2-methylthiazol-4-yl, 2-methylthiazol-5-yl, [1,2,3]triazol-2-yl, [1,2,4]triazol-3-yl, [1,2,4]triazol-4-yl, 4-methyl-[1,2,4]triazol-3-yl, 2-methyl-[1,2,3]triazol-4-yl, [1,3,4]-oxadiazol-2-yl, [1,2,4]-oxadiazol-3-yl, [1,2,4]-oxadiazol-5-yl, [1,2,3]-oxadiazol-5-yl, [1,3,4]-oxadiazol-2-yl, 5-methyl-[1,3,4]-oxadiazol-2-yl, 5-methyl-[1,2,4]-oxadiazol-3-yl, [1,2,3]thiadiazol-4-yl, tetrazol-5-yl, 2-methyltetrazol-5-yl, 1-methyltetrazol-5-yl, furazan-3-yl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl and 2-methylpyrimidin-4-yl.

The heterocyclic ring is unsubstituted or substituted by one substituent which is preferably selected from halogen, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl, C₁-C₄-alkoxy and

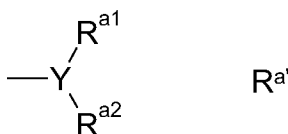
fluorinated C₁-C₄-alkoxy and in particular from halogen, in particular fluorine, C₁-C₄-alkyl, especially methyl, and fluorinated C₁-C₄-alkyl, especially fluorinated methyl.

In a preferred embodiment, R^a is selected from the group consisting of halogen, C₁-C₆-alkyl, C₁-C₆-hydroxyalkyl, fluorinated C₁-C₄-alkyl, C₁-C₄-alkoxy, fluorinated C₁-C₄-alkoxy, C₁-C₄-alkoxy-C₁-C₄-alkoxy, C₂-C₄-alkenyl, fluorinated C₂-C₄-alkenyl, NR⁶R⁷, ONR⁶R⁷, C₁-C₆-alkylene-NR⁶R⁷, where R⁶ and R⁷ are independently of each other H, C₁-C₄-alkyl or C₁-C₄-alkoxy, ureido (NHCONH₂) C₃-C₆-cycloalkyl, fluorinated C₃-C₆-cycloalkyl, acetyl, carboxyl, hydroxy, cyano, nitro, benzoxy, methylsulfanyl, fluoro-methylsulfanyl, difluoromethylsulfanyl, trifluoromethylsulfanyl, methylsulfonyl and one of the above-mentioned saturated or unsaturated 3- to 7-membered heterocyclic rings, in particular azetidin-1-yl, 2-methylazetidinyl, 3-methoxyazetidinyl, 3-hydroxyazetidinyl, 3-fluoroazetidinyl, 2,2-difluoroazetidin-1-yl, pyrrolidin-1-yl, pyrrolidin-2-yl, pyrrolidin-3-yl, 2- and 3-fluoropyrrolidin-1-yl, 2,2-difluoropyrrolidin-1-yl, 3,3-difluoropyrrolidin-1-yl, 2- and 3-methylpyrrolidin-1-yl, 1-methylpyrrolidin-2-yl, 2,2-dimethylpyrrolidin-1-yl, 3,3-dimethylpyrrolidin-1-yl, 2-oxo-pyrrolidin-1-yl, 2- and 3-trifluoromethylpyrrolidin-1-yl, 2-oxo-oxazolidin-1-yl, piperidin-1-yl, 2-methylpiperidin-1-yl, 2-fluoropiperidin-1-yl, 2,2-difluoropiperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, 1-oxothiomorpholin-4-yl, 1,1-dioxothiomorpholin-4-yl, pyrrol-1-yl, pyrrol-2-yl, pyrrol-3-yl, 1-methylpyrrol-2-yl, 1-methylpyrrol-3-yl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, 1-methylpyrazol-4-yl, 4-fluoropyrazol-1-yl, imidazol-1-yl, imidazol-2-yl, 1-methylimidazol-2-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, isoxazol-3-yl, isoxazol-4-yl, isoxazol-5-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, 2-methylthiazol-4-yl, 2-methylthiazol-5-yl, [1,2,3]triazol-1-yl, [1,2,4]triazol-1-yl, [1,2,3]triazol-2-yl, [1,2,4]triazol-3-yl, [1,2,4]triazol-4-yl, 4-methyl-[1,2,4]triazol-3-yl, 2-methyl-[1,2,3]triazol-4-yl, [1,3,4]-oxadiazol-2-yl, [1,2,4]-oxadiazol-3-yl, [1,2,4]-oxadiazol-5-yl, [1,2,3]-oxadiazol-5-yl, [1,3,4]-oxadiazol-2-yl, 5-methyl-[1,3,4]-oxadiazol-2-yl, 5-methyl-[1,2,4]-oxadiazol-3-yl, [1,2,3]thiadiazol-4-yl, tetrazol-1-yl, tetrazol-5-yl, 2-methyltetrazol-5-yl, 1-methyltetrazol-5-yl, furazan-3-yl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl and 2-methylpyrimidin-4-yl.

In a more preferred embodiment, R^a is selected from the group consisting of halogen, C₁-C₆-alkyl, fluorinated C₁-C₄-alkyl, C₁-C₄-alkoxy, OCF₃, OCHF₂, OCH₂F, 2-fluoroethoxy, 2,2-difluoroethoxy, 2,2,2-trifluoroethoxy, 1,1,2,2-tetrafluoroethoxy, 1,1,2,2,2-pentafluoroethoxy, C₂-C₄-alkenyl, C₃-C₆-cycloalkyl, fluorinated C₃-C₆-cycloalkyl, ureido, acetyl, acetylamino, carboxyl, hydroxy, cyano, nitro, benzoxy, trifluoromethylsulfanyl, methylsulfonyl, azetidin-1-yl, 2-methylazetidinyl, 3-methoxyazetidinyl, 3-hydroxyazetidinyl, 3-fluoroazetidinyl, 2,2-difluoroazetidin-1-yl, pyrrolidin-1-yl, pyrrolidin-2-yl, pyrrolidin-3-yl, 2- and 3-fluoropyrrolidin-1-yl, 2,2-difluoropyrrolidin-1-yl, 3,3-difluoropyrrolidin-1-yl, 2- and 3-methylpyrrolidin-1-yl, 1-methylpyrrolidin-2-yl, 2,2-

dimethylpyrrolidin-1-yl, 3,3-dimethylpyrrolidin-1-yl, 2-oxo-pyrrolidin-1-yl, 2- and 3-trifluoromethylpyrrolidin-1-yl, 2-oxo-oxazolidin-1-yl, piperidin-1-yl, 2-methylpiperidin-1-yl, 2-fluoropiperidin-1-yl, 2,2-difluoropiperidin-1-yl, piperazin-1-yl, 4-methylpiperazin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, 1-oxothiomorpholin-4-yl, 1,1-dioxothiomorpholin-4-yl, pyrrol-1-yl, pyrrol-2-yl, pyrrol-3-yl, 1-methylpyrrol-2-yl, 1-methylpyrrol-3-yl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, 1-methylpyrazol-4-yl, 4-fluoropyrazol-1-yl, imidazol-1-yl, imidazol-2-yl, 1-methylimidazol-2-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, isoxazol-3-yl, isoxazol-4-yl, isoxazol-5-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, 2-methylthiazol-4-yl, 2-methylthiazol-5-yl, [1,2,3]triazol-1-yl, [1,2,4]triazol-1-yl, [1,2,3]triazol-2-yl, [1,2,4]triazol-3-yl, [1,2,4]triazol-4-yl, 4-methyl-[1,2,4]triazol-3-yl, 2-methyl-[1,2,3]triazol-4-yl, [1,3,4]-oxadiazol-2-yl, [1,2,4]-oxadiazol-3-yl, [1,2,4]-oxadiazol-5-yl, [1,2,3]-oxadiazol-5-yl, [1,3,4]-oxadiazol-2-yl, 5-methyl-[1,3,4]-oxadiazol-2-yl, 5-methyl-[1,2,4]-oxadiazol-3-yl, [1,2,3]thiadiazol-4-yl, tetrazol-1-yl, tetrazol-5-yl, 2-methyltetrazol-5-yl, 1-methyltetrazol-5-yl, furazan-3-yl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl and 2-methylpyrimidin-4-yl.

In an alternatively preferred embodiment, R^a has the formula $R^{a'}$



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wherein

Y is N, CH or CF,

R^{a1} and R^{a2} are independently of each other selected from C_1 - C_2 -alkyl, in particular methyl, 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

R^{a1} and R^{a2} form a radical $(CH_2)_m$ wherein 1 or 2 of the hydrogen atoms may be replaced by fluorine and wherein m 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 .

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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 of the formula $R^{a'}$ 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,

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2,2-difluoropropyl, 3,3-difluoropropyl, 3,3,3-trifluoropropyl, cyclopropyl, cyclobutyl, 1-fluorocyclopropyl, (S)- and (R)-2,2-difluorocyclopropyl and 2-fluorocyclopropyl.

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.

R^b and R^c , independently of each other, are H, halogen, CH_3 , OCH_3 , CH_2F , OCH_2F , CHF_2 , $OCHF_2$, CF_3 , OCF_3 , CH_2CH_2F , OCH_2CH_2F , CH_2CHF_2 , OCH_2CHF_2 , CH_2CF_3 or OCH_2CF_3 . If both R^b and R^c are different from H, it is preferred that one of R^b and R^c is selected from halogen and the other is selected from halogen, CH_3 , OCH_3 , CH_2F , OCH_2F , CHF_2 , $OCHF_2$, CF_3 , OCF_3 , CH_2CH_2F , OCH_2CH_2F , CH_2CHF_2 , OCH_2CHF_2 , CH_2CF_3 and OCH_2CF_3 and specifically from CH_3 , OCH_3 , CH_2F , OCH_2F , CHF_2 , $OCHF_2$, CF_3 , OCF_3 , CH_2CH_2F and OCH_2CH_2F .

Preferred examples for Ar, where Ar is a radical of formula (A), (B), (C), (D) or (E), are in particular the following: 3-methylphenyl, 3-ethylphenyl, 3-propylphenyl, 3-isopropylphenyl, 3-sec-butylphenyl, 3-isobutylphenyl, 3-tert-butylphenyl, 3-(1,1-dimethylpropyl)-phenyl, 3-vinylphenyl, 3-isopropenylphenyl, 3-fluorophenyl, 3-chlorophenyl, 3-bromophenyl, 3-iodophenyl, 3-(fluoromethyl)phenyl, 3-(difluoromethyl)phenyl, 3-(trifluoromethyl)phenyl, 3,5-bis(trifluoromethyl)phenyl, 3-(1-fluoroethyl)-phenyl, 3-((S)-1-fluoroethyl)-phenyl, 3-((R)-1-fluoroethyl)-phenyl, 3-(2-fluoroethyl)-phenyl, 3-(1,1-difluoroethyl)-phenyl, 3-(2,2-difluoroethyl)-phenyl, 3-(2,2,2-trifluoroethyl)-phenyl, 3-(3-fluoropropyl)-phenyl, 3-(2-fluoropropyl)-phenyl, 3-((S)-2-fluoropropyl)-phenyl, 3-((R)-2-fluoropropyl)-phenyl, 3-(3,3-difluoropropyl)-phenyl, 3-(3,3,3-trifluoropropyl)-phenyl, 3-(1-fluoro-1-methylethyl)-phenyl, 3-(2-fluoro-1-methylethyl)-phenyl, 3-((S)-2-fluoro-1-methylethyl)-phenyl, 3-((R)-2-fluoro-1-methylethyl)-phenyl, 3-(2,2-difluoro-1-methylethyl)-phenyl, 3-((S)-2,2-difluoro-1-methylethyl)-phenyl, 3-((R)-2,2-difluoro-1-methylethyl)-phenyl, 3-(2,2,2-trifluoro-1-methylethyl)-phenyl, 3-((S)-2,2,2-trifluoro-1-methylethyl)-phenyl, 3-((R)-2,2,2-trifluoro-1-methylethyl)-phenyl, 3-(2-fluoro-1-fluoromethylethyl)-phenyl, 3-(1-difluoromethyl-2,2-difluoroethyl)-phenyl, 3-(1,1-dimethyl-2-fluoroethyl)-phenyl, 3-methoxyphenyl, 3-ethoxyphenyl, 3-propoxyphenyl, 3-isopropoxyphenyl, 3-butoxyphenyl, 3-(fluoromethoxy)-phenyl, 3-(difluoromethoxy)-phenyl, 3-(trifluoromethoxy)-phenyl, 3-(2-fluoroethoxy)-phenyl, 3-(2,2-difluoroethoxy)-phenyl, 3-(2,2,2-trifluoroethoxy)-phenyl, 3-(1,1,2,2-tetrafluoroethoxy)-phenyl, 3-cyclopropylphenyl, 3-cyclobutylphenyl, 3-cyclopentylphenyl, 3-(2,2-difluorocyclopropyl)-phenyl, 3,4-difluorophenyl, 3,5-dichlorophenyl, 2,3-dichlorophenyl, 2,5-dichlorophenyl, 4-bromo-3-fluorophenyl, 3-bromo-2-fluorophenyl, 2-bromo-3-fluorophenyl, 3-chloro-4-fluorophenyl, 3-bromo-2,5-difluorophenyl, 4-bromo-2,5-difluorophenyl, 5-bromo-2,4-difluorophenyl, 3-bromo-2,4-difluorophenyl, 4-chloro-3-(trifluoromethyl)-phenyl, 2-chloro-5-(trifluoromethyl)-phenyl,

2-fluoro-5-(trifluoromethyl)-phenyl, 4-fluoro-3-(trifluoromethyl)-phenyl, 3-fluoro-5-(trifluoromethyl)-phenyl, 4-bromo-3-(trifluoromethyl)-phenyl, 3-bromo-5-(trifluoromethyl)-phenyl, 2-bromo-5-(trifluoromethyl)-phenyl, 5-bromo-2-methoxyphenyl, 3-bromo-4-methoxyphenyl, 3-bromo-4-(trifluoromethoxy)-phenyl, 3,5-dibromo-4-(2-fluoroethoxy)-phenyl, 2-fluoro-3-isopropylphenyl, 4-fluoro-3-isopropylphenyl, 3-(1-hydroxy-1-methylethyl)-phenyl, 3-(2-hydroxy-2-methylpropyl)-phenyl, 3-acetylphenyl, 3-acetylamino-phenyl, 3-carboxyphenyl, 3-cyanophenyl, 3-nitrophenyl, 3-hydroxyphenyl, 3-(O-benzyl)-phenyl, 3-(2-methoxyethoxy)-phenyl, 3-(CH₂-N(CH₃)₂)-phenyl, 3-(NH-CO-NH₂)-phenyl, 3-(methylsulfanyl)-phenyl, 3-(fluoromethylsulfanyl)-phenyl, 3-(difluoromethylsulfanyl)-phenyl, 3-(trifluoromethylsulfanyl)-phenyl, 3-(methylsulfonyl)-phenyl, 3-(N-methoxy-N-methyl-amino)-phenyl, 3-(methoxyamino)-phenyl, 3-(ethoxyamino)-phenyl, 3-(N-methylaminooxy)-phenyl, 3-(N,N-dimethylaminooxy)-phenyl, 3-cyanophenyl, 2,5-dimethylphenyl, 2,5-di(trifluoromethyl)-phenyl, 3,5-di(trifluoromethyl)-phenyl, 2,5-dimethoxyphenyl, 2-methoxy-5-methylphenyl, 2-methoxy-5-(trifluoromethyl)-phenyl, 3-(azetidin-1-yl)-phenyl, 3-(2-methylazetidin-1-yl)-phenyl, 3-((S)-2-methylazetidin-1-yl)-phenyl, 3-((R)-2-methylazetidin-1-yl)-phenyl, 3-(3-fluoroazetidin-1-yl)-phenyl, 3-(2,2-difluoroazetidin-1-yl)-phenyl, 3-(3-methoxyazetidin-1-yl)-phenyl, 3-(3-hydroxyazetidin-1-yl)-phenyl, 3-(pyrrolidin-1-yl)-phenyl, 3-(pyrrolidin-2-yl)-phenyl, 3-((S)-pyrrolidin-2-yl)-phenyl, 3-((R)-pyrrolidin-2-yl)-phenyl, 3-(pyrrolidin-3-yl)-phenyl, 3-((S)-pyrrolidin-3-yl)-phenyl, 3-((R)-pyrrolidin-3-yl)-phenyl, 3-(pyrrolidin-1-yl)-5-(trifluoromethyl)-phenyl, 5-(pyrrolidin-1-yl)-2-methoxyphenyl, 3-(pyrrolidin-1-yl)-4-methoxyphenyl, 5-(pyrrolidin-1-yl)-2,4-difluorophenyl, 3-(pyrrolidin-1-yl)-2,4-difluorophenyl, 3-(2-fluoropyrrolidin-1-yl)-phenyl, 3-((S)-2-fluoropyrrolidin-1-yl)-phenyl, 3-((R)-2-fluoropyrrolidin-1-yl)-phenyl, 3-(3-fluoropyrrolidin-1-yl)-phenyl, 3-((S)-3-fluoropyrrolidin-1-yl)-phenyl, 3-((R)-3-fluoropyrrolidin-1-yl)-phenyl, 3-(2,2-difluoropyrrolidin-1-yl)-phenyl, 3-(3,3-difluoropyrrolidin-1-yl)-phenyl, 3-(2-methylpyrrolidin-1-yl)-phenyl, 3-((S)-2-methylpyrrolidin-1-yl)-phenyl, 3-((R)-2-methylpyrrolidin-1-yl)-phenyl, 3-(3-methylpyrrolidin-1-yl)-phenyl, 3-((S)-3-methylpyrrolidin-1-yl)-phenyl, 3-((R)-3-methylpyrrolidin-1-yl)-phenyl, 3-(1-methylpyrrolidin-2-yl)-phenyl, 3-((S)-1-methylpyrrolidin-2-yl)-phenyl, 3-((R)-1-methylpyrrolidin-2-yl)-phenyl, 3-(1-methylpyrrolidin-3-yl)-phenyl, 3-((S)-1-methylpyrrolidin-3-yl)-phenyl, 3-((R)-1-methylpyrrolidin-3-yl)-phenyl, 3-(2,2-dimethylpyrrolidin-1-yl)-phenyl, 3-(3,3-dimethylpyrrolidin-1-yl)-phenyl, 3-(2-trifluoromethylpyrrolidin-1-yl)-phenyl, 3-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl, 3-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl, 3-(3-trifluoromethylpyrrolidin-1-yl)-phenyl, 3-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl, 3-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl, 3-(2-oxopyrrolidin-1-yl)-phenyl, 3-(2-oxo-oxazolidin-3-yl)-phenyl, 3-(piperidin-1-yl)-phenyl, 3-(2-methylpiperidin-1-yl)-phenyl, 3-((S)-2-methylpiperidin-1-yl)-phenyl, 3-((R)-2-methylpiperidin-1-yl)-phenyl, 3-(2-fluoropiperidin-1-yl)-phenyl, 3-((S)-2-fluoropiperidin-1-yl)-phenyl, 3-((R)-2-fluoropiperidin-1-yl)-phenyl, 3-(2,2-

difluoropiperidin-1-yl)-phenyl, 3-(piperazin-1-yl)-phenyl, 3-(4-methylpiperazin-1-yl)-phenyl, 3-(morpholin-4-yl)-phenyl, 3-(morpholin-4-yl)-5-(trifluoromethyl)-phenyl, 5-(morpholin-4-yl)-2-methoxyphenyl, 3-(morpholin-4-yl)-4-methoxyphenyl, 5-(morpholin-4-yl)-2,4-difluorophenyl, 3-(morpholin-4-yl)-2,4-difluorophenyl, 3-(thiomorpholin-4-yl)-phenyl, 3-(1-oxo-thiomorpholin-4-yl)-phenyl, 3-(1,1-dioxo-thiomorpholin-4-yl)-phenyl, 3-(pyrrol-1-yl)-phenyl, 3-(pyrrol-2-yl)-phenyl, 3-(pyrrol-3-yl)-phenyl, 3-(1-methylpyrrol-2-yl)-phenyl, 3-(1-methylpyrrol-3-yl)-phenyl, 3-(furan-2-yl)-phenyl, 3-(furan-3-yl)-phenyl, 3-(thiophen-2-yl)-phenyl, 3-(thiophen-3-yl)-phenyl, 3-(5-propylthien-2-yl)-phenyl, 3-(pyrazol-1-yl)-phenyl, 3-(pyrazol-3-yl)-phenyl, 3-(pyrazol-4-yl)-phenyl, 3-(1-methyl-1H-pyrazol-4-yl)-phenyl, 3-(1-ethyl-1H-pyrazol-4-yl)-phenyl, 3-(1-methyl-1H-pyrazol-5-yl)-phenyl, 3-(4-fluoropyrazol-1-yl)-phenyl, 3-(1H-imidazol-2-yl)-phenyl, 3-(imidazol-1-yl)-phenyl, 3-(1-methylimidazol-2-yl)-phenyl, 3-(oxazol-2-yl)-phenyl, 3-(oxazol-4-yl)-phenyl, 3-(oxazol-5-yl)-phenyl, 4-fluoro-3-(oxazol-4-yl)-phenyl, 3-(isoxazol-3-yl)-phenyl, 3-(isoxazol-4-yl)-phenyl, 3-(isoxazol-5-yl)-phenyl, 3-(thiazol-2-yl)-phenyl, 3-(thiazol-4-yl)-phenyl, 3-(thiazol-5-yl)-phenyl, 3-(2-methylthiazol-4-yl)-phenyl, 3-(2-methylthiazol-5-yl)-phenyl, 3-([1,2,3]-triazol-1-yl)-phenyl, 3-([1,2,4]-triazol-1-yl)-phenyl, 3-([1,2,3]-triazol-2-yl)-phenyl, 3-(4H-[1,2,4]-triazol-3-yl)-phenyl, 3-([1,2,4]-triazol-4-yl)-phenyl, 3-(2H-[1,2,3]-triazol-4-yl)-phenyl, 3-(4-methyl-4H-[1,2,4]-triazol-3-yl)-phenyl, 3-(2-methyl-2H-[1,2,3]-triazol-4-yl)-phenyl, 3-([1,3,4]-oxadiazol-2-yl)-phenyl, 3-(5-methyl-[1,3,4]-oxadiazol-2-yl)-phenyl, 3-([1,2,4]-oxadiazol-3-yl)-phenyl, 3-(5-methyl-[1,2,4]-oxadiazol-3-yl)-phenyl, 3-([1,2,4]-oxadiazol-5-yl)-phenyl, 3-([1,2,3]-oxadiazol-4-yl)-phenyl, 3-([1,2,3]-oxadiazol-5-yl)-phenyl, 3-([1,2,3]-thiadiazol-4-yl)-phenyl, 3-(1H-tetrazol-5-yl)-phenyl, 3-(tetrazol-1-yl)-phenyl, 3-(2-methyl-2H-tetrazol-5-yl)-phenyl, 3-(1-methyl-1H-tetrazol-5-yl)-phenyl, 3-furazan-3-yl-phenyl, 3-(pyrid-2-yl)-phenyl, 3-(pyrid-3-yl)-phenyl, 3-(pyrid-4-yl)-phenyl, 3-(pyrimidin-2-yl)-phenyl, 3-(pyrimidin-4-yl)-phenyl, 3-(2-methylpyrimidin-4-yl)-phenyl, 3-(pyrimidin-5-yl)-phenyl, 5-bromopyridin-3-yl, 3-bromo-2-chloropyridin-5-yl, 4-methylpyridin-2-yl, 6-methylpyridin-2-yl, 4-(trifluoromethyl)-pyridin-2-yl, 6-(trifluoromethyl)-pyridin-2-yl, 5-(trifluoromethyl)-pyridin-3-yl, 5-(pyrrolidin-1-yl)-pyridin-3-yl, 3-(pyrrolidin-1-yl)-2-chloropyridin-5-yl and 3-(morpholin-4-yl)-2-chloropyridin-5-yl.

In an alternatively preferred embodiment; Ar is a group of the formulae (F) or (G), (F) being particularly preferred.

In compounds I, wherein Ar is a radical (F), R^d is preferably selected from halogen, hydroxyl, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl, C₁-C₄-alkylsulfonyl, fluorinated C₁-C₄-alkylsulfonyl, phenylsulfonyl, pyridylsulfonyl, phenyl, where the phenyl and the pyridyl radical in the 3 last-mentioned radicals may be unsubstituted or may carry 1 to 3 substituents selected from C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl and halogen, R⁹-CO-NR⁶-C₁-C₂-alkylene, CH₂-pyridyl, where the pyridyl radical may be unsubstituted or may carry 1

- to 3 substituents selected from C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl and halogen, and a saturated, partially unsaturated or aromatic 5- or 6-membered heterocyclic ring comprising as ring members 1, 2 or 3 heteroatoms selected from N, O and S and/or 1, 2 or 3 heteroatom-containing groups selected from NR⁸, where R⁸ is H, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl, C₁-C₄-alkylcarbonyl or fluorinated C₁-C₄-alkylcarbonyl, and where the heterocyclic ring may carry 1, 2 or 3 substituents selected from hydroxy, halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl, C₁-C₆-alkoxy, fluorinated C₁-C₆-alkoxy, C₁-C₆-alkylthio, fluorinated C₁-C₆-alkylthio, NR⁶R⁷-C₁-C₆-alkylene, carboxyl and C₁-C₄-alkyoxycarbonyl, where R⁶, R⁷ and R⁹ are as defined above.
- More preferably, R^d is selected from halogen, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl, C₁-C₄-alkylsulfonyl, fluorinated C₁-C₄-alkylsulfonyl, phenylsulfonyl, where the phenyl radical may be unsubstituted or may carry 1 to 3 substituents selected from C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl and halogen, and a 5- or 6-membered heteroaromatic ring comprising as ring members one nitrogen atom or one group NR⁸, where R⁸ is H or C₁-C₄-alkyl, and optionally one or two further heteroatoms selected from N, O, S, and where the heteroaromatic ring may carry 1, 2 or 3 substituents selected from halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl, C₁-C₆-alkoxy, fluorinated C₁-C₆-alkoxy, C₁-C₆-alkylthio and fluorinated C₁-C₆-alkylthio.
- Even more preferably, R^d is selected from halogen, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl, phenylsulfonyl, where the phenyl radical may be unsubstituted or may carry 1 to 3 substituents selected from C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl and halogen, and a 5- or 6-membered heteroaromatic ring comprising as ring members one nitrogen atom or one group NR⁸, where R⁸ is H or C₁-C₄-alkyl, and optionally one or two further heteroatoms selected from N, O, S, and where the heteroaromatic ring may carry 1, 2 or 3 substituents selected from halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl, C₁-C₆-alkoxy, fluorinated C₁-C₆-alkoxy, C₁-C₆-alkylthio and fluorinated C₁-C₆-alkylthio.
- The 5-membered heteroaromatic radical can be bound via a ring carbon atom or a nitrogen ring atom.
- The 5- or 6-membered heteroaromatic radical is preferably selected from oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, pyridyl and pyrimidyl. In case the heteroaromatic radical is substituted, it carries preferably one substituent which is preferably selected from halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl, C₁-C₆-alkoxy, fluorinated C₁-C₆-alkoxy, C₁-C₆-alkylthio and fluorinated C₁-C₆-alkylthio and more preferably from F, CH₃, CH₂F, CHF₂, CF₃, OCH₃, OCH₂F, OCHF₂, OCF₃, SCH₃, SCH₂F, SCHF₂ and SCF₃.

k is preferably 0, 1 or 2, more preferably 0 or 1 and in particular 1.

The thienyl radical (F) can be bound to the sulfonyl group SO₂ via its 2- or 3-position, the 2-position (= C-atom adjacent to the ring S atom (S = 1-position)) being preferred. If the thienyl radical carries one radical R^d, this is preferably bound in the 4- or 5-position, more preferably in the 5-position (relative to the 2- or 3-position of the ring atom bound to the sulfonyl group). If the thienyl radical carries two radicals R^d, these are preferably bound in the 4- and 5-position.

Particularly preferred Ar radicals (F) are selected from thien-2-yl, thien-3-yl, 3-chlorothien-2-yl, 4-chlorothien-2-yl, 5-chlorothien-2-yl, 3-bromothien-2-yl, 4-bromothien-2-yl, 5-bromothien-2-yl, 4,5-dichlorothien-2-yl, 4,5-dibromothien-2-yl, 4-bromo-5-chlorothien-2-yl, 3-bromo-5-chlorothien-2-yl, 5-methylthien-2-yl, 5-ethylthien-2-yl, 5-propylthien-2-yl, 5-trifluoromethylthien-2-yl, 5-phenylthien-2-yl, 5-(pyrid-2-yl)-thien-2-yl, 5-(phenylsulfonyl)-thien-2-yl, 4-(phenylsulfonyl)-thien-2-yl, 5-(pyrid-2-ylsulfonyl)-thien-2-yl, 5-(3-chloro-5-trifluoro-pyrid-2-ylsulfonyl)-thien-2-yl, 5-(benzoylaminomethyl)-thien-2-yl, 5-((4-chlorobenzoyl)aminomethyl)-thien-2-yl, 5-(acetylaminomethyl)-thien-2-yl, 5-(pyrazol-1-yl)-thien-2-yl, 5-(pyrazol-3-yl)-thien-2-yl, 5-(pyrazol-4-yl)-thien-2-yl, 5-(pyrazol-5-yl)-thien-2-yl, 5-(4-fluoropyrazol-1-yl)-thien-2-yl, 5-(1-methyl-5-trifluoromethyl-(1H)-pyrazol-3-yl)-thien-2-yl, 5-(1-methyl-3-trifluoromethyl-(1H)-pyrazol-5-yl)-thien-2-yl, 5-(4-carboxy-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl, 5-(4-aminomethyl-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl, 5-(isoxazol-3-yl)-thien-2-yl, 5-(isoxazol-4-yl)-thien-2-yl, 5-(isoxazol-5-yl)-thien-2-yl, 5-(5-trifluoromethylisoxazol-3-yl)-thien-2-yl, 5-(oxazol-2-yl)-thien-2-yl, 5-(oxazol-4-yl)-thien-2-yl, 5-(oxazol-5-yl)-thien-2-yl, 5-(2-methyloxazol-4-yl)-thien-2-yl, 5-(2-methyloxazol-5-yl)-thien-2-yl, 5-(isothiazol-3-yl)-thien-2-yl, 5-(isothiazol-4-yl)-thien-2-yl, 5-(isothiazol-5-yl)-thien-2-yl, 5-(5-trifluoromethylisothiazol-3-yl)-thien-2-yl, 5-(thiazol-2-yl)-thien-2-yl, 5-(thiazol-4-yl)-thien-2-yl, 5-(thiazol-5-yl)-thien-2-yl, 5-(2-methylthiazol-4-yl)-thien-2-yl, 5-(2-methylthiazol-5-yl)-thien-2-yl, 5-([1,2,3]-oxadiazol-4-yl)-thien-2-yl, 5-([1,2,3]-thiadiazol-4-yl)-thien-2-yl, 5-(pyrimidin-2-yl)-thien-2-yl, 5-(pyrimidin-4-yl)-thien-2-yl, 5-(pyrimidin-5-yl)-thien-2-yl, 5-(2-methylthiopyrimidin-4-yl)-thien-2-yl, 5-([1,3]-dioxolan-2-yl)-thien-2-yl, 3-([1,3]-dioxolan-2-yl)-thien-2-yl, 5-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)-methyl)-thien-2-yl, 5-[3-chloro-5-(trifluoromethyl)-pyrid-2-ylsulfonyl]-thien-2-yl, 2-chlorothien-3-yl, 4-chlorothien-3-yl, 5-chlorothien-3-yl, 2-bromothien-3-yl, 4-bromothien-3-yl, 5-bromothien-3-yl, 2,5-dichlorothien-3-yl, 2,5-dibromothien-3-yl, 2,4,5-trichlorothien-3-yl, 4-bromo-2,5-dichlorothien-3-yl, 2-chloro-5-methylsulfonylthien-3-yl, 2,5-dimethylthien-3-yl, 4-hydroxythien-3-yl, 2-phenylthien-3-yl, 4-phenyl-5-(trifluoromethyl)-thien-3-yl and 2-methoxycarbonyl-4-phenyl-5-(trifluoromethyl)-thien-3-yl.

In compounds I, wherein Ar is a radical (G), R^e is preferably selected from H, halogen, C₁-C₄-alkyl and fluorinated C₁-C₄-alkyl, more preferably from halogen, C₁-C₄-alkyl and fluorinated C₁-C₄-alkyl and more preferably from C₁-C₄-alkyl, specifically CH₃.

- 5 R^f is preferably selected from halogen, C₁-C₄-alkyl and fluorinated C₁-C₄-alkyl, more preferably from halogen, specifically chlorine.

j is preferably 0 or 1, in particular 1. In case j is 1, R^f is preferably bound at the 4- or in particular at the 5-position (relative to the 3-position of R^e).

- 10 In compounds I, wherein Ar is a radical (G), n is specifically 0.

- Particularly preferred Ar radicals (G) are selected from benzo[b]thiophen-2-yl, benzo[b]thiophen-3-yl, 3-methyl-benzo[b]thiophen-2-yl, 5-methyl-benzo[b]thiophen-2-yl, 5-fluoro-3-methyl-benzo[b]thiophen-2-yl, 5-chloro-3-methyl-benzo[b]thiophen-2-yl and
15 5-bromo-3-methyl-benzo[b]thiophen-2-yl.

- In one preferred embodiment, A is 1,3-phenylene. In this case, the radicals R¹, R², R³, R⁴, E and Ar with its variables R^a, R^b, R^c, R^d, R^e and R^f have the above general or preferred meanings.

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- In an alternatively preferred embodiment, A is 1,4-phenylene. In this case, the radicals R¹, R², R³, R⁴, E and Ar with its variables R^a, R^b, R^c, R^d, R^e and R^f have the above general or preferred meanings. However, R^a in this case is preferably selected from the group consisting of C₁-C₆-alkyl, C₁-C₆-hydroxyalkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₂-C₆-
25 alkenyl, fluorinated C₂-C₆-alkenyl, C₃-C₆-cycloalkyl, fluorinated C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₁-C₆-hydroxyalkoxy, C₁-C₆-alkoxy-C₁-C₆-alkoxy, C₁-C₆-alkylthio, fluorinated C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, fluorinated C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, fluorinated C₁-C₆-alkylsulfonyl, phenylsulfonyl, benzyloxy, phenoxy, where the phenyl radical in the 3 last-mentioned radicals may be unsubstituted or may carry 1 to 3 substituents selected from C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl and halogen, CN, nitro, C₁-
30 C₆-alkylcarbonyl, fluorinated C₁-C₆-alkylcarbonyl, C₁-C₆-alkylcarbonylamino, fluorinated C₁-C₆-alkylcarbonylamino, carboxy, NH-C(O)-NR⁶R⁷, NR⁶R⁷, NR⁶R⁷-C₁-C₆-alkylene, O-NR⁶R⁷, where R⁶ and R⁷ are, independently of each other, H, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl or C₁-C₄-alkoxy or may form, together with N, a 4-, 5- or 6-membered saturated or unsaturated ring, or is a saturated or unsaturated 3- to 7-membered heterocyclic ring comprising as ring members 1, 2, 3 or 4 heteroatoms selected from N, O and S and/or 1, 2 or 3 heteroatom-containing groups selected from NR⁸, where R⁸ is as defined above, SO, SO₂ and CO, and where the heterocyclic ring may carry 1, 2 or 3 substituents selected from hydroxy, halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl and
40 C₁-C₆-alkoxy. More preferably, R^a in this case is selected from the group consisting of

C₁-C₆-alkyl, C₁-C₆-hydroxyalkyl, C₁-C₄-alkoxy, C₁-C₄-alkoxy-C₁-C₄-alkoxy, C₂-C₄-alkenyl, fluorinated C₂-C₄-alkenyl, NR⁶R⁷, ONR⁶R⁷, C₁-C₆-alkylene-NR⁶R⁷, where R⁶ and R⁷ are independently of each other H, C₁-C₄-alkyl or C₁-C₄-alkoxy, ureido (NHCONH₂) C₃-C₆-cycloalkyl, fluorinated C₃-C₆-cycloalkyl, acetyl, carboxyl, hydroxy, cyano, nitro, benzoxy, methylsulfanyl, fluoromethylsulfanyl, difluoromethylsulfanyl, trifluoromethylsulfanyl, methylsulfonyl and one of the above-mentioned saturated or unsaturated 3- to 7-membered heterocyclic rings, in particular azetidin-1-yl, 2-methylazetidinyl, 3-methoxyazetidinyl, 3-hydroxyazetidinyl, 3-fluoroazetidinyl, 2,2-difluoroazetidin-1-yl, pyrrolidin-1-yl, pyrrolidin-2-yl, pyrrolidin-3-yl, 2- and 3-fluoropyrrolidin-1-yl, 2,2-difluoropyrrolidin-1-yl, 3,3-difluoropyrrolidin-1-yl, 2- and 3-methylpyrrolidin-1-yl, 1-methylpyrrolidin-2-yl, 2,2-dimethylpyrrolidin-1-yl, 3,3-dimethylpyrrolidin-1-yl, 2-oxo-pyrrolidin-1-yl, 2- and 3-trifluoromethylpyrrolidin-1-yl, 2-oxo-oxazolidin-1-yl, piperidin-1-yl, 2-methylpiperidin-1-yl, 3-(2-fluoropiperidin-1-yl)-phenyl, 3-((S)-2-fluoropiperidin-1-yl)-phenyl, 3-((R)-2-fluoropiperidin-1-yl)-phenyl, 3-(2,2-difluoropiperidin-1-yl)-phenyl, piperazin-1-yl, 4-methylpiperazin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, 1-oxothiomorpholin-4-yl, 1,1-dioxothiomorpholin-4-yl, pyrrol-1-yl, pyrrol-2-yl, pyrrol-3-yl, 1-methylpyrrol-2-yl, 1-methylpyrrol-3-yl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, 1-methylpyrazol-4-yl, 4-fluoropyrazol-1-yl, imidazol-1-yl, imidazol-2-yl, 1-methylimidazol-2-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, isoxazol-3-yl, isoxazol-4-yl, isoxazol-5-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, 2-methylthiazol-4-yl, 2-methylthiazol-5-yl, [1,2,3]triazol-1-yl, [1,2,4]triazol-1-yl, [1,2,3]triazol-2-yl, [1,2,4]triazol-3-yl, [1,2,4]triazol-4-yl, 4-methyl-[1,2,4]triazol-3-yl, 2-methyl-[1,2,3]triazol-4-yl, [1,3,4]-oxadiazol-2-yl, [1,2,4]-oxadiazol-3-yl, [1,2,4]-oxadiazol-5-yl, [1,2,3]-oxadiazol-5-yl, [1,3,4]-oxadiazol-2-yl, 5-methyl-[1,3,4]-oxadiazol-2-yl, 5-methyl-[1,2,4]-oxadiazol-3-yl, [1,2,3]thiadiazol-4-yl, tetrazol-1-yl, tetrazol-5-yl, 2-methyltetrazol-5-yl, 1-methyltetrazol-5-yl, furazan-3-yl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl and 2-methylpyrimidin-4-yl.

Even more preferably, R^a in this case is selected from the group consisting of C₁-C₆-alkyl, C₁-C₄-alkoxy, C₂-C₄-alkenyl, C₃-C₆-cycloalkyl, fluorinated C₃-C₆-cycloalkyl, ureido, acetyl, acetylamino, carboxyl, hydroxy, cyano, nitro, benzoxy, trifluoromethylsulfanyl, methylsulfonyl, azetidin-1-yl, 2-methylazetidinyl, 3-methoxyazetidinyl, 3-hydroxyazetidinyl, 3-fluoroazetidinyl, 2,2-difluoroazetidin-1-yl, pyrrolidin-1-yl, pyrrolidin-2-yl, pyrrolidin-3-yl, 2- and 3-fluoropyrrolidin-1-yl, 2,2-difluoropyrrolidin-1-yl, 3,3-difluoropyrrolidin-1-yl, 2- and 3-methylpyrrolidin-1-yl, 1-methylpyrrolidin-2-yl, 2,2-dimethylpyrrolidin-1-yl, 3,3-dimethylpyrrolidin-1-yl, 2-oxo-pyrrolidin-1-yl, 2- and 3-trifluoromethylpyrrolidin-1-yl, 2-oxo-oxazolidin-1-yl, piperidin-1-yl, 2-methylpiperidin-1-yl, 3-(2-fluoropiperidin-1-yl)-phenyl, 3-((S)-2-fluoropiperidin-1-yl)-phenyl, 3-((R)-2-fluoropiperidin-1-yl)-phenyl, 3-(2,2-difluoropiperidin-1-yl)-phenyl, piperazin-1-yl, 4-methylpiperazin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, 1-oxothiomorpholin-4-yl, 1,1-

dioxothiomorpholin-4-yl, pyrrol-1-yl, pyrrol-2-yl, pyrrol-3-yl, 1-methylpyrrol-2-yl, 1-methylpyrrol-3-yl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, 1-methylpyrazol-4-yl, 4-fluoropyrazol-1-yl, imidazol-1-yl, imidazol-2-yl, 1-methylimidazol-2-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, isoxazol-3-yl, isoxazol-4-yl, isoxazol-5-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, 2-methylthiazol-4-yl, 2-methylthiazol-5-yl, [1,2,3]triazol-1-yl, [1,2,4]triazol-1-yl, [1,2,3]triazol-2-yl, [1,2,4]triazol-3-yl, [1,2,4]triazol-4-yl, 4-methyl-[1,2,4]triazol-3-yl, 2-methyl-[1,2,3]triazol-4-yl, [1,3,4]-oxadiazol-2-yl, [1,2,4]-oxadiazol-3-yl, [1,2,4]-oxadiazol-5-yl, [1,2,3]-oxadiazol-5-yl, [1,3,4]-oxadiazol-2-yl, 5-methyl-[1,3,4]-oxadiazol-2-yl, 5-methyl-[1,2,4]-oxadiazol-3-yl, [1,2,3]thiadiazol-4-yl, tetrazol-1-yl, tetrazol-5-yl, 2-methyltetrazol-5-yl, 1-methyltetrazol-5-yl, furazan-3-yl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, 4-methylpyridin-2-yl, 6-methylpyridin-2-yl, 5-bromopyridin-2-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl and 2-methylpyrimidin-4-yl.

In this case, i.e. if A is 1,4-phenylene, preferred examples for Ar are in particular the following: 3-methylphenyl, 3-ethylphenyl, 3-propylphenyl, 3-isopropylphenyl, 3-sec-butylphenyl, 3-isobutylphenyl, 3-tert-butylphenyl, 3-(1,1-dimethylpropyl)-phenyl, 3-vinylphenyl, 3-isopropenylphenyl, 3-methoxyphenyl, 3-ethoxyphenyl, 3-propoxyphenyl, 3-isopropoxyphenyl, 3-butoxyphenyl, 3-cyclopropylphenyl, 3-cyclobutylphenyl, 3-cyclopentylphenyl, 3-(2,2-difluorocyclopropyl)-phenyl, 3-(1-hydroxy-1-methylethyl)-phenyl, 3-(2-hydroxy-2-methylpropyl)-phenyl, 3-(cyanophenyl, 2,5-dimethylphenyl, 2,5-di-(trifluoromethyl)-phenyl, 3,5-di-(trifluoromethyl)-phenyl, 2,5-dimethoxyphenyl, 2-methoxy-5-methylphenyl, 2-methoxy-5-(trifluoromethyl)-phenyl, 3-acetylphenyl, 3-acetylaminophenyl, 3-carboxyphenyl, 3-cyanophenyl, 3-nitrophenyl, 3-hydroxyphenyl, 3-(O-benzyl)-phenyl, 3-(2-methoxyethoxy)-phenyl, 3-(CH₂-N(CH₃)₂)-phenyl, 3-(NH-CO-NH₂)-phenyl, 3-(methylsulfanyl)-phenyl, 3-(fluoromethylsulfanyl)-phenyl, 3-(difluoromethylsulfanyl)-phenyl, 3-(trifluoromethylsulfanyl)-phenyl, 3-(methylsulfonyl)-phenyl, 3-(N-methoxy-N-methyl-amino)-phenyl, 3-(methoxyamino)-phenyl, 3-(ethoxyamino)-phenyl, 3-(N-methylaminooxy)-phenyl, 3-(N,N-dimethylaminooxy)-phenyl, 3-(azetidin-1-yl)-phenyl, 3-(2-methylazetidin-1-yl)-phenyl, 3-((S)-2-methylazetidin-1-yl)-phenyl, 3-((R)-2-methylazetidin-1-yl)-phenyl, 3-(3-fluoroazetidin-1-yl)-phenyl, 3-(2,2-difluoroazetidin-1-yl)-phenyl, 3-(3-methoxyazetidin-1-yl)-phenyl, 3-(3-hydroxyazetidin-1-yl)-phenyl, 3-(pyrrolidin-1-yl)-phenyl, 3-(pyrrolidin-2-yl)-phenyl, 3-((S)-pyrrolidin-2-yl)-phenyl, 3-((R)-pyrrolidin-2-yl)-phenyl, 3-(pyrrolidin-3-yl)-phenyl, 3-((S)-pyrrolidin-3-yl)-phenyl, 3-((R)-pyrrolidin-3-yl)-phenyl, 3-(pyrrolidin-1-yl)-5-(trifluoromethyl)-phenyl, 5-(pyrrolidin-1-yl)-2-methoxyphenyl, 3-(pyrrolidin-1-yl)-4-methoxyphenyl, 5-(pyrrolidin-1-yl)-2,4-difluorophenyl, 3-(pyrrolidin-1-yl)-2,4-difluorophenyl, 3-(2-fluoropyrrolidin-1-yl)-phenyl, 3-((S)-2-fluoropyrrolidin-1-yl)-phenyl, 3-((R)-2-fluoropyrrolidin-1-yl)-phenyl, 3-(3-fluoropyrrolidin-1-yl)-phenyl, 3-((S)-3-fluoropyrrolidin-1-yl)-phenyl, 3-((R)-3-fluoropyrrolidin-1-yl)-phenyl, 3-(2,2-difluoropyrrolidin-1-yl)-phenyl, 3-(3,3-difluoropyrrolidin-1-yl)-phenyl, 3-(2-

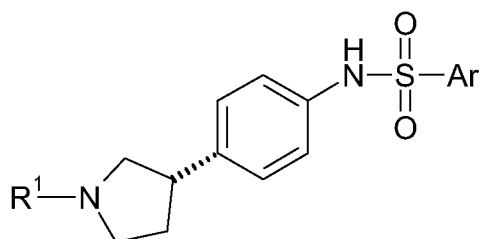
methylpyrrolidin-1-yl)-phenyl, 3-((S)-2-methylpyrrolidin-1-yl)-phenyl, 3-((R)-2-methylpyrrolidin-1-yl)-phenyl, 3-(3-methylpyrrolidin-1-yl)-phenyl, 3-((S)-3-methylpyrrolidin-1-yl)-phenyl, 3-((R)-3-methylpyrrolidin-1-yl)-phenyl, 3-(1-methylpyrrolidin-2-yl)-phenyl, 3-((S)-1-methylpyrrolidin-2-yl)-phenyl, 3-((R)-1-methylpyrrolidin-2-yl)-phenyl, 3-(1-methylpyrrolidin-3-yl)-phenyl, 3-((S)-1-methylpyrrolidin-3-yl)-phenyl, 3-((R)-1-methylpyrrolidin-3-yl)-phenyl, 3-(2,2-dimethylpyrrolidin-1-yl)-phenyl, 3-(3,3-dimethylpyrrolidin-1-yl)-phenyl, 3-(2-trifluoromethylpyrrolidin-1-yl)-phenyl, 3-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl, 3-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl, 3-(3-trifluoromethylpyrrolidin-1-yl)-phenyl, 3-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl, 3-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl, 3-(2-oxopyrrolidin-1-yl)-phenyl, 3-(2-oxo-oxazolidin-3-yl)-phenyl, 3-(piperidin-1-yl)-phenyl, 3-(2-methylpiperidin-1-yl)-phenyl, 3-((S)-2-methylpiperidin-1-yl)-phenyl, 3-((R)-2-methylpiperidin-1-yl)-phenyl, 3-(2-fluoropiperidin-1-yl)-phenyl, 3-((S)-2-fluoropiperidin-1-yl)-phenyl, 3-((R)-2-fluoropiperidin-1-yl)-phenyl, 3-(2,2-difluoropiperidin-1-yl)-phenyl, 3-(piperazin-1-yl)-phenyl, 3-(4-methylpiperazin-1-yl)-phenyl, 3-(morpholin-4-yl)-phenyl, 3-(morpholin-4-yl)-5-(trifluoromethyl)-phenyl, 5-(morpholin-4-yl)-2-methoxyphenyl, 3-(morpholin-4-yl)-4-methoxyphenyl, 5-(morpholin-4-yl)-2,4-difluorophenyl, 3-(morpholin-4-yl)-2,4-difluorophenyl, 3-(thiomorpholin-4-yl)-phenyl, 3-(1-oxo-thiomorpholin-4-yl)-phenyl, 3-(1,1-dioxo-thiomorpholin-4-yl)-phenyl, 3-(pyrrol-1-yl)-phenyl, 3-(pyrrol-2-yl)-phenyl, 3-(pyrrol-3-yl)-phenyl, 3-(1-methylpyrrol-2-yl)-phenyl, 3-(1-methylpyrrol-3-yl)-phenyl, 3-(furan-2-yl)-phenyl, 3-(furan-3-yl)-phenyl, 3-(thiophen-2-yl)-phenyl, 3-(thiophen-3-yl)-phenyl, 3-(5-propylthien-2-yl)-phenyl, 3-(pyrazol-1-yl)-phenyl, 3-(pyrazol-3-yl)-phenyl, 3-(pyrazol-4-yl)-phenyl, 3-(1-methyl-1H-pyrazol-4-yl)-phenyl, 3-(1-ethyl-1H-pyrazol-4-yl)-phenyl, 3-(1-methyl-1H-pyrazol-5-yl)-phenyl, 3-(4-fluoropyrazol-1-yl)-phenyl, 3-(1H-imidazol-2-yl)-phenyl, 3-(imidazol-1-yl)-phenyl, 3-(1-methylimidazol-2-yl)-phenyl, 3-(oxazol-2-yl)-phenyl, 3-(oxazol-4-yl)-phenyl, 3-(oxazol-5-yl)-phenyl, 4-fluoro-3-(oxazol-4-yl)-phenyl, 3-(isoxazol-3-yl)-phenyl, 3-(isoxazol-4-yl)-phenyl, 3-(isoxazol-5-yl)-phenyl, 3-(thiazol-2-yl)-phenyl, 3-(thiazol-4-yl)-phenyl, 3-(thiazol-5-yl)-phenyl, 3-(2-methylthiazol-4-yl)-phenyl, 3-(2-methylthiazol-5-yl)-phenyl, 3-([1,2,3]-triazol-1-yl)-phenyl, 3-([1,2,4]-triazol-1-yl)-phenyl, 3-([1,2,3]-triazol-2-yl)-phenyl, 3-(4H-[1,2,4]-triazol-3-yl)-phenyl, 3-([1,2,4]-triazol-4-yl)-phenyl, 3-(2H-[1,2,3]-triazol-4-yl)-phenyl, 3-(4-methyl-4H-[1,2,4]-triazol-3-yl)-phenyl, 3-(2-methyl-2H-[1,2,3]-triazol-4-yl)-phenyl, 3-([1,3,4]-oxadiazol-2-yl)-phenyl, 3-(5-methyl-[1,3,4]-oxadiazol-2-yl)-phenyl, 3-([1,2,4]-oxadiazol-3-yl)-phenyl, 3-(5-methyl-[1,2,4]-oxadiazol-3-yl)-phenyl, 3-([1,2,4]-oxadiazol-5-yl)-phenyl, 3-([1,2,3]-oxadiazol-4-yl)-phenyl, 3-([1,2,3]-oxadiazol-5-yl)-phenyl, 3-([1,2,3]-thiadiazol-4-yl)-phenyl, 3-(1H-tetrazol-5-yl)-phenyl, 3-(tetrazol-1-yl)-phenyl, 3-(2-methyl-2H-tetrazol-5-yl)-phenyl, 3-(1-methyl-1H-tetrazol-5-yl)-phenyl, 3-furazan-3-yl-phenyl, 3-(pyrid-2-yl)-phenyl, 3-(pyrid-3-yl)-phenyl, 3-(pyrid-4-yl)-phenyl, 3-(pyrimidin-2-yl)-phenyl, 3-(pyrimidin-4-yl)-phenyl, 3-(2-methylpyrimidin-4-yl)-phenyl, 3-(pyrimidin-5-yl)-phenyl, 5-bromopyridin-3-yl, 3-bromo-2-

chloropyridin-5-yl, 4-methylpyridin-2-yl, 6-methylpyridin-2-yl, 4-(trifluoromethyl)-pyridin-2-yl, 6-(trifluoromethyl)-pyridin-2-yl, 5-(trifluoromethyl)-pyridin-3-yl, 5-(pyrrolidin-1-yl)-pyridin-3-yl, 3-(pyrrolidin-1-yl)-2-chloropyridin-5-yl and 3-(morpholin-4-yl)-2-chloropyridin-5-yl.

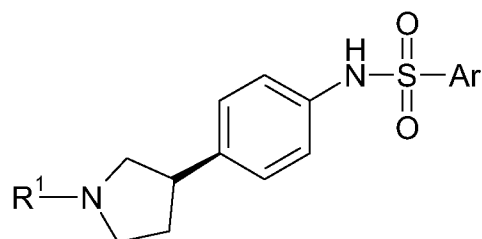
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Particularly preferred compounds I are those of formulae I.a, I.b, I.c, I.d, I.e, I.f, I.g, I.h, I.i, I.k, I.l, I.m, I.n, I.o, I.p, I.q, I.r, I.s and I.t, wherein R¹ and Ar have the above-defined meanings. Preferred meanings of R¹ and Ar are as defined above.

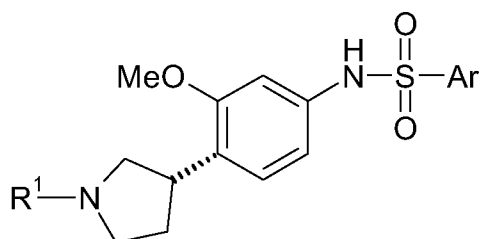
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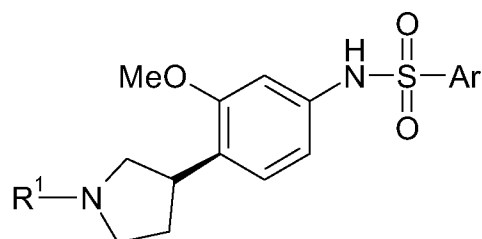
I.a



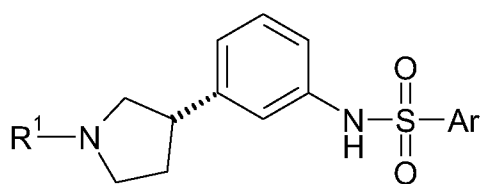
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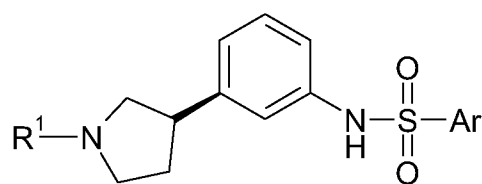
I.c



I.d

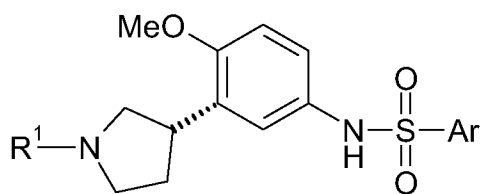


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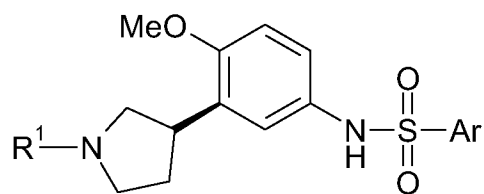


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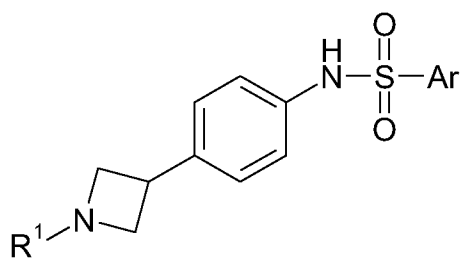
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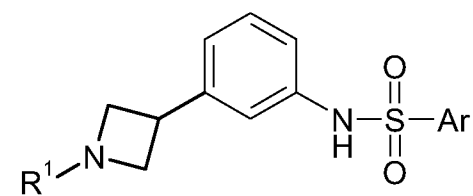
I.g



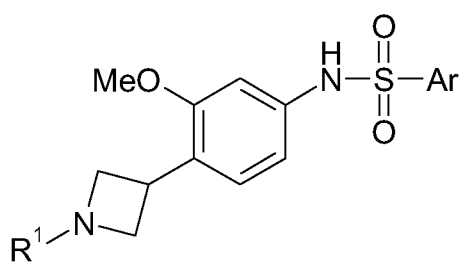
I.h



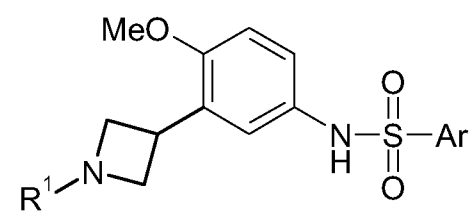
I.i



I.j

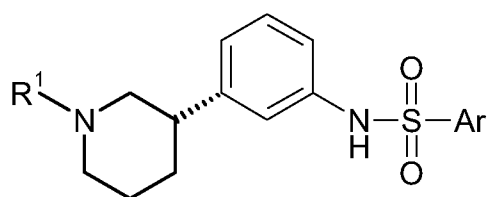


I.k

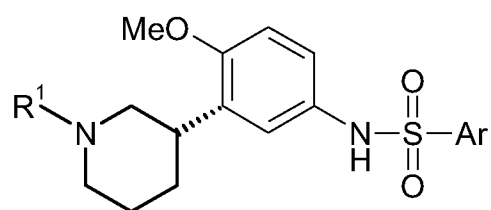


I.l

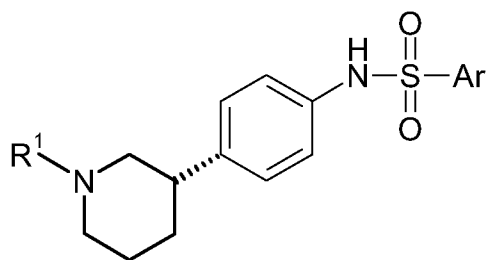
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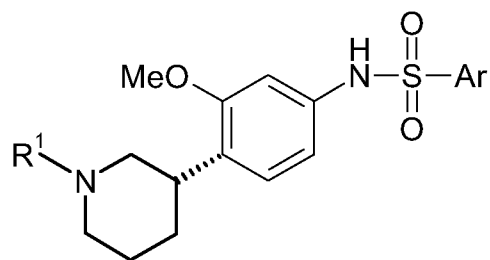
I.m



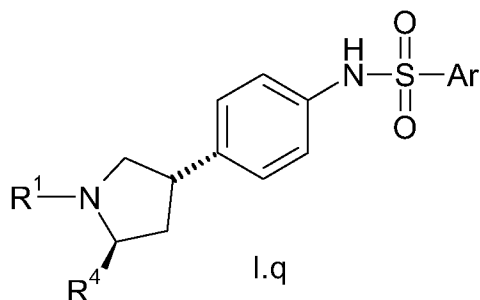
I.n



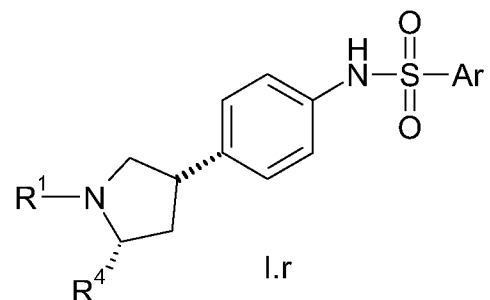
I.o



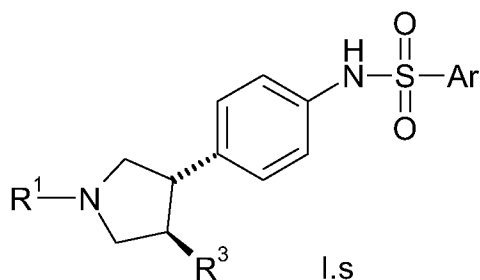
I.p



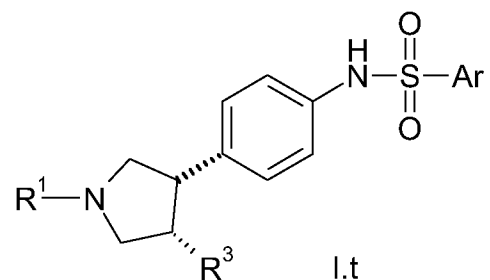
I.q



I.r



I.s



I.t

5

Examples of preferred compounds which are represented by the formulae I.q, I.r, I.s and I.t are listed in following tables 1 to :

10 Table 1

Compounds of the formula I.q in which R⁴ is methyl and the combination of R¹ and Ar for a compound corresponds in each case to one row of Table A

Table 2

Compounds of the formula I.q in which R⁴ is fluoromethyl and the combination of R¹ and Ar for a compound corresponds in each case to one row of Table A

15

Table 3

Compounds of the formula I.q in which R⁴ is difluoromethyl and the combination of R¹ and Ar for a compound corresponds in each case to one row of Table A

Table 4

Compounds of the formula I.q in which R⁴ is trifluoromethyl and the combination of R¹ and Ar for a compound corresponds in each case to one row of Table A

20

Table 5

Compounds of the formula I.r in which R⁴ is methyl and the combination of R¹ and Ar for a compound corresponds in each case to one row of Table A

Table 6

- 5 Compounds of the formula I.r in which R⁴ is fluoromethyl and the combination of R¹ and Ar for a compound corresponds in each case to one row of Table A

Table 7

Compounds of the formula I.r in which R⁴ is difluoromethyl and the combination of R¹ and Ar for a compound corresponds in each case to one row of Table A

10 Table 8

Compounds of the formula I.r in which R⁴ is trifluoromethyl and the combination of R¹ and Ar for a compound corresponds in each case to one row of Table A

Table 9

- 15 Compounds of the formula I.s in which R³ is methyl and the combination of R¹ and Ar for a compound corresponds in each case to one row of Table A

Table 10

Compounds of the formula I.s in which R³ is fluoromethyl and the combination of R¹ and Ar for a compound corresponds in each case to one row of Table A

Table 11

- 20 Compounds of the formula I.s in which R³ is difluoromethyl and the combination of R¹ and Ar for a compound corresponds in each case to one row of Table A

Table 12

Compounds of the formula I.r in which R³ is trifluoromethyl and the combination of R¹ and Ar for a compound corresponds in each case to one row of Table A

25 Table 13

Compounds of the formula I.t in which R³ is methyl and the combination of R¹ and Ar for a compound corresponds in each case to one row of Table A

Table 14

- 30 Compounds of the formula I.t in which R³ is fluoromethyl and the combination of R¹ and Ar for a compound corresponds in each case to one row of Table A

Table 15

Compounds of the formula I.t in which R³ is difluoromethyl and the combination of R¹ and Ar for a compound corresponds in each case to one row of Table A

Table 16

- 35 Compounds of the formula I.t in which R³ is trifluoromethyl and the combination of R¹ and Ar for a compound corresponds in each case to one row of Table A

- 40 Examples of preferred compounds which are represented by the formulae I.a, I.b, I.c, I.d, I.e, I.f, I.g, I.h, I.i, I.k, I.l, I.m, I.n, I.o, I.p, I.q, I.r, I.s and I.t are the individual com-

pounds listed above, where the variables Ar and R¹ have the meanings given in one row of table A.

Table A

5

No.	R ¹	Ar
1.	propyl	3-methylphenyl
2.	propyl	3-ethylphenyl
3.	propyl	3-propylphenyl
4.	propyl	3-isopropylphenyl
5.	propyl	3-sec-butylphenyl
6.	propyl	3-tert-butylphenyl
7.	propyl	3-isobutylphenyl
8.	propyl	3-(1,1-dimethylpropyl)-phenyl
9.	propyl	3-vinylphenyl
10.	propyl	3-isopropenylphenyl
11.	propyl	3-fluorophenyl
12.	propyl	3-chlorophenyl
13.	propyl	3-bromophenyl
14.	propyl	3-iodophenyl
15.	propyl	3-(fluoromethyl)phenyl
16.	propyl	3-(difluoromethyl)phenyl
17.	propyl	3-(trifluoromethyl)phenyl
18.	propyl	3,5-bis(trifluoromethyl)phenyl
19.	propyl	3-(1-fluoroethyl)-phenyl
20.	propyl	3-((S)-1-fluoroethyl)-phenyl
21.	propyl	3-((R)-1-fluoroethyl)-phenyl
22.	propyl	3-(2-fluoroethyl)-phenyl
23.	propyl	3-(1,1-difluoroethyl)-phenyl
24.	propyl	3-(2,2-difluoroethyl)-phenyl
25.	propyl	3-(2,2,2-trifluoroethyl)-phenyl
26.	propyl	3-(3-fluoropropyl)-phenyl
27.	propyl	3-(2-fluoropropyl)-phenyl
28.	propyl	3-((S)-2-fluoropropyl)-phenyl
29.	propyl	3-((R)-2-fluoropropyl)-phenyl
30.	propyl	3-(3,3-difluoropropyl)-phenyl
31.	propyl	3-(3,3,3-trifluoropropyl)-phenyl
32.	propyl	3-(1-fluoro-1-methylethyl)-phenyl
33.	propyl	3-(2-fluoro-1-methylethyl)-phenyl

No.	R ¹	Ar
34.	propyl	3-((S)-2-fluoro-1-methylethyl)-phenyl
35.	propyl	3-((R)-2-fluoro-1-methylethyl)-phenyl
36.	propyl	3-(2,2-difluoro-1-methylethyl)-phenyl
37.	propyl	3-((S)-2,2-difluoro-1-methylethyl)-phenyl
38.	propyl	3-((R)-2,2-difluoro-1-methylethyl)-phenyl
39.	propyl	3-(2,2,2-trifluoro-1-methylethyl)-phenyl
40.	propyl	3-((S)-2,2,2-trifluoro-1-methylethyl)-phenyl
41.	propyl	3-((R)-2,2,2-trifluoro-1-methylethyl)-phenyl
42.	propyl	3-(2-fluoro-1-fluoromethylethyl)-phenyl
43.	propyl	3-(1-difluoromethyl-2,2-difluoroethyl)-phenyl
44.	propyl	3-(1,1-dimethyl-2-fluoroethyl)-phenyl
45.	propyl	3-methoxyphenyl
46.	propyl	3-ethoxyphenyl
47.	propyl	3-propoxyphenyl
48.	propyl	3-isopropoxyphenyl
49.	propyl	3-butoxyphenyl
50.	propyl	3-(fluoromethoxy)-phenyl
51.	propyl	3-(difluoromethoxy)-phenyl
52.	propyl	3-(trifluoromethoxy)-phenyl
53.	propyl	3-(2-fluoroethoxy)-phenyl
54.	propyl	3-(2,2-difluoroethoxy)-phenyl
55.	propyl	3-(2,2,2-trifluoroethoxy)-phenyl
56.	propyl	3-(1,1,2,2-tetrafluoroethoxy)-phenyl
57.	propyl	3-cyclopropylphenyl
58.	propyl	3-cyclobutylphenyl
59.	propyl	3-cyclopentylphenyl
60.	propyl	3-(2,2-difluorocyclopropyl)-phenyl
61.	propyl	3,4-difluorophenyl
62.	propyl	3-bromo-2-fluorophenyl
63.	propyl	2-bromo-3-fluorophenyl
64.	propyl	3-bromo-2,5-difluorophenyl
65.	propyl	5-bromo-2,4-difluorophenyl
66.	propyl	3-bromo-2,4-difluorophenyl
67.	propyl	4-chloro-3-(trifluoromethyl)-phenyl
68.	propyl	2-chloro-5-(trifluoromethyl)-phenyl
69.	propyl	2-fluoro-5-(trifluoromethyl)-phenyl
70.	propyl	4-fluoro-3-(trifluoromethyl)-phenyl
71.	propyl	3-fluoro-5-(trifluoromethyl)-phenyl

No.	R ¹	Ar
72.	propyl	4-bromo-3-(trifluoromethyl)-phenyl
73.	propyl	3-bromo-5-(trifluoromethyl)-phenyl
74.	propyl	2-bromo-5-(trifluoromethyl)-phenyl
75.	propyl	5-bromo-2-methoxyphenyl
76.	propyl	3-bromo-4-methoxyphenyl
77.	propyl	2-fluoro-3-isopropylphenyl
78.	propyl	4-fluoro-3-isopropylphenyl
79.	propyl	3-(1-hydroxy-1-methylethyl)-phenyl
80.	propyl	3-(2-hydroxy-2-methylpropyl)-phenyl
81.	propyl	3-acetylphenyl
82.	propyl	3-acetylaminophenyl
83.	propyl	3-carboxyphenyl
84.	propyl	3-cyanophenyl
85.	propyl	3-nitrophenyl
86.	propyl	3-hydroxyphenyl
87.	propyl	3-(O-benzyl)-phenyl
88.	propyl	3-(2-methoxyethoxy)-phenyl
89.	propyl	3-(CH ₂ -N(CH ₃) ₂)-phenyl
90.	propyl	3-(NH-CO-NH ₂)-phenyl
91.	propyl	3-(methylsulfanyl)-phenyl
92.	propyl	3-(fluoromethylsulfanyl)-phenyl
93.	propyl	3-(difluoromethylsulfanyl)-phenyl
94.	propyl	3-(trifluoromethylsulfanyl)-phenyl
95.	propyl	3-(methylsulfonyl)-phenyl
96.	propyl	3-(N-methoxy-N-methyl-amino)-phenyl
97.	propyl	3-(methoxyamino)-phenyl
98.	propyl	3-(ethoxyamino)-phenyl
99.	propyl	3-(N-methylaminooxy)-phenyl
100.	propyl	3-(N,N-dimethylaminooxy)-phenyl
101.	propyl	3-(azetidin-1-yl)-phenyl
102.	propyl	3-(2-methylazetidin-1-yl)-phenyl
103.	propyl	3-((S)-2-methylazetidin-1-yl)-phenyl
104.	propyl	3-((R)-2-methylazetidin-1-yl)-phenyl
105.	propyl	3-(3-fluoroazetidin-1-yl)-phenyl
106.	propyl	3-(2,2-difluoroazetidin-1-yl)-phenyl
107.	propyl	3-(3-methoxyazetidin-1-yl)-phenyl
108.	propyl	3-(3-hydroxyazetidin-1-yl)-phenyl
109.	propyl	3-(pyrrolidin-1-yl)-phenyl

No.	R ¹	Ar
110.	propyl	3-(pyrrolidin-2-yl)-phenyl
111.	propyl	3-((S)-pyrrolidin-2-yl)-phenyl
112.	propyl	3-((R)-pyrrolidin-2-yl)-phenyl
113.	propyl	3-(pyrrolidin-3-yl)-phenyl
114.	propyl	3-((S)-pyrrolidin-3-yl)-phenyl
115.	propyl	3-((R)-pyrrolidin-3-yl)-phenyl
116.	propyl	3-(pyrrolidin-1-yl)-5-(trifluoromethyl)-phenyl
117.	propyl	5-(pyrrolidin-1-yl)-2-methoxyphenyl
118.	propyl	3-(pyrrolidin-1-yl)-4-methoxyphenyl
119.	propyl	5-(pyrrolidin-1-yl)-2,4-difluorophenyl
120.	propyl	3-(pyrrolidin-1-yl)-2,4-difluorophenyl
121.	propyl	3-(2-fluoropyrrolidin-1-yl)-phenyl
122.	propyl	3-((S)-2-fluoropyrrolidin-1-yl)-phenyl
123.	propyl	3-((R)-2-fluoropyrrolidin-1-yl)-phenyl
124.	propyl	3-(3-fluoropyrrolidin-1-yl)-phenyl
125.	propyl	3-((S)-3-fluoropyrrolidin-1-yl)-phenyl
126.	propyl	3-((R)-3-fluoropyrrolidin-1-yl)-phenyl
127.	propyl	3-(2,2-difluoropyrrolidin-1-yl)-phenyl
128.	propyl	3-(3,3-difluoropyrrolidin-1-yl)-phenyl
129.	propyl	3-(2-methylpyrrolidin-1-yl)-phenyl
130.	propyl	3-((S)-2-methylpyrrolidin-1-yl)-phenyl
131.	propyl	3-((R)-2-methylpyrrolidin-1-yl)-phenyl
132.	propyl	3-(3-methylpyrrolidin-1-yl)-phenyl
133.	propyl	3-((S)-3-methylpyrrolidin-1-yl)-phenyl
134.	propyl	3-((R)-3-methylpyrrolidin-1-yl)-phenyl
135.	propyl	3-(1-methylpyrrolidin-2-yl)-phenyl
136.	propyl	3-((S)-1-methylpyrrolidin-2-yl)-phenyl
137.	propyl	3-((R)-1-methylpyrrolidin-2-yl)-phenyl
138.	propyl	3-(1-methylpyrrolidin-3-yl)-phenyl
139.	propyl	3-((S)-1-methylpyrrolidin-3-yl)-phenyl
140.	propyl	3-((R)-1-methylpyrrolidin-3-yl)-phenyl
141.	propyl	3-(2,2-dimethylpyrrolidin-1-yl)-phenyl
142.	propyl	3-(3,3-dimethylpyrrolidin-1-yl)-phenyl
143.	propyl	3-(2-trifluoromethylpyrrolidin-1-yl)-phenyl
144.	propyl	3-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
145.	propyl	3-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
146.	propyl	3-(3-trifluoromethylpyrrolidin-1-yl)-phenyl
147.	propyl	3-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl

No.	R ¹	Ar
148.	propyl	3-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
149.	propyl	3-(2-oxopyrrolidin-1-yl)-phenyl
150.	propyl	3-(2-oxo-oxazolidin-3-yl)-phenyl
151.	propyl	3-(piperidin-1-yl)-phenyl
152.	propyl	3-(2-methylpiperidin-1-yl)-phenyl
153.	propyl	3-((S)-2-methylpiperidin-1-yl)-phenyl
154.	propyl	3-((R)-2-methylpiperidin-1-yl)-phenyl
155.	propyl	3-(2-fluoropiperidin-1-yl)-phenyl
156.	propyl	3-((S)-2-fluoropiperidin-1-yl)-phenyl
157.	propyl	3-((R)-2-fluoropiperidin-1-yl)-phenyl
158.	propyl	3-(2,2-difluoropiperidin-1-yl)-phenyl
159.	propyl	3-(piperazin-1-yl)-phenyl
160.	propyl	3-(4-methylpiperazin-1-yl)-phenyl
161.	propyl	3-(morpholin-4-yl)-phenyl
162.	propyl	3-(morpholin-4-yl)-5-(trifluoromethyl)-phenyl
163.	propyl	5-(morpholin-4-yl)-2-methoxyphenyl
164.	propyl	3-(morpholin-4-yl)-4-methoxyphenyl
165.	propyl	5-(morpholin-4-yl)-2,4-difluorophenyl
166.	propyl	3-(morpholin-4-yl)-2,4-difluorophenyl
167.	propyl	3-(thiomorpholin-4-yl)-phenyl
168.	propyl	3-(1-oxo-thiomorpholin-4-yl)-phenyl
169.	propyl	3-(1,1-dioxo-thiomorpholin-4-yl)-phenyl
170.	propyl	3-(pyrrol-1-yl)-phenyl
171.	propyl	3-(pyrrol-2-yl)-phenyl
172.	propyl	3-(pyrrol-3-yl)-phenyl
173.	propyl	3-(1-methylpyrrol-2-yl)-phenyl
174.	propyl	3-(1-methylpyrrol-3-yl)-phenyl
175.	propyl	3-(furan-2-yl)-phenyl
176.	propyl	3-(furan-3-yl)-phenyl
177.	propyl	3-(thiophen-2-yl)-phenyl
178.	propyl	3-(thiophen-3-yl)-phenyl
179.	propyl	3-(5-propylthien-2-yl)-phenyl
180.	propyl	3-(pyrazol-1-yl)-phenyl
181.	propyl	3-(pyrazol-3-yl)-phenyl
182.	propyl	3-(pyrazol-4-yl)-phenyl
183.	propyl	3-(4-fluoropyrazol-1-yl)-phenyl
184.	propyl	3-(1-methyl-1H-pyrazol-4-yl)-phenyl
185.	propyl	3-(1-ethyl-1H-pyrazol-4-yl)-phenyl

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

No.	R ¹	Ar
224.	propyl	3-(pyrid-4-yl)-phenyl
225.	propyl	3-(pyrimidin-2-yl)-phenyl
226.	propyl	3-(2-methylpyrimidin-4-yl)-phenyl
227.	propyl	3-(pyrimidin-4-yl)-phenyl
228.	propyl	3-(pyrimidin-5-yl)-phenyl
229.	propyl	5-bromopyridin-3-yl
230.	propyl	3-bromo-2-chloropyridin-5-yl
231.	propyl	4-methylpyridin-2-yl
232.	propyl	6-methylpyridin-2-yl
233.	propyl	4-(trifluoromethyl)-pyridin-2-yl
234.	propyl	6-(trifluoromethyl)-pyridin-2-yl
235.	propyl	5-(trifluoromethyl)-pyridin-3-yl
236.	propyl	5-(pyrrolidin-1-yl)-pyridin-3-yl
237.	propyl	3-(pyrrolidin-1-yl)-2-chloropyridin-5-yl
238.	propyl	3-(morpholin-4-yl)-2-chloropyridin-5-yl
239.	propyl	2-(morpholin-4-yl)-pyridin-5-yl
240.	propyl	2-phenoxy-pyridin-5-yl
241.	propyl	2,3-dichlorophenyl
242.	propyl	2,5-dichlorophenyl
243.	propyl	3,5-dichlorophenyl
244.	propyl	3-chloro-4-fluorophenyl
245.	propyl	4-bromo-2,5-dichlorophenyl
246.	propyl	3-bromo-4-(trifluoromethoxy)phenyl
247.	propyl	3,5-dibromo-4-(2-fluoroethoxy)-phenyl
248.	propyl	2,5-dimethylphenyl
249.	propyl	2,5-di-(trifluoromethyl)-phenyl
250.	propyl	3,5-di-(trifluoromethyl)-phenyl
251.	propyl	2,5-dimethoxyphenyl
252.	propyl	2-methoxy-5-methylphenyl
253.	propyl	2-methoxy-5-(trifluoromethyl)-phenyl
254.	propyl	4-fluoro-3-(oxazol-4-yl)-phenyl
255.	propyl	thien-2-yl
256.	propyl	thien-3-yl
257.	propyl	3-chlorothien-2-yl
258.	propyl	4-chlorothien-2-yl
259.	propyl	5-chlorothien-2-yl
260.	propyl	3-bromothien-2-yl
261.	propyl	4-bromothien-2-yl

No.	R ¹	Ar
262.	propyl	5-bromothien-2-yl
263.	propyl	4,5-dichlorothien-2-yl
264.	propyl	4,5-dibromothien-2-yl
265.	propyl	4-bromo-5-chlorothien-2-yl
266.	propyl	3-bromo-5-chlorothien-2-yl
267.	propyl	5-methylthien-2-yl
268.	propyl	5-ethylthien-2-yl
269.	propyl	5-propylthien-2-yl
270.	propyl	5-(trifluoromethyl)-thien-2-yl
271.	propyl	5-phenylthien-2-yl
272.	propyl	5-(pyrid-2-yl)-thien-2-yl
273.	propyl	5-(phenylsulfonyl)-thien-2-yl
274.	propyl	4-(phenylsulfonyl)-thien-2-yl
275.	propyl	5-(pyrid-2-ylsulfonyl)-thien-2-yl
276.	propyl	5-(3-chloro-5-trifluoro-pyrid-2-ylsulfonyl)-thien-2-yl
277.	propyl	5-(benzoylaminomethyl)-thien-2-yl
278.	propyl	5-((4-chlorobenzoyl)aminomethyl)-thien-2-yl
279.	propyl	5-(acetylaminomethyl)-thien-2-yl
280.	propyl	5-(pyrazol-1-yl)-thien-2-yl
281.	propyl	5-(pyrazol-3-yl)-thien-2-yl
282.	propyl	5-(pyrazol-4-yl)-thien-2-yl
283.	propyl	5-(pyrazol-5-yl)-thien-2-yl
284.	propyl	5-(4-fluoropyrazol-1-yl)-thien-2-yl
285.	propyl	5-(1-methyl-5-trifluoromethyl-(1H)-pyrazol-3-yl)-thien-2-yl
286.	propyl	5-(1-methyl-3-trifluoromethyl-(1H)-pyrazol-5-yl)-thien-2-yl
287.	propyl	5-(4-carboxy-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
288.	propyl	5-(4-aminomethyl-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
289.	propyl	5-(isoxazol-3-yl)-thien-2-yl
290.	propyl	5-(isoxazol-4-yl)-thien-2-yl
291.	propyl	5-(isoxazol-5-yl)-thien-2-yl
292.	propyl	5-(5-trifluoromethylisoxazol-3-yl)-thien-2-yl
293.	propyl	5-(oxazol-2-yl)-thien-2-yl
294.	propyl	5-(oxazol-4-yl)-thien-2-yl

No.	R ¹	Ar
295.	propyl	5-(oxazol-5-yl)-thien-2-yl
296.	propyl	5-(2-methyloxazol-4-yl)-thien-2-yl
297.	propyl	5-(2-methyloxazol-5-yl)-thien-2-yl
298.	propyl	5-(isothiazol-3-yl)-thien-2-yl
299.	propyl	5-(isothiazol-4-yl)-thien-2-yl
300.	propyl	5-(isothiazol-5-yl)-thien-2-yl
301.	propyl	5-(5-trifluoromethylisothiazol-3-yl)-thien-2-yl
302.	propyl	5-(thiazol-2-yl)-thien-2-yl
303.	propyl	5-(thiazol-4-yl)-thien-2-yl
304.	propyl	5-(thiazol-5-yl)-thien-2-yl
305.	propyl	5-(2-methylthiazol-4-yl)-thien-2-yl
306.	propyl	5-(2-methylthiazol-5-yl)-thien-2-yl
307.	propyl	5-([1,2,3]-oxadiazol-4-yl)-thien-2-yl
308.	propyl	5-([1,2,3]-thiadiazol-4-yl)-thien-2-yl
309.	propyl	5-(pyrimidin-2-yl)-thien-2-yl
310.	propyl	5-(pyrimidin-4-yl)-thien-2-yl
311.	propyl	5-(pyrimidin-5-yl)-thien-2-yl
312.	propyl	5-(2-methylthiopyrimidin-4-yl)-thien-2-yl
313.	propyl	5-([1,3]-dioxolan-2-yl)-thien-2-yl
314.	propyl	3-([1,3]-dioxolan-2-yl)-thien-2-yl
315.	propyl	5-((3-chloro-5-(trifluoromethyl)-pyridin-2-yl)-methyl)-thien-2-yl
316.	propyl	5-[3-chloro-5-(trifluoromethyl)-pyrid-2-ylsulfonyl]-thien-2-yl
317.	propyl	2-chlorothien-3-yl
318.	propyl	4-chlorothien-3-yl
319.	propyl	5-chlorothien-3-yl
320.	propyl	2-bromothien-3-yl
321.	propyl	4-bromothien-3-yl
322.	propyl	5-bromothien-3-yl
323.	propyl	2,5-dichlorothien-3-yl
324.	propyl	2,5-dibromothien-3-yl
325.	propyl	2,4,5-trichlorothien-3-yl
326.	propyl	4-bromo-2,5-dichlorothien-3-yl
327.	propyl	2-chloro-5-methylsulfonylthien-3-yl
328.	propyl	2,5-dimethylthien-3-yl
329.	propyl	4-hydroxythien-3-yl
330.	propyl	2-phenylthien-3-yl

No.	R ¹	Ar
331.	propyl	4-phenyl-5-(trifluoromethyl)-thien-3-yl
332.	propyl	2-methoxycarbonyl-4-phenyl-5-(trifluoromethyl)-thien-3-yl
333.	propyl	benzo[b]thiophen-2-yl
334.	propyl	benzo[b]thiophen-3-yl
335.	propyl	3-methyl-benzo[b]thiophen-2-yl
336.	propyl	5-methyl-benzo[b]thiophen-2-yl
337.	propyl	5-fluoro-3-methyl-benzo[b]thiophen-2-yl
338.	propyl	5-chloro-3-methyl-benzo[b]thiophen-2-yl
339.	propyl	5-bromo-3-methyl-benzo[b]thiophen-2-yl
340.	ethyl	3-methylphenyl
341.	ethyl	3-ethylphenyl
342.	ethyl	3-propylphenyl
343.	ethyl	3-isopropylphenyl
344.	ethyl	3-sec-butylphenyl
345.	ethyl	3-tert-butylphenyl
346.	ethyl	3-isobutylphenyl
347.	ethyl	3-(1,1-dimethylpropyl)-phenyl
348.	ethyl	3-vinylphenyl
349.	ethyl	3-isopropenylphenyl
350.	ethyl	3-fluorophenyl
351.	ethyl	3-chlorophenyl
352.	ethyl	3-bromophenyl
353.	ethyl	3-iodophenyl
354.	ethyl	3-(fluoromethyl)phenyl
355.	ethyl	3-(difluoromethyl)phenyl
356.	ethyl	3-(trifluoromethyl)phenyl
357.	ethyl	3,5-bis(trifluoromethyl)phenyl
358.	ethyl	3-(1-fluoroethyl)-phenyl
359.	ethyl	3-((S)-1-fluoroethyl)-phenyl
360.	ethyl	3-((R)-1-fluoroethyl)-phenyl
361.	ethyl	3-(2-fluoroethyl)-phenyl
362.	ethyl	3-(1,1-difluoroethyl)-phenyl
363.	ethyl	3-(2,2-difluoroethyl)-phenyl
364.	ethyl	3-(2,2,2-trifluoroethyl)-phenyl
365.	ethyl	3-(3-fluoropropyl)-phenyl
366.	ethyl	3-(2-fluoropropyl)-phenyl
367.	ethyl	3-((S)-2-fluoropropyl)-phenyl

No.	R ¹	Ar
368.	ethyl	3-((R)-2-fluoropropyl)-phenyl
369.	ethyl	3-(3,3-difluoropropyl)-phenyl
370.	ethyl	3-(3,3,3-trifluoropropyl)-phenyl
371.	ethyl	3-(1-fluoro-1-methylethyl)-phenyl
372.	ethyl	3-(2-fluoro-1-methylethyl)-phenyl
373.	ethyl	3-((S)-2-fluoro-1-methylethyl)-phenyl
374.	ethyl	3-((R)-2-fluoro-1-methylethyl)-phenyl
375.	ethyl	3-(2,2-difluoro-1-methylethyl)-phenyl
376.	ethyl	3-((S)-2,2-difluoro-1-methylethyl)-phenyl
377.	ethyl	3-((R)-2,2-difluoro-1-methylethyl)-phenyl
378.	ethyl	3-(2,2,2-trifluoro-1-methylethyl)-phenyl
379.	ethyl	3-((S)-2,2,2-trifluoro-1-methylethyl)-phenyl
380.	ethyl	3-((R)-2,2,2-trifluoro-1-methylethyl)-phenyl
381.	ethyl	3-(2-fluoro-1-fluoromethylethyl)-phenyl
382.	ethyl	3-(1-difluoromethyl-2,2-difluoroethyl)-phenyl
383.	ethyl	3-(1,1-dimethyl-2-fluoroethyl)-phenyl
384.	ethyl	3-methoxyphenyl
385.	ethyl	3-ethoxyphenyl
386.	ethyl	3-propoxyphenyl
387.	ethyl	3-isopropoxyphenyl
388.	ethyl	3-butoxyphenyl
389.	ethyl	3-(fluoromethoxy)-phenyl
390.	ethyl	3-(difluoromethoxy)-phenyl
391.	ethyl	3-(trifluoromethoxy)-phenyl
392.	ethyl	3-(2-fluoroethoxy)-phenyl
393.	ethyl	3-(2,2-difluoroethoxy)-phenyl
394.	ethyl	3-(2,2,2-trifluoroethoxy)-phenyl
395.	ethyl	3-(1,1,2,2-tetrafluoroethoxy)-phenyl
396.	ethyl	3-cyclopropylphenyl
397.	ethyl	3-cyclobutylphenyl
398.	ethyl	3-cyclopentylphenyl
399.	ethyl	3-(2,2-difluorocyclopropyl)-phenyl
400.	ethyl	3,4-difluorophenyl
401.	ethyl	3-bromo-2-fluorophenyl
402.	ethyl	2-bromo-3-fluorophenyl
403.	ethyl	3-bromo-2,5-difluorophenyl
404.	ethyl	5-bromo-2,4-difluorophenyl
405.	ethyl	3-bromo-2,4-difluorophenyl

No.	R ¹	Ar
406.	ethyl	4-chloro-3-(trifluoromethyl)-phenyl
407.	ethyl	2-chloro-5-(trifluoromethyl)-phenyl
408.	ethyl	2-fluoro-5-(trifluoromethyl)-phenyl
409.	ethyl	4-fluoro-3-(trifluoromethyl)-phenyl
410.	ethyl	3-fluoro-5-(trifluoromethyl)-phenyl
411.	ethyl	4-bromo-3-(trifluoromethyl)-phenyl
412.	ethyl	3-bromo-5-(trifluoromethyl)-phenyl
413.	ethyl	2-bromo-5-(trifluoromethyl)-phenyl
414.	ethyl	5-bromo-2-methoxyphenyl
415.	ethyl	3-bromo-4-methoxyphenyl
416.	ethyl	2-fluoro-3-isopropylphenyl
417.	ethyl	4-fluoro-3-isopropylphenyl
418.	ethyl	3-(1-hydroxy-1-methylethyl)-phenyl
419.	ethyl	3-(2-hydroxy-2-methylpropyl)-phenyl
420.	ethyl	3-acetylphenyl
421.	ethyl	3-acetylaminophenyl
422.	ethyl	3-carboxyphenyl
423.	ethyl	3-cyanophenyl
424.	ethyl	3-nitrophenyl
425.	ethyl	3-hydroxyphenyl
426.	ethyl	3-(O-benzyl)-phenyl
427.	ethyl	3-(2-methoxyethoxy)-phenyl
428.	ethyl	3-(CH ₂ -N(CH ₃) ₂)-phenyl
429.	ethyl	3-(NH-CO-NH ₂)-phenyl
430.	ethyl	3-(methylsulfanyl)-phenyl
431.	ethyl	3-(fluoromethylsulfanyl)-phenyl
432.	ethyl	3-(difluoromethylsulfanyl)-phenyl
433.	ethyl	3-(trifluoromethylsulfanyl)-phenyl
434.	ethyl	3-(methylsulfonyl)-phenyl
435.	ethyl	3-(N-methoxy-N-methyl-amino)-phenyl
436.	ethyl	3-(methoxyamino)-phenyl
437.	ethyl	3-(ethoxyamino)-phenyl
438.	ethyl	3-(N-methylaminooxy)-phenyl
439.	ethyl	3-(N,N-dimethylaminooxy)-phenyl
440.	ethyl	3-(azetidin-1-yl)-phenyl
441.	ethyl	3-(2-methylazetidin-1-yl)-phenyl
442.	ethyl	3-((S)-2-methylazetidin-1-yl)-phenyl
443.	ethyl	3-((R)-2-methylazetidin-1-yl)-phenyl

No.	R ¹	Ar
444.	ethyl	3-(3-fluoroazetidin-1-yl)-phenyl
445.	ethyl	3-(2,2-difluoroazetidin-1-yl)-phenyl
446.	ethyl	3-(3-methoxyazetidin-1-yl)-phenyl
447.	ethyl	3-(3-hydroxyazetidin-1-yl)-phenyl
448.	ethyl	3-(pyrrolidin-1-yl)-phenyl
449.	ethyl	3-(pyrrolidin-2-yl)-phenyl
450.	ethyl	3-((S)-pyrrolidin-2-yl)-phenyl
451.	ethyl	3-((R)-pyrrolidin-2-yl)-phenyl
452.	ethyl	3-(pyrrolidin-3-yl)-phenyl
453.	ethyl	3-((S)-pyrrolidin-3-yl)-phenyl
454.	ethyl	3-((R)-pyrrolidin-3-yl)-phenyl
455.	ethyl	3-(pyrrolidin-1-yl)-5-(trifluoromethyl)-phenyl
456.	ethyl	5-(pyrrolidin-1-yl)-2-methoxyphenyl
457.	ethyl	3-(pyrrolidin-1-yl)-4-methoxyphenyl
458.	ethyl	5-(pyrrolidin-1-yl)-2,4-difluorophenyl
459.	ethyl	3-(pyrrolidin-1-yl)-2,4-difluorophenyl
460.	ethyl	3-(2-fluoropyrrolidin-1-yl)-phenyl
461.	ethyl	3-((S)-2-fluoropyrrolidin-1-yl)-phenyl
462.	ethyl	3-((R)-2-fluoropyrrolidin-1-yl)-phenyl
463.	ethyl	3-(3-fluoropyrrolidin-1-yl)-phenyl
464.	ethyl	3-((S)-3-fluoropyrrolidin-1-yl)-phenyl
465.	ethyl	3-((R)-3-fluoropyrrolidin-1-yl)-phenyl
466.	ethyl	3-(2,2-difluoropyrrolidin-1-yl)-phenyl
467.	ethyl	3-(3,3-difluoropyrrolidin-1-yl)-phenyl
468.	ethyl	3-(2-methylpyrrolidin-1-yl)-phenyl
469.	ethyl	3-((S)-2-methylpyrrolidin-1-yl)-phenyl
470.	ethyl	3-((R)-2-methylpyrrolidin-1-yl)-phenyl
471.	ethyl	3-(3-methylpyrrolidin-1-yl)-phenyl
472.	ethyl	3-((S)-3-methylpyrrolidin-1-yl)-phenyl
473.	ethyl	3-((R)-3-methylpyrrolidin-1-yl)-phenyl
474.	ethyl	3-(1-methylpyrrolidin-2-yl)-phenyl
475.	ethyl	3-((S)-1-methylpyrrolidin-2-yl)-phenyl
476.	ethyl	3-((R)-1-methylpyrrolidin-2-yl)-phenyl
477.	ethyl	3-(1-methylpyrrolidin-3-yl)-phenyl
478.	ethyl	3-((S)-1-methylpyrrolidin-3-yl)-phenyl
479.	ethyl	3-((R)-1-methylpyrrolidin-3-yl)-phenyl
480.	ethyl	3-(2,2-dimethylpyrrolidin-1-yl)-phenyl
481.	ethyl	3-(3,3-dimethylpyrrolidin-1-yl)-phenyl

No.	R ¹	Ar
482.	ethyl	3-(2-trifluoromethylpyrrolidin-1-yl)-phenyl
483.	ethyl	3-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
484.	ethyl	3-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
485.	ethyl	3-(3-trifluoromethylpyrrolidin-1-yl)-phenyl
486.	ethyl	3-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
487.	ethyl	3-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
488.	ethyl	3-(2-oxopyrrolidin-1-yl)-phenyl
489.	ethyl	3-(2-oxo-oxazolidin-3-yl)-phenyl
490.	ethyl	3-(piperidin-1-yl)-phenyl
491.	ethyl	3-(2-methylpiperidin-1-yl)-phenyl
492.	ethyl	3-((S)-2-methylpiperidin-1-yl)-phenyl
493.	ethyl	3-((R)-2-methylpiperidin-1-yl)-phenyl
494.	ethyl	3-(2-fluoropiperidin-1-yl)-phenyl
495.	ethyl	3-((S)-2-fluoropiperidin-1-yl)-phenyl
496.	ethyl	3-((R)-2-fluoropiperidin-1-yl)-phenyl
497.	ethyl	3-(2,2-difluoropiperidin-1-yl)-phenyl
498.	ethyl	3-(piperazin-1-yl)-phenyl
499.	ethyl	3-(4-methylpiperazin-1-yl)-phenyl
500.	ethyl	3-(morpholin-4-yl)-phenyl
501.	ethyl	3-(morpholin-4-yl)-5-(trifluoromethyl)-phenyl
502.	ethyl	5-(morpholin-4-yl)-2-methoxyphenyl
503.	ethyl	3-(morpholin-4-yl)-4-methoxyphenyl
504.	ethyl	5-(morpholin-4-yl)-2,4-difluorophenyl
505.	ethyl	3-(morpholin-4-yl)-2,4-difluorophenyl
506.	ethyl	3-(thiomorpholin-4-yl)-phenyl
507.	ethyl	3-(1-oxo-thiomorpholin-4-yl)-phenyl
508.	ethyl	3-(1,1-dioxo-thiomorpholin-4-yl)-phenyl
509.	ethyl	3-(pyrrol-1-yl)-phenyl
510.	ethyl	3-(pyrrol-2-yl)-phenyl
511.	ethyl	3-(pyrrol-3-yl)-phenyl
512.	ethyl	3-(1-methylpyrrol-2-yl)-phenyl
513.	ethyl	3-(1-methylpyrrol-3-yl)-phenyl
514.	ethyl	3-(furan-2-yl)-phenyl
515.	ethyl	3-(furan-3-yl)-phenyl
516.	ethyl	3-(thiophen-2-yl)-phenyl
517.	ethyl	3-(thiophen-3-yl)-phenyl
518.	ethyl	3-(5-propylthien-2-yl)-phenyl
519.	ethyl	3-(pyrazol-1-yl)-phenyl

No.	R ¹	Ar
520.	ethyl	3-(pyrazol-3-yl)-phenyl
521.	ethyl	3-(pyrazol-4-yl)-phenyl
522.	ethyl	3-(4-fluoropyrazol-1-yl)-phenyl
523.	ethyl	3-(1-methyl-1H-pyrazol-4-yl)-phenyl
524.	ethyl	3-(1-ethyl-1H-pyrazol-4-yl)-phenyl
525.	ethyl	3-(1-methyl-1H-pyrazol-5-yl)-phenyl
526.	ethyl	3-(1H-imidazol-2-yl)-phenyl
527.	ethyl	3-(imidazol-1-yl)-phenyl
528.	ethyl	3-(1-methylimidazol-2-yl)-phenyl
529.	ethyl	3-(oxazol-2-yl)-phenyl
530.	ethyl	3-(oxazol-4-yl)-phenyl
531.	ethyl	3-(oxazol-5-yl)-phenyl
532.	ethyl	3-(isoxazol-3-yl)-phenyl
533.	ethyl	3-(isoxazol-4-yl)-phenyl
534.	ethyl	3-(isoxazol-5-yl)-phenyl
535.	ethyl	3-(thiazol-2-yl)-phenyl
536.	ethyl	3-(thiazol-4-yl)-phenyl
537.	ethyl	3-(thiazol-5-yl)-phenyl
538.	ethyl	3-(2-methylthiazol-4-yl)-phenyl
539.	ethyl	3-(2-methylthiazol-5-yl)-phenyl
540.	ethyl	3-([1,2,3]-triazol-1-yl)-phenyl
541.	ethyl	3-([1,2,4]-triazol-1-yl)-phenyl
542.	ethyl	3-([1,2,3]-triazol-2-yl)-phenyl
543.	ethyl	3-(4H-[1,2,4]-triazol-3-yl)-phenyl
544.	ethyl	3-([1,2,4]-triazol-4-yl)-phenyl
545.	ethyl	3-(2H-[1,2,3]-triazol-4-yl)-phenyl
546.	ethyl	3-(4-methyl-4H-[1,2,4]-triazol-3-yl)-phenyl
547.	ethyl	3-(2-methyl-2H-[1,2,3]-triazol-4-yl)-phenyl
548.	ethyl	3-([1,3,4]-oxadiazol-2-yl)-phenyl
549.	ethyl	3-(5-methyl-[1,3,4]-oxadiazol-2-yl)-phenyl
550.	ethyl	3-([1,2,4]-oxadiazol-3-yl)-phenyl
551.	ethyl	3-(5-methyl-[1,2,4]-oxadiazol-3-yl)-phenyl
552.	ethyl	3-([1,2,4]-oxadiazol-5-yl)-phenyl
553.	ethyl	3-([1,2,3]-oxadiazol-4-yl)-phenyl
554.	ethyl	3-([1,2,3]-oxadiazol-5-yl)-phenyl
555.	ethyl	3-([1,2,3]-thiadiazol-4-yl)-phenyl
556.	ethyl	3-(1H-tetrazol-5-yl)-phenyl
557.	ethyl	3-(tetrazol-1-yl)-phenyl

No.	R ¹	Ar
558.	ethyl	3-(2-methyl-2H-tetrazol-5-yl)-phenyl
559.	ethyl	3-(1-methyl-1H-tetrazol-5-yl)-phenyl
560.	ethyl	3-furazan-3-yl-phenyl
561.	ethyl	3-(pyrid-2-yl)-phenyl
562.	ethyl	3-(pyrid-3-yl)-phenyl
563.	ethyl	3-(pyrid-4-yl)-phenyl
564.	ethyl	3-(pyrimidin-2-yl)-phenyl
565.	ethyl	3-(2-methylpyrimidin-4-yl)-phenyl
566.	ethyl	3-(pyrimidin-4-yl)-phenyl
567.	ethyl	3-(pyrimidin-5-yl)-phenyl
568.	ethyl	5-bromopyridin-3-yl
569.	ethyl	3-bromo-2-chloropyridin-5-yl
570.	ethyl	4-methylpyridin-2-yl
571.	ethyl	6-methylpyridin-2-yl
572.	ethyl	4-(trifluoromethyl)-pyridin-2-yl
573.	ethyl	6-(trifluoromethyl)-pyridin-2-yl
574.	ethyl	5-(trifluoromethyl)-pyridin-3-yl
575.	ethyl	5-(pyrrolidin-1-yl)-pyridin-3-yl
576.	ethyl	3-(pyrrolidin-1-yl)-2-chloropyridin-5-yl
577.	ethyl	3-(morpholin-4-yl)-2-chloropyridin-5-yl
578.	ethyl	2-(morpholin-4-yl)-pyridin-5-yl
579.	ethyl	2-phenoxy-pyridin-5-yl
580.	ethyl	2,3-dichlorophenyl
581.	ethyl	2,5-dichlorophenyl
582.	ethyl	3,5-dichlorophenyl
583.	ethyl	3-chloro-4-fluorophenyl
584.	ethyl	4-bromo-2,5-dichlorophenyl
585.	ethyl	3-bromo-4-(trifluoromethoxy)phenyl
586.	ethyl	3,5-dibromo-4-(2-fluoroethoxy)-phenyl
587.	ethyl	2,5-dimethylphenyl
588.	ethyl	2,5-di-(trifluoromethyl)-phenyl
589.	ethyl	3,5-di-(trifluoromethyl)-phenyl
590.	ethyl	2,5-dimethoxyphenyl
591.	ethyl	2-methoxy-5-methylphenyl
592.	ethyl	2-methoxy-5-(trifluoromethyl)-phenyl
593.	ethyl	4-fluoro-3-(oxazol-4-yl)-phenyl
594.	ethyl	thien-2-yl
595.	ethyl	thien-3-yl

No.	R ¹	Ar
596.	ethyl	3-chlorothien-2-yl
597.	ethyl	4-chlorothien-2-yl
598.	ethyl	5-chlorothien-2-yl
599.	ethyl	3-bromothien-2-yl
600.	ethyl	4-bromothien-2-yl
601.	ethyl	5-bromothien-2-yl
602.	ethyl	4,5-dichlorothien-2-yl
603.	ethyl	4,5-dibromothien-2-yl
604.	ethyl	4-bromo-5-chlorothien-2-yl
605.	ethyl	3-bromo-5-chlorothien-2-yl
606.	ethyl	5-methylthien-2-yl
607.	ethyl	5-ethylthien-2-yl
608.	ethyl	5-propylthien-2-yl
609.	ethyl	5-trifluoromethylthien-2-yl
610.	ethyl	5-phenylthien-2-yl
611.	ethyl	5-(pyrid-2-yl)-thien-2-yl
612.	ethyl	5-(phenylsulfonyl)-thien-2-yl
613.	ethyl	4-(phenylsulfonyl)-thien-2-yl
614.	ethyl	5-(pyrid-2-ylsulfonyl)-thien-2-yl
615.	ethyl	5-(3-chloro-5-trifluoro-pyrid-2-ylsulfonyl)-thien-2-yl
616.	ethyl	5-(benzoylaminomethyl)-thien-2-yl
617.	ethyl	5-((4-chlorobenzoyl)aminomethyl)-thien-2-yl
618.	ethyl	5-(acetylaminomethyl)-thien-2-yl
619.	ethyl	5-(pyrazol-1-yl)-thien-2-yl
620.	ethyl	5-(pyrazol-3-yl)-thien-2-yl
621.	ethyl	5-(pyrazol-4-yl)-thien-2-yl
622.	ethyl	5-(pyrazol-5-yl)-thien-2-yl
623.	ethyl	5-(4-fluoropyrazol-1-yl)-thien-2-yl
624.	ethyl	5-(1-methyl-5-trifluoromethyl-(1H)-pyrazol-3-yl)-thien-2-yl
625.	ethyl	5-(1-methyl-3-trifluoromethyl-(1H)-pyrazol-5-yl)-thien-2-yl
626.	ethyl	5-(4-carboxy-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
627.	ethyl	5-(4-aminomethyl-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
628.	ethyl	5-(isoxazol-3-yl)-thien-2-yl

No.	R ¹	Ar
629.	ethyl	5-(isoxazol-4-yl)-thien-2-yl
630.	ethyl	5-(isoxazol-5-yl)-thien-2-yl
631.	ethyl	5-(5-trifluoromethylisoxazol-3-yl)-thien-2-yl
632.	ethyl	5-(oxazol-2-yl)-thien-2-yl
633.	ethyl	5-(oxazol-4-yl)-thien-2-yl
634.	ethyl	5-(oxazol-5-yl)-thien-2-yl
635.	ethyl	5-(2-methyloxazol-4-yl)-thien-2-yl
636.	ethyl	5-(2-methyloxazol-5-yl)-thien-2-yl
637.	ethyl	5-(isothiazol-3-yl)-thien-2-yl
638.	ethyl	5-(isothiazol-4-yl)-thien-2-yl
639.	ethyl	5-(isothiazol-5-yl)-thien-2-yl
640.	ethyl	5-(5-trifluoromethylisothiazol-3-yl)-thien-2-yl
641.	ethyl	5-(thiazol-2-yl)-thien-2-yl
642.	ethyl	5-(thiazol-4-yl)-thien-2-yl
643.	ethyl	5-(thiazol-5-yl)-thien-2-yl
644.	ethyl	5-(2-methylthiazol-4-yl)-thien-2-yl
645.	ethyl	5-(2-methylthiazol-5-yl)-thien-2-yl
646.	ethyl	5-([1,2,3]-oxadiazol-4-yl)-thien-2-yl
647.	ethyl	5-([1,2,3]-thiadiazol-4-yl)-thien-2-yl
648.	ethyl	5-(pyrimidin-2-yl)-thien-2-yl
649.	ethyl	5-(pyrimidin-4-yl)-thien-2-yl
650.	ethyl	5-(pyrimidin-5-yl)-thien-2-yl
651.	ethyl	5-(2-methylthiopyrimidin-4-yl)-thien-2-yl
652.	ethyl	5-([1,3]-dioxolan-2-yl)-thien-2-yl
653.	ethyl	3-([1,3]-dioxolan-2-yl)-thien-2-yl
654.	ethyl	5-((3-chloro-5-(trifluoromethyl)-pyridin-2-yl)-methyl)-thien-2-yl
655.	ethyl	5-[3-chloro-5-(trifluoromethyl)-pyrid-2-ylsulfonyl]-thien-2-yl
656.	ethyl	2-chlorothien-3-yl
657.	ethyl	4-chlorothien-3-yl
658.	ethyl	5-chlorothien-3-yl
659.	ethyl	2-bromothien-3-yl
660.	ethyl	4-bromothien-3-yl
661.	ethyl	5-bromothien-3-yl
662.	ethyl	2,5-dichlorothien-3-yl
663.	ethyl	2,5-dibromothien-3-yl
664.	ethyl	2,4,5-trichlorothien-3-yl

No.	R ¹	Ar
665.	ethyl	4-bromo-2,5-dichlorothien-3-yl
666.	ethyl	2-chloro-5-methylsulfonylthien-3-yl
667.	ethyl	2,5-dimethylthien-3-yl
668.	ethyl	4-hydroxythien-3-yl
669.	ethyl	2-phenylthien-3-yl
670.	ethyl	4-phenyl-5-(trifluoromethyl)-thien-3-yl
671.	ethyl	2-methoxycarbonyl-4-phenyl-5-(trifluoromethyl)-thien-3-yl
672.	ethyl	benzo[b]thiophen-2-yl
673.	ethyl	benzo[b]thiophen-3-yl
674.	ethyl	3-methyl-benzo[b]thiophen-2-yl
675.	ethyl	5-methyl-benzo[b]thiophen-2-yl
676.	ethyl	5-fluoro-3-methyl-benzo[b]thiophen-2-yl
677.	ethyl	5-chloro-3-methyl-benzo[b]thiophen-2-yl
678.	ethyl	5-bromo-3-methyl-benzo[b]thiophen-2-yl
679.	methyl	3-methylphenyl
680.	methyl	3-ethylphenyl
681.	methyl	3-propylphenyl
682.	methyl	3-isopropylphenyl
683.	methyl	3-sec-butylphenyl
684.	methyl	3-tert-butylphenyl
685.	methyl	3-isobutylphenyl
686.	methyl	3-(1,1-dimethylpropyl)-phenyl
687.	methyl	3-vinylphenyl
688.	methyl	3-isopropenylphenyl
689.	methyl	3-fluorophenyl
690.	methyl	3-chlorophenyl
691.	methyl	3-bromophenyl
692.	methyl	3-iodophenyl
693.	methyl	3-(fluoromethyl)phenyl
694.	methyl	3-(difluoromethyl)phenyl
695.	methyl	3-(trifluoromethyl)phenyl
696.	methyl	3,5-bis(trifluoromethyl)phenyl
697.	methyl	3-(1-fluoroethyl)-phenyl
698.	methyl	3-((S)-1-fluoroethyl)-phenyl
699.	methyl	3-((R)-1-fluoroethyl)-phenyl
700.	methyl	3-(2-fluoroethyl)-phenyl
701.	methyl	3-(1,1-difluoroethyl)-phenyl

No.	R ¹	Ar
702.	methyl	3-(2,2-difluoroethyl)-phenyl
703.	methyl	3-(2,2,2-trifluoroethyl)-phenyl
704.	methyl	3-(3-fluoropropyl)-phenyl
705.	methyl	3-(2-fluoropropyl)-phenyl
706.	methyl	3-((S)-2-fluoropropyl)-phenyl
707.	methyl	3-((R)-2-fluoropropyl)-phenyl
708.	methyl	3-(3,3-difluoropropyl)-phenyl
709.	methyl	3-(3,3,3-trifluoropropyl)-phenyl
710.	methyl	3-(1-fluoro-1-methylethyl)-phenyl
711.	methyl	3-(2-fluoro-1-methylethyl)-phenyl
712.	methyl	3-((S)-2-fluoro-1-methylethyl)-phenyl
713.	methyl	3-((R)-2-fluoro-1-methylethyl)-phenyl
714.	methyl	3-(2,2-difluoro-1-methylethyl)-phenyl
715.	methyl	3-((S)-2,2-difluoro-1-methylethyl)-phenyl
716.	methyl	3-((R)-2,2-difluoro-1-methylethyl)-phenyl
717.	methyl	3-(2,2,2-trifluoro-1-methylethyl)-phenyl
718.	methyl	3-((S)-2,2,2-trifluoro-1-methylethyl)-phenyl
719.	methyl	3-((R)-2,2,2-trifluoro-1-methylethyl)-phenyl
720.	methyl	3-(2-fluoro-1-fluoromethylethyl)-phenyl
721.	methyl	3-(1-difluoromethyl-2,2-difluoroethyl)-phenyl
722.	methyl	3-(1,1-dimethyl-2-fluoroethyl)-phenyl
723.	methyl	3-methoxyphenyl
724.	methyl	3-ethoxyphenyl
725.	methyl	3-propoxyphenyl
726.	methyl	3-isopropoxyphenyl
727.	methyl	3-butoxyphenyl
728.	methyl	3-(fluoromethoxy)-phenyl
729.	methyl	3-(difluoromethoxy)-phenyl
730.	methyl	3-(trifluoromethoxy)-phenyl
731.	methyl	3-(2-fluoroethoxy)-phenyl
732.	methyl	3-(2,2-difluoroethoxy)-phenyl
733.	methyl	3-(2,2,2-trifluoroethoxy)-phenyl
734.	methyl	3-(1,1,2,2-tetrafluoroethoxy)-phenyl
735.	methyl	3-cyclopropylphenyl
736.	methyl	3-cyclobutylphenyl
737.	methyl	3-cyclopentylphenyl
738.	methyl	3-(2,2-difluorocyclopropyl)-phenyl
739.	methyl	3,4-difluorophenyl

No.	R ¹	Ar
740.	methyl	3-bromo-2-fluorophenyl
741.	methyl	2-bromo-3-fluorophenyl
742.	methyl	3-bromo-2,5-difluorophenyl
743.	methyl	5-bromo-2,4-difluorophenyl
744.	methyl	3-bromo-2,4-difluorophenyl
745.	methyl	4-chloro-3-(trifluoromethyl)-phenyl
746.	methyl	2-chloro-5-(trifluoromethyl)-phenyl
747.	methyl	2-fluoro-5-(trifluoromethyl)-phenyl
748.	methyl	4-fluoro-3-(trifluoromethyl)-phenyl
749.	methyl	3-fluoro-5-(trifluoromethyl)-phenyl
750.	methyl	4-bromo-3-(trifluoromethyl)-phenyl
751.	methyl	3-bromo-5-(trifluoromethyl)-phenyl
752.	methyl	2-bromo-5-(trifluoromethyl)-phenyl
753.	methyl	5-bromo-2-methoxyphenyl
754.	methyl	3-bromo-4-methoxyphenyl
755.	methyl	2-fluoro-3-isopropylphenyl
756.	methyl	4-fluoro-3-isopropylphenyl
757.	methyl	3-(1-hydroxy-1-methylethyl)-phenyl
758.	methyl	3-(2-hydroxy-2-methylpropyl)-phenyl
759.	methyl	3-acetylphenyl
760.	methyl	3-acetylaminophenyl
761.	methyl	3-carboxyphenyl
762.	methyl	3-cyanophenyl
763.	methyl	3-nitrophenyl
764.	methyl	3-hydroxyphenyl
765.	methyl	3-(O-benzyl)-phenyl
766.	methyl	3-(2-methoxyethoxy)-phenyl
767.	methyl	3-(CH ₂ -N(CH ₃) ₂)-phenyl
768.	methyl	3-(NH-CO-NH ₂)-phenyl
769.	methyl	3-(methylsulfanyl)-phenyl
770.	methyl	3-(fluoromethylsulfanyl)-phenyl
771.	methyl	3-(difluoromethylsulfanyl)-phenyl
772.	methyl	3-(trifluoromethylsulfanyl)-phenyl
773.	methyl	3-(methylsulfonyl)-phenyl
774.	methyl	3-(N-methoxy-N-methyl-amino)-phenyl
775.	methyl	3-(methoxyamino)-phenyl
776.	methyl	3-(ethoxyamino)-phenyl
777.	methyl	3-(N-methylaminooxy)-phenyl

No.	R ¹	Ar
778.	methyl	3-(N,N-dimethylaminooxy)-phenyl
779.	methyl	3-(azetidin-1-yl)-phenyl
780.	methyl	3-(2-methylazetidin-1-yl)-phenyl
781.	methyl	3-((S)-2-methylazetidin-1-yl)-phenyl
782.	methyl	3-((R)-2-methylazetidin-1-yl)-phenyl
783.	methyl	3-(3-fluoroazetidin-1-yl)-phenyl
784.	methyl	3-(2,2-difluoroazetidin-1-yl)-phenyl
785.	methyl	3-(3-methoxyazetidin-1-yl)-phenyl
786.	methyl	3-(3-hydroxyazetidin-1-yl)-phenyl
787.	methyl	3-(pyrrolidin-1-yl)-phenyl
788.	methyl	3-(pyrrolidin-2-yl)-phenyl
789.	methyl	3-((S)-pyrrolidin-2-yl)-phenyl
790.	methyl	3-((R)-pyrrolidin-2-yl)-phenyl
791.	methyl	3-(pyrrolidin-3-yl)-phenyl
792.	methyl	3-((S)-pyrrolidin-3-yl)-phenyl
793.	methyl	3-((R)-pyrrolidin-3-yl)-phenyl
794.	methyl	3-(pyrrolidin-1-yl)-5-(trifluoromethyl)-phenyl
795.	methyl	5-(pyrrolidin-1-yl)-2-methoxyphenyl
796.	methyl	3-(pyrrolidin-1-yl)-4-methoxyphenyl
797.	methyl	5-(pyrrolidin-1-yl)-2,4-difluorophenyl
798.	methyl	3-(pyrrolidin-1-yl)-2,4-difluorophenyl
799.	methyl	3-(2-fluoropyrrolidin-1-yl)-phenyl
800.	methyl	3-((S)-2-fluoropyrrolidin-1-yl)-phenyl
801.	methyl	3-((R)-2-fluoropyrrolidin-1-yl)-phenyl
802.	methyl	3-(3-fluoropyrrolidin-1-yl)-phenyl
803.	methyl	3-((S)-3-fluoropyrrolidin-1-yl)-phenyl
804.	methyl	3-((R)-3-fluoropyrrolidin-1-yl)-phenyl
805.	methyl	3-(2,2-difluoropyrrolidin-1-yl)-phenyl
806.	methyl	3-(3,3-difluoropyrrolidin-1-yl)-phenyl
807.	methyl	3-(2-methylpyrrolidin-1-yl)-phenyl
808.	methyl	3-((S)-2-methylpyrrolidin-1-yl)-phenyl
809.	methyl	3-((R)-2-methylpyrrolidin-1-yl)-phenyl
810.	methyl	3-(3-methylpyrrolidin-1-yl)-phenyl
811.	methyl	3-((S)-3-methylpyrrolidin-1-yl)-phenyl
812.	methyl	3-((R)-3-methylpyrrolidin-1-yl)-phenyl
813.	methyl	3-(1-methylpyrrolidin-2-yl)-phenyl
814.	methyl	3-((S)-1-methylpyrrolidin-2-yl)-phenyl
815.	methyl	3-((R)-1-methylpyrrolidin-2-yl)-phenyl

No.	R ¹	Ar
816.	methyl	3-(1-methylpyrrolidin-3-yl)-phenyl
817.	methyl	3-((S)-1-methylpyrrolidin-3-yl)-phenyl
818.	methyl	3-((R)-1-methylpyrrolidin-3-yl)-phenyl
819.	methyl	3-(2,2-dimethylpyrrolidin-1-yl)-phenyl
820.	methyl	3-(3,3-dimethylpyrrolidin-1-yl)-phenyl
821.	methyl	3-(2-trifluoromethylpyrrolidin-1-yl)-phenyl
822.	methyl	3-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
823.	methyl	3-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
824.	methyl	3-(3-trifluoromethylpyrrolidin-1-yl)-phenyl
825.	methyl	3-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
826.	methyl	3-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
827.	methyl	3-(2-oxopyrrolidin-1-yl)-phenyl
828.	methyl	3-(2-oxo-oxazolidin-3-yl)-phenyl
829.	methyl	3-(piperidin-1-yl)-phenyl
830.	methyl	3-(2-methylpiperidin-1-yl)-phenyl
831.	methyl	3-((S)-2-methylpiperidin-1-yl)-phenyl
832.	methyl	3-((R)-2-methylpiperidin-1-yl)-phenyl
833.	methyl	3-(2-fluoropiperidin-1-yl)-phenyl
834.	methyl	3-((S)-2-fluoropiperidin-1-yl)-phenyl
835.	methyl	3-((R)-2-fluoropiperidin-1-yl)-phenyl
836.	methyl	3-(2,2-difluoropiperidin-1-yl)-phenyl
837.	methyl	3-(piperazin-1-yl)-phenyl
838.	methyl	3-(4-methylpiperazin-1-yl)-phenyl
839.	methyl	3-(morpholin-4-yl)-phenyl
840.	methyl	3-(morpholin-4-yl)-5-(trifluoromethyl)-phenyl
841.	methyl	5-(morpholin-4-yl)-2-methoxyphenyl
842.	methyl	3-(morpholin-4-yl)-4-methoxyphenyl
843.	methyl	5-(morpholin-4-yl)-2,4-difluorophenyl
844.	methyl	3-(morpholin-4-yl)-2,4-difluorophenyl
845.	methyl	3-(thiomorpholin-4-yl)-phenyl
846.	methyl	3-(1-oxo-thiomorpholin-4-yl)-phenyl
847.	methyl	3-(1,1-dioxo-thiomorpholin-4-yl)-phenyl
848.	methyl	3-(pyrrol-1-yl)-phenyl
849.	methyl	3-(pyrrol-2-yl)-phenyl
850.	methyl	3-(pyrrol-3-yl)-phenyl
851.	methyl	3-(1-methylpyrrol-2-yl)-phenyl
852.	methyl	3-(1-methylpyrrol-3-yl)-phenyl
853.	methyl	3-(furan-2-yl)-phenyl

No.	R ¹	Ar
854.	methyl	3-(furan-3-yl)-phenyl
855.	methyl	3-(thiophen-2-yl)-phenyl
856.	methyl	3-(thiophen-3-yl)-phenyl
857.	methyl	3-(5-propylthien-2-yl)-phenyl
858.	methyl	3-(pyrazol-1-yl)-phenyl
859.	methyl	3-(pyrazol-3-yl)-phenyl
860.	methyl	3-(pyrazol-4-yl)-phenyl
861.	methyl	3-(4-fluoropyrazol-1-yl)-phenyl
862.	methyl	3-(1-methyl-1H-pyrazol-4-yl)-phenyl
863.	methyl	3-(1-ethyl-1H-pyrazol-4-yl)-phenyl
864.	methyl	3-(1-methyl-1H-pyrazol-5-yl)-phenyl
865.	methyl	3-(1H-imidazol-2-yl)-phenyl
866.	methyl	3-(imidazol-1-yl)-phenyl
867.	methyl	3-(1-methylimidazol-2-yl)-phenyl
868.	methyl	3-(oxazol-2-yl)-phenyl
869.	methyl	3-(oxazol-4-yl)-phenyl
870.	methyl	3-(oxazol-5-yl)-phenyl
871.	methyl	3-(isoxazol-3-yl)-phenyl
872.	methyl	3-(isoxazol-4-yl)-phenyl
873.	methyl	3-(isoxazol-5-yl)-phenyl
874.	methyl	3-(thiazol-2-yl)-phenyl
875.	methyl	3-(thiazol-4-yl)-phenyl
876.	methyl	3-(thiazol-5-yl)-phenyl
877.	methyl	3-(2-methylthiazol-4-yl)-phenyl
878.	methyl	3-(2-methylthiazol-5-yl)-phenyl
879.	methyl	3-([1,2,3]-triazol-1-yl)-phenyl
880.	methyl	3-([1,2,4]-triazol-1-yl)-phenyl
881.	methyl	3-([1,2,3]-triazol-2-yl)-phenyl
882.	methyl	3-(4H-[1,2,4]-triazol-3-yl)-phenyl
883.	methyl	3-([1,2,4]-triazol-4-yl)-phenyl
884.	methyl	3-(2H-[1,2,3]-triazol-4-yl)-phenyl
885.	methyl	3-(4-methyl-4H-[1,2,4]-triazol-3-yl)-phenyl
886.	methyl	3-(2-methyl-2H-[1,2,3]-triazol-4-yl)-phenyl
887.	methyl	3-([1,3,4]-oxadiazol-2-yl)-phenyl
888.	methyl	3-(5-methyl-[1,3,4]-oxadiazol-2-yl)-phenyl
889.	methyl	3-([1,2,4]-oxadiazol-3-yl)-phenyl
890.	methyl	3-(5-methyl-[1,2,4]-oxadiazol-3-yl)-phenyl
891.	methyl	3-([1,2,4]-oxadiazol-5-yl)-phenyl

No.	R ¹	Ar
892.	methyl	3-([1,2,3]-oxadiazol-4-yl)-phenyl
893.	methyl	3-([1,2,3]-oxadiazol-5-yl)-phenyl
894.	methyl	3-([1,2,3]-thiadiazol-4-yl)-phenyl
895.	methyl	3-(1H-tetrazol-5-yl)-phenyl
896.	methyl	3-(tetrazol-1-yl)-phenyl
897.	methyl	3-(2-methyl-2H-tetrazol-5-yl)-phenyl
898.	methyl	3-(1-methyl-1H-tetrazol-5-yl)-phenyl
899.	methyl	3-furazan-3-yl-phenyl
900.	methyl	3-(pyrid-2-yl)-phenyl
901.	methyl	3-(pyrid-3-yl)-phenyl
902.	methyl	3-(pyrid-4-yl)-phenyl
903.	methyl	3-(pyrimidin-2-yl)-phenyl
904.	methyl	3-(2-methylpyrimidin-4-yl)-phenyl
905.	methyl	3-(pyrimidin-4-yl)-phenyl
906.	methyl	3-(pyrimidin-5-yl)-phenyl
907.	methyl	5-bromopyridin-3-yl
908.	methyl	3-bromo-2-chloropyridin-5-yl
909.	methyl	4-methylpyridin-2-yl
910.	methyl	6-methylpyridin-2-yl
911.	methyl	4-(trifluoromethyl)-pyridin-2-yl
912.	methyl	6-(trifluoromethyl)-pyridin-2-yl
913.	methyl	5-(trifluoromethyl)-pyridin-3-yl
914.	methyl	5-(pyrrolidin-1-yl)-pyridin-3-yl
915.	methyl	3-(pyrrolidin-1-yl)-2-chloropyridin-5-yl
916.	methyl	3-(morpholin-4-yl)-2-chloropyridin-5-yl
917.	methyl	2-(morpholin-4-yl)-pyridin-5-yl
918.	methyl	2-phenoxy pyridin-5-yl
919.	methyl	2,3-dichlorophenyl
920.	methyl	2,5-dichlorophenyl
921.	methyl	3,5-dichlorophenyl
922.	methyl	3-chloro-4-fluorophenyl
923.	methyl	4-bromo-2,5-dichlorophenyl
924.	methyl	3-bromo-4-(trifluoromethoxy)phenyl
925.	methyl	3,5-dibromo-4-(2-fluoroethoxy)-phenyl
926.	methyl	2,5-dimethylphenyl
927.	methyl	2,5-di-(trifluoromethyl)-phenyl
928.	methyl	3,5-di-(trifluoromethyl)-phenyl
929.	methyl	2,5-dimethoxyphenyl

No.	R ¹	Ar
930.	methyl	2-methoxy-5-methylphenyl
931.	methyl	2-methoxy-5-(trifluoromethyl)-phenyl
932.	methyl	4-fluoro-3-(oxazol-4-yl)-phenyl
933.	methyl	thien-2-yl
934.	methyl	thien-3-yl
935.	methyl	3-chlorothien-2-yl
936.	methyl	4-chlorothien-2-yl
937.	methyl	5-chlorothien-2-yl
938.	methyl	3-bromothien-2-yl
939.	methyl	4-bromothien-2-yl
940.	methyl	5-bromothien-2-yl
941.	methyl	4,5-dichlorothien-2-yl
942.	methyl	4,5-dibromothien-2-yl
943.	methyl	4-bromo-5-chlorothien-2-yl
944.	methyl	3-bromo-5-chlorothien-2-yl
945.	methyl	5-methylthien-2-yl
946.	methyl	5-ethylthien-2-yl
947.	methyl	5-propylthien-2-yl
948.	methyl	5-trifluoromethylthien-2-yl
949.	methyl	5-phenylthien-2-yl
950.	methyl	5-(pyrid-2-yl)-thien-2-yl
951.	methyl	5-(phenylsulfonyl)-thien-2-yl
952.	methyl	4-(phenylsulfonyl)-thien-2-yl
953.	methyl	5-(pyrid-2-ylsulfonyl)-thien-2-yl
954.	methyl	5-(3-chloro-5-trifluoro-pyrid-2-ylsulfonyl)-thien-2-yl
955.	methyl	5-(benzoylaminomethyl)-thien-2-yl
956.	methyl	5-((4-chlorobenzoyl)aminomethyl)-thien-2-yl
957.	methyl	5-(acetylaminomethyl)-thien-2-yl
958.	methyl	5-(pyrazol-1-yl)-thien-2-yl
959.	methyl	5-(pyrazol-3-yl)-thien-2-yl
960.	methyl	5-(pyrazol-4-yl)-thien-2-yl
961.	methyl	5-(pyrazol-5-yl)-thien-2-yl
962.	methyl	5-(4-fluoropyrazol-1-yl)-thien-2-yl
963.	methyl	5-(1-methyl-5-trifluoromethyl-(1H)-pyrazol-3-yl)-thien-2-yl
964.	methyl	5-(1-methyl-3-trifluoromethyl-(1H)-pyrazol-5-yl)-thien-2-yl

No.	R ¹	Ar
965.	methyl	5-(4-carboxy-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
966.	methyl	5-(4-aminomethyl-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
967.	methyl	5-(isoxazol-3-yl)-thien-2-yl
968.	methyl	5-(isoxazol-4-yl)-thien-2-yl
969.	methyl	5-(isoxazol-5-yl)-thien-2-yl
970.	methyl	5-(5-trifluoromethylisoxazol-3-yl)-thien-2-yl
971.	methyl	5-(oxazol-2-yl)-thien-2-yl
972.	methyl	5-(oxazol-4-yl)-thien-2-yl
973.	methyl	5-(oxazol-5-yl)-thien-2-yl
974.	methyl	5-(2-methyloxazol-4-yl)-thien-2-yl
975.	methyl	5-(2-methyloxazol-5-yl)-thien-2-yl
976.	methyl	5-(isothiazol-3-yl)-thien-2-yl
977.	methyl	5-(isothiazol-4-yl)-thien-2-yl
978.	methyl	5-(isothiazol-5-yl)-thien-2-yl
979.	methyl	5-(5-trifluoromethylisothiazol-3-yl)-thien-2-yl
980.	methyl	5-(thiazol-2-yl)-thien-2-yl
981.	methyl	5-(thiazol-4-yl)-thien-2-yl
982.	methyl	5-(thiazol-5-yl)-thien-2-yl
983.	methyl	5-(2-methylthiazol-4-yl)-thien-2-yl
984.	methyl	5-(2-methylthiazol-5-yl)-thien-2-yl
985.	methyl	5-([1,2,3]-oxadiazol-4-yl)-thien-2-yl
986.	methyl	5-([1,2,3]-thiadiazol-4-yl)-thien-2-yl
987.	methyl	5-(pyrimidin-2-yl)-thien-2-yl
988.	methyl	5-(pyrimidin-4-yl)-thien-2-yl
989.	methyl	5-(pyrimidin-5-yl)-thien-2-yl
990.	methyl	5-(2-methylthiopyrimidin-4-yl)-thien-2-yl
991.	methyl	5-([1,3]-dioxolan-2-yl)-thien-2-yl
992.	methyl	3-([1,3]-dioxolan-2-yl)-thien-2-yl
993.	methyl	5-((3-chloro-5-(trifluoromethyl)-pyridin-2-yl)-methyl)-thien-2-yl
994.	methyl	5-[3-chloro-5-(trifluoromethyl)-pyrid-2-ylsulfonyl]-thien-2-yl
995.	methyl	2-chlorothien-3-yl
996.	methyl	4-chlorothien-3-yl
997.	methyl	5-chlorothien-3-yl
998.	methyl	2-bromothien-3-yl

No.	R ¹	Ar
999.	methyl	4-bromothien-3-yl
1000.	methyl	5-bromothien-3-yl
1001.	methyl	2,5-dichlorothien-3-yl
1002.	methyl	2,5-dibromothien-3-yl
1003.	methyl	2,4,5-trichlorothien-3-yl
1004.	methyl	4-bromo-2,5-dichlorothien-3-yl
1005.	methyl	2-chloro-5-methylsulfonylthien-3-yl
1006.	methyl	2,5-dimethylthien-3-yl
1007.	methyl	4-hydroxythien-3-yl
1008.	methyl	2-phenylthien-3-yl
1009.	methyl	4-phenyl-5-(trifluoromethyl)-thien-3-yl
1010.	methyl	2-methoxycarbonyl-4-phenyl-5-(trifluoromethyl)-thien-3-yl
1011.	methyl	benzo[b]thiophen-2-yl
1012.	methyl	benzo[b]thiophen-3-yl
1013.	methyl	3-methyl-benzo[b]thiophen-2-yl
1014.	methyl	5-methyl-benzo[b]thiophen-2-yl
1015.	methyl	5-fluoro-3-methyl-benzo[b]thiophen-2-yl
1016.	methyl	5-chloro-3-methyl-benzo[b]thiophen-2-yl
1017.	methyl	5-bromo-3-methyl-benzo[b]thiophen-2-yl
1018.	H	3-methylphenyl
1019.	H	3-ethylphenyl
1020.	H	3-propylphenyl
1021.	H	3-isopropylphenyl
1022.	H	3-sec-butylphenyl
1023.	H	3-tert-butylphenyl
1024.	H	3-isobutylphenyl
1025.	H	3-(1,1-dimethylpropyl)-phenyl
1026.	H	3-vinylphenyl
1027.	H	3-isopropenylphenyl
1028.	H	3-fluorophenyl
1029.	H	3-chlorophenyl
1030.	H	3-bromophenyl
1031.	H	3-iodophenyl
1032.	H	3-(fluoromethyl)phenyl
1033.	H	3-(difluoromethyl)phenyl
1034.	H	3-(trifluoromethyl)phenyl
1035.	H	3,5-bis(trifluoromethyl)phenyl

No.	R ¹	Ar
1036.	H	3-(1-fluoroethyl)-phenyl
1037.	H	3-((S)-1-fluoroethyl)-phenyl
1038.	H	3-((R)-1-fluoroethyl)-phenyl
1039.	H	3-(2-fluoroethyl)-phenyl
1040.	H	3-(1,1-difluoroethyl)-phenyl
1041.	H	3-(2,2-difluoroethyl)-phenyl
1042.	H	3-(2,2,2-trifluoroethyl)-phenyl
1043.	H	3-(3-fluoropropyl)-phenyl
1044.	H	3-(2-fluoropropyl)-phenyl
1045.	H	3-((S)-2-fluoropropyl)-phenyl
1046.	H	3-((R)-2-fluoropropyl)-phenyl
1047.	H	3-(3,3-difluoropropyl)-phenyl
1048.	H	3-(3,3,3-trifluoropropyl)-phenyl
1049.	H	3-(1-fluoro-1-methylethyl)-phenyl
1050.	H	3-(2-fluoro-1-methylethyl)-phenyl
1051.	H	3-((S)-2-fluoro-1-methylethyl)-phenyl
1052.	H	3-((R)-2-fluoro-1-methylethyl)-phenyl
1053.	H	3-(2,2-difluoro-1-methylethyl)-phenyl
1054.	H	3-((S)-2,2-difluoro-1-methylethyl)-phenyl
1055.	H	3-((R)-2,2-difluoro-1-methylethyl)-phenyl
1056.	H	3-(2,2,2-trifluoro-1-methylethyl)-phenyl
1057.	H	3-((S)-2,2,2-trifluoro-1-methylethyl)-phenyl
1058.	H	3-((R)-2,2,2-trifluoro-1-methylethyl)-phenyl
1059.	H	3-(2-fluoro-1-fluoromethylethyl)-phenyl
1060.	H	3-(1-difluoromethyl-2,2-difluoroethyl)-phenyl
1061.	H	3-(1,1-dimethyl-2-fluoroethyl)-phenyl
1062.	H	3-methoxyphenyl
1063.	H	3-ethoxyphenyl
1064.	H	3-propoxyphenyl
1065.	H	3-isopropoxyphenyl
1066.	H	3-butoxyphenyl
1067.	H	3-(fluoromethoxy)-phenyl
1068.	H	3-(difluoromethoxy)-phenyl
1069.	H	3-(trifluoromethoxy)-phenyl
1070.	H	3-(2-fluoroethoxy)-phenyl
1071.	H	3-(2,2-difluoroethoxy)-phenyl
1072.	H	3-(2,2,2-trifluoroethoxy)-phenyl
1073.	H	3-(1,1,2,2-tetrafluoroethoxy)-phenyl

No.	R ¹	Ar
1074.	H	3-cyclopropylphenyl
1075.	H	3-cyclobutylphenyl
1076.	H	3-cyclopentylphenyl
1077.	H	3-(2,2-difluorocyclopropyl)-phenyl
1078.	H	3,4-difluorophenyl
1079.	H	3-bromo-2-fluorophenyl
1080.	H	2-bromo-3-fluorophenyl
1081.	H	3-bromo-2,5-difluorophenyl
1082.	H	5-bromo-2,4-difluorophenyl
1083.	H	3-bromo-2,4-difluorophenyl
1084.	H	4-chloro-3-(trifluoromethyl)-phenyl
1085.	H	2-chloro-5-(trifluoromethyl)-phenyl
1086.	H	2-fluoro-5-(trifluoromethyl)-phenyl
1087.	H	4-fluoro-3-(trifluoromethyl)-phenyl
1088.	H	3-fluoro-5-(trifluoromethyl)-phenyl
1089.	H	4-bromo-3-(trifluoromethyl)-phenyl
1090.	H	3-bromo-5-(trifluoromethyl)-phenyl
1091.	H	2-bromo-5-(trifluoromethyl)-phenyl
1092.	H	5-bromo-2-methoxyphenyl
1093.	H	3-bromo-4-methoxyphenyl
1094.	H	2-fluoro-3-isopropylphenyl
1095.	H	4-fluoro-3-isopropylphenyl
1096.	H	3-(1-hydroxy-1-methylethyl)-phenyl
1097.	H	3-(2-hydroxy-2-methylpropyl)-phenyl
1098.	H	3-acetylphenyl
1099.	H	3-acetylaminophenyl
1100.	H	3-carboxyphenyl
1101.	H	3-cyanophenyl
1102.	H	3-nitrophenyl
1103.	H	3-hydroxyphenyl
1104.	H	3-(O-benzyl)-phenyl
1105.	H	3-(2-methoxyethoxy)-phenyl
1106.	H	3-(CH ₂ -N(CH ₃) ₂)-phenyl
1107.	H	3-(NH-CO-NH ₂)-phenyl
1108.	H	3-(methylsulfanyl)-phenyl
1109.	H	3-(fluoromethylsulfanyl)-phenyl
1110.	H	3-(difluoromethylsulfanyl)-phenyl
1111.	H	3-(trifluoromethylsulfanyl)-phenyl

No.	R ¹	Ar
1112.	H	3-(methylsulfonyl)-phenyl
1113.	H	3-(N-methoxy-N-methyl-amino)-phenyl
1114.	H	3-(methoxyamino)-phenyl
1115.	H	3-(ethoxyamino)-phenyl
1116.	H	3-(N-methylaminooxy)-phenyl
1117.	H	3-(N,N-dimethylaminooxy)-phenyl
1118.	H	3-(azetidin-1-yl)-phenyl
1119.	H	3-(2-methylazetidin-1-yl)-phenyl
1120.	H	3-((S)-2-methylazetidin-1-yl)-phenyl
1121.	H	3-((R)-2-methylazetidin-1-yl)-phenyl
1122.	H	3-(3-fluoroazetidin-1-yl)-phenyl
1123.	H	3-(2,2-difluoroazetidin-1-yl)-phenyl
1124.	H	3-(3-methoxyazetidin-1-yl)-phenyl
1125.	H	3-(3-hydroxyazetidin-1-yl)-phenyl
1126.	H	3-(pyrrolidin-1-yl)-phenyl
1127.	H	3-(pyrrolidin-2-yl)-phenyl
1128.	H	3-((S)-pyrrolidin-2-yl)-phenyl
1129.	H	3-((R)-pyrrolidin-2-yl)-phenyl
1130.	H	3-(pyrrolidin-3-yl)-phenyl
1131.	H	3-((S)-pyrrolidin-3-yl)-phenyl
1132.	H	3-((R)-pyrrolidin-3-yl)-phenyl
1133.	H	3-(pyrrolidin-1-yl)-5-(trifluoromethyl)-phenyl
1134.	H	5-(pyrrolidin-1-yl)-2-methoxyphenyl
1135.	H	3-(pyrrolidin-1-yl)-4-methoxyphenyl
1136.	H	5-(pyrrolidin-1-yl)-2,4-difluorophenyl
1137.	H	3-(pyrrolidin-1-yl)-2,4-difluorophenyl
1138.	H	3-(2-fluoropyrrolidin-1-yl)-phenyl
1139.	H	3-((S)-2-fluoropyrrolidin-1-yl)-phenyl
1140.	H	3-((R)-2-fluoropyrrolidin-1-yl)-phenyl
1141.	H	3-(3-fluoropyrrolidin-1-yl)-phenyl
1142.	H	3-((S)-3-fluoropyrrolidin-1-yl)-phenyl
1143.	H	3-((R)-3-fluoropyrrolidin-1-yl)-phenyl
1144.	H	3-(2,2-difluoropyrrolidin-1-yl)-phenyl
1145.	H	3-(3,3-difluoropyrrolidin-1-yl)-phenyl
1146.	H	3-(2-methylpyrrolidin-1-yl)-phenyl
1147.	H	3-((S)-2-methylpyrrolidin-1-yl)-phenyl
1148.	H	3-((R)-2-methylpyrrolidin-1-yl)-phenyl
1149.	H	3-(3-methylpyrrolidin-1-yl)-phenyl

No.	R ¹	Ar
1150.	H	3-((S)-3-methylpyrrolidin-1-yl)-phenyl
1151.	H	3-((R)-3-methylpyrrolidin-1-yl)-phenyl
1152.	H	3-(1-methylpyrrolidin-2-yl)-phenyl
1153.	H	3-((S)-1-methylpyrrolidin-2-yl)-phenyl
1154.	H	3-((R)-1-methylpyrrolidin-2-yl)-phenyl
1155.	H	3-(1-methylpyrrolidin-3-yl)-phenyl
1156.	H	3-((S)-1-methylpyrrolidin-3-yl)-phenyl
1157.	H	3-((R)-1-methylpyrrolidin-3-yl)-phenyl
1158.	H	3-(2,2-dimethylpyrrolidin-1-yl)-phenyl
1159.	H	3-(3,3-dimethylpyrrolidin-1-yl)-phenyl
1160.	H	3-(2-trifluoromethylpyrrolidin-1-yl)-phenyl
1161.	H	3-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
1162.	H	3-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
1163.	H	3-(3-trifluoromethylpyrrolidin-1-yl)-phenyl
1164.	H	3-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
1165.	H	3-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
1166.	H	3-(2-oxopyrrolidin-1-yl)-phenyl
1167.	H	3-(2-oxo-oxazolidin-3-yl)-phenyl
1168.	H	3-(piperidin-1-yl)-phenyl
1169.	H	3-(2-methylpiperidin-1-yl)-phenyl
1170.	H	3-((S)-2-methylpiperidin-1-yl)-phenyl
1171.	H	3-((R)-2-methylpiperidin-1-yl)-phenyl
1172.	H	3-(2-fluoropiperidin-1-yl)-phenyl
1173.	H	3-((S)-2-fluoropiperidin-1-yl)-phenyl
1174.	H	3-((R)-2-fluoropiperidin-1-yl)-phenyl
1175.	H	3-(2,2-difluoropiperidin-1-yl)-phenyl
1176.	H	3-(piperazin-1-yl)-phenyl
1177.	H	3-(4-methylpiperazin-1-yl)-phenyl
1178.	H	3-(morpholin-4-yl)-phenyl
1179.	H	3-(morpholin-4-yl)-5-(trifluoromethyl)-phenyl
1180.	H	5-(morpholin-4-yl)-2-methoxyphenyl
1181.	H	3-(morpholin-4-yl)-4-methoxyphenyl
1182.	H	5-(morpholin-4-yl)-2,4-difluorophenyl
1183.	H	3-(morpholin-4-yl)-2,4-difluorophenyl
1184.	H	3-(thiomorpholin-4-yl)-phenyl
1185.	H	3-(1-oxo-thiomorpholin-4-yl)-phenyl
1186.	H	3-(1,1-dioxo-thiomorpholin-4-yl)-phenyl
1187.	H	3-(pyrrol-1-yl)-phenyl

No.	R ¹	Ar
1188.	H	3-(pyrrol-2-yl)-phenyl
1189.	H	3-(pyrrol-3-yl)-phenyl
1190.	H	3-(1-methylpyrrol-2-yl)-phenyl
1191.	H	3-(1-methylpyrrol-3-yl)-phenyl
1192.	H	3-(furan-2-yl)-phenyl
1193.	H	3-(furan-3-yl)-phenyl
1194.	H	3-(thiophen-2-yl)-phenyl
1195.	H	3-(thiophen-3-yl)-phenyl
1196.	H	3-(5-propylthien-2-yl)-phenyl
1197.	H	3-(pyrazol-1-yl)-phenyl
1198.	H	3-(pyrazol-3-yl)-phenyl
1199.	H	3-(pyrazol-4-yl)-phenyl
1200.	H	3-(4-fluoropyrazol-1-yl)-phenyl
1201.	H	3-(1-methyl-1H-pyrazol-4-yl)-phenyl
1202.	H	3-(1-ethyl-1H-pyrazol-4-yl)-phenyl
1203.	H	3-(1-methyl-1H-pyrazol-5-yl)-phenyl
1204.	H	3-(1H-imidazol-2-yl)-phenyl
1205.	H	3-(imidazol-1-yl)-phenyl
1206.	H	3-(1-methylimidazol-2-yl)-phenyl
1207.	H	3-(oxazol-2-yl)-phenyl
1208.	H	3-(oxazol-4-yl)-phenyl
1209.	H	3-(oxazol-5-yl)-phenyl
1210.	H	3-(isoxazol-3-yl)-phenyl
1211.	H	3-(isoxazol-4-yl)-phenyl
1212.	H	3-(isoxazol-5-yl)-phenyl
1213.	H	3-(thiazol-2-yl)-phenyl
1214.	H	3-(thiazol-4-yl)-phenyl
1215.	H	3-(thiazol-5-yl)-phenyl
1216.	H	3-(2-methylthiazol-4-yl)-phenyl
1217.	H	3-(2-methylthiazol-5-yl)-phenyl
1218.	H	3-([1,2,3]-triazol-1-yl)-phenyl
1219.	H	3-([1,2,4]-triazol-1-yl)-phenyl
1220.	H	3-([1,2,3]-triazol-2-yl)-phenyl
1221.	H	3-(4H-[1,2,4]-triazol-3-yl)-phenyl
1222.	H	3-([1,2,4]-triazol-4-yl)-phenyl
1223.	H	3-(2H-[1,2,3]-triazol-4-yl)-phenyl
1224.	H	3-(4-methyl-4H-[1,2,4]-triazol-3-yl)-phenyl
1225.	H	3-(2-methyl-2H-[1,2,3]-triazol-4-yl)-phenyl

No.	R ¹	Ar
1226.	H	3-([1,3,4]-oxadiazol-2-yl)-phenyl
1227.	H	3-(5-methyl-[1,3,4]-oxadiazol-2-yl)-phenyl
1228.	H	3-([1,2,4]-oxadiazol-3-yl)-phenyl
1229.	H	3-(5-methyl-[1,2,4]-oxadiazol-3-yl)-phenyl
1230.	H	3-([1,2,4]-oxadiazol-5-yl)-phenyl
1231.	H	3-([1,2,3]-oxadiazol-4-yl)-phenyl
1232.	H	3-([1,2,3]-oxadiazol-5-yl)-phenyl
1233.	H	3-([1,2,3]-thiadiazol-4-yl)-phenyl
1234.	H	3-(1H-tetrazol-5-yl)-phenyl
1235.	H	3-(tetrazol-1-yl)-phenyl
1236.	H	3-(2-methyl-2H-tetrazol-5-yl)-phenyl
1237.	H	3-(1-methyl-1H-tetrazol-5-yl)-phenyl
1238.	H	3-furazan-3-yl-phenyl
1239.	H	3-(pyrid-2-yl)-phenyl
1240.	H	3-(pyrid-3-yl)-phenyl
1241.	H	3-(pyrid-4-yl)-phenyl
1242.	H	3-(pyrimidin-2-yl)-phenyl
1243.	H	3-(2-methylpyrimidin-4-yl)-phenyl
1244.	H	3-(pyrimidin-4-yl)-phenyl
1245.	H	3-(pyrimidin-5-yl)-phenyl
1246.	H	5-bromopyridin-3-yl
1247.	H	3-bromo-2-chloropyridin-5-yl
1248.	H	4-methylpyridin-2-yl
1249.	H	6-methylpyridin-2-yl
1250.	H	4-(trifluoromethyl)-pyridin-2-yl
1251.	H	6-(trifluoromethyl)-pyridin-2-yl
1252.	H	5-(trifluoromethyl)-pyridin-3-yl
1253.	H	5-(pyrrolidin-1-yl)-pyridin-3-yl
1254.	H	3-(pyrrolidin-1-yl)-2-chloropyridin-5-yl
1255.	H	3-(morpholin-4-yl)-2-chloropyridin-5-yl
1256.	H	2-(morpholin-4-yl)-pyridin-5-yl
1257.	H	2-phenoxy-pyridin-5-yl
1258.	H	2,3-dichlorophenyl
1259.	H	2,5-dichlorophenyl
1260.	H	3,5-dichlorophenyl
1261.	H	3-chloro-4-fluorophenyl
1262.	H	4-bromo-2,5-dichlorophenyl
1263.	H	3-bromo-4-(trifluoromethoxy)phenyl

No.	R ¹	Ar
1264.	H	3,5-dibromo-4-(2-fluoroethoxy)-phenyl
1265.	H	2,5-dimethylphenyl
1266.	H	2,5-di-(trifluoromethyl)-phenyl
1267.	H	3,5-di-(trifluoromethyl)-phenyl
1268.	H	2,5-dimethoxyphenyl
1269.	H	2-methoxy-5-methylphenyl
1270.	H	2-methoxy-5-(trifluoromethyl)-phenyl
1271.	H	4-fluoro-3-(oxazol-4-yl)-phenyl
1272.	H	thien-2-yl
1273.	H	thien-3-yl
1274.	H	3-chlorothien-2-yl
1275.	H	4-chlorothien-2-yl
1276.	H	5-chlorothien-2-yl
1277.	H	3-bromothien-2-yl
1278.	H	4-bromothien-2-yl
1279.	H	5-bromothien-2-yl
1280.	H	4,5-dichlorothien-2-yl
1281.	H	4,5-dibromothien-2-yl
1282.	H	4-bromo-5-chlorothien-2-yl
1283.	H	3-bromo-5-chlorothien-2-yl
1284.	H	5-methylthien-2-yl
1285.	H	5-ethylthien-2-yl
1286.	H	5-propylthien-2-yl
1287.	H	5-trifluoromethylthien-2-yl
1288.	H	5-phenylthien-2-yl
1289.	H	5-(pyrid-2-yl)-thien-2-yl
1290.	H	5-(phenylsulfonyl)-thien-2-yl
1291.	H	4-(phenylsulfonyl)-thien-2-yl
1292.	H	5-(pyrid-2-ylsulfonyl)-thien-2-yl
1293.	H	5-(3-chloro-5-trifluoro-pyrid-2-ylsulfonyl)-thien-2-yl
1294.	H	5-(benzoylaminomethyl)-thien-2-yl
1295.	H	5-((4-chlorobenzoyl)aminomethyl)-thien-2-yl
1296.	H	5-(acetylaminomethyl)-thien-2-yl
1297.	H	5-(pyrazol-1-yl)-thien-2-yl
1298.	H	5-(pyrazol-3-yl)-thien-2-yl
1299.	H	5-(pyrazol-4-yl)-thien-2-yl
1300.	H	5-(pyrazol-5-yl)-thien-2-yl

No.	R ¹	Ar
1301.	H	5-(4-fluoropyrazol-1-yl)-thien-2-yl
1302.	H	5-(1-methyl-5-trifluoromethyl-(1H)-pyrazol-3-yl)-thien-2-yl
1303.	H	5-(1-methyl-3-trifluoromethyl-(1H)-pyrazol-5-yl)-thien-2-yl
1304.	H	5-(4-carboxy-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
1305.	H	5-(4-aminomethyl-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
1306.	H	5-(isoxazol-3-yl)-thien-2-yl
1307.	H	5-(isoxazol-4-yl)-thien-2-yl
1308.	H	5-(isoxazol-5-yl)-thien-2-yl
1309.	H	5-(5-trifluoromethylisoxazol-3-yl)-thien-2-yl
1310.	H	5-(oxazol-2-yl)-thien-2-yl
1311.	H	5-(oxazol-4-yl)-thien-2-yl
1312.	H	5-(oxazol-5-yl)-thien-2-yl
1313.	H	5-(2-methyloxazol-4-yl)-thien-2-yl
1314.	H	5-(2-methyloxazol-5-yl)-thien-2-yl
1315.	H	5-(isothiazol-3-yl)-thien-2-yl
1316.	H	5-(isothiazol-4-yl)-thien-2-yl
1317.	H	5-(isothiazol-5-yl)-thien-2-yl
1318.	H	5-(5-trifluoromethylisothiazol-3-yl)-thien-2-yl
1319.	H	5-(thiazol-2-yl)-thien-2-yl
1320.	H	5-(thiazol-4-yl)-thien-2-yl
1321.	H	5-(thiazol-5-yl)-thien-2-yl
1322.	H	5-(2-methylthiazol-4-yl)-thien-2-yl
1323.	H	5-(2-methylthiazol-5-yl)-thien-2-yl
1324.	H	5-([1,2,3]-oxadiazol-4-yl)-thien-2-yl
1325.	H	5-([1,2,3]-thiadiazol-4-yl)-thien-2-yl
1326.	H	5-(pyrimidin-2-yl)-thien-2-yl
1327.	H	5-(pyrimidin-4-yl)-thien-2-yl
1328.	H	5-(pyrimidin-5-yl)-thien-2-yl
1329.	H	5-(2-methylthiopyrimidin-4-yl)-thien-2-yl
1330.	H	5-([1,3]-dioxolan-2-yl)-thien-2-yl
1331.	H	3-([1,3]-dioxolan-2-yl)-thien-2-yl
1332.	H	5-((3-chloro-5-(trifluoromethyl)-pyridin-2-yl)-methyl)-thien-2-yl
1333.	H	5-[3-chloro-5-(trifluoromethyl)-pyrid-2-ylsulfonyl]-

No.	R ¹	Ar
		thien-2-yl
1334.	H	2-chlorothien-3-yl
1335.	H	4-chlorothien-3-yl
1336.	H	5-chlorothien-3-yl
1337.	H	2-bromothien-3-yl
1338.	H	4-bromothien-3-yl
1339.	H	5-bromothien-3-yl
1340.	H	2,5-dichlorothien-3-yl
1341.	H	2,5-dibromothien-3-yl
1342.	H	2,4,5-trichlorothien-3-yl
1343.	H	4-bromo-2,5-dichlorothien-3-yl
1344.	H	2-chloro-5-methylsulfonylthien-3-yl
1345.	H	2,5-dimethylthien-3-yl
1346.	H	4-hydroxythien-3-yl
1347.	H	2-phenylthien-3-yl
1348.	H	4-phenyl-5-(trifluoromethyl)-thien-3-yl
1349.	H	2-methoxycarbonyl-4-phenyl-5-(trifluoromethyl)-thien-3-yl
1350.	H	benzo[b]thiophen-2-yl
1351.	H	benzo[b]thiophen-3-yl
1352.	H	3-methyl-benzo[b]thiophen-2-yl
1353.	H	5-methyl-benzo[b]thiophen-2-yl
1354.	H	5-fluoro-3-methyl-benzo[b]thiophen-2-yl
1355.	H	5-chloro-3-methyl-benzo[b]thiophen-2-yl
1356.	H	5-bromo-3-methyl-benzo[b]thiophen-2-yl
1357.	3-fluoropropyl	3-methylphenyl
1358.	3-fluoropropyl	3-ethylphenyl
1359.	3-fluoropropyl	3-propylphenyl
1360.	3-fluoropropyl	3-isopropylphenyl
1361.	3-fluoropropyl	3-sec-butylphenyl
1362.	3-fluoropropyl	3-tert-butylphenyl
1363.	3-fluoropropyl	3-isobutylphenyl
1364.	3-fluoropropyl	3-(1,1-dimethylpropyl)-phenyl
1365.	3-fluoropropyl	3-vinylphenyl
1366.	3-fluoropropyl	3-isopropenylphenyl
1367.	3-fluoropropyl	3-fluorophenyl
1368.	3-fluoropropyl	3-chlorophenyl
1369.	3-fluoropropyl	3-bromophenyl

No.	R ¹	Ar
1370.	3-fluoropropyl	3-iodophenyl
1371.	3-fluoropropyl	3-(fluoromethyl)phenyl
1372.	3-fluoropropyl	3-(difluoromethyl)phenyl
1373.	3-fluoropropyl	3-(trifluoromethyl)phenyl
1374.	3-fluoropropyl	3,5-bis(trifluoromethyl)phenyl
1375.	3-fluoropropyl	3-(1-fluoroethyl)-phenyl
1376.	3-fluoropropyl	3-((S)-1-fluoroethyl)-phenyl
1377.	3-fluoropropyl	3-((R)-1-fluoroethyl)-phenyl
1378.	3-fluoropropyl	3-(2-fluoroethyl)-phenyl
1379.	3-fluoropropyl	3-(1,1-difluoroethyl)-phenyl
1380.	3-fluoropropyl	3-(2,2-difluoroethyl)-phenyl
1381.	3-fluoropropyl	3-(2,2,2-trifluoroethyl)-phenyl
1382.	3-fluoropropyl	3-(3-fluoropropyl)-phenyl
1383.	3-fluoropropyl	3-(2-fluoropropyl)-phenyl
1384.	3-fluoropropyl	3-((S)-2-fluoropropyl)-phenyl
1385.	3-fluoropropyl	3-((R)-2-fluoropropyl)-phenyl
1386.	3-fluoropropyl	3-(3,3-difluoropropyl)-phenyl
1387.	3-fluoropropyl	3-(3,3,3-trifluoropropyl)-phenyl
1388.	3-fluoropropyl	3-(1-fluoro-1-methylethyl)-phenyl
1389.	3-fluoropropyl	3-(2-fluoro-1-methylethyl)-phenyl
1390.	3-fluoropropyl	3-((S)-2-fluoro-1-methylethyl)-phenyl
1391.	3-fluoropropyl	3-((R)-2-fluoro-1-methylethyl)-phenyl
1392.	3-fluoropropyl	3-(2,2-difluoro-1-methylethyl)-phenyl
1393.	3-fluoropropyl	3-((S)-2,2-difluoro-1-methylethyl)-phenyl
1394.	3-fluoropropyl	3-((R)-2,2-difluoro-1-methylethyl)-phenyl
1395.	3-fluoropropyl	3-(2,2,2-trifluoro-1-methylethyl)-phenyl
1396.	3-fluoropropyl	3-((S)-2,2,2-trifluoro-1-methylethyl)-phenyl
1397.	3-fluoropropyl	3-((R)-2,2,2-trifluoro-1-methylethyl)-phenyl
1398.	3-fluoropropyl	3-(2-fluoro-1-fluoromethylethyl)-phenyl
1399.	3-fluoropropyl	3-(1-difluoromethyl-2,2-difluoroethyl)-phenyl
1400.	3-fluoropropyl	3-(1,1-dimethyl-2-fluoroethyl)-phenyl
1401.	3-fluoropropyl	3-methoxyphenyl
1402.	3-fluoropropyl	3-ethoxyphenyl
1403.	3-fluoropropyl	3-propoxyphenyl
1404.	3-fluoropropyl	3-isopropoxyphenyl
1405.	3-fluoropropyl	3-butoxyphenyl
1406.	3-fluoropropyl	3-(fluoromethoxy)-phenyl
1407.	3-fluoropropyl	3-(difluoromethoxy)-phenyl

No.	R ¹	Ar
1408.	3-fluoropropyl	3-(trifluoromethoxy)-phenyl
1409.	3-fluoropropyl	3-(2-fluoroethoxy)-phenyl
1410.	3-fluoropropyl	3-(2,2-difluoroethoxy)-phenyl
1411.	3-fluoropropyl	3-(2,2,2-trifluoroethoxy)-phenyl
1412.	3-fluoropropyl	3-(1,1,2,2-tetrafluoroethoxy)-phenyl
1413.	3-fluoropropyl	3-cyclopropylphenyl
1414.	3-fluoropropyl	3-cyclobutylphenyl
1415.	3-fluoropropyl	3-cyclopentylphenyl
1416.	3-fluoropropyl	3-(2,2-difluorocyclopropyl)-phenyl
1417.	3-fluoropropyl	3,4-difluorophenyl
1418.	3-fluoropropyl	3-bromo-2-fluorophenyl
1419.	3-fluoropropyl	2-bromo-3-fluorophenyl
1420.	3-fluoropropyl	3-bromo-2,5-difluorophenyl
1421.	3-fluoropropyl	5-bromo-2,4-difluorophenyl
1422.	3-fluoropropyl	3-bromo-2,4-difluorophenyl
1423.	3-fluoropropyl	4-chloro-3-(trifluoromethyl)-phenyl
1424.	3-fluoropropyl	2-chloro-5-(trifluoromethyl)-phenyl
1425.	3-fluoropropyl	2-fluoro-5-(trifluoromethyl)-phenyl
1426.	3-fluoropropyl	4-fluoro-3-(trifluoromethyl)-phenyl
1427.	3-fluoropropyl	3-fluoro-5-(trifluoromethyl)-phenyl
1428.	3-fluoropropyl	4-bromo-3-(trifluoromethyl)-phenyl
1429.	3-fluoropropyl	3-bromo-5-(trifluoromethyl)-phenyl
1430.	3-fluoropropyl	2-bromo-5-(trifluoromethyl)-phenyl
1431.	3-fluoropropyl	5-bromo-2-methoxyphenyl
1432.	3-fluoropropyl	3-bromo-4-methoxyphenyl
1433.	3-fluoropropyl	2-fluoro-3-isopropylphenyl
1434.	3-fluoropropyl	4-fluoro-3-isopropylphenyl
1435.	3-fluoropropyl	3-(1-hydroxy-1-methylethyl)-phenyl
1436.	3-fluoropropyl	3-(2-hydroxy-2-methylpropyl)-phenyl
1437.	3-fluoropropyl	3-acetylphenyl
1438.	3-fluoropropyl	3-acetylamino-phenyl
1439.	3-fluoropropyl	3-carboxyphenyl
1440.	3-fluoropropyl	3-cyanophenyl
1441.	3-fluoropropyl	3-nitrophenyl
1442.	3-fluoropropyl	3-hydroxyphenyl
1443.	3-fluoropropyl	3-(O-benzyl)-phenyl
1444.	3-fluoropropyl	3-(2-methoxyethoxy)-phenyl
1445.	3-fluoropropyl	3-(CH ₂ -N(CH ₃) ₂)-phenyl

No.	R ¹	Ar
1446.	3-fluoropropyl	3-(NH-CO-NH ₂)-phenyl
1447.	3-fluoropropyl	3-(methylsulfanyl)-phenyl
1448.	3-fluoropropyl	3-(fluoromethylsulfanyl)-phenyl
1449.	3-fluoropropyl	3-(difluoromethylsulfanyl)-phenyl
1450.	3-fluoropropyl	3-(trifluoromethylsulfanyl)-phenyl
1451.	3-fluoropropyl	3-(methylsulfonyl)-phenyl
1452.	3-fluoropropyl	3-(N-methoxy-N-methyl-amino)-phenyl
1453.	3-fluoropropyl	3-(methoxyamino)-phenyl
1454.	3-fluoropropyl	3-(ethoxyamino)-phenyl
1455.	3-fluoropropyl	3-(N-methylaminooxy)-phenyl
1456.	3-fluoropropyl	3-(N,N-dimethylaminooxy)-phenyl
1457.	3-fluoropropyl	3-(azetidin-1-yl)-phenyl
1458.	3-fluoropropyl	3-(2-methylazetidin-1-yl)-phenyl
1459.	3-fluoropropyl	3-((S)-2-methylazetidin-1-yl)-phenyl
1460.	3-fluoropropyl	3-((R)-2-methylazetidin-1-yl)-phenyl
1461.	3-fluoropropyl	3-(3-fluoroazetidin-1-yl)-phenyl
1462.	3-fluoropropyl	3-(2,2-difluoroazetidin-1-yl)-phenyl
1463.	3-fluoropropyl	3-(3-methoxyazetidin-1-yl)-phenyl
1464.	3-fluoropropyl	3-(3-hydroxyazetidin-1-yl)-phenyl
1465.	3-fluoropropyl	3-(pyrrolidin-1-yl)-phenyl
1466.	3-fluoropropyl	3-(pyrrolidin-2-yl)-phenyl
1467.	3-fluoropropyl	3-((S)-pyrrolidin-2-yl)-phenyl
1468.	3-fluoropropyl	3-((R)-pyrrolidin-2-yl)-phenyl
1469.	3-fluoropropyl	3-(pyrrolidin-3-yl)-phenyl
1470.	3-fluoropropyl	3-((S)-pyrrolidin-3-yl)-phenyl
1471.	3-fluoropropyl	3-((R)-pyrrolidin-3-yl)-phenyl
1472.	3-fluoropropyl	3-(pyrrolidin-1-yl)-5-(trifluoromethyl)-phenyl
1473.	3-fluoropropyl	5-(pyrrolidin-1-yl)-2-methoxyphenyl
1474.	3-fluoropropyl	3-(pyrrolidin-1-yl)-4-methoxyphenyl
1475.	3-fluoropropyl	5-(pyrrolidin-1-yl)-2,4-difluorophenyl
1476.	3-fluoropropyl	3-(pyrrolidin-1-yl)-2,4-difluorophenyl
1477.	3-fluoropropyl	3-(2-fluoropyrrolidin-1-yl)-phenyl
1478.	3-fluoropropyl	3-((S)-2-fluoropyrrolidin-1-yl)-phenyl
1479.	3-fluoropropyl	3-((R)-2-fluoropyrrolidin-1-yl)-phenyl
1480.	3-fluoropropyl	3-(3-fluoropyrrolidin-1-yl)-phenyl
1481.	3-fluoropropyl	3-((S)-3-fluoropyrrolidin-1-yl)-phenyl
1482.	3-fluoropropyl	3-((R)-3-fluoropyrrolidin-1-yl)-phenyl
1483.	3-fluoropropyl	3-(2,2-difluoropyrrolidin-1-yl)-phenyl

No.	R ¹	Ar
1484.	3-fluoropropyl	3-(3,3-difluoropyrrolidin-1-yl)-phenyl
1485.	3-fluoropropyl	3-(2-methylpyrrolidin-1-yl)-phenyl
1486.	3-fluoropropyl	3-((S)-2-methylpyrrolidin-1-yl)-phenyl
1487.	3-fluoropropyl	3-((R)-2-methylpyrrolidin-1-yl)-phenyl
1488.	3-fluoropropyl	3-(3-methylpyrrolidin-1-yl)-phenyl
1489.	3-fluoropropyl	3-((S)-3-methylpyrrolidin-1-yl)-phenyl
1490.	3-fluoropropyl	3-((R)-3-methylpyrrolidin-1-yl)-phenyl
1491.	3-fluoropropyl	3-(1-methylpyrrolidin-2-yl)-phenyl
1492.	3-fluoropropyl	3-((S)-1-methylpyrrolidin-2-yl)-phenyl
1493.	3-fluoropropyl	3-((R)-1-methylpyrrolidin-2-yl)-phenyl
1494.	3-fluoropropyl	3-(1-methylpyrrolidin-3-yl)-phenyl
1495.	3-fluoropropyl	3-((S)-1-methylpyrrolidin-3-yl)-phenyl
1496.	3-fluoropropyl	3-((R)-1-methylpyrrolidin-3-yl)-phenyl
1497.	3-fluoropropyl	3-(2,2-dimethylpyrrolidin-1-yl)-phenyl
1498.	3-fluoropropyl	3-(3,3-dimethylpyrrolidin-1-yl)-phenyl
1499.	3-fluoropropyl	3-(2-trifluoromethylpyrrolidin-1-yl)-phenyl
1500.	3-fluoropropyl	3-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
1501.	3-fluoropropyl	3-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
1502.	3-fluoropropyl	3-(3-trifluoromethylpyrrolidin-1-yl)-phenyl
1503.	3-fluoropropyl	3-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
1504.	3-fluoropropyl	3-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
1505.	3-fluoropropyl	3-(2-oxopyrrolidin-1-yl)-phenyl
1506.	3-fluoropropyl	3-(2-oxo-oxazolidin-3-yl)-phenyl
1507.	3-fluoropropyl	3-(piperidin-1-yl)-phenyl
1508.	3-fluoropropyl	3-(2-methylpiperidin-1-yl)-phenyl
1509.	3-fluoropropyl	3-((S)-2-methylpiperidin-1-yl)-phenyl
1510.	3-fluoropropyl	3-((R)-2-methylpiperidin-1-yl)-phenyl
1511.	3-fluoropropyl	3-(2-fluoropiperidin-1-yl)-phenyl
1512.	3-fluoropropyl	3-((S)-2-fluoropiperidin-1-yl)-phenyl
1513.	3-fluoropropyl	3-((R)-2-fluoropiperidin-1-yl)-phenyl
1514.	3-fluoropropyl	3-(2,2-difluoropiperidin-1-yl)-phenyl
1515.	3-fluoropropyl	3-(piperazin-1-yl)-phenyl
1516.	3-fluoropropyl	3-(4-methylpiperazin-1-yl)-phenyl
1517.	3-fluoropropyl	3-(morpholin-4-yl)-phenyl
1518.	3-fluoropropyl	3-(morpholin-4-yl)-5-(trifluoromethyl)-phenyl
1519.	3-fluoropropyl	5-(morpholin-4-yl)-2-methoxyphenyl
1520.	3-fluoropropyl	3-(morpholin-4-yl)-4-methoxyphenyl
1521.	3-fluoropropyl	5-(morpholin-4-yl)-2,4-difluorophenyl

No.	R ¹	Ar
1522.	3-fluoropropyl	3-(morpholin-4-yl)-2,4-difluorophenyl
1523.	3-fluoropropyl	3-(thiomorpholin-4-yl)-phenyl
1524.	3-fluoropropyl	3-(1-oxo-thiomorpholin-4-yl)-phenyl
1525.	3-fluoropropyl	3-(1,1-dioxo-thiomorpholin-4-yl)-phenyl
1526.	3-fluoropropyl	3-(pyrrol-1-yl)-phenyl
1527.	3-fluoropropyl	3-(pyrrol-2-yl)-phenyl
1528.	3-fluoropropyl	3-(pyrrol-3-yl)-phenyl
1529.	3-fluoropropyl	3-(1-methylpyrrol-2-yl)-phenyl
1530.	3-fluoropropyl	3-(1-methylpyrrol-3-yl)-phenyl
1531.	3-fluoropropyl	3-(furan-2-yl)-phenyl
1532.	3-fluoropropyl	3-(furan-3-yl)-phenyl
1533.	3-fluoropropyl	3-(thiophen-2-yl)-phenyl
1534.	3-fluoropropyl	3-(thiophen-3-yl)-phenyl
1535.	3-fluoropropyl	3-(5-propylthien-2-yl)-phenyl
1536.	3-fluoropropyl	3-(pyrazol-1-yl)-phenyl
1537.	3-fluoropropyl	3-(pyrazol-3-yl)-phenyl
1538.	3-fluoropropyl	3-(pyrazol-4-yl)-phenyl
1539.	3-fluoropropyl	3-(4-fluoropyrazol-1-yl)-phenyl
1540.	3-fluoropropyl	3-(1-methyl-1H-pyrazol-4-yl)-phenyl
1541.	3-fluoropropyl	3-(1-ethyl-1H-pyrazol-4-yl)-phenyl
1542.	3-fluoropropyl	3-(1-methyl-1H-pyrazol-5-yl)-phenyl
1543.	3-fluoropropyl	3-(1H-imidazol-2-yl)-phenyl
1544.	3-fluoropropyl	3-(imidazol-1-yl)-phenyl
1545.	3-fluoropropyl	3-(1-methylimidazol-2-yl)-phenyl
1546.	3-fluoropropyl	3-(oxazol-2-yl)-phenyl
1547.	3-fluoropropyl	3-(oxazol-4-yl)-phenyl
1548.	3-fluoropropyl	3-(oxazol-5-yl)-phenyl
1549.	3-fluoropropyl	3-(isoxazol-3-yl)-phenyl
1550.	3-fluoropropyl	3-(isoxazol-4-yl)-phenyl
1551.	3-fluoropropyl	3-(isoxazol-5-yl)-phenyl
1552.	3-fluoropropyl	3-(thiazol-2-yl)-phenyl
1553.	3-fluoropropyl	3-(thiazol-4-yl)-phenyl
1554.	3-fluoropropyl	3-(thiazol-5-yl)-phenyl
1555.	3-fluoropropyl	3-(2-methylthiazol-4-yl)-phenyl
1556.	3-fluoropropyl	3-(2-methylthiazol-5-yl)-phenyl
1557.	3-fluoropropyl	3-([1,2,3]-triazol-1-yl)-phenyl
1558.	3-fluoropropyl	3-([1,2,4]-triazol-1-yl)-phenyl
1559.	3-fluoropropyl	3-([1,2,3]-triazol-2-yl)-phenyl

No.	R ¹	Ar
1560.	3-fluoropropyl	3-(4H-[1,2,4]-triazol-3-yl)-phenyl
1561.	3-fluoropropyl	3-([1,2,4]-triazol-4-yl)-phenyl
1562.	3-fluoropropyl	3-(2H-[1,2,3]-triazol-4-yl)-phenyl
1563.	3-fluoropropyl	3-(4-methyl-4H-[1,2,4]-triazol-3-yl)-phenyl
1564.	3-fluoropropyl	3-(2-methyl-2H-[1,2,3]-triazol-4-yl)-phenyl
1565.	3-fluoropropyl	3-([1,3,4]-oxadiazol-2-yl)-phenyl
1566.	3-fluoropropyl	3-(5-methyl-[1,3,4]-oxadiazol-2-yl)-phenyl
1567.	3-fluoropropyl	3-([1,2,4]-oxadiazol-3-yl)-phenyl
1568.	3-fluoropropyl	3-(5-methyl-[1,2,4]-oxadiazol-3-yl)-phenyl
1569.	3-fluoropropyl	3-([1,2,4]-oxadiazol-5-yl)-phenyl
1570.	3-fluoropropyl	3-([1,2,3]-oxadiazol-4-yl)-phenyl
1571.	3-fluoropropyl	3-([1,2,3]-oxadiazol-5-yl)-phenyl
1572.	3-fluoropropyl	3-([1,2,3]-thiadiazol-4-yl)-phenyl
1573.	3-fluoropropyl	3-(1H-tetrazol-5-yl)-phenyl
1574.	3-fluoropropyl	3-(tetrazol-1-yl)-phenyl
1575.	3-fluoropropyl	3-(2-methyl-2H-tetrazol-5-yl)-phenyl
1576.	3-fluoropropyl	3-(1-methyl-1H-tetrazol-5-yl)-phenyl
1577.	3-fluoropropyl	3-furazan-3-yl-phenyl
1578.	3-fluoropropyl	3-(pyrid-2-yl)-phenyl
1579.	3-fluoropropyl	3-(pyrid-3-yl)-phenyl
1580.	3-fluoropropyl	3-(pyrid-4-yl)-phenyl
1581.	3-fluoropropyl	3-(pyrimidin-2-yl)-phenyl
1582.	3-fluoropropyl	3-(2-methylpyrimidin-4-yl)-phenyl
1583.	3-fluoropropyl	3-(pyrimidin-4-yl)-phenyl
1584.	3-fluoropropyl	3-(pyrimidin-5-yl)-phenyl
1585.	3-fluoropropyl	5-bromopyridin-3-yl
1586.	3-fluoropropyl	3-bromo-2-chloropyridin-5-yl
1587.	3-fluoropropyl	4-methylpyridin-2-yl
1588.	3-fluoropropyl	6-methylpyridin-2-yl
1589.	3-fluoropropyl	4-(trifluoromethyl)-pyridin-2-yl
1590.	3-fluoropropyl	6-(trifluoromethyl)-pyridin-2-yl
1591.	3-fluoropropyl	5-(trifluoromethyl)-pyridin-3-yl
1592.	3-fluoropropyl	5-(pyrrolidin-1-yl)-pyridin-3-yl
1593.	3-fluoropropyl	3-(pyrrolidin-1-yl)-2-chloropyridin-5-yl
1594.	3-fluoropropyl	3-(morpholin-4-yl)-2-chloropyridin-5-yl
1595.	3-fluoropropyl	2-(morpholin-4-yl)-pyridin-5-yl
1596.	3-fluoropropyl	2-phenoxy-pyridin-5-yl
1597.	3-fluoropropyl	2,3-dichlorophenyl

No.	R ¹	Ar
1598.	3-fluoropropyl	2,5-dichlorophenyl
1599.	3-fluoropropyl	3,5-dichlorophenyl
1600.	3-fluoropropyl	3-chloro-4-fluorophenyl
1601.	3-fluoropropyl	4-bromo-2,5-dichlorophenyl
1602.	3-fluoropropyl	3-bromo-4-(trifluoromethoxy)phenyl
1603.	3-fluoropropyl	3,5-dibromo-4-(2-fluoroethoxy)-phenyl
1604.	3-fluoropropyl	2,5-dimethylphenyl
1605.	3-fluoropropyl	2,5-di-(trifluoromethyl)-phenyl
1606.	3-fluoropropyl	3,5-di-(trifluoromethyl)-phenyl
1607.	3-fluoropropyl	2,5-dimethoxyphenyl
1608.	3-fluoropropyl	2-methoxy-5-methylphenyl
1609.	3-fluoropropyl	2-methoxy-5-(trifluoromethyl)-phenyl
1610.	3-fluoropropyl	4-fluoro-3-(oxazol-4-yl)-phenyl
1611.	3-fluoropropyl	thien-2-yl
1612.	3-fluoropropyl	thien-3-yl
1613.	3-fluoropropyl	3-chlorothien-2-yl
1614.	3-fluoropropyl	4-chlorothien-2-yl
1615.	3-fluoropropyl	5-chlorothien-2-yl
1616.	3-fluoropropyl	3-bromothien-2-yl
1617.	3-fluoropropyl	4-bromothien-2-yl
1618.	3-fluoropropyl	5-bromothien-2-yl
1619.	3-fluoropropyl	4,5-dichlorothien-2-yl
1620.	3-fluoropropyl	4,5-dibromothien-2-yl
1621.	3-fluoropropyl	4-bromo-5-chlorothien-2-yl
1622.	3-fluoropropyl	3-bromo-5-chlorothien-2-yl
1623.	3-fluoropropyl	5-methylthien-2-yl
1624.	3-fluoropropyl	5-ethylthien-2-yl
1625.	3-fluoropropyl	5-propylthien-2-yl
1626.	3-fluoropropyl	5-trifluoromethylthien-2-yl
1627.	3-fluoropropyl	5-phenylthien-2-yl
1628.	3-fluoropropyl	5-(pyrid-2-yl)-thien-2-yl
1629.	3-fluoropropyl	5-(phenylsulfonyl)-thien-2-yl
1630.	3-fluoropropyl	4-(phenylsulfonyl)-thien-2-yl
1631.	3-fluoropropyl	5-(pyrid-2-ylsulfonyl)-thien-2-yl
1632.	3-fluoropropyl	5-(3-chloro-5-trifluoro-pyrid-2-ylsulfonyl)-thien-2-yl
1633.	3-fluoropropyl	5-(benzoylaminomethyl)-thien-2-yl
1634.	3-fluoropropyl	5-((4-chlorobenzoyl)aminomethyl)-thien-2-yl

No.	R ¹	Ar
1635.	3-fluoropropyl	5-(acetaminomethyl)-thien-2-yl
1636.	3-fluoropropyl	5-(pyrazol-1-yl)-thien-2-yl
1637.	3-fluoropropyl	5-(pyrazol-3-yl)-thien-2-yl
1638.	3-fluoropropyl	5-(pyrazol-4-yl)-thien-2-yl
1639.	3-fluoropropyl	5-(pyrazol-5-yl)-thien-2-yl
1640.	3-fluoropropyl	5-(4-fluoropyrazol-1-yl)-thien-2-yl
1641.	3-fluoropropyl	5-(1-methyl-5-trifluoromethyl-(1H)-pyrazol-3-yl)-thien-2-yl
1642.	3-fluoropropyl	5-(1-methyl-3-trifluoromethyl-(1H)-pyrazol-5-yl)-thien-2-yl
1643.	3-fluoropropyl	5-(4-carboxy-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
1644.	3-fluoropropyl	5-(4-aminomethyl-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
1645.	3-fluoropropyl	5-(isoxazol-3-yl)-thien-2-yl
1646.	3-fluoropropyl	5-(isoxazol-4-yl)-thien-2-yl
1647.	3-fluoropropyl	5-(isoxazol-5-yl)-thien-2-yl
1648.	3-fluoropropyl	5-(5-trifluoromethylisoxazol-3-yl)-thien-2-yl
1649.	3-fluoropropyl	5-(oxazol-2-yl)-thien-2-yl
1650.	3-fluoropropyl	5-(oxazol-4-yl)-thien-2-yl
1651.	3-fluoropropyl	5-(oxazol-5-yl)-thien-2-yl
1652.	3-fluoropropyl	5-(2-methyloxazol-4-yl)-thien-2-yl
1653.	3-fluoropropyl	5-(2-methyloxazol-5-yl)-thien-2-yl
1654.	3-fluoropropyl	5-(isothiazol-3-yl)-thien-2-yl
1655.	3-fluoropropyl	5-(isothiazol-4-yl)-thien-2-yl
1656.	3-fluoropropyl	5-(isothiazol-5-yl)-thien-2-yl
1657.	3-fluoropropyl	5-(5-trifluoromethylisothiazol-3-yl)-thien-2-yl
1658.	3-fluoropropyl	5-(thiazol-2-yl)-thien-2-yl
1659.	3-fluoropropyl	5-(thiazol-4-yl)-thien-2-yl
1660.	3-fluoropropyl	5-(thiazol-5-yl)-thien-2-yl
1661.	3-fluoropropyl	5-(2-methylthiazol-4-yl)-thien-2-yl
1662.	3-fluoropropyl	5-(2-methylthiazol-5-yl)-thien-2-yl
1663.	3-fluoropropyl	5-([1,2,3]-oxadiazol-4-yl)-thien-2-yl
1664.	3-fluoropropyl	5-([1,2,3]-thiadiazol-4-yl)-thien-2-yl
1665.	3-fluoropropyl	5-(pyrimidin-2-yl)-thien-2-yl
1666.	3-fluoropropyl	5-(pyrimidin-4-yl)-thien-2-yl
1667.	3-fluoropropyl	5-(pyrimidin-5-yl)-thien-2-yl
1668.	3-fluoropropyl	5-(2-methylthiopyrimidin-4-yl)-thien-2-yl

No.	R ¹	Ar
1669.	3-fluoropropyl	5-([1,3]-dioxolan-2-yl)-thien-2-yl
1670.	3-fluoropropyl	3-([1,3]-dioxolan-2-yl)-thien-2-yl thien-2-yl
1671.	3-fluoropropyl	5-((3-chloro-5-(trifluoromethyl)-pyridin-2-yl)-methyl)-thien-2-yl
1672.	3-fluoropropyl	5-[3-chloro-5-(trifluoromethyl)-pyrid-2-ylsulfonyl]-thien-2-yl
1673.	3-fluoropropyl	2-chlorothien-3-yl
1674.	3-fluoropropyl	4-chlorothien-3-yl
1675.	3-fluoropropyl	5-chlorothien-3-yl
1676.	3-fluoropropyl	2-bromothien-3-yl
1677.	3-fluoropropyl	4-bromothien-3-yl
1678.	3-fluoropropyl	5-bromothien-3-yl
1679.	3-fluoropropyl	2,5-dichlorothien-3-yl
1680.	3-fluoropropyl	2,5-dibromothien-3-yl
1681.	3-fluoropropyl	2,4,5-trichlorothien-3-yl
1682.	3-fluoropropyl	4-bromo-2,5-dichlorothien-3-yl
1683.	3-fluoropropyl	2-chloro-5-methylsulfonylthien-3-yl
1684.	3-fluoropropyl	2,5-dimethylthien-3-yl
1685.	3-fluoropropyl	4-hydroxythien-3-yl
1686.	3-fluoropropyl	2-phenylthien-3-yl
1687.	3-fluoropropyl	4-phenyl-5-(trifluoromethyl)-thien-3-yl
1688.	3-fluoropropyl	2-methoxycarbonyl-4-phenyl-5-(trifluoromethyl)-thien-3-yl
1689.	3-fluoropropyl	benzo[b]thiophen-2-yl
1690.	3-fluoropropyl	benzo[b]thiophen-3-yl
1691.	3-fluoropropyl	3-methyl-benzo[b]thiophen-2-yl
1692.	3-fluoropropyl	5-methyl-benzo[b]thiophen-2-yl
1693.	3-fluoropropyl	5-fluoro-3-methyl-benzo[b]thiophen-2-yl
1694.	3-fluoropropyl	5-chloro-3-methyl-benzo[b]thiophen-2-yl
1695.	3-fluoropropyl	5-bromo-3-methyl-benzo[b]thiophen-2-yl
1696.	2-fluoroethyl	3-methylphenyl
1697.	2-fluoroethyl	3-ethylphenyl
1698.	2-fluoroethyl	3-propylphenyl
1699.	2-fluoroethyl	3-isopropylphenyl
1700.	2-fluoroethyl	3-sec-butylphenyl
1701.	2-fluoroethyl	3-tert-butylphenyl
1702.	2-fluoroethyl	3-isobutylphenyl
1703.	2-fluoroethyl	3-(1,1-dimethylpropyl)-phenyl

No.	R ¹	Ar
1704.	2-fluoroethyl	3-vinylphenyl
1705.	2-fluoroethyl	3-isopropenylphenyl
1706.	2-fluoroethyl	3-fluorophenyl
1707.	2-fluoroethyl	3-chlorophenyl
1708.	2-fluoroethyl	3-bromophenyl
1709.	2-fluoroethyl	3-iodophenyl
1710.	2-fluoroethyl	3-(fluoromethyl)phenyl
1711.	2-fluoroethyl	3-(difluoromethyl)phenyl
1712.	2-fluoroethyl	3-(trifluoromethyl)phenyl
1713.	2-fluoroethyl	3,5-bis(trifluoromethyl)phenyl
1714.	2-fluoroethyl	3-(1-fluoroethyl)-phenyl
1715.	2-fluoroethyl	3-((S)-1-fluoroethyl)-phenyl
1716.	2-fluoroethyl	3-((R)-1-fluoroethyl)-phenyl
1717.	2-fluoroethyl	3-(2-fluoroethyl)-phenyl
1718.	2-fluoroethyl	3-(1,1-difluoroethyl)-phenyl
1719.	2-fluoroethyl	3-(2,2-difluoroethyl)-phenyl
1720.	2-fluoroethyl	3-(2,2,2-trifluoroethyl)-phenyl
1721.	2-fluoroethyl	3-(3-fluoropropyl)-phenyl
1722.	2-fluoroethyl	3-(2-fluoropropyl)-phenyl
1723.	2-fluoroethyl	3-((S)-2-fluoropropyl)-phenyl
1724.	2-fluoroethyl	3-((R)-2-fluoropropyl)-phenyl
1725.	2-fluoroethyl	3-(3,3-difluoropropyl)-phenyl
1726.	2-fluoroethyl	3-(3,3,3-trifluoropropyl)-phenyl
1727.	2-fluoroethyl	3-(1-fluoro-1-methylethyl)-phenyl
1728.	2-fluoroethyl	3-(2-fluoro-1-methylethyl)-phenyl
1729.	2-fluoroethyl	3-((S)-2-fluoro-1-methylethyl)-phenyl
1730.	2-fluoroethyl	3-((R)-2-fluoro-1-methylethyl)-phenyl
1731.	2-fluoroethyl	3-(2,2-difluoro-1-methylethyl)-phenyl
1732.	2-fluoroethyl	3-((S)-2,2-difluoro-1-methylethyl)-phenyl
1733.	2-fluoroethyl	3-((R)-2,2-difluoro-1-methylethyl)-phenyl
1734.	2-fluoroethyl	3-(2,2,2-trifluoro-1-methylethyl)-phenyl
1735.	2-fluoroethyl	3-((S)-2,2,2-trifluoro-1-methylethyl)-phenyl
1736.	2-fluoroethyl	3-((R)-2,2,2-trifluoro-1-methylethyl)-phenyl
1737.	2-fluoroethyl	3-(2-fluoro-1-fluoromethylethyl)-phenyl
1738.	2-fluoroethyl	3-(1-difluoromethyl-2,2-difluoroethyl)-phenyl
1739.	2-fluoroethyl	3-(1,1-dimethyl-2-fluoroethyl)-phenyl
1740.	2-fluoroethyl	3-methoxyphenyl
1741.	2-fluoroethyl	3-ethoxyphenyl

No.	R ¹	Ar
1742.	2-fluoroethyl	3-propoxyphenyl
1743.	2-fluoroethyl	3-isopropoxyphenyl
1744.	2-fluoroethyl	3-butoxyphenyl
1745.	2-fluoroethyl	3-(fluoromethoxy)-phenyl
1746.	2-fluoroethyl	3-(difluoromethoxy)-phenyl
1747.	2-fluoroethyl	3-(trifluoromethoxy)-phenyl
1748.	2-fluoroethyl	3-(2-fluoroethoxy)-phenyl
1749.	2-fluoroethyl	3-(2,2-difluoroethoxy)-phenyl
1750.	2-fluoroethyl	3-(2,2,2-trifluoroethoxy)-phenyl
1751.	2-fluoroethyl	3-(1,1,2,2-tetrafluoroethoxy)-phenyl
1752.	2-fluoroethyl	3-cyclopropylphenyl
1753.	2-fluoroethyl	3-cyclobutylphenyl
1754.	2-fluoroethyl	3-cyclopentylphenyl
1755.	2-fluoroethyl	3-(2,2-difluorocyclopropyl)-phenyl
1756.	2-fluoroethyl	3,4-difluorophenyl
1757.	2-fluoroethyl	3-bromo-2-fluorophenyl
1758.	2-fluoroethyl	2-bromo-3-fluorophenyl
1759.	2-fluoroethyl	3-bromo-2,5-difluorophenyl
1760.	2-fluoroethyl	5-bromo-2,4-difluorophenyl
1761.	2-fluoroethyl	3-bromo-2,4-difluorophenyl
1762.	2-fluoroethyl	4-chloro-3-(trifluoromethyl)-phenyl
1763.	2-fluoroethyl	2-chloro-5-(trifluoromethyl)-phenyl
1764.	2-fluoroethyl	2-fluoro-5-(trifluoromethyl)-phenyl
1765.	2-fluoroethyl	4-fluoro-3-(trifluoromethyl)-phenyl
1766.	2-fluoroethyl	3-fluoro-5-(trifluoromethyl)-phenyl
1767.	2-fluoroethyl	4-bromo-3-(trifluoromethyl)-phenyl
1768.	2-fluoroethyl	3-bromo-5-(trifluoromethyl)-phenyl
1769.	2-fluoroethyl	2-bromo-5-(trifluoromethyl)-phenyl
1770.	2-fluoroethyl	5-bromo-2-methoxyphenyl
1771.	2-fluoroethyl	3-bromo-4-methoxyphenyl
1772.	2-fluoroethyl	2-fluoro-3-isopropylphenyl
1773.	2-fluoroethyl	4-fluoro-3-isopropylphenyl
1774.	2-fluoroethyl	3-(1-hydroxy-1-methylethyl)-phenyl
1775.	2-fluoroethyl	3-(2-hydroxy-2-methylpropyl)-phenyl
1776.	2-fluoroethyl	3-acetylphenyl
1777.	2-fluoroethyl	3-acetylamino-phenyl
1778.	2-fluoroethyl	3-carboxyphenyl
1779.	2-fluoroethyl	3-cyanophenyl

No.	R ¹	Ar
1780.	2-fluoroethyl	3-nitrophenyl
1781.	2-fluoroethyl	3-hydroxyphenyl
1782.	2-fluoroethyl	3-(O-benzyl)-phenyl
1783.	2-fluoroethyl	3-(2-methoxyethoxy)-phenyl
1784.	2-fluoroethyl	3-(CH ₂ -N(CH ₃) ₂)-phenyl
1785.	2-fluoroethyl	3-(NH-CO-NH ₂)-phenyl
1786.	2-fluoroethyl	3-(methylsulfanyl)-phenyl
1787.	2-fluoroethyl	3-(fluoromethylsulfanyl)-phenyl
1788.	2-fluoroethyl	3-(difluoromethylsulfanyl)-phenyl
1789.	2-fluoroethyl	3-(trifluoromethylsulfanyl)-phenyl
1790.	2-fluoroethyl	3-(methylsulfonyl)-phenyl
1791.	2-fluoroethyl	3-(N-methoxy-N-methyl-amino)-phenyl
1792.	2-fluoroethyl	3-(methoxyamino)-phenyl
1793.	2-fluoroethyl	3-(ethoxyamino)-phenyl
1794.	2-fluoroethyl	3-(N-methylaminooxy)-phenyl
1795.	2-fluoroethyl	3-(N,N-dimethylaminooxy)-phenyl
1796.	2-fluoroethyl	3-(azetidin-1-yl)-phenyl
1797.	2-fluoroethyl	3-(2-methylazetidin-1-yl)-phenyl
1798.	2-fluoroethyl	3-((S)-2-methylazetidin-1-yl)-phenyl
1799.	2-fluoroethyl	3-((R)-2-methylazetidin-1-yl)-phenyl
1800.	2-fluoroethyl	3-(3-fluoroazetidin-1-yl)-phenyl
1801.	2-fluoroethyl	3-(2,2-difluoroazetidin-1-yl)-phenyl
1802.	2-fluoroethyl	3-(3-methoxyazetidin-1-yl)-phenyl
1803.	2-fluoroethyl	3-(3-hydroxyazetidin-1-yl)-phenyl
1804.	2-fluoroethyl	3-(pyrrolidin-1-yl)-phenyl
1805.	2-fluoroethyl	3-(pyrrolidin-2-yl)-phenyl
1806.	2-fluoroethyl	3-((S)-pyrrolidin-2-yl)-phenyl
1807.	2-fluoroethyl	3-((R)-pyrrolidin-2-yl)-phenyl
1808.	2-fluoroethyl	3-(pyrrolidin-3-yl)-phenyl
1809.	2-fluoroethyl	3-((S)-pyrrolidin-3-yl)-phenyl
1810.	2-fluoroethyl	3-((R)-pyrrolidin-3-yl)-phenyl
1811.	2-fluoroethyl	3-(pyrrolidin-1-yl)-5-(trifluoromethyl)-phenyl
1812.	2-fluoroethyl	5-(pyrrolidin-1-yl)-2-methoxyphenyl
1813.	2-fluoroethyl	3-(pyrrolidin-1-yl)-4-methoxyphenyl
1814.	2-fluoroethyl	5-(pyrrolidin-1-yl)-2,4-difluorophenyl
1815.	2-fluoroethyl	3-(pyrrolidin-1-yl)-2,4-difluorophenyl
1816.	2-fluoroethyl	3-(2-fluoropyrrolidin-1-yl)-phenyl
1817.	2-fluoroethyl	3-((S)-2-fluoropyrrolidin-1-yl)-phenyl

No.	R ¹	Ar
1818.	2-fluoroethyl	3-((R)-2-fluoropyrrolidin-1-yl)-phenyl
1819.	2-fluoroethyl	3-(3-fluoropyrrolidin-1-yl)-phenyl
1820.	2-fluoroethyl	3-((S)-3-fluoropyrrolidin-1-yl)-phenyl
1821.	2-fluoroethyl	3-((R)-3-fluoropyrrolidin-1-yl)-phenyl
1822.	2-fluoroethyl	3-(2,2-difluoropyrrolidin-1-yl)-phenyl
1823.	2-fluoroethyl	3-(3,3-difluoropyrrolidin-1-yl)-phenyl
1824.	2-fluoroethyl	3-(2-methylpyrrolidin-1-yl)-phenyl
1825.	2-fluoroethyl	3-((S)-2-methylpyrrolidin-1-yl)-phenyl
1826.	2-fluoroethyl	3-((R)-2-methylpyrrolidin-1-yl)-phenyl
1827.	2-fluoroethyl	3-(3-methylpyrrolidin-1-yl)-phenyl
1828.	2-fluoroethyl	3-((S)-3-methylpyrrolidin-1-yl)-phenyl
1829.	2-fluoroethyl	3-((R)-3-methylpyrrolidin-1-yl)-phenyl
1830.	2-fluoroethyl	3-(1-methylpyrrolidin-2-yl)-phenyl
1831.	2-fluoroethyl	3-((S)-1-methylpyrrolidin-2-yl)-phenyl
1832.	2-fluoroethyl	3-((R)-1-methylpyrrolidin-2-yl)-phenyl
1833.	2-fluoroethyl	3-(1-methylpyrrolidin-3-yl)-phenyl
1834.	2-fluoroethyl	3-((S)-1-methylpyrrolidin-3-yl)-phenyl
1835.	2-fluoroethyl	3-((R)-1-methylpyrrolidin-3-yl)-phenyl
1836.	2-fluoroethyl	3-(2,2-dimethylpyrrolidin-1-yl)-phenyl
1837.	2-fluoroethyl	3-(3,3-dimethylpyrrolidin-1-yl)-phenyl
1838.	2-fluoroethyl	3-(2-trifluoromethylpyrrolidin-1-yl)-phenyl
1839.	2-fluoroethyl	3-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
1840.	2-fluoroethyl	3-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
1841.	2-fluoroethyl	3-(3-trifluoromethylpyrrolidin-1-yl)-phenyl
1842.	2-fluoroethyl	3-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
1843.	2-fluoroethyl	3-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
1844.	2-fluoroethyl	3-(2-oxopyrrolidin-1-yl)-phenyl
1845.	2-fluoroethyl	3-(2-oxo-oxazolidin-3-yl)-phenyl
1846.	2-fluoroethyl	3-(piperidin-1-yl)-phenyl
1847.	2-fluoroethyl	3-(2-methylpiperidin-1-yl)-phenyl
1848.	2-fluoroethyl	3-((S)-2-methylpiperidin-1-yl)-phenyl
1849.	2-fluoroethyl	3-((R)-2-methylpiperidin-1-yl)-phenyl
1850.	2-fluoroethyl	3-(2-fluoropiperidin-1-yl)-phenyl
1851.	2-fluoroethyl	3-((S)-2-fluoropiperidin-1-yl)-phenyl
1852.	2-fluoroethyl	3-((R)-2-fluoropiperidin-1-yl)-phenyl
1853.	2-fluoroethyl	3-(2,2-difluoropiperidin-1-yl)-phenyl
1854.	2-fluoroethyl	3-(piperazin-1-yl)-phenyl
1855.	2-fluoroethyl	3-(4-methylpiperazin-1-yl)-phenyl

No.	R ¹	Ar
1856.	2-fluoroethyl	3-(morpholin-4-yl)-phenyl
1857.	2-fluoroethyl	3-(morpholin-4-yl)-5-(trifluoromethyl)-phenyl
1858.	2-fluoroethyl	5-(morpholin-4-yl)-2-methoxyphenyl
1859.	2-fluoroethyl	3-(morpholin-4-yl)-4-methoxyphenyl
1860.	2-fluoroethyl	5-(morpholin-4-yl)-2,4-difluorophenyl
1861.	2-fluoroethyl	3-(morpholin-4-yl)-2,4-difluorophenyl
1862.	2-fluoroethyl	3-(thiomorpholin-4-yl)-phenyl
1863.	2-fluoroethyl	3-(1-oxo-thiomorpholin-4-yl)-phenyl
1864.	2-fluoroethyl	3-(1,1-dioxo-thiomorpholin-4-yl)-phenyl
1865.	2-fluoroethyl	3-(pyrrol-1-yl)-phenyl
1866.	2-fluoroethyl	3-(pyrrol-2-yl)-phenyl
1867.	2-fluoroethyl	3-(pyrrol-3-yl)-phenyl
1868.	2-fluoroethyl	3-(1-methylpyrrol-2-yl)-phenyl
1869.	2-fluoroethyl	3-(1-methylpyrrol-3-yl)-phenyl
1870.	2-fluoroethyl	3-(furan-2-yl)-phenyl
1871.	2-fluoroethyl	3-(furan-3-yl)-phenyl
1872.	2-fluoroethyl	3-(thiophen-2-yl)-phenyl
1873.	2-fluoroethyl	3-(thiophen-3-yl)-phenyl
1874.	2-fluoroethyl	3-(5-propylthien-2-yl)-phenyl
1875.	2-fluoroethyl	3-(pyrazol-1-yl)-phenyl
1876.	2-fluoroethyl	3-(pyrazol-3-yl)-phenyl
1877.	2-fluoroethyl	3-(pyrazol-4-yl)-phenyl
1878.	2-fluoroethyl	3-(4-fluoropyrazol-1-yl)-phenyl
1879.	2-fluoroethyl	3-(1-methyl-1H-pyrazol-4-yl)-phenyl
1880.	2-fluoroethyl	3-(1-ethyl-1H-pyrazol-4-yl)-phenyl
1881.	2-fluoroethyl	3-(1-methyl-1H-pyrazol-5-yl)-phenyl
1882.	2-fluoroethyl	3-(1H-imidazol-2-yl)-phenyl
1883.	2-fluoroethyl	3-(imidazol-1-yl)-phenyl
1884.	2-fluoroethyl	3-(1-methylimidazol-2-yl)-phenyl
1885.	2-fluoroethyl	3-(oxazol-2-yl)-phenyl
1886.	2-fluoroethyl	3-(oxazol-4-yl)-phenyl
1887.	2-fluoroethyl	3-(oxazol-5-yl)-phenyl
1888.	2-fluoroethyl	3-(isoxazol-3-yl)-phenyl
1889.	2-fluoroethyl	3-(isoxazol-4-yl)-phenyl
1890.	2-fluoroethyl	3-(isoxazol-5-yl)-phenyl
1891.	2-fluoroethyl	3-(thiazol-2-yl)-phenyl
1892.	2-fluoroethyl	3-(thiazol-4-yl)-phenyl
1893.	2-fluoroethyl	3-(thiazol-5-yl)-phenyl

No.	R ¹	Ar
1894.	2-fluoroethyl	3-(2-methylthiazol-4-yl)-phenyl
1895.	2-fluoroethyl	3-(2-methylthiazol-5-yl)-phenyl
1896.	2-fluoroethyl	3-([1,2,3]-triazol-1-yl)-phenyl
1897.	2-fluoroethyl	3-([1,2,4]-triazol-1-yl)-phenyl
1898.	2-fluoroethyl	3-([1,2,3]-triazol-2-yl)-phenyl
1899.	2-fluoroethyl	3-(4H-[1,2,4]-triazol-3-yl)-phenyl
1900.	2-fluoroethyl	3-([1,2,4]-triazol-4-yl)-phenyl
1901.	2-fluoroethyl	3-(2H-[1,2,3]-triazol-4-yl)-phenyl
1902.	2-fluoroethyl	3-(4-methyl-4H-[1,2,4]-triazol-3-yl)-phenyl
1903.	2-fluoroethyl	3-(2-methyl-2H-[1,2,3]-triazol-4-yl)-phenyl
1904.	2-fluoroethyl	3-([1,3,4]-oxadiazol-2-yl)-phenyl
1905.	2-fluoroethyl	3-(5-methyl-[1,3,4]-oxadiazol-2-yl)-phenyl
1906.	2-fluoroethyl	3-([1,2,4]-oxadiazol-3-yl)-phenyl
1907.	2-fluoroethyl	3-(5-methyl-[1,2,4]-oxadiazol-3-yl)-phenyl
1908.	2-fluoroethyl	3-([1,2,4]-oxadiazol-5-yl)-phenyl
1909.	2-fluoroethyl	3-([1,2,3]-oxadiazol-4-yl)-phenyl
1910.	2-fluoroethyl	3-([1,2,3]-oxadiazol-5-yl)-phenyl
1911.	2-fluoroethyl	3-([1,2,3]-thiadiazol-4-yl)-phenyl
1912.	2-fluoroethyl	3-(1H-tetrazol-5-yl)-phenyl
1913.	2-fluoroethyl	3-(tetrazol-1-yl)-phenyl
1914.	2-fluoroethyl	3-(2-methyl-2H-tetrazol-5-yl)-phenyl
1915.	2-fluoroethyl	3-(1-methyl-1H-tetrazol-5-yl)-phenyl
1916.	2-fluoroethyl	3-furazan-3-yl-phenyl
1917.	2-fluoroethyl	3-(pyrid-2-yl)-phenyl
1918.	2-fluoroethyl	3-(pyrid-3-yl)-phenyl
1919.	2-fluoroethyl	3-(pyrid-4-yl)-phenyl
1920.	2-fluoroethyl	3-(pyrimidin-2-yl)-phenyl
1921.	2-fluoroethyl	3-(2-methylpyrimidin-4-yl)-phenyl
1922.	2-fluoroethyl	3-(pyrimidin-4-yl)-phenyl
1923.	2-fluoroethyl	3-(pyrimidin-5-yl)-phenyl
1924.	2-fluoroethyl	5-bromopyridin-3-yl
1925.	2-fluoroethyl	3-bromo-2-chloropyridin-5-yl
1926.	2-fluoroethyl	4-methylpyridin-2-yl
1927.	2-fluoroethyl	6-methylpyridin-2-yl
1928.	2-fluoroethyl	4-(trifluoromethyl)-pyridin-2-yl
1929.	2-fluoroethyl	6-(trifluoromethyl)-pyridin-2-yl
1930.	2-fluoroethyl	5-(trifluoromethyl)-pyridin-3-yl
1931.	2-fluoroethyl	5-(pyrrolidin-1-yl)-pyridin-3-yl

No.	R ¹	Ar
1932.	2-fluoroethyl	3-(pyrrolidin-1-yl)-2-chloropyridin-5-yl
1933.	2-fluoroethyl	3-(morpholin-4-yl)-2-chloropyridin-5-yl
1934.	2-fluoroethyl	2-(morpholin-4-yl)-pyridin-5-yl
1935.	2-fluoroethyl	2-phenoxy-pyridin-5-yl
1936.	2-fluoroethyl	2,3-dichlorophenyl
1937.	2-fluoroethyl	2,5-dichlorophenyl
1938.	2-fluoroethyl	3,5-dichlorophenyl
1939.	2-fluoroethyl	3-chloro-4-fluorophenyl
1940.	2-fluoroethyl	4-bromo-2,5-dichlorophenyl
1941.	2-fluoroethyl	3-bromo-4-(trifluoromethoxy)phenyl
1942.	2-fluoroethyl	3,5-dibromo-4-(2-fluoroethoxy)-phenyl
1943.	2-fluoroethyl	2,5-dimethylphenyl
1944.	2-fluoroethyl	2,5-di-(trifluoromethyl)-phenyl
1945.	2-fluoroethyl	3,5-di-(trifluoromethyl)-phenyl
1946.	2-fluoroethyl	2,5-dimethoxyphenyl
1947.	2-fluoroethyl	2-methoxy-5-methylphenyl
1948.	2-fluoroethyl	2-methoxy-5-(trifluoromethyl)-phenyl
1949.	2-fluoroethyl	4-fluoro-3-(oxazol-4-yl)-phenyl
1950.	2-fluoroethyl	thien-2-yl
1951.	2-fluoroethyl	thien-3-yl
1952.	2-fluoroethyl	3-chlorothien-2-yl
1953.	2-fluoroethyl	4-chlorothien-2-yl
1954.	2-fluoroethyl	5-chlorothien-2-yl
1955.	2-fluoroethyl	3-bromothien-2-yl
1956.	2-fluoroethyl	4-bromothien-2-yl
1957.	2-fluoroethyl	5-bromothien-2-yl
1958.	2-fluoroethyl	4,5-dichlorothien-2-yl
1959.	2-fluoroethyl	4,5-dibromothien-2-yl
1960.	2-fluoroethyl	4-bromo-5-chlorothien-2-yl
1961.	2-fluoroethyl	3-bromo-5-chlorothien-2-yl
1962.	2-fluoroethyl	5-methylthien-2-yl
1963.	2-fluoroethyl	5-ethylthien-2-yl
1964.	2-fluoroethyl	5-propylthien-2-yl
1965.	2-fluoroethyl	5-trifluoromethylthien-2-yl
1966.	2-fluoroethyl	5-phenylthien-2-yl
1967.	2-fluoroethyl	5-(pyrid-2-yl)-thien-2-yl
1968.	2-fluoroethyl	5-(phenylsulfonyl)-thien-2-yl
1969.	2-fluoroethyl	4-(phenylsulfonyl)-thien-2-yl

No.	R ¹	Ar
1970.	2-fluoroethyl	5-(pyrid-2-ylsulfonyl)-thien-2-yl
1971.	2-fluoroethyl	5-(3-chloro-5-trifluoro-pyrid-2-ylsulfonyl)-thien-2-yl
1972.	2-fluoroethyl	5-(benzoylaminomethyl)-thien-2-yl
1973.	2-fluoroethyl	5-((4-chlorobenzoyl)aminomethyl)-thien-2-yl
1974.	2-fluoroethyl	5-(acetylaminomethyl)-thien-2-yl
1975.	2-fluoroethyl	5-(pyrazol-1-yl)-thien-2-yl
1976.	2-fluoroethyl	5-(pyrazol-3-yl)-thien-2-yl
1977.	2-fluoroethyl	5-(pyrazol-4-yl)-thien-2-yl
1978.	2-fluoroethyl	5-(pyrazol-5-yl)-thien-2-yl
1979.	2-fluoroethyl	5-(4-fluoropyrazol-1-yl)-thien-2-yl
1980.	2-fluoroethyl	5-(1-methyl-5-trifluoromethyl-(1H)-pyrazol-3-yl)-thien-2-yl
1981.	2-fluoroethyl	5-(1-methyl-3-trifluoromethyl-(1H)-pyrazol-5-yl)-thien-2-yl
1982.	2-fluoroethyl	5-(4-carboxy-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
1983.	2-fluoroethyl	5-(4-aminomethyl-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
1984.	2-fluoroethyl	5-(isoxazol-3-yl)-thien-2-yl
1985.	2-fluoroethyl	5-(isoxazol-4-yl)-thien-2-yl
1986.	2-fluoroethyl	5-(isoxazol-5-yl)-thien-2-yl
1987.	2-fluoroethyl	5-(5-trifluoromethylisoxazol-3-yl)-thien-2-yl
1988.	2-fluoroethyl	5-(oxazol-2-yl)-thien-2-yl
1989.	2-fluoroethyl	5-(oxazol-4-yl)-thien-2-yl
1990.	2-fluoroethyl	5-(oxazol-5-yl)-thien-2-yl
1991.	2-fluoroethyl	5-(2-methyloxazol-4-yl)-thien-2-yl
1992.	2-fluoroethyl	5-(2-methyloxazol-5-yl)-thien-2-yl
1993.	2-fluoroethyl	5-(isothiazol-3-yl)-thien-2-yl
1994.	2-fluoroethyl	5-(isothiazol-4-yl)-thien-2-yl
1995.	2-fluoroethyl	5-(isothiazol-5-yl)-thien-2-yl
1996.	2-fluoroethyl	5-(5-trifluoromethylisothiazol-3-yl)-thien-2-yl
1997.	2-fluoroethyl	5-(thiazol-2-yl)-thien-2-yl
1998.	2-fluoroethyl	5-(thiazol-4-yl)-thien-2-yl
1999.	2-fluoroethyl	5-(thiazol-5-yl)-thien-2-yl
2000.	2-fluoroethyl	5-(2-methylthiazol-4-yl)-thien-2-yl
2001.	2-fluoroethyl	5-(2-methylthiazol-5-yl)-thien-2-yl
2002.	2-fluoroethyl	5-([1,2,3]-oxadiazol-4-yl)-thien-2-yl

No.	R ¹	Ar
2003.	2-fluoroethyl	5-([1,2,3]-thiadiazol-4-yl)-thien-2-yl
2004.	2-fluoroethyl	5-(pyrimidin-2-yl)-thien-2-yl
2005.	2-fluoroethyl	5-(pyrimidin-4-yl)-thien-2-yl
2006.	2-fluoroethyl	5-(pyrimidin-5-yl)-thien-2-yl
2007.	2-fluoroethyl	5-(2-methylthiopyrimidin-4-yl)-thien-2-yl
2008.	2-fluoroethyl	5-([1,3]-dioxolan-2-yl)-thien-2-yl
2009.	2-fluoroethyl	3-([1,3]-dioxolan-2-yl)-thien-2-yl thien-2-yl
2010.	2-fluoroethyl	5-((3-chloro-5-(trifluoromethyl)-pyridin-2-yl)-methyl)-thien-2-yl
2011.	2-fluoroethyl	5-[3-chloro-5-(trifluoromethyl)-pyrid-2-ylsulfonyl]-thien-2-yl
2012.	2-fluoroethyl	2-chlorothien-3-yl
2013.	2-fluoroethyl	4-chlorothien-3-yl
2014.	2-fluoroethyl	5-chlorothien-3-yl
2015.	2-fluoroethyl	2-bromothien-3-yl
2016.	2-fluoroethyl	4-bromothien-3-yl
2017.	2-fluoroethyl	5-bromothien-3-yl
2018.	2-fluoroethyl	2,5-dichlorothien-3-yl
2019.	2-fluoroethyl	2,5-dibromothien-3-yl
2020.	2-fluoroethyl	2,4,5-trichlorothien-3-yl
2021.	2-fluoroethyl	4-bromo-2,5-dichlorothien-3-yl
2022.	2-fluoroethyl	2-chloro-5-methylsulfonylthien-3-yl
2023.	2-fluoroethyl	2,5-dimethylthien-3-yl
2024.	2-fluoroethyl	4-hydroxythien-3-yl
2025.	2-fluoroethyl	2-phenylthien-3-yl
2026.	2-fluoroethyl	4-phenyl-5-(trifluoromethyl)-thien-3-yl
2027.	2-fluoroethyl	2-methoxycarbonyl-4-phenyl-5-(trifluoromethyl)-thien-3-yl
2028.	2-fluoroethyl	benzo[b]thiophen-2-yl
2029.	2-fluoroethyl	benzo[b]thiophen-3-yl
2030.	2-fluoroethyl	3-methyl-benzo[b]thiophen-2-yl
2031.	2-fluoroethyl	5-methyl-benzo[b]thiophen-2-yl
2032.	2-fluoroethyl	5-fluoro-3-methyl-benzo[b]thiophen-2-yl
2033.	2-fluoroethyl	5-chloro-3-methyl-benzo[b]thiophen-2-yl
2034.	2-fluoroethyl	5-bromo-3-methyl-benzo[b]thiophen-2-yl
2035.	cyclopropylmethyl	3-methylphenyl
2036.	cyclopropylmethyl	3-ethylphenyl
2037.	cyclopropylmethyl	3-propylphenyl

No.	R ¹	Ar
2038.	cyclopropylmethyl	3-isopropylphenyl
2039.	cyclopropylmethyl	3-sec-butylphenyl
2040.	cyclopropylmethyl	3-tert-butylphenyl
2041.	cyclopropylmethyl	3-isobutylphenyl
2042.	cyclopropylmethyl	3-(1,1-dimethylpropyl)-phenyl
2043.	cyclopropylmethyl	3-vinylphenyl
2044.	cyclopropylmethyl	3-isopropenylphenyl
2045.	cyclopropylmethyl	3-fluorophenyl
2046.	cyclopropylmethyl	3-chlorophenyl
2047.	cyclopropylmethyl	3-bromophenyl
2048.	cyclopropylmethyl	3-iodophenyl
2049.	cyclopropylmethyl	3-(fluoromethyl)phenyl
2050.	cyclopropylmethyl	3-(difluoromethyl)phenyl
2051.	cyclopropylmethyl	3-(trifluoromethyl)phenyl
2052.	cyclopropylmethyl	3,5-bis(trifluoromethyl)phenyl
2053.	cyclopropylmethyl	3-(1-fluoroethyl)-phenyl
2054.	cyclopropylmethyl	3-((S)-1-fluoroethyl)-phenyl
2055.	cyclopropylmethyl	3-((R)-1-fluoroethyl)-phenyl
2056.	cyclopropylmethyl	3-(2-fluoroethyl)-phenyl
2057.	cyclopropylmethyl	3-(1,1-difluoroethyl)-phenyl
2058.	cyclopropylmethyl	3-(2,2-difluoroethyl)-phenyl
2059.	cyclopropylmethyl	3-(2,2,2-trifluoroethyl)-phenyl
2060.	cyclopropylmethyl	3-(3-fluoropropyl)-phenyl
2061.	cyclopropylmethyl	3-(2-fluoropropyl)-phenyl
2062.	cyclopropylmethyl	3-((S)-2-fluoropropyl)-phenyl
2063.	cyclopropylmethyl	3-((R)-2-fluoropropyl)-phenyl
2064.	cyclopropylmethyl	3-(3,3-difluoropropyl)-phenyl
2065.	cyclopropylmethyl	3-(3,3,3-trifluoropropyl)-phenyl
2066.	cyclopropylmethyl	3-(1-fluoro-1-methylethyl)-phenyl
2067.	cyclopropylmethyl	3-(2-fluoro-1-methylethyl)-phenyl
2068.	cyclopropylmethyl	3-((S)-2-fluoro-1-methylethyl)-phenyl
2069.	cyclopropylmethyl	3-((R)-2-fluoro-1-methylethyl)-phenyl
2070.	cyclopropylmethyl	3-(2,2-difluoro-1-methylethyl)-phenyl
2071.	cyclopropylmethyl	3-((S)-2,2-difluoro-1-methylethyl)-phenyl
2072.	cyclopropylmethyl	3-((R)-2,2-difluoro-1-methylethyl)-phenyl
2073.	cyclopropylmethyl	3-(2,2,2-trifluoro-1-methylethyl)-phenyl
2074.	cyclopropylmethyl	3-((S)-2,2,2-trifluoro-1-methylethyl)-phenyl
2075.	cyclopropylmethyl	3-((R)-2,2,2-trifluoro-1-methylethyl)-phenyl

No.	R ¹	Ar
2076.	cyclopropylmethyl	3-(2-fluoro-1-fluoromethylethyl)-phenyl
2077.	cyclopropylmethyl	3-(1-difluoromethyl-2,2-difluoroethyl)-phenyl
2078.	cyclopropylmethyl	3-(1,1-dimethyl-2-fluoroethyl)-phenyl
2079.	cyclopropylmethyl	3-methoxyphenyl
2080.	cyclopropylmethyl	3-ethoxyphenyl
2081.	cyclopropylmethyl	3-propoxyphenyl
2082.	cyclopropylmethyl	3-isopropoxyphenyl
2083.	cyclopropylmethyl	3-butoxyphenyl
2084.	cyclopropylmethyl	3-(fluoromethoxy)-phenyl
2085.	cyclopropylmethyl	3-(difluoromethoxy)-phenyl
2086.	cyclopropylmethyl	3-(trifluoromethoxy)-phenyl
2087.	cyclopropylmethyl	3-(2-fluoroethoxy)-phenyl
2088.	cyclopropylmethyl	3-(2,2-difluoroethoxy)-phenyl
2089.	cyclopropylmethyl	3-(2,2,2-trifluoroethoxy)-phenyl
2090.	cyclopropylmethyl	3-(1,1,2,2-tetrafluoroethoxy)-phenyl
2091.	cyclopropylmethyl	3-cyclopropylphenyl
2092.	cyclopropylmethyl	3-cyclobutylphenyl
2093.	cyclopropylmethyl	3-cyclopentylphenyl
2094.	cyclopropylmethyl	3-(2,2-difluorocyclopropyl)-phenyl
2095.	cyclopropylmethyl	3,4-difluorophenyl
2096.	cyclopropylmethyl	3-bromo-2-fluorophenyl
2097.	cyclopropylmethyl	2-bromo-3-fluorophenyl
2098.	cyclopropylmethyl	3-bromo-2,5-difluorophenyl
2099.	cyclopropylmethyl	5-bromo-2,4-difluorophenyl
2100.	cyclopropylmethyl	3-bromo-2,4-difluorophenyl
2101.	cyclopropylmethyl	4-chloro-3-(trifluoromethyl)-phenyl
2102.	cyclopropylmethyl	2-chloro-5-(trifluoromethyl)-phenyl
2103.	cyclopropylmethyl	2-fluoro-5-(trifluoromethyl)-phenyl
2104.	cyclopropylmethyl	4-fluoro-3-(trifluoromethyl)-phenyl
2105.	cyclopropylmethyl	3-fluoro-5-(trifluoromethyl)-phenyl
2106.	cyclopropylmethyl	4-bromo-3-(trifluoromethyl)-phenyl
2107.	cyclopropylmethyl	3-bromo-5-(trifluoromethyl)-phenyl
2108.	cyclopropylmethyl	2-bromo-5-(trifluoromethyl)-phenyl
2109.	cyclopropylmethyl	5-bromo-2-methoxyphenyl
2110.	cyclopropylmethyl	3-bromo-4-methoxyphenyl
2111.	cyclopropylmethyl	2-fluoro-3-isopropylphenyl
2112.	cyclopropylmethyl	4-fluoro-3-isopropylphenyl
2113.	cyclopropylmethyl	3-(1-hydroxy-1-methylethyl)-phenyl

No.	R ¹	Ar
2114.	cyclopropylmethyl	3-(2-hydroxy-2-methylpropyl)-phenyl
2115.	cyclopropylmethyl	3-acetylphenyl
2116.	cyclopropylmethyl	3-acetylamino-phenyl
2117.	cyclopropylmethyl	3-carboxyphenyl
2118.	cyclopropylmethyl	3-cyanophenyl
2119.	cyclopropylmethyl	3-nitrophenyl
2120.	cyclopropylmethyl	3-hydroxyphenyl
2121.	cyclopropylmethyl	3-(O-benzyl)-phenyl
2122.	cyclopropylmethyl	3-(2-methoxyethoxy)-phenyl
2123.	cyclopropylmethyl	3-(CH ₂ -N(CH ₃) ₂)-phenyl
2124.	cyclopropylmethyl	3-(NH-CO-NH ₂)-phenyl
2125.	cyclopropylmethyl	3-(methylsulfanyl)-phenyl
2126.	cyclopropylmethyl	3-(fluoromethylsulfanyl)-phenyl
2127.	cyclopropylmethyl	3-(difluoromethylsulfanyl)-phenyl
2128.	cyclopropylmethyl	3-(trifluoromethylsulfanyl)-phenyl
2129.	cyclopropylmethyl	3-(methylsulfonyl)-phenyl
2130.	cyclopropylmethyl	3-(N-methoxy-N-methyl-amino)-phenyl
2131.	cyclopropylmethyl	3-(methoxyamino)-phenyl
2132.	cyclopropylmethyl	3-(ethoxyamino)-phenyl
2133.	cyclopropylmethyl	3-(N-methylaminooxy)-phenyl
2134.	cyclopropylmethyl	3-(N,N-dimethylaminoxy)-phenyl
2135.	cyclopropylmethyl	3-(azetidin-1-yl)-phenyl
2136.	cyclopropylmethyl	3-(2-methylazetidin-1-yl)-phenyl
2137.	cyclopropylmethyl	3-((S)-2-methylazetidin-1-yl)-phenyl
2138.	cyclopropylmethyl	3-((R)-2-methylazetidin-1-yl)-phenyl
2139.	cyclopropylmethyl	3-(3-fluoroazetidin-1-yl)-phenyl
2140.	cyclopropylmethyl	3-(2,2-difluoroazetidin-1-yl)-phenyl
2141.	cyclopropylmethyl	3-(3-methoxyazetidin-1-yl)-phenyl
2142.	cyclopropylmethyl	3-(3-hydroxyazetidin-1-yl)-phenyl
2143.	cyclopropylmethyl	3-(pyrrolidin-1-yl)-phenyl
2144.	cyclopropylmethyl	3-(pyrrolidin-2-yl)-phenyl
2145.	cyclopropylmethyl	3-((S)-pyrrolidin-2-yl)-phenyl
2146.	cyclopropylmethyl	3-((R)-pyrrolidin-2-yl)-phenyl
2147.	cyclopropylmethyl	3-(pyrrolidin-3-yl)-phenyl
2148.	cyclopropylmethyl	3-((S)-pyrrolidin-3-yl)-phenyl
2149.	cyclopropylmethyl	3-((R)-pyrrolidin-3-yl)-phenyl
2150.	cyclopropylmethyl	3-(pyrrolidin-1-yl)-5-(trifluoromethyl)-phenyl
2151.	cyclopropylmethyl	5-(pyrrolidin-1-yl)-2-methoxyphenyl

No.	R ¹	Ar
2152.	cyclopropylmethyl	3-(pyrrolidin-1-yl)-4-methoxyphenyl
2153.	cyclopropylmethyl	5-(pyrrolidin-1-yl)-2,4-difluorophenyl
2154.	cyclopropylmethyl	3-(pyrrolidin-1-yl)-2,4-difluorophenyl
2155.	cyclopropylmethyl	3-(2-fluoropyrrolidin-1-yl)-phenyl
2156.	cyclopropylmethyl	3-((S)-2-fluoropyrrolidin-1-yl)-phenyl
2157.	cyclopropylmethyl	3-((R)-2-fluoropyrrolidin-1-yl)-phenyl
2158.	cyclopropylmethyl	3-(3-fluoropyrrolidin-1-yl)-phenyl
2159.	cyclopropylmethyl	3-((S)-3-fluoropyrrolidin-1-yl)-phenyl
2160.	cyclopropylmethyl	3-((R)-3-fluoropyrrolidin-1-yl)-phenyl
2161.	cyclopropylmethyl	3-(2,2-difluoropyrrolidin-1-yl)-phenyl
2162.	cyclopropylmethyl	3-(3,3-difluoropyrrolidin-1-yl)-phenyl
2163.	cyclopropylmethyl	3-(2-methylpyrrolidin-1-yl)-phenyl
2164.	cyclopropylmethyl	3-((S)-2-methylpyrrolidin-1-yl)-phenyl
2165.	cyclopropylmethyl	3-((R)-2-methylpyrrolidin-1-yl)-phenyl
2166.	cyclopropylmethyl	3-(3-methylpyrrolidin-1-yl)-phenyl
2167.	cyclopropylmethyl	3-((S)-3-methylpyrrolidin-1-yl)-phenyl
2168.	cyclopropylmethyl	3-((R)-3-methylpyrrolidin-1-yl)-phenyl
2169.	cyclopropylmethyl	3-(1-methylpyrrolidin-2-yl)-phenyl
2170.	cyclopropylmethyl	3-((S)-1-methylpyrrolidin-2-yl)-phenyl
2171.	cyclopropylmethyl	3-((R)-1-methylpyrrolidin-2-yl)-phenyl
2172.	cyclopropylmethyl	3-(1-methylpyrrolidin-3-yl)-phenyl
2173.	cyclopropylmethyl	3-((S)-1-methylpyrrolidin-3-yl)-phenyl
2174.	cyclopropylmethyl	3-((R)-1-methylpyrrolidin-3-yl)-phenyl
2175.	cyclopropylmethyl	3-(2,2-dimethylpyrrolidin-1-yl)-phenyl
2176.	cyclopropylmethyl	3-(3,3-dimethylpyrrolidin-1-yl)-phenyl
2177.	cyclopropylmethyl	3-(2-trifluoromethylpyrrolidin-1-yl)-phenyl
2178.	cyclopropylmethyl	3-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
2179.	cyclopropylmethyl	3-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
2180.	cyclopropylmethyl	3-(3-trifluoromethylpyrrolidin-1-yl)-phenyl
2181.	cyclopropylmethyl	3-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
2182.	cyclopropylmethyl	3-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
2183.	cyclopropylmethyl	3-(2-oxopyrrolidin-1-yl)-phenyl
2184.	cyclopropylmethyl	3-(2-oxo-oxazolidin-3-yl)-phenyl
2185.	cyclopropylmethyl	3-(piperidin-1-yl)-phenyl
2186.	cyclopropylmethyl	3-(2-methylpiperidin-1-yl)-phenyl
2187.	cyclopropylmethyl	3-((S)-2-methylpiperidin-1-yl)-phenyl
2188.	cyclopropylmethyl	3-((R)-2-methylpiperidin-1-yl)-phenyl
2189.	cyclopropylmethyl	3-(2-fluoropiperidin-1-yl)-phenyl

No.	R ¹	Ar
2190.	cyclopropylmethyl	3-((S)-2-fluoropiperidin-1-yl)-phenyl
2191.	cyclopropylmethyl	3-((R)-2-fluoropiperidin-1-yl)-phenyl
2192.	cyclopropylmethyl	3-(2,2-difluoropiperidin-1-yl)-phenyl
2193.	cyclopropylmethyl	3-(piperazin-1-yl)-phenyl
2194.	cyclopropylmethyl	3-(4-methylpiperazin-1-yl)-phenyl
2195.	cyclopropylmethyl	3-(morpholin-4-yl)-phenyl
2196.	cyclopropylmethyl	3-(morpholin-4-yl)-5-(trifluoromethyl)-phenyl
2197.	cyclopropylmethyl	5-(morpholin-4-yl)-2-methoxyphenyl
2198.	cyclopropylmethyl	3-(morpholin-4-yl)-4-methoxyphenyl
2199.	cyclopropylmethyl	5-(morpholin-4-yl)-2,4-difluorophenyl
2200.	cyclopropylmethyl	3-(morpholin-4-yl)-2,4-difluorophenyl
2201.	cyclopropylmethyl	3-(thiomorpholin-4-yl)-phenyl
2202.	cyclopropylmethyl	3-(1-oxo-thiomorpholin-4-yl)-phenyl
2203.	cyclopropylmethyl	3-(1,1-dioxo-thiomorpholin-4-yl)-phenyl
2204.	cyclopropylmethyl	3-(pyrrol-1-yl)-phenyl
2205.	cyclopropylmethyl	3-(pyrrol-2-yl)-phenyl
2206.	cyclopropylmethyl	3-(pyrrol-3-yl)-phenyl
2207.	cyclopropylmethyl	3-(1-methylpyrrol-2-yl)-phenyl
2208.	cyclopropylmethyl	3-(1-methylpyrrol-3-yl)-phenyl
2209.	cyclopropylmethyl	3-(furan-2-yl)-phenyl
2210.	cyclopropylmethyl	3-(furan-3-yl)-phenyl
2211.	cyclopropylmethyl	3-(thiophen-2-yl)-phenyl
2212.	cyclopropylmethyl	3-(thiophen-3-yl)-phenyl
2213.	cyclopropylmethyl	3-(5-propylthien-2-yl)-phenyl
2214.	cyclopropylmethyl	3-(pyrazol-1-yl)-phenyl
2215.	cyclopropylmethyl	3-(pyrazol-3-yl)-phenyl
2216.	cyclopropylmethyl	3-(pyrazol-4-yl)-phenyl
2217.	cyclopropylmethyl	3-(4-fluoropyrazol-1-yl)-phenyl
2218.	cyclopropylmethyl	3-(1-methyl-1H-pyrazol-4-yl)-phenyl
2219.	cyclopropylmethyl	3-(1-ethyl-1H-pyrazol-4-yl)-phenyl
2220.	cyclopropylmethyl	3-(1-methyl-1H-pyrazol-5-yl)-phenyl
2221.	cyclopropylmethyl	3-(1H-imidazol-2-yl)-phenyl
2222.	cyclopropylmethyl	3-(imidazol-1-yl)-phenyl
2223.	cyclopropylmethyl	3-(1-methylimidazol-2-yl)-phenyl
2224.	cyclopropylmethyl	3-(oxazol-2-yl)-phenyl
2225.	cyclopropylmethyl	3-(oxazol-4-yl)-phenyl
2226.	cyclopropylmethyl	3-(oxazol-5-yl)-phenyl
2227.	cyclopropylmethyl	3-(isoxazol-3-yl)-phenyl

No.	R ¹	Ar
2228.	cyclopropylmethyl	3-(isoxazol-4-yl)-phenyl
2229.	cyclopropylmethyl	3-(isoxazol-5-yl)-phenyl
2230.	cyclopropylmethyl	3-(thiazol-2-yl)-phenyl
2231.	cyclopropylmethyl	3-(thiazol-4-yl)-phenyl
2232.	cyclopropylmethyl	3-(thiazol-5-yl)-phenyl
2233.	cyclopropylmethyl	3-(2-methylthiazol-4-yl)-phenyl
2234.	cyclopropylmethyl	3-(2-methylthiazol-5-yl)-phenyl
2235.	cyclopropylmethyl	3-([1,2,3]-triazol-1-yl)-phenyl
2236.	cyclopropylmethyl	3-([1,2,4]-triazol-1-yl)-phenyl
2237.	cyclopropylmethyl	3-([1,2,3]-triazol-2-yl)-phenyl
2238.	cyclopropylmethyl	3-(4H-[1,2,4]-triazol-3-yl)-phenyl
2239.	cyclopropylmethyl	3-([1,2,4]-triazol-4-yl)-phenyl
2240.	cyclopropylmethyl	3-(2H-[1,2,3]-triazol-4-yl)-phenyl
2241.	cyclopropylmethyl	3-(4-methyl-4H-[1,2,4]-triazol-3-yl)-phenyl
2242.	cyclopropylmethyl	3-(2-methyl-2H-[1,2,3]-triazol-4-yl)-phenyl
2243.	cyclopropylmethyl	3-([1,3,4]-oxadiazol-2-yl)-phenyl
2244.	cyclopropylmethyl	3-(5-methyl-[1,3,4]-oxadiazol-2-yl)-phenyl
2245.	cyclopropylmethyl	3-([1,2,4]-oxadiazol-3-yl)-phenyl
2246.	cyclopropylmethyl	3-(5-methyl-[1,2,4]-oxadiazol-3-yl)-phenyl
2247.	cyclopropylmethyl	3-([1,2,4]-oxadiazol-5-yl)-phenyl
2248.	cyclopropylmethyl	3-([1,2,3]-oxadiazol-4-yl)-phenyl
2249.	cyclopropylmethyl	3-([1,2,3]-oxadiazol-5-yl)-phenyl
2250.	cyclopropylmethyl	3-([1,2,3]-thiadiazol-4-yl)-phenyl
2251.	cyclopropylmethyl	3-(1H-tetrazol-5-yl)-phenyl
2252.	cyclopropylmethyl	3-(tetrazol-1-yl)-phenyl
2253.	cyclopropylmethyl	3-(2-methyl-2H-tetrazol-5-yl)-phenyl
2254.	cyclopropylmethyl	3-(1-methyl-1H-tetrazol-5-yl)-phenyl
2255.	cyclopropylmethyl	3-furazan-3-yl-phenyl
2256.	cyclopropylmethyl	3-(pyrid-2-yl)-phenyl
2257.	cyclopropylmethyl	3-(pyrid-3-yl)-phenyl
2258.	cyclopropylmethyl	3-(pyrid-4-yl)-phenyl
2259.	cyclopropylmethyl	3-(pyrimidin-2-yl)-phenyl
2260.	cyclopropylmethyl	3-(2-methylpyrimidin-4-yl)-phenyl
2261.	cyclopropylmethyl	3-(pyrimidin-4-yl)-phenyl
2262.	cyclopropylmethyl	3-(pyrimidin-5-yl)-phenyl
2263.	cyclopropylmethyl	5-bromopyridin-3-yl
2264.	cyclopropylmethyl	3-bromo-2-chloropyridin-5-yl
2265.	cyclopropylmethyl	4-methylpyridin-2-yl

No.	R ¹	Ar
2266.	cyclopropylmethyl	6-methylpyridin-2-yl
2267.	cyclopropylmethyl	4-(trifluoromethyl)-pyridin-2-yl
2268.	cyclopropylmethyl	6-(trifluoromethyl)-pyridin-2-yl
2269.	cyclopropylmethyl	5-(trifluoromethyl)-pyridin-3-yl
2270.	cyclopropylmethyl	5-(pyrrolidin-1-yl)-pyridin-3-yl
2271.	cyclopropylmethyl	3-(pyrrolidin-1-yl)-2-chloropyridin-5-yl
2272.	cyclopropylmethyl	3-(morpholin-4-yl)-2-chloropyridin-5-yl
2273.	cyclopropylmethyl	2-(morpholin-4-yl)-pyridin-5-yl
2274.	cyclopropylmethyl	2-phenoxy-pyridin-5-yl
2275.	cyclopropylmethyl	2,3-dichlorophenyl
2276.	cyclopropylmethyl	2,5-dichlorophenyl
2277.	cyclopropylmethyl	3,5-dichlorophenyl
2278.	cyclopropylmethyl	3-chloro-4-fluorophenyl
2279.	cyclopropylmethyl	4-bromo-2,5-dichlorophenyl
2280.	cyclopropylmethyl	3-bromo-4-(trifluoromethoxy)phenyl
2281.	cyclopropylmethyl	3,5-dibromo-4-(2-fluoroethoxy)-phenyl
2282.	cyclopropylmethyl	2,5-dimethylphenyl
2283.	cyclopropylmethyl	2,5-di-(trifluoromethyl)-phenyl
2284.	cyclopropylmethyl	3,5-di-(trifluoromethyl)-phenyl
2285.	cyclopropylmethyl	2,5-dimethoxyphenyl
2286.	cyclopropylmethyl	2-methoxy-5-methylphenyl
2287.	cyclopropylmethyl	2-methoxy-5-(trifluoromethyl)-phenyl
2288.	cyclopropylmethyl	4-fluoro-3-(oxazol-4-yl)-phenyl
2289.	cyclopropylmethyl	thien-2-yl
2290.	cyclopropylmethyl	thien-3-yl
2291.	cyclopropylmethyl	3-chlorothien-2-yl
2292.	cyclopropylmethyl	4-chlorothien-2-yl
2293.	cyclopropylmethyl	5-chlorothien-2-yl
2294.	cyclopropylmethyl	3-bromothien-2-yl
2295.	cyclopropylmethyl	4-bromothien-2-yl
2296.	cyclopropylmethyl	5-bromothien-2-yl
2297.	cyclopropylmethyl	4,5-dichlorothien-2-yl
2298.	cyclopropylmethyl	4,5-dibromothien-2-yl
2299.	cyclopropylmethyl	4-bromo-5-chlorothien-2-yl
2300.	cyclopropylmethyl	3-bromo-5-chlorothien-2-yl
2301.	cyclopropylmethyl	5-methylthien-2-yl
2302.	cyclopropylmethyl	5-ethylthien-2-yl
2303.	cyclopropylmethyl	5-propylthien-2-yl

No.	R ¹	Ar
2304.	cyclopropylmethyl	5-trifluoromethylthien-2-yl
2305.	cyclopropylmethyl	5-phenylthien-2-yl
2306.	cyclopropylmethyl	5-(pyrid-2-yl)-thien-2-yl
2307.	cyclopropylmethyl	5-(phenylsulfonyl)-thien-2-yl
2308.	cyclopropylmethyl	4-(phenylsulfonyl)-thien-2-yl
2309.	cyclopropylmethyl	5-(pyrid-2-ylsulfonyl)-thien-2-yl
2310.	cyclopropylmethyl	5-(3-chloro-5-trifluoro-pyrid-2-ylsulfonyl)-thien-2-yl
2311.	cyclopropylmethyl	5-(benzoylaminomethyl)-thien-2-yl
2312.	cyclopropylmethyl	5-((4-chlorobenzoyl)aminomethyl)-thien-2-yl
2313.	cyclopropylmethyl	5-(acetylaminomethyl)-thien-2-yl
2314.	cyclopropylmethyl	5-(pyrazol-1-yl)-thien-2-yl
2315.	cyclopropylmethyl	5-(pyrazol-3-yl)-thien-2-yl
2316.	cyclopropylmethyl	5-(pyrazol-4-yl)-thien-2-yl
2317.	cyclopropylmethyl	5-(pyrazol-5-yl)-thien-2-yl
2318.	cyclopropylmethyl	5-(4-fluoropyrazol-1-yl)-thien-2-yl
2319.	cyclopropylmethyl	5-(1-methyl-5-trifluoromethyl-(1H)-pyrazol-3-yl)-thien-2-yl
2320.	cyclopropylmethyl	5-(1-methyl-3-trifluoromethyl-(1H)-pyrazol-5-yl)-thien-2-yl
2321.	cyclopropylmethyl	5-(4-carboxy-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
2322.	cyclopropylmethyl	5-(4-aminomethyl-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
2323.	cyclopropylmethyl	5-(isoxazol-3-yl)-thien-2-yl
2324.	cyclopropylmethyl	5-(isoxazol-4-yl)-thien-2-yl
2325.	cyclopropylmethyl	5-(isoxazol-5-yl)-thien-2-yl
2326.	cyclopropylmethyl	5-(5-trifluoromethylisoxazol-3-yl)-thien-2-yl
2327.	cyclopropylmethyl	5-(oxazol-2-yl)-thien-2-yl
2328.	cyclopropylmethyl	5-(oxazol-4-yl)-thien-2-yl
2329.	cyclopropylmethyl	5-(oxazol-5-yl)-thien-2-yl
2330.	cyclopropylmethyl	5-(2-methyloxazol-4-yl)-thien-2-yl
2331.	cyclopropylmethyl	5-(2-methyloxazol-5-yl)-thien-2-yl
2332.	cyclopropylmethyl	5-(isothiazol-3-yl)-thien-2-yl
2333.	cyclopropylmethyl	5-(isothiazol-4-yl)-thien-2-yl
2334.	cyclopropylmethyl	5-(isothiazol-5-yl)-thien-2-yl
2335.	cyclopropylmethyl	5-(5-trifluoromethylisothiazol-3-yl)-thien-2-yl
2336.	cyclopropylmethyl	5-(thiazol-2-yl)-thien-2-yl

No.	R ¹	Ar
2337.	cyclopropylmethyl	5-(thiazol-4-yl)-thien-2-yl
2338.	cyclopropylmethyl	5-(thiazol-5-yl)-thien-2-yl
2339.	cyclopropylmethyl	5-(2-methylthiazol-4-yl)-thien-2-yl
2340.	cyclopropylmethyl	5-(2-methylthiazol-5-yl)-thien-2-yl
2341.	cyclopropylmethyl	5-([1,2,3]-oxadiazol-4-yl)-thien-2-yl
2342.	cyclopropylmethyl	5-([1,2,3]-thiadiazol-4-yl)-thien-2-yl
2343.	cyclopropylmethyl	5-(pyrimidin-2-yl)-thien-2-yl
2344.	cyclopropylmethyl	5-(pyrimidin-4-yl)-thien-2-yl
2345.	cyclopropylmethyl	5-(pyrimidin-5-yl)-thien-2-yl
2346.	cyclopropylmethyl	5-(2-methylthiopyrimidin-4-yl)-thien-2-yl
2347.	cyclopropylmethyl	5-([1,3]-dioxolan-2-yl)-thien-2-yl
2348.	cyclopropylmethyl	3-([1,3]-dioxolan-2-yl)-thien-2-yl thien-2-yl
2349.	cyclopropylmethyl	5-((3-chloro-5-(trifluoromethyl)-pyridin-2-yl)-methyl)-thien-2-yl
2350.	cyclopropylmethyl	5-[3-chloro-5-(trifluoromethyl)-pyrid-2-ylsulfonyl]-thien-2-yl
2351.	cyclopropylmethyl	2-chlorothien-3-yl
2352.	cyclopropylmethyl	4-chlorothien-3-yl
2353.	cyclopropylmethyl	5-chlorothien-3-yl
2354.	cyclopropylmethyl	2-bromothien-3-yl
2355.	cyclopropylmethyl	4-bromothien-3-yl
2356.	cyclopropylmethyl	5-bromothien-3-yl
2357.	cyclopropylmethyl	2,5-dichlorothien-3-yl
2358.	cyclopropylmethyl	2,5-dibromothien-3-yl
2359.	cyclopropylmethyl	2,4,5-trichlorothien-3-yl
2360.	cyclopropylmethyl	4-bromo-2,5-dichlorothien-3-yl
2361.	cyclopropylmethyl	2-chloro-5-methylsulfonylthien-3-yl
2362.	cyclopropylmethyl	2,5-dimethylthien-3-yl
2363.	cyclopropylmethyl	4-hydroxythien-3-yl
2364.	cyclopropylmethyl	2-phenylthien-3-yl
2365.	cyclopropylmethyl	4-phenyl-5-(trifluoromethyl)-thien-3-yl
2366.	cyclopropylmethyl	2-methoxycarbonyl-4-phenyl-5-(trifluoromethyl)-thien-3-yl
2367.	cyclopropylmethyl	benzo[b]thiophen-2-yl
2368.	cyclopropylmethyl	benzo[b]thiophen-3-yl
2369.	cyclopropylmethyl	3-methyl-benzo[b]thiophen-2-yl
2370.	cyclopropylmethyl	5-methyl-benzo[b]thiophen-2-yl
2371.	cyclopropylmethyl	5-fluoro-3-methyl-benzo[b]thiophen-2-yl

No.	R ¹	Ar
2372.	cyclopropylmethyl	5-chloro-3-methyl-benzo[b]thiophen-2-yl
2373.	cyclopropylmethyl	5-bromo-3-methyl-benzo[b]thiophen-2-yl
2374.	allyl	3-methylphenyl
2375.	allyl	3-ethylphenyl
2376.	allyl	3-propylphenyl
2377.	allyl	3-isopropylphenyl
2378.	allyl	3-sec-butylphenyl
2379.	allyl	3-tert-butylphenyl
2380.	allyl	3-isobutylphenyl
2381.	allyl	3-(1,1-dimethylpropyl)-phenyl
2382.	allyl	3-vinylphenyl
2383.	allyl	3-isopropenylphenyl
2384.	allyl	3-fluorophenyl
2385.	allyl	3-chlorophenyl
2386.	allyl	3-bromophenyl
2387.	allyl	3-iodophenyl
2388.	allyl	3-(fluoromethyl)phenyl
2389.	allyl	3-(difluoromethyl)phenyl
2390.	allyl	3-(trifluoromethyl)phenyl
2391.	allyl	3,5-bis(trifluoromethyl)phenyl
2392.	allyl	3-(1-fluoroethyl)-phenyl
2393.	allyl	3-((S)-1-fluoroethyl)-phenyl
2394.	allyl	3-((R)-1-fluoroethyl)-phenyl
2395.	allyl	3-(2-fluoroethyl)-phenyl
2396.	allyl	3-(1,1-difluoroethyl)-phenyl
2397.	allyl	3-(2,2-difluoroethyl)-phenyl
2398.	allyl	3-(2,2,2-trifluoroethyl)-phenyl
2399.	allyl	3-(3-fluoropropyl)-phenyl
2400.	allyl	3-(2-fluoropropyl)-phenyl
2401.	allyl	3-((S)-2-fluoropropyl)-phenyl
2402.	allyl	3-((R)-2-fluoropropyl)-phenyl
2403.	allyl	3-(3,3-difluoropropyl)-phenyl
2404.	allyl	3-(3,3,3-trifluoropropyl)-phenyl
2405.	allyl	3-(1-fluoro-1-methylethyl)-phenyl
2406.	allyl	3-(2-fluoro-1-methylethyl)-phenyl
2407.	allyl	3-((S)-2-fluoro-1-methylethyl)-phenyl
2408.	allyl	3-((R)-2-fluoro-1-methylethyl)-phenyl
2409.	allyl	3-(2,2-difluoro-1-methylethyl)-phenyl

No.	R ¹	Ar
2410.	allyl	3-((S)-2,2-difluoro-1-methylethyl)-phenyl
2411.	allyl	3-((R)-2,2-difluoro-1-methylethyl)-phenyl
2412.	allyl	3-(2,2,2-trifluoro-1-methylethyl)-phenyl
2413.	allyl	3-((S)-2,2,2-trifluoro-1-methylethyl)-phenyl
2414.	allyl	3-((R)-2,2,2-trifluoro-1-methylethyl)-phenyl
2415.	allyl	3-(2-fluoro-1-fluoromethylethyl)-phenyl
2416.	allyl	3-(1-difluoromethyl-2,2-difluoroethyl)-phenyl
2417.	allyl	3-(1,1-dimethyl-2-fluoroethyl)-phenyl
2418.	allyl	3-methoxyphenyl
2419.	allyl	3-ethoxyphenyl
2420.	allyl	3-propoxyphenyl
2421.	allyl	3-isopropoxyphenyl
2422.	allyl	3-butoxyphenyl
2423.	allyl	3-(fluoromethoxy)-phenyl
2424.	allyl	3-(difluoromethoxy)-phenyl
2425.	allyl	3-(trifluoromethoxy)-phenyl
2426.	allyl	3-(2-fluoroethoxy)-phenyl
2427.	allyl	3-(2,2-difluoroethoxy)-phenyl
2428.	allyl	3-(2,2,2-trifluoroethoxy)-phenyl
2429.	allyl	3-(1,1,2,2-tetrafluoroethoxy)-phenyl
2430.	allyl	3-cyclopropylphenyl
2431.	allyl	3-cyclobutylphenyl
2432.	allyl	3-cyclopentylphenyl
2433.	allyl	3-(2,2-difluorocyclopropyl)-phenyl
2434.	allyl	3,4-difluorophenyl
2435.	allyl	3-bromo-2-fluorophenyl
2436.	allyl	2-bromo-3-fluorophenyl
2437.	allyl	3-bromo-2,5-difluorophenyl
2438.	allyl	5-bromo-2,4-difluorophenyl
2439.	allyl	3-bromo-2,4-difluorophenyl
2440.	allyl	4-chloro-3-(trifluoromethyl)-phenyl
2441.	allyl	2-chloro-5-(trifluoromethyl)-phenyl
2442.	allyl	2-fluoro-5-(trifluoromethyl)-phenyl
2443.	allyl	4-fluoro-3-(trifluoromethyl)-phenyl
2444.	allyl	3-fluoro-5-(trifluoromethyl)-phenyl
2445.	allyl	4-bromo-3-(trifluoromethyl)-phenyl
2446.	allyl	3-bromo-5-(trifluoromethyl)-phenyl
2447.	allyl	2-bromo-5-(trifluoromethyl)-phenyl

No.	R ¹	Ar
2448.	allyl	5-bromo-2-methoxyphenyl
2449.	allyl	3-bromo-4-methoxyphenyl
2450.	allyl	2-fluoro-3-isopropylphenyl
2451.	allyl	4-fluoro-3-isopropylphenyl
2452.	allyl	3-(1-hydroxy-1-methylethyl)-phenyl
2453.	allyl	3-(2-hydroxy-2-methylpropyl)-phenyl
2454.	allyl	3-acetylphenyl
2455.	allyl	3-acetylamino-phenyl
2456.	allyl	3-carboxyphenyl
2457.	allyl	3-cyanophenyl
2458.	allyl	3-nitrophenyl
2459.	allyl	3-hydroxyphenyl
2460.	allyl	3-(O-benzyl)-phenyl
2461.	allyl	3-(2-methoxyethoxy)-phenyl
2462.	allyl	3-(CH ₂ -N(CH ₃) ₂)-phenyl
2463.	allyl	3-(NH-CO-NH ₂)-phenyl
2464.	allyl	3-(methylsulfanyl)-phenyl
2465.	allyl	3-(fluoromethylsulfanyl)-phenyl
2466.	allyl	3-(difluoromethylsulfanyl)-phenyl
2467.	allyl	3-(trifluoromethylsulfanyl)-phenyl
2468.	allyl	3-(methylsulfonyl)-phenyl
2469.	allyl	3-(N-methoxy-N-methyl-amino)-phenyl
2470.	allyl	3-(methoxyamino)-phenyl
2471.	allyl	3-(ethoxyamino)-phenyl
2472.	allyl	3-(N-methylamino-oxy)-phenyl
2473.	allyl	3-(N,N-dimethylamino-oxy)-phenyl
2474.	allyl	3-(azetidin-1-yl)-phenyl
2475.	allyl	3-(2-methylazetidin-1-yl)-phenyl
2476.	allyl	3-((S)-2-methylazetidin-1-yl)-phenyl
2477.	allyl	3-((R)-2-methylazetidin-1-yl)-phenyl
2478.	allyl	3-(3-fluoroazetidin-1-yl)-phenyl
2479.	allyl	3-(2,2-difluoroazetidin-1-yl)-phenyl
2480.	allyl	3-(3-methoxyazetidin-1-yl)-phenyl
2481.	allyl	3-(3-hydroxyazetidin-1-yl)-phenyl
2482.	allyl	3-(pyrrolidin-1-yl)-phenyl
2483.	allyl	3-(pyrrolidin-2-yl)-phenyl
2484.	allyl	3-((S)-pyrrolidin-2-yl)-phenyl

No.	R ¹	Ar
2485.	allyl	3-((R)-pyrrolidin-2-yl)-phenyl
2486.	allyl	3-(pyrrolidin-3-yl)-phenyl
2487.	allyl	3-((S)-pyrrolidin-3-yl)-phenyl
2488.	allyl	3-((R)-pyrrolidin-3-yl)-phenyl
2489.	allyl	3-(pyrrolidin-1-yl)-5-(trifluoromethyl)-phenyl
2490.	allyl	5-(pyrrolidin-1-yl)-2-methoxyphenyl
2491.	allyl	3-(pyrrolidin-1-yl)-4-methoxyphenyl
2492.	allyl	5-(pyrrolidin-1-yl)-2,4-difluorophenyl
2493.	allyl	3-(pyrrolidin-1-yl)-2,4-difluorophenyl
2494.	allyl	3-(2-fluoropyrrolidin-1-yl)-phenyl
2495.	allyl	3-((S)-2-fluoropyrrolidin-1-yl)-phenyl
2496.	allyl	3-((R)-2-fluoropyrrolidin-1-yl)-phenyl
2497.	allyl	3-(3-fluoropyrrolidin-1-yl)-phenyl
2498.	allyl	3-((S)-3-fluoropyrrolidin-1-yl)-phenyl
2499.	allyl	3-((R)-3-fluoropyrrolidin-1-yl)-phenyl
2500.	allyl	3-(2,2-difluoropyrrolidin-1-yl)-phenyl
2501.	allyl	3-(3,3-difluoropyrrolidin-1-yl)-phenyl
2502.	allyl	3-(2-methylpyrrolidin-1-yl)-phenyl
2503.	allyl	3-((S)-2-methylpyrrolidin-1-yl)-phenyl
2504.	allyl	3-((R)-2-methylpyrrolidin-1-yl)-phenyl
2505.	allyl	3-(3-methylpyrrolidin-1-yl)-phenyl
2506.	allyl	3-((S)-3-methylpyrrolidin-1-yl)-phenyl
2507.	allyl	3-((R)-3-methylpyrrolidin-1-yl)-phenyl
2508.	allyl	3-(1-methylpyrrolidin-2-yl)-phenyl
2509.	allyl	3-((S)-1-methylpyrrolidin-2-yl)-phenyl
2510.	allyl	3-((R)-1-methylpyrrolidin-2-yl)-phenyl
2511.	allyl	3-(1-methylpyrrolidin-3-yl)-phenyl
2512.	allyl	3-((S)-1-methylpyrrolidin-3-yl)-phenyl
2513.	allyl	3-((R)-1-methylpyrrolidin-3-yl)-phenyl
2514.	allyl	3-(2,2-dimethylpyrrolidin-1-yl)-phenyl
2515.	allyl	3-(3,3-dimethylpyrrolidin-1-yl)-phenyl
2516.	allyl	3-(2-trifluoromethylpyrrolidin-1-yl)-phenyl
2517.	allyl	3-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
2518.	allyl	3-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
2519.	allyl	3-(3-trifluoromethylpyrrolidin-1-yl)-phenyl
2520.	allyl	3-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
2521.	allyl	3-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
2522.	allyl	3-(2-oxopyrrolidin-1-yl)-phenyl

No.	R ¹	Ar
2523.	allyl	3-(2-oxo-oxazolidin-3-yl)-phenyl
2524.	allyl	3-(piperidin-1-yl)-phenyl
2525.	allyl	3-(2-methylpiperidin-1-yl)-phenyl
2526.	allyl	3-((S)-2-methylpiperidin-1-yl)-phenyl
2527.	allyl	3-((R)-2-methylpiperidin-1-yl)-phenyl
2528.	allyl	3-(2-fluoropiperidin-1-yl)-phenyl
2529.	allyl	3-((S)-2-fluoropiperidin-1-yl)-phenyl
2530.	allyl	3-((R)-2-fluoropiperidin-1-yl)-phenyl
2531.	allyl	3-(2,2-difluoropiperidin-1-yl)-phenyl
2532.	allyl	3-(piperazin-1-yl)-phenyl
2533.	allyl	3-(4-methylpiperazin-1-yl)-phenyl
2534.	allyl	3-(morpholin-4-yl)-phenyl
2535.	allyl	3-(morpholin-4-yl)-5-(trifluoromethyl)-phenyl
2536.	allyl	5-(morpholin-4-yl)-2-methoxyphenyl
2537.	allyl	3-(morpholin-4-yl)-4-methoxyphenyl
2538.	allyl	5-(morpholin-4-yl)-2,4-difluorophenyl
2539.	allyl	3-(morpholin-4-yl)-2,4-difluorophenyl
2540.	allyl	3-(thiomorpholin-4-yl)-phenyl
2541.	allyl	3-(1-oxo-thiomorpholin-4-yl)-phenyl
2542.	allyl	3-(1,1-dioxo-thiomorpholin-4-yl)-phenyl
2543.	allyl	3-(pyrrol-1-yl)-phenyl
2544.	allyl	3-(pyrrol-2-yl)-phenyl
2545.	allyl	3-(pyrrol-3-yl)-phenyl
2546.	allyl	3-(1-methylpyrrol-2-yl)-phenyl
2547.	allyl	3-(1-methylpyrrol-3-yl)-phenyl
2548.	allyl	3-(furan-2-yl)-phenyl
2549.	allyl	3-(furan-3-yl)-phenyl
2550.	allyl	3-(thiophen-2-yl)-phenyl
2551.	allyl	3-(thiophen-3-yl)-phenyl
2552.	allyl	3-(5-propylthien-2-yl)-phenyl
2553.	allyl	3-(pyrazol-1-yl)-phenyl
2554.	allyl	3-(pyrazol-3-yl)-phenyl
2555.	allyl	3-(pyrazol-4-yl)-phenyl
2556.	allyl	3-(4-fluoropyrazol-1-yl)-phenyl
2557.	allyl	3-(1-methyl-1H-pyrazol-4-yl)-phenyl
2558.	allyl	3-(1-ethyl-1H-pyrazol-4-yl)-phenyl
2559.	allyl	3-(1-methyl-1H-pyrazol-5-yl)-phenyl
2560.	allyl	3-(1H-imidazol-2-yl)-phenyl

No.	R ¹	Ar
2561.	allyl	3-(imidazol-1-yl)-phenyl
2562.	allyl	3-(1-methylimidazol-2-yl)-phenyl
2563.	allyl	3-(oxazol-2-yl)-phenyl
2564.	allyl	3-(oxazol-4-yl)-phenyl
2565.	allyl	3-(oxazol-5-yl)-phenyl
2566.	allyl	3-(isoxazol-3-yl)-phenyl
2567.	allyl	3-(isoxazol-4-yl)-phenyl
2568.	allyl	3-(isoxazol-5-yl)-phenyl
2569.	allyl	3-(thiazol-2-yl)-phenyl
2570.	allyl	3-(thiazol-4-yl)-phenyl
2571.	allyl	3-(thiazol-5-yl)-phenyl
2572.	allyl	3-(2-methylthiazol-4-yl)-phenyl
2573.	allyl	3-(2-methylthiazol-5-yl)-phenyl
2574.	allyl	3-([1,2,3]-triazol-1-yl)-phenyl
2575.	allyl	3-([1,2,4]-triazol-1-yl)-phenyl
2576.	allyl	3-([1,2,3]-triazol-2-yl)-phenyl
2577.	allyl	3-(4H-[1,2,4]-triazol-3-yl)-phenyl
2578.	allyl	3-([1,2,4]-triazol-4-yl)-phenyl
2579.	allyl	3-(2H-[1,2,3]-triazol-4-yl)-phenyl
2580.	allyl	3-(4-methyl-4H-[1,2,4]-triazol-3-yl)-phenyl
2581.	allyl	3-(2-methyl-2H-[1,2,3]-triazol-4-yl)-phenyl
2582.	allyl	3-([1,3,4]-oxadiazol-2-yl)-phenyl
2583.	allyl	3-(5-methyl-[1,3,4]-oxadiazol-2-yl)-phenyl
2584.	allyl	3-([1,2,4]-oxadiazol-3-yl)-phenyl
2585.	allyl	3-(5-methyl-[1,2,4]-oxadiazol-3-yl)-phenyl
2586.	allyl	3-([1,2,4]-oxadiazol-5-yl)-phenyl
2587.	allyl	3-([1,2,3]-oxadiazol-4-yl)-phenyl
2588.	allyl	3-([1,2,3]-oxadiazol-5-yl)-phenyl
2589.	allyl	3-([1,2,3]-thiadiazol-4-yl)-phenyl
2590.	allyl	3-(1H-tetrazol-5-yl)-phenyl
2591.	allyl	3-(tetrazol-1-yl)-phenyl
2592.	allyl	3-(2-methyl-2H-tetrazol-5-yl)-phenyl
2593.	allyl	3-(1-methyl-1H-tetrazol-5-yl)-phenyl
2594.	allyl	3-furazan-3-yl-phenyl
2595.	allyl	3-(pyrid-2-yl)-phenyl
2596.	allyl	3-(pyrid-3-yl)-phenyl
2597.	allyl	3-(pyrid-4-yl)-phenyl
2598.	allyl	3-(pyrimidin-2-yl)-phenyl

No.	R ¹	Ar
2599.	allyl	3-(2-methylpyrimidin-4-yl)-phenyl
2600.	allyl	3-(pyrimidin-4-yl)-phenyl
2601.	allyl	3-(pyrimidin-5-yl)-phenyl
2602.	allyl	5-bromopyridin-3-yl
2603.	allyl	3-bromo-2-chloropyridin-5-yl
2604.	allyl	4-methylpyridin-2-yl
2605.	allyl	6-methylpyridin-2-yl
2606.	allyl	4-(trifluoromethyl)-pyridin-2-yl
2607.	allyl	6-(trifluoromethyl)-pyridin-2-yl
2608.	allyl	5-(trifluoromethyl)-pyridin-3-yl
2609.	allyl	5-(pyrrolidin-1-yl)-pyridin-3-yl
2610.	allyl	3-(pyrrolidin-1-yl)-2-chloropyridin-5-yl
2611.	allyl	3-(morpholin-4-yl)-2-chloropyridin-5-yl
2612.	allyl	2-(morpholin-4-yl)-pyridin-5-yl
2613.	allyl	2-phenoxy-pyridin-5-yl
2614.	allyl	2,3-dichlorophenyl
2615.	allyl	2,5-dichlorophenyl
2616.	allyl	3,5-dichlorophenyl
2617.	allyl	3-chloro-4-fluorophenyl
2618.	allyl	4-bromo-2,5-dichlorophenyl
2619.	allyl	3-bromo-4-(trifluoromethoxy)phenyl
2620.	allyl	3,5-dibromo-4-(2-fluoroethoxy)-phenyl
2621.	allyl	2,5-dimethylphenyl
2622.	allyl	2,5-di-(trifluoromethyl)-phenyl
2623.	allyl	3,5-di-(trifluoromethyl)-phenyl
2624.	allyl	2,5-dimethoxyphenyl
2625.	allyl	2-methoxy-5-methylphenyl
2626.	allyl	2-methoxy-5-(trifluoromethyl)-phenyl
2627.	allyl	4-fluoro-3-(oxazol-4-yl)-phenyl
2628.	allyl	thien-2-yl
2629.	allyl	thien-3-yl
2630.	allyl	3-chlorothien-2-yl
2631.	allyl	4-chlorothien-2-yl
2632.	allyl	5-chlorothien-2-yl
2633.	allyl	3-bromothien-2-yl
2634.	allyl	4-bromothien-2-yl
2635.	allyl	5-bromothien-2-yl
2636.	allyl	4,5-dichlorothien-2-yl

No.	R ¹	Ar
2637.	allyl	4,5-dibromothien-2-yl
2638.	allyl	4-bromo-5-chlorothien-2-yl
2639.	allyl	3-bromo-5-chlorothien-2-yl
2640.	allyl	5-methylthien-2-yl
2641.	allyl	5-ethylthien-2-yl
2642.	allyl	5-propylthien-2-yl
2643.	allyl	5-trifluoromethylthien-2-yl
2644.	allyl	5-phenylthien-2-yl
2645.	allyl	5-(pyrid-2-yl)-thien-2-yl
2646.	allyl	5-(phenylsulfonyl)-thien-2-yl
2647.	allyl	4-(phenylsulfonyl)-thien-2-yl
2648.	allyl	5-(pyrid-2-ylsulfonyl)-thien-2-yl
2649.	allyl	5-(3-chloro-5-trifluoro-pyrid-2-ylsulfonyl)-thien-2-yl
2650.	allyl	5-(benzoylaminomethyl)-thien-2-yl
2651.	allyl	5-((4-chlorobenzoyl)aminomethyl)-thien-2-yl
2652.	allyl	5-(acetylaminomethyl)-thien-2-yl
2653.	allyl	5-(pyrazol-1-yl)-thien-2-yl
2654.	allyl	5-(pyrazol-3-yl)-thien-2-yl
2655.	allyl	5-(pyrazol-4-yl)-thien-2-yl
2656.	allyl	5-(pyrazol-5-yl)-thien-2-yl
2657.	allyl	5-(4-fluoropyrazol-1-yl)-thien-2-yl
2658.	allyl	5-(1-methyl-5-trifluoromethyl-(1H)-pyrazol-3-yl)-thien-2-yl
2659.	allyl	5-(1-methyl-3-trifluoromethyl-(1H)-pyrazol-5-yl)-thien-2-yl
2660.	allyl	5-(4-carboxy-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
2661.	allyl	5-(4-aminomethyl-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
2662.	allyl	5-(isoxazol-3-yl)-thien-2-yl
2663.	allyl	5-(isoxazol-4-yl)-thien-2-yl
2664.	allyl	5-(isoxazol-5-yl)-thien-2-yl
2665.	allyl	5-(5-trifluoromethylisoxazol-3-yl)-thien-2-yl
2666.	allyl	5-(oxazol-2-yl)-thien-2-yl
2667.	allyl	5-(oxazol-4-yl)-thien-2-yl
2668.	allyl	5-(oxazol-5-yl)-thien-2-yl
2669.	allyl	5-(2-methyloxazol-4-yl)-thien-2-yl

No.	R ¹	Ar
2670.	allyl	5-(2-methyloxazol-5-yl)-thien-2-yl
2671.	allyl	5-(isothiazol-3-yl)-thien-2-yl
2672.	allyl	5-(isothiazol-4-yl)-thien-2-yl
2673.	allyl	5-(isothiazol-5-yl)-thien-2-yl
2674.	allyl	5-(5-trifluoromethylisothiazol-3-yl)-thien-2-yl
2675.	allyl	5-(thiazol-2-yl)-thien-2-yl
2676.	allyl	5-(thiazol-4-yl)-thien-2-yl
2677.	allyl	5-(thiazol-5-yl)-thien-2-yl
2678.	allyl	5-(2-methylthiazol-4-yl)-thien-2-yl
2679.	allyl	5-(2-methylthiazol-5-yl)-thien-2-yl
2680.	allyl	5-([1,2,3]-oxadiazol-4-yl)-thien-2-yl
2681.	allyl	5-([1,2,3]-thiadiazol-4-yl)-thien-2-yl
2682.	allyl	5-(pyrimidin-2-yl)-thien-2-yl
2683.	allyl	5-(pyrimidin-4-yl)-thien-2-yl
2684.	allyl	5-(pyrimidin-5-yl)-thien-2-yl
2685.	allyl	5-(2-methylthiopyrimidin-4-yl)-thien-2-yl
2686.	allyl	5-([1,3]-dioxolan-2-yl)-thien-2-yl
2687.	allyl	3-([1,3]-dioxolan-2-yl)-thien-2-yl thien-2-yl
2688.	allyl	5-((3-chloro-5-(trifluoromethyl)-pyridin-2-yl)-methyl)-thien-2-yl
2689.	allyl	5-[3-chloro-5-(trifluoromethyl)-pyrid-2-ylsulfonyl]-thien-2-yl
2690.	allyl	2-chlorothien-3-yl
2691.	allyl	4-chlorothien-3-yl
2692.	allyl	5-chlorothien-3-yl
2693.	allyl	2-bromothien-3-yl
2694.	allyl	4-bromothien-3-yl
2695.	allyl	5-bromothien-3-yl
2696.	allyl	2,5-dichlorothien-3-yl
2697.	allyl	2,5-dibromothien-3-yl
2698.	allyl	2,4,5-trichlorothien-3-yl
2699.	allyl	4-bromo-2,5-dichlorothien-3-yl
2700.	allyl	2-chloro-5-methylsulfonylthien-3-yl
2701.	allyl	2,5-dimethylthien-3-yl
2702.	allyl	4-hydroxythien-3-yl
2703.	allyl	2-phenylthien-3-yl
2704.	allyl	4-phenyl-5-(trifluoromethyl)-thien-3-yl
2705.	allyl	2-methoxycarbonyl-4-phenyl-5-(trifluoromethyl)-

No.	R ¹	Ar
		thien-3-yl
2706.	allyl	benzo[b]thiophen-2-yl
2707.	allyl	benzo[b]thiophen-3-yl
2708.	allyl	3-methyl-benzo[b]thiophen-2-yl
2709.	allyl	5-methyl-benzo[b]thiophen-2-yl
2710.	allyl	5-fluoro-3-methyl-benzo[b]thiophen-2-yl
2711.	allyl	5-chloro-3-methyl-benzo[b]thiophen-2-yl
2712.	allyl	5-bromo-3-methyl-benzo[b]thiophen-2-yl
2713.	benzyl	3-methylphenyl
2714.	benzyl	3-ethylphenyl
2715.	benzyl	3-propylphenyl
2716.	benzyl	3-isopropylphenyl
2717.	benzyl	3-sec-butylphenyl
2718.	benzyl	3-tert-butylphenyl
2719.	benzyl	3-isobutylphenyl
2720.	benzyl	3-(1,1-dimethylpropyl)-phenyl
2721.	benzyl	3-vinylphenyl
2722.	benzyl	3-isopropenylphenyl
2723.	benzyl	3-fluorophenyl
2724.	benzyl	3-chlorophenyl
2725.	benzyl	3-bromophenyl
2726.	benzyl	3-iodophenyl
2727.	benzyl	3-(fluoromethyl)phenyl
2728.	benzyl	3-(difluoromethyl)phenyl
2729.	benzyl	3-(trifluoromethyl)phenyl
2730.	benzyl	3,5-bis(trifluoromethyl)phenyl
2731.	benzyl	3-(1-fluoroethyl)-phenyl
2732.	benzyl	3-((S)-1-fluoroethyl)-phenyl
2733.	benzyl	3-((R)-1-fluoroethyl)-phenyl
2734.	benzyl	3-(2-fluoroethyl)-phenyl
2735.	benzyl	3-(1,1-difluoroethyl)-phenyl
2736.	benzyl	3-(2,2-difluoroethyl)-phenyl
2737.	benzyl	3-(2,2,2-trifluoroethyl)-phenyl
2738.	benzyl	3-(3-fluoropropyl)-phenyl
2739.	benzyl	3-(2-fluoropropyl)-phenyl
2740.	benzyl	3-((S)-2-fluoropropyl)-phenyl
2741.	benzyl	3-((R)-2-fluoropropyl)-phenyl
2742.	benzyl	3-(3,3-difluoropropyl)-phenyl

No.	R ¹	Ar
2743.	benzyl	3-(3,3,3-trifluoropropyl)-phenyl
2744.	benzyl	3-(1-fluoro-1-methylethyl)-phenyl
2745.	benzyl	3-(2-fluoro-1-methylethyl)-phenyl
2746.	benzyl	3-((S)-2-fluoro-1-methylethyl)-phenyl
2747.	benzyl	3-((R)-2-fluoro-1-methylethyl)-phenyl
2748.	benzyl	3-(2,2-difluoro-1-methylethyl)-phenyl
2749.	benzyl	3-((S)-2,2-difluoro-1-methylethyl)-phenyl
2750.	benzyl	3-((R)-2,2-difluoro-1-methylethyl)-phenyl
2751.	benzyl	3-(2,2,2-trifluoro-1-methylethyl)-phenyl
2752.	benzyl	3-((S)-2,2,2-trifluoro-1-methylethyl)-phenyl
2753.	benzyl	3-((R)-2,2,2-trifluoro-1-methylethyl)-phenyl
2754.	benzyl	3-(2-fluoro-1-fluoromethylethyl)-phenyl
2755.	benzyl	3-(1-difluoromethyl-2,2-difluoroethyl)-phenyl
2756.	benzyl	3-(1,1-dimethyl-2-fluoroethyl)-phenyl
2757.	benzyl	3-methoxyphenyl
2758.	benzyl	3-ethoxyphenyl
2759.	benzyl	3-propoxyphenyl
2760.	benzyl	3-isopropoxyphenyl
2761.	benzyl	3-butoxyphenyl
2762.	benzyl	3-(fluoromethoxy)-phenyl
2763.	benzyl	3-(difluoromethoxy)-phenyl
2764.	benzyl	3-(trifluoromethoxy)-phenyl
2765.	benzyl	3-(2-fluoroethoxy)-phenyl
2766.	benzyl	3-(2,2-difluoroethoxy)-phenyl
2767.	benzyl	3-(2,2,2-trifluoroethoxy)-phenyl
2768.	benzyl	3-(1,1,2,2-tetrafluoroethoxy)-phenyl
2769.	benzyl	3-cyclopropylphenyl
2770.	benzyl	3-cyclobutylphenyl
2771.	benzyl	3-cyclopentylphenyl
2772.	benzyl	3-(2,2-difluorocyclopropyl)-phenyl
2773.	benzyl	3,4-difluorophenyl
2774.	benzyl	3-bromo-2-fluorophenyl
2775.	benzyl	2-bromo-3-fluorophenyl
2776.	benzyl	3-bromo-2,5-difluorophenyl
2777.	benzyl	5-bromo-2,4-difluorophenyl
2778.	benzyl	3-bromo-2,4-difluorophenyl
2779.	benzyl	4-chloro-3-(trifluoromethyl)-phenyl
2780.	benzyl	2-chloro-5-(trifluoromethyl)-phenyl

No.	R ¹	Ar
2781.	benzyl	2-fluoro-5-(trifluoromethyl)-phenyl
2782.	benzyl	4-fluoro-3-(trifluoromethyl)-phenyl
2783.	benzyl	3-fluoro-5-(trifluoromethyl)-phenyl
2784.	benzyl	4-bromo-3-(trifluoromethyl)-phenyl
2785.	benzyl	3-bromo-5-(trifluoromethyl)-phenyl
2786.	benzyl	2-bromo-5-(trifluoromethyl)-phenyl
2787.	benzyl	5-bromo-2-methoxyphenyl
2788.	benzyl	3-bromo-4-methoxyphenyl
2789.	benzyl	2-fluoro-3-isopropylphenyl
2790.	benzyl	4-fluoro-3-isopropylphenyl
2791.	benzyl	3-(1-hydroxy-1-methylethyl)-phenyl
2792.	benzyl	3-(2-hydroxy-2-methylpropyl)-phenyl
2793.	benzyl	3-acetylphenyl
2794.	benzyl	3-acetylamino-phenyl
2795.	benzyl	3-carboxyphenyl
2796.	benzyl	3-cyanophenyl
2797.	benzyl	3-nitrophenyl
2798.	benzyl	3-hydroxyphenyl
2799.	benzyl	3-(O-benzyl)-phenyl
2800.	benzyl	3-(2-methoxyethoxy)-phenyl
2801.	benzyl	3-(CH ₂ -N(CH ₃) ₂)-phenyl
2802.	benzyl	3-(NH-CO-NH ₂)-phenyl
2803.	benzyl	3-(methylsulfanyl)-phenyl
2804.	benzyl	3-(fluoromethylsulfanyl)-phenyl
2805.	benzyl	3-(difluoromethylsulfanyl)-phenyl
2806.	benzyl	3-(trifluoromethylsulfanyl)-phenyl
2807.	benzyl	3-(methylsulfonyl)-phenyl
2808.	benzyl	3-(N-methoxy-N-methyl-amino)-phenyl
2809.	benzyl	3-(methoxyamino)-phenyl
2810.	benzyl	3-(ethoxyamino)-phenyl
2811.	benzyl	3-(N-methylamino-oxy)-phenyl
2812.	benzyl	3-(N,N-dimethylamino-oxy)-phenyl
2813.	benzyl	3-(azetidin-1-yl)-phenyl
2814.	benzyl	3-(2-methylazetidin-1-yl)-phenyl
2815.	benzyl	3-((S)-2-methylazetidin-1-yl)-phenyl
2816.	benzyl	3-((R)-2-methylazetidin-1-yl)-phenyl
2817.	benzyl	3-(3-fluoroazetidin-1-yl)-phenyl

No.	R ¹	Ar
2818.	benzyl	3-(2,2-difluoroazetidin-1-yl)-phenyl
2819.	benzyl	3-(3-methoxyazetidin-1-yl)-phenyl
2820.	benzyl	3-(3-hydroxyazetidin-1-yl)-phenyl
2821.	benzyl	3-(pyrrolidin-1-yl)-phenyl
2822.	benzyl	3-(pyrrolidin-2-yl)-phenyl
2823.	benzyl	3-((S)-pyrrolidin-2-yl)-phenyl
2824.	benzyl	3-((R)-pyrrolidin-2-yl)-phenyl
2825.	benzyl	3-(pyrrolidin-3-yl)-phenyl
2826.	benzyl	3-((S)-pyrrolidin-3-yl)-phenyl
2827.	benzyl	3-((R)-pyrrolidin-3-yl)-phenyl
2828.	benzyl	3-(pyrrolidin-1-yl)-5-(trifluoromethyl)-phenyl
2829.	benzyl	5-(pyrrolidin-1-yl)-2-methoxyphenyl
2830.	benzyl	3-(pyrrolidin-1-yl)-4-methoxyphenyl
2831.	benzyl	5-(pyrrolidin-1-yl)-2,4-difluorophenyl
2832.	benzyl	3-(pyrrolidin-1-yl)-2,4-difluorophenyl
2833.	benzyl	3-(2-fluoropyrrolidin-1-yl)-phenyl
2834.	benzyl	3-((S)-2-fluoropyrrolidin-1-yl)-phenyl
2835.	benzyl	3-((R)-2-fluoropyrrolidin-1-yl)-phenyl
2836.	benzyl	3-(3-fluoropyrrolidin-1-yl)-phenyl
2837.	benzyl	3-((S)-3-fluoropyrrolidin-1-yl)-phenyl
2838.	benzyl	3-((R)-3-fluoropyrrolidin-1-yl)-phenyl
2839.	benzyl	3-(2,2-difluoropyrrolidin-1-yl)-phenyl
2840.	benzyl	3-(3,3-difluoropyrrolidin-1-yl)-phenyl
2841.	benzyl	3-(2-methylpyrrolidin-1-yl)-phenyl
2842.	benzyl	3-((S)-2-methylpyrrolidin-1-yl)-phenyl
2843.	benzyl	3-((R)-2-methylpyrrolidin-1-yl)-phenyl
2844.	benzyl	3-(3-methylpyrrolidin-1-yl)-phenyl
2845.	benzyl	3-((S)-3-methylpyrrolidin-1-yl)-phenyl
2846.	benzyl	3-((R)-3-methylpyrrolidin-1-yl)-phenyl
2847.	benzyl	3-(1-methylpyrrolidin-2-yl)-phenyl
2848.	benzyl	3-((S)-1-methylpyrrolidin-2-yl)-phenyl
2849.	benzyl	3-((R)-1-methylpyrrolidin-2-yl)-phenyl
2850.	benzyl	3-(1-methylpyrrolidin-3-yl)-phenyl
2851.	benzyl	3-((S)-1-methylpyrrolidin-3-yl)-phenyl
2852.	benzyl	3-((R)-1-methylpyrrolidin-3-yl)-phenyl
2853.	benzyl	3-(2,2-dimethylpyrrolidin-1-yl)-phenyl
2854.	benzyl	3-(3,3-dimethylpyrrolidin-1-yl)-phenyl
2855.	benzyl	3-(2-trifluoromethylpyrrolidin-1-yl)-phenyl

No.	R ¹	Ar
2856.	benzyl	3-((S)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
2857.	benzyl	3-((R)-2-trifluoromethylpyrrolidin-1-yl)-phenyl
2858.	benzyl	3-(3-trifluoromethylpyrrolidin-1-yl)-phenyl
2859.	benzyl	3-((S)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
2860.	benzyl	3-((R)-3-trifluoromethylpyrrolidin-1-yl)-phenyl
2861.	benzyl	3-(2-oxopyrrolidin-1-yl)-phenyl
2862.	benzyl	3-(2-oxo-oxazolidin-3-yl)-phenyl
2863.	benzyl	3-(piperidin-1-yl)-phenyl
2864.	benzyl	3-(2-methylpiperidin-1-yl)-phenyl
2865.	benzyl	3-((S)-2-methylpiperidin-1-yl)-phenyl
2866.	benzyl	3-((R)-2-methylpiperidin-1-yl)-phenyl
2867.	benzyl	3-(2-fluoropiperidin-1-yl)-phenyl
2868.	benzyl	3-((S)-2-fluoropiperidin-1-yl)-phenyl
2869.	benzyl	3-((R)-2-fluoropiperidin-1-yl)-phenyl
2870.	benzyl	3-(2,2-difluoropiperidin-1-yl)-phenyl
2871.	benzyl	3-(piperazin-1-yl)-phenyl
2872.	benzyl	3-(4-methylpiperazin-1-yl)-phenyl
2873.	benzyl	3-(morpholin-4-yl)-phenyl
2874.	benzyl	3-(morpholin-4-yl)-5-(trifluoromethyl)-phenyl
2875.	benzyl	5-(morpholin-4-yl)-2-methoxyphenyl
2876.	benzyl	3-(morpholin-4-yl)-4-methoxyphenyl
2877.	benzyl	5-(morpholin-4-yl)-2,4-difluorophenyl
2878.	benzyl	3-(morpholin-4-yl)-2,4-difluorophenyl
2879.	benzyl	3-(thiomorpholin-4-yl)-phenyl
2880.	benzyl	3-(1-oxo-thiomorpholin-4-yl)-phenyl
2881.	benzyl	3-(1,1-dioxo-thiomorpholin-4-yl)-phenyl
2882.	benzyl	3-(pyrrol-1-yl)-phenyl
2883.	benzyl	3-(pyrrol-2-yl)-phenyl
2884.	benzyl	3-(pyrrol-3-yl)-phenyl
2885.	benzyl	3-(1-methylpyrrol-2-yl)-phenyl
2886.	benzyl	3-(1-methylpyrrol-3-yl)-phenyl
2887.	benzyl	3-(furan-2-yl)-phenyl
2888.	benzyl	3-(furan-3-yl)-phenyl
2889.	benzyl	3-(thiophen-2-yl)-phenyl
2890.	benzyl	3-(thiophen-3-yl)-phenyl
2891.	benzyl	3-(5-propylthien-2-yl)-phenyl
2892.	benzyl	3-(pyrazol-1-yl)-phenyl
2893.	benzyl	3-(pyrazol-3-yl)-phenyl

No.	R ¹	Ar
2894.	benzyl	3-(pyrazol-4-yl)-phenyl
2895.	benzyl	3-(4-fluoropyrazol-1-yl)-phenyl
2896.	benzyl	3-(1-methyl-1H-pyrazol-4-yl)-phenyl
2897.	benzyl	3-(1-ethyl-1H-pyrazol-4-yl)-phenyl
2898.	benzyl	3-(1-methyl-1H-pyrazol-5-yl)-phenyl
2899.	benzyl	3-(1H-imidazol-2-yl)-phenyl
2900.	benzyl	3-(imidazol-1-yl)-phenyl
2901.	benzyl	3-(1-methylimidazol-2-yl)-phenyl
2902.	benzyl	3-(oxazol-2-yl)-phenyl
2903.	benzyl	3-(oxazol-4-yl)-phenyl
2904.	benzyl	3-(oxazol-5-yl)-phenyl
2905.	benzyl	3-(isoxazol-3-yl)-phenyl
2906.	benzyl	3-(isoxazol-4-yl)-phenyl
2907.	benzyl	3-(isoxazol-5-yl)-phenyl
2908.	benzyl	3-(thiazol-2-yl)-phenyl
2909.	benzyl	3-(thiazol-4-yl)-phenyl
2910.	benzyl	3-(thiazol-5-yl)-phenyl
2911.	benzyl	3-(2-methylthiazol-4-yl)-phenyl
2912.	benzyl	3-(2-methylthiazol-5-yl)-phenyl
2913.	benzyl	3-([1,2,3]-triazol-1-yl)-phenyl
2914.	benzyl	3-([1,2,4]-triazol-1-yl)-phenyl
2915.	benzyl	3-([1,2,3]-triazol-2-yl)-phenyl
2916.	benzyl	3-(4H-[1,2,4]-triazol-3-yl)-phenyl
2917.	benzyl	3-([1,2,4]-triazol-4-yl)-phenyl
2918.	benzyl	3-(2H-[1,2,3]-triazol-4-yl)-phenyl
2919.	benzyl	3-(4-methyl-4H-[1,2,4]-triazol-3-yl)-phenyl
2920.	benzyl	3-(2-methyl-2H-[1,2,3]-triazol-4-yl)-phenyl
2921.	benzyl	3-([1,3,4]-oxadiazol-2-yl)-phenyl
2922.	benzyl	3-(5-methyl-[1,3,4]-oxadiazol-2-yl)-phenyl
2923.	benzyl	3-([1,2,4]-oxadiazol-3-yl)-phenyl
2924.	benzyl	3-(5-methyl-[1,2,4]-oxadiazol-3-yl)-phenyl
2925.	benzyl	3-([1,2,4]-oxadiazol-5-yl)-phenyl
2926.	benzyl	3-([1,2,3]-oxadiazol-4-yl)-phenyl
2927.	benzyl	3-([1,2,3]-oxadiazol-5-yl)-phenyl
2928.	benzyl	3-([1,2,3]-thiadiazol-4-yl)-phenyl
2929.	benzyl	3-(1H-tetrazol-5-yl)-phenyl
2930.	benzyl	3-(tetrazol-1-yl)-phenyl
2931.	benzyl	3-(2-methyl-2H-tetrazol-5-yl)-phenyl

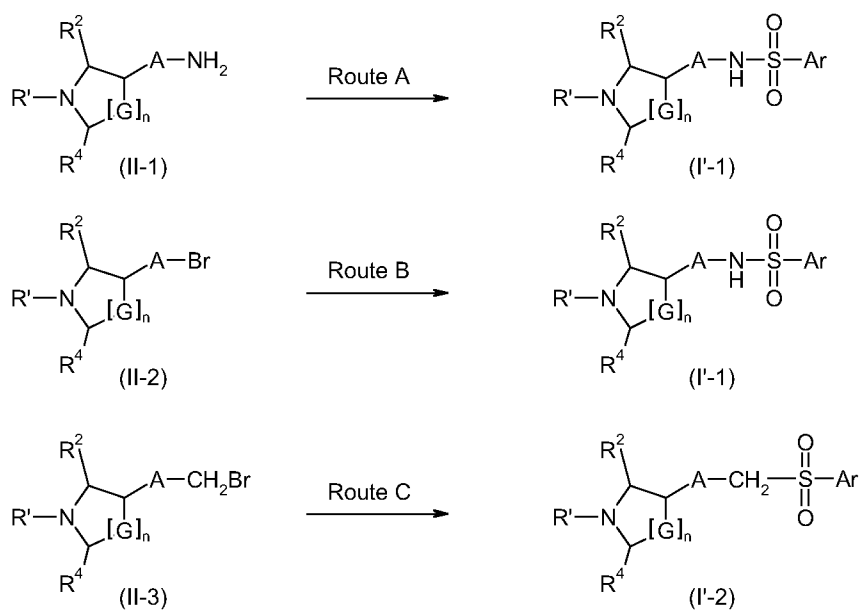
No.	R ¹	Ar
2932.	benzyl	3-(1-methyl-1H-tetrazol-5-yl)-phenyl
2933.	benzyl	3-furazan-3-yl-phenyl
2934.	benzyl	3-(pyrid-2-yl)-phenyl
2935.	benzyl	3-(pyrid-3-yl)-phenyl
2936.	benzyl	3-(pyrid-4-yl)-phenyl
2937.	benzyl	3-(pyrimidin-2-yl)-phenyl
2938.	benzyl	3-(2-methylpyrimidin-4-yl)-phenyl
2939.	benzyl	3-(pyrimidin-4-yl)-phenyl
2940.	benzyl	3-(pyrimidin-5-yl)-phenyl
2941.	benzyl	5-bromopyridin-3-yl
2942.	benzyl	3-bromo-2-chloropyridin-5-yl
2943.	benzyl	4-methylpyridin-2-yl
2944.	benzyl	6-methylpyridin-2-yl
2945.	benzyl	4-(trifluoromethyl)-pyridin-2-yl
2946.	benzyl	6-(trifluoromethyl)-pyridin-2-yl
2947.	benzyl	5-(trifluoromethyl)-pyridin-3-yl
2948.	benzyl	5-(pyrrolidin-1-yl)-pyridin-3-yl
2949.	benzyl	3-(pyrrolidin-1-yl)-2-chloropyridin-5-yl
2950.	benzyl	3-(morpholin-4-yl)-2-chloropyridin-5-yl
2951.	benzyl	2-(morpholin-4-yl)-pyridin-5-yl
2952.	benzyl	2-phenoxy-pyridin-5-yl
2953.	benzyl	2,3-dichlorophenyl
2954.	benzyl	2,5-dichlorophenyl
2955.	benzyl	3,5-dichlorophenyl
2956.	benzyl	3-chloro-4-fluorophenyl
2957.	benzyl	4-bromo-2,5-dichlorophenyl
2958.	benzyl	3-bromo-4-(trifluoromethoxy)phenyl
2959.	benzyl	3,5-dibromo-4-(2-fluoroethoxy)-phenyl
2960.	benzyl	2,5-dimethylphenyl
2961.	benzyl	2,5-di-(trifluoromethyl)-phenyl
2962.	benzyl	3,5-di-(trifluoromethyl)-phenyl
2963.	benzyl	2,5-dimethoxyphenyl
2964.	benzyl	2-methoxy-5-methylphenyl
2965.	benzyl	2-methoxy-5-(trifluoromethyl)-phenyl
2966.	benzyl	4-fluoro-3-(oxazol-4-yl)-phenyl
2967.	benzyl	thien-2-yl
2968.	benzyl	thien-3-yl
2969.	benzyl	3-chlorothien-2-yl

No.	R ¹	Ar
2970.	benzyl	4-chlorothien-2-yl
2971.	benzyl	5-chlorothien-2-yl
2972.	benzyl	3-bromothien-2-yl
2973.	benzyl	4-bromothien-2-yl
2974.	benzyl	5-bromothien-2-yl
2975.	benzyl	4,5-dichlorothien-2-yl
2976.	benzyl	4,5-dibromothien-2-yl
2977.	benzyl	4-bromo-5-chlorothien-2-yl
2978.	benzyl	3-bromo-5-chlorothien-2-yl
2979.	benzyl	5-methylthien-2-yl
2980.	benzyl	5-ethylthien-2-yl
2981.	benzyl	5-propylthien-2-yl
2982.	benzyl	5-trifluoromethylthien-2-yl
2983.	benzyl	5-phenylthien-2-yl
2984.	benzyl	5-(pyrid-2-yl)-thien-2-yl
2985.	benzyl	5-(phenylsulfonyl)-thien-2-yl
2986.	benzyl	4-(phenylsulfonyl)-thien-2-yl
2987.	benzyl	5-(pyrid-2-ylsulfonyl)-thien-2-yl
2988.	benzyl	5-(3-chloro-5-trifluoro-pyrid-2-ylsulfonyl)-thien-2-yl
2989.	benzyl	5-(benzoylaminomethyl)-thien-2-yl
2990.	benzyl	5-((4-chlorobenzoyl)aminomethyl)-thien-2-yl
2991.	benzyl	5-(acetylaminomethyl)-thien-2-yl
2992.	benzyl	5-(pyrazol-1-yl)-thien-2-yl
2993.	benzyl	5-(pyrazol-3-yl)-thien-2-yl
2994.	benzyl	5-(pyrazol-4-yl)-thien-2-yl
2995.	benzyl	5-(pyrazol-5-yl)-thien-2-yl
2996.	benzyl	5-(4-fluoropyrazol-1-yl)-thien-2-yl
2997.	benzyl	5-(1-methyl-5-trifluoromethyl-(1H)-pyrazol-3-yl)-thien-2-yl
2998.	benzyl	5-(1-methyl-3-trifluoromethyl-(1H)-pyrazol-5-yl)-thien-2-yl
2999.	benzyl	5-(4-carboxy-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
3000.	benzyl	5-(4-aminomethyl-1-methyl-5-methylthio-(1H)-pyrazol-3-yl)-thien-2-yl
3001.	benzyl	5-(isoxazol-3-yl)-thien-2-yl
3002.	benzyl	5-(isoxazol-4-yl)-thien-2-yl

No.	R ¹	Ar
3003.	benzyl	5-(isoxazol-5-yl)-thien-2-yl
3004.	benzyl	5-(5-trifluoromethylisoxazol-3-yl)-thien-2-yl
3005.	benzyl	5-(oxazol-2-yl)-thien-2-yl
3006.	benzyl	5-(oxazol-4-yl)-thien-2-yl
3007.	benzyl	5-(oxazol-5-yl)-thien-2-yl
3008.	benzyl	5-(2-methyloxazol-4-yl)-thien-2-yl
3009.	benzyl	5-(2-methyloxazol-5-yl)-thien-2-yl
3010.	benzyl	5-(isothiazol-3-yl)-thien-2-yl
3011.	benzyl	5-(isothiazol-4-yl)-thien-2-yl
3012.	benzyl	5-(isothiazol-5-yl)-thien-2-yl
3013.	benzyl	5-(5-trifluoromethylisothiazol-3-yl)-thien-2-yl
3014.	benzyl	5-(thiazol-2-yl)-thien-2-yl
3015.	benzyl	5-(thiazol-4-yl)-thien-2-yl
3016.	benzyl	5-(thiazol-5-yl)-thien-2-yl
3017.	benzyl	5-(2-methylthiazol-4-yl)-thien-2-yl
3018.	benzyl	5-(2-methylthiazol-5-yl)-thien-2-yl
3019.	benzyl	5-([1,2,3]-oxadiazol-4-yl)-thien-2-yl
3020.	benzyl	5-([1,2,3]-thiadiazol-4-yl)-thien-2-yl
3021.	benzyl	5-(pyrimidin-2-yl)-thien-2-yl
3022.	benzyl	5-(pyrimidin-4-yl)-thien-2-yl
3023.	benzyl	5-(pyrimidin-5-yl)-thien-2-yl
3024.	benzyl	5-(2-methylthiopyrimidin-4-yl)-thien-2-yl
3025.	benzyl	5-([1,3]-dioxolan-2-yl)-thien-2-yl
3026.	benzyl	3-([1,3]-dioxolan-2-yl)-thien-2-yl
3027.	benzyl	5-((3-chloro-5-(trifluoromethyl)-pyridin-2-yl)-methyl)-thien-2-yl
3028.	benzyl	5-[3-chloro-5-(trifluoromethyl)-pyrid-2-ylsulfonyl]-thien-2-yl
3029.	benzyl	2-chlorothien-3-yl
3030.	benzyl	4-chlorothien-3-yl
3031.	benzyl	5-chlorothien-3-yl
3032.	benzyl	2-bromothien-3-yl
3033.	benzyl	4-bromothien-3-yl
3034.	benzyl	5-bromothien-3-yl
3035.	benzyl	2,5-dichlorothien-3-yl
3036.	benzyl	2,5-dibromothien-3-yl
3037.	benzyl	2,4,5-trichlorothien-3-yl
3038.	benzyl	4-bromo-2,5-dichlorothien-3-yl

No.	R ¹	Ar
3039.	benzyl	2-chloro-5-methylsulfonylthien-3-yl
3040.	benzyl	2,5-dimethylthien-3-yl
3041.	benzyl	4-hydroxythien-3-yl
3042.	benzyl	2-phenylthien-3-yl
3043.	benzyl	4-phenyl-5-(trifluoromethyl)-thien-3-yl
3044.	benzyl	2-methoxycarbonyl-4-phenyl-5-(trifluoromethyl)-thien-3-yl
3045.	benzyl	benzo[b]thiophen-2-yl
3046.	benzyl	benzo[b]thiophen-3-yl
3047.	benzyl	3-methyl-benzo[b]thiophen-2-yl
3048.	benzyl	5-methyl-benzo[b]thiophen-2-yl
3049.	benzyl	5-fluoro-3-methyl-benzo[b]thiophen-2-yl
3050.	benzyl	5-chloro-3-methyl-benzo[b]thiophen-2-yl
3051.	benzyl	5-bromo-3-methyl-benzo[b]thiophen-2-yl

Compounds I of the present invention can be synthesized as outlined in the synthetic routes A, B and C below.



Scheme 1:

In scheme 1, A, Ar, G, n, R², and R⁴ are as defined above. R' is either R¹ or is a precursor of R¹.

Route A

In route A, the amino compound (II-1) is reacted with a suitable sulfonic acid derivative to give the sulfonamide (I-1) ($E = NH$). A suitable sulfonic acid derivative is e.g. the sulfonyl chloride $Ar-SO_2Cl$. The sulfonation reaction is preferably carried out in the presence of a base, according to standard procedures in the art. In the reaction depicted in the above scheme 1, the sulfonation 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 page 444ff 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 with $Cl-SO_2-Ar$ 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 (II-1).

Prior to the sulfonation reaction, the radical NH_2 can be converted into a $NR^{5'}$ group, in which $R^{5'}$ has the meanings different from hydrogen which are specified for R^5 (not shown in scheme 1).

If in the resulting sulfonamide (I'-1) R' is not the desired radical R^1 but a precursor thereof, the compound can be modified as outlined below to obtain the desired substituent R^1 . A precursor is a radical which can be easily removed and replaced by the desired group R^1 or which can be modified to give R^1 . The precursor can also be an N-protective group.

If R' is allyl, the allyl group can be cleaved to obtain a compound wherein R' is hydrogen. The cleavage of the allyl group is achieved, for example, by reacting compound (I'-1) [$R' = allyl$] with an allyl trapping agent, such as mercaptobenzoic acid or 1,3-dimethylbarbituric acid, in the presence of catalytic quantities of palladium (0) com-

pounds 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 R' is benzyl, this substituent may also be cleaved to obtain a compound (I'-1) wherein R' is H. The reaction conditions for the cleavage are known in the art. Typically, the benzyl group is removed by a hydrogenation reaction in the presence of a suitable Pd catalyst, such as Pd on carbon or palladium hydroxide.

R' can also be a protective group. The protective group may be removed to yield a compound (I'-1) wherein R' is H. Suitable protective groups are known in the art and are, for example, selected from tert-butoxycarbonyl (boc), benzyloxycarbonyl (Cbz), 9-fluorenylmethoxycarbonyl (Fmoc), triphenylmethyl (Trt) and nitrobenzenesulfonyl (Nps). A preferred protective group is boc. The protective groups can be removed by known methods, such as treatment of the protected amine with an acid, e.g. halogen acid, such as HCl or HBr, or trifluoroacetic acid, or by hydrogenation, optionally in the presence of a Pd catalyst.

The resulting compound, wherein R' is H, can then be reacted, in a known manner, in the sense of an alkylation, with a compound R¹-X. In this compound, R¹ is C₁-C₄-alkyl, C₃-C₆-cycloalkyl, C₁-C₄-haloalkyl, C₁-C₄-alkoxy-C₁-C₄-alkyl or C₃-C₆-cycloalkyl-C₁-C₄-alkyl and X is a nucleophilically displaceable leaving group, e.g. halogen, trifluoroacetate, alkylsulfonate, arylsulfonate, alkyl sulfate and the like. The reaction 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.

The alkylation can also be achieved, in the sense of a reductive amination, by reacting the compound (I'-1), wherein $R' = H$, 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.

In case R' is hydrogen, the resulting sulfonamide (I'-1) can further be reacted with an acyl halide to obtain a compound of the formula I wherein R^1 is C_1 - C_3 -alkylcarbonyl. The carbonyl group in these compounds can be reduced with diborane to obtain compounds of the general formula I, wherein R^1 is C_2 - C_4 -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 Jerry 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).

20 Route B

In route B, the bromo substituted compound (II-2) is reacted with an appropriate sulfonamide $ArSO_2NHR^5$ to give the sulfonamide (I'-1). The reaction is generally carried out under activating conditions, e.g. under microwave conditions. Pd, especially Pd(0), or Cu catalysts may also be used for coupling (see, e.g. Org. Lett. 2000, 2, 1101; J. Am. Chem. Soc. 2002, 124, 6043; Org. Lett. 2003, 5, 4373; Tetrahedron Lett. 2003, 44, 3385). Examples for suitable Pd (0) catalysts are tetrakis(triphenylphosphine)-palladium(0) and $Pd_2(dba)_3$ (tris(dibenzylideneacetone) -dipalladium(0)), which are customarily used in the presence of a tri(substituted)phosphine, e.g. a triarylphosphine such as triphenylphosphine, tritolylphosphine or xantphos, tri(cyclo)alkylphosphine such as tris-n-butylphosphine, tris(tert.-butyl)phosphine or tris(cyclohexylphosphine). This route is especially useful in cases where the corresponding sulfonyl chloride is not available.

Alternatively, the bromo substituent may be replaced by an amino substituent, e.g. by reacting with a benzophenone imine or with lithium bis(trimethylsilyl)amide in the presence of a palladium(0) compound such as 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, e.g., J. Org. Chem., 68 (1993) pp 8274-8276, or J. Org. Chem. 2000, 65, 2612. The resulting amino compound may then be subjected to the sulfonation reaction of route A.

5 Route C

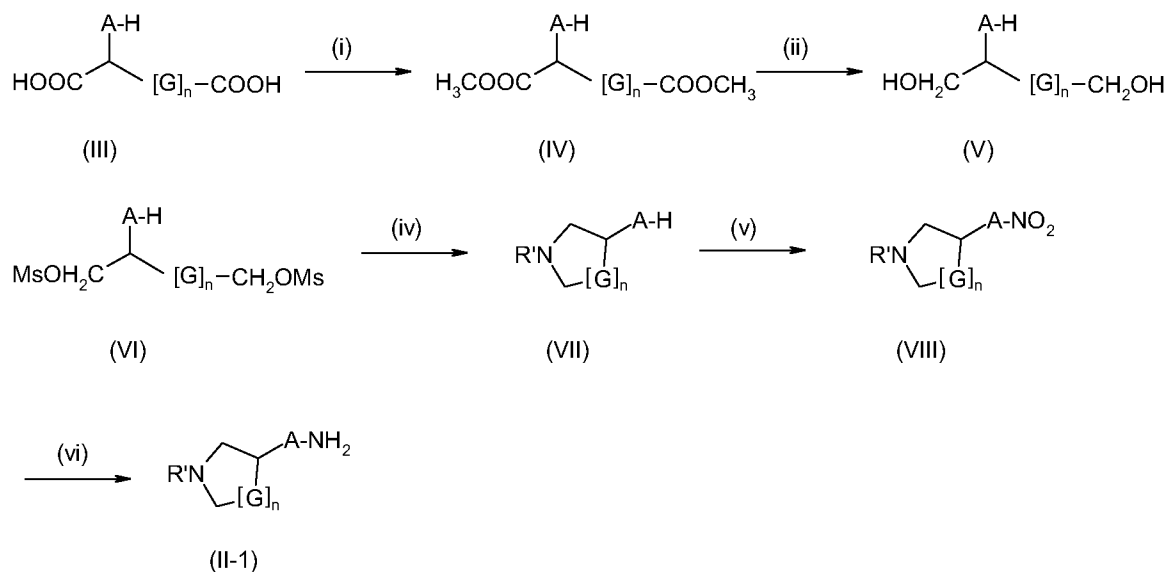
In route C, compound (II-3) is reacted with a mercapto compound HS-Ar in the presence of a base, such as sodium hydride or sodium alkoxide or with an alkali metal salt thereof thereby yielding a thioether compound. The thioether moiety is then oxidized to
10 a sulfone moiety, e.g. by oxone, to yield the sulfone (I'-2).

The substituent Ar can be varied by either using different sulfonyl chlorides or by modifying the substituents of the group Ar after the formation of the sulfonamide (I'-1) or the sulfone (I'-2) by known methods. For example, a bromine substituent of the Ar group
15 may be replaced by an N-bound pyrrolidinyl group according to the procedure described in Tetrahedron Asym. 1999, 10, 1831. This Pd-mediated coupling is generally applicable to all nitrogen-containing heterocycles such as azetidiny, pyrazolidiny, imidazolidiny, piperidiny, piperaziny, morpholiny and the like. The reaction is also applicable to heterocyclic compounds carrying one or more substituents such as halogen,
20 alkyl or fluorinated alkyl. A bromine substituent of the Ar group may further be replaced by an isopropenyl group according to a Stille coupling where the bromo compound is reacted with an alkenyl tributyl stannate in the presence of an appropriate Pd coupling catalyst, e.g. tetrakis(triphenylphosphine) palladium(0) (see, e.g. Tetrahedron, 2003, 59(34), 6545 and Bioorg. Med. Chem. 1999, 7(5), 665). The isopropenyl group may
25 then be converted into the isopropyl group by known hydrogenation methods.

Compounds of formula (II) (II-1, II-2 and II-3) can be synthesized by as shown below.

1. Synthesis of compounds (II-1)

Scheme 2



In scheme 2, A, G, n and R' are as defined above.

- 5 The conversion of the acid (III) into its methyl ester (IV) is performed by standard techniques, e.g. as described in Jerry March, *Advanced Organic Chemistry*, John Wiley, 3rd edition, page 348ff. For instance, the acid is transformed into the corresponding acid chloride, e.g. by reacting it with SOCl_2 . The chloride is then converted into the ester by reaction with methanol.

10

- The reduction in step (ii) is suitably carried out under standard conditions for the conversion of carboxylic esters into alcohols. Appropriate reaction conditions and reducing agents are described, e.g. in Jerry March, *Advanced Organic Chemistry*, John Wiley, 3rd edition, page 1093ff. Typical reducing agents are metal hydrides and complex hydrides. Examples of suitable metal hydrides include BH_3 , 9-BBN, AlH_3 and $\text{AlH}(\text{i-Bu})_2$ (DIBAL-H), suitably in the presence of complexing solvents, such as tetrahydrofuran and diethylether. Complex hydrides are e.g. NaBH_4 , LiAlH_4 and $\text{LiAlH}(\text{OR})_3$, where R is C_1 - C_4 -alkyl, such as methyl, ethyl, isobutyl or tert-butyl. A preferred reducing agent is LiAlH_4 . The reduction is suitably carried out in complexing solvents, such as open-chain and cyclic ethers, e.g. tetrahydrofuran, diethyl ether, dipropyl ether, diisopropyl ether, dibutyl ether and methylbutyl ether. A preferred solvent is tetrahydrofuran.
- 15
- 20

- In the mesylation step (iii), the alcohol functionality is converted into a better leaving group. The mesylation is performed under standard conditions, e.g. by reacting the alcohol with methanesulfonyl chloride in the presence of a base. Suitable bases are, among others, alkyl amines, such as diethyl amine, triethyl amine and ethyldiisopropyl amine. In this step, other functionalities representing good leaving groups, such as
- 25

trifluoroacetate, other alkylsulfonates, arylsulfonates, e.g. tosylates, alkyl sulfates and the like tosylate, may be introduced instead of the methansulfonyl group.

5 In the cyclisation step (iv), compound (VI) or a suitable derivative thereof is reacted with a primary amine $\text{NH}_2\text{R}'$. In case the primary amine is a liquid, it may also be used as solvent, no further solvent being necessary. If the amine is viscous or a solid, the reaction is advantageously carried out in a suitable solvent.

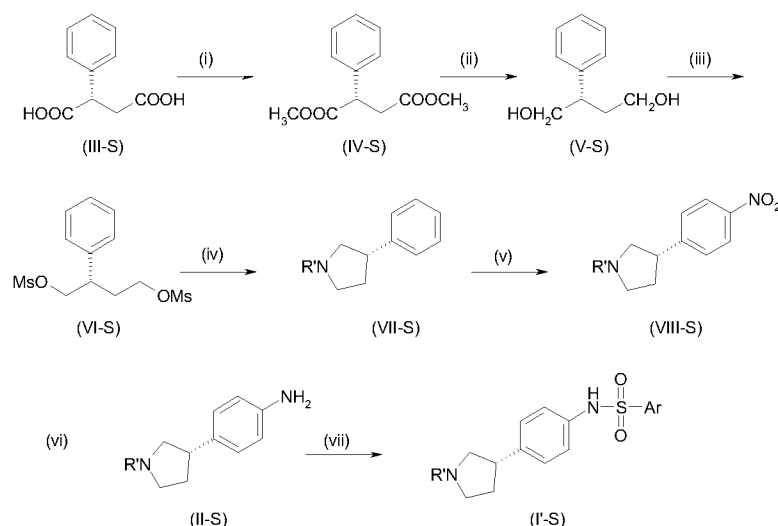
10 The reaction of step (v) takes place under the reaction conditions which are customary for a nitration reaction on an aromatic radical and which are described, for example, in Jerry March, *Advanced Organic Chemistry*, John Wiley, 3rd edition, page 468ff, Tetrahedron 1999, 55(33), pp. 10243-10252, J. Med. Chem. 1997, 40(22), pp. 3679-3686 and Synthetic Communications, 1993, 23(5), pp. 591-599. For example, compound (VII) is reacted with concentrated nitric acid or a nitrate, such as potassium or sodium
15 nitrate, in the presence of concentrated sulfuric acid. The resulting product (VIII) may in the form of different regioisomers (e.g. ortho, meta or para, if A is phenyl or a 6-membered hetaryl. In the case of A being phenyl or a 6-membered hetaryl, the para-nitro compound generally predominates. However, some ortho product may also be obtained, whereas the meta product is not produced at all or only in neglectable
20 amounts. By separating ortho and para products, compounds of formula I, wherein A is 1,4-bound phenyl, are accessible via the reaction path shown in scheme 2.

In step (vi), the nitro group in (VIII) is reduced to an NH_2 group. Subsequently, the NH_2 group can be converted into a $-\text{NR}^5$ group, in which R^5 has the meanings different
25 from hydrogen which are specified for R^5 . The reaction conditions which are required for step (vi) correspond to the customary conditions for reducing aromatic nitro groups which have been described 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 react-
30 ing 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.
35 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 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
40 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 nitro compound, 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 VII with tin(II) chloride is preferably carried out in an inert organic solvent, preferably an alcohol such as methanol, ethanol, isopropanol or butanol.

For compounds, wherein n is 1 and A is phenylene (i.e. (I) is N-(pyrrolidin-3-yl)-phenyl-sulfonamide), starting compound (III) is e.g. commercially available (S) or (R) phenylsuccinic acid or a racemic mixture thereof. By starting from enantiomerically pure (S)- or (R)-compound (III), pure (S)- or (R) may be obtained:

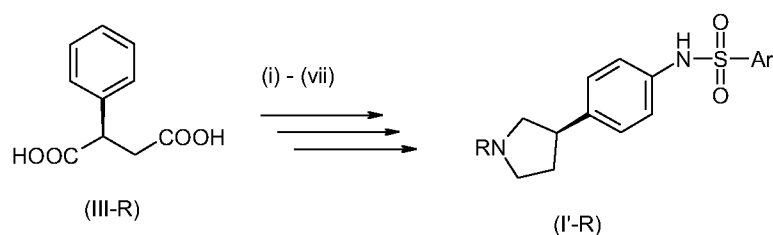
a) (S) isomer



In step (i), commercially available (S)-phenylsuccinic acid (II-S) is converted into the methyl ester (III); this is reduced to the alcohol (IV) which is reacted with methanesulfonylchloride. Cyclisation with a primary amine gives the phenyl pyrrolidine (VI). The phenyl group is first nitrated, then the nitro group is reduced to an amino function which is reacted with a sulfonyl chloride to give the desired sulfonyl amide (I'-S).

a) (R) isomer

The (R)-isomer can be obtained in an analogous way starting from commercially available (R)-phenylsuccinic acid (III-R):



5 c) Isomeric mixtures

Isomeric mixtures of compound I'-S and I'-R can be obtained by starting from racemic III or from a mixture of III-S and III-R.

- 10 The skilled person will appreciate that the synthesis described in scheme 2 is also suitable for the preparation of compounds (II) and consequently for compounds (I), wherein R^2 , R^3 and R^4 are different from H, e.g. by starting from the correspondingly substituted compound (III). The same applies to the synthesis of enantiomerically pure (I) which can be synthesized by starting from the corresponding enantiomer (III).

15

2. Synthesis of compounds (II-2)

- Compounds of formula (II-2) can be synthesized by carrying out in step (v) of scheme 2 a halogenation instead of a nitration. Halogenation reactions of aryl and hetaryl groups are widespread standard methods and are, e.g., discussed in Jerry March, Advanced Organic Chemistry, John Wiley, 3rd edition page 476 ff.
- 20

3. Synthesis of compounds (II-3)

- 25 The synthesis of these compounds also belongs to standard reaction methods and can be performed by monohalogenating the methyl group of a methyl-substituted aryl or hetaryl compound.

4. Synthesis of enantiomerically pure compounds I

30

- In addition to the method described in item 1., enantiomerically pure compounds (I) can also be obtained by applying standard resolution techniques to suitable precursors thereof. For instance, compound VIII (see scheme 2 above) or compounds (II-2) or (II-3) (see scheme 1 above), wherein R' is a suitable protective group, such as benzyl, may be reacted with tartaric acid or a derivative thereof (e.g. diethyltartrate, dipropyltartrate, diisopropyltartrate, etc.) to afford two diastomeric salts. These can be sepa-
- 35

rated in a customary manner, e.g. by extraction or chromatographic methods or preferably by fractionated crystallization. The thus separated diastereomeric salts are then converted into enantiomerically pure compounds VIII, II-2 or II-3 by reacting the salts with a suitable base to afford the S- or R-enantiomers of compounds VIII, II-2 or II-3.

- 5 Suitable bases are, e.g., alkali metal hydroxides, such as potassium hydroxide and sodium hydroxide, alkaline earth metal hydroxides, such as magnesium hydroxide and calcium hydroxide, alkali metal carbonates, such as sodium carbonate and potassium carbonate, alkaline earth metal carbonates, such as magnesium carbonate and calcium carbonate, alkali metal oxides such as sodium oxide and potassium oxide, and
10 alkaline earth metal oxides, such as magnesium oxide and calcium oxide; organic bases, such as alcoholates, e.g. sodium methanolate, sodium ethanolate or sodium-tert-butanolate, amines, such as dimethylamine, trimethylamine, diethylamine, triethylamine, dipropylamine, tripropylamine, diisopropylamine, diisopropylethylamine and the like, and nitrogen-containing basic heterocyclic compounds, such as pyridine, picoline
15 und lutidine.

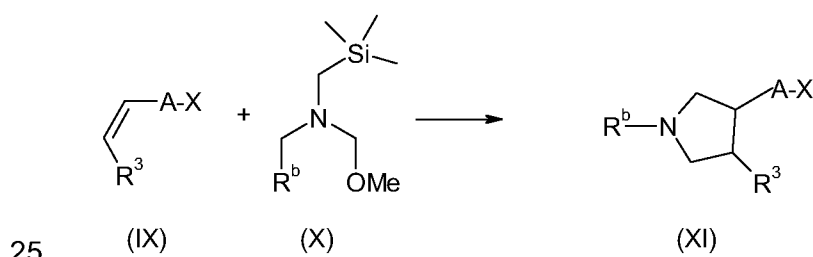
5. Specific syntheses

5.1 Synthesis of compounds, wherein n is 1 (pyrrolidinyll sulfone derivatives)

20

5.1.1

Scheme 3:



In scheme 3, A and R^3 are as defined above.

- 30 The pyrrolidine ring is also available by a [3+2] dipolar cycloaddition of a non-stabilized azomethine ylid to a 1-alkenylaryl or hetaryl derivative (IX) (e.g. a vinyl benzene, $R^3 = H$). This procedure is generally described in J. Org. Chem 1987, 52, 235. The precursor of the ylid, the amine $N(CH_2R^b)(CH_2SiMe_3)(CH_2OCH_3)$ (X), is commercially available or can be synthesized from $NH_2(CH_2R^b)$, Me_3SiCH_2Cl and $HCHO$ in the presence
35 of methanol.

The 1-alkenyl-(hetero)aromatic compound (IX) can be synthesized e.g. by a Stille coupling of a halogeno benzene, e.g. a bromo benzene, with the corresponding alkenyl tributyl stannate, such as vinyl or isobutenyl tributyl stannate, in the presence of an appropriate Pd coupling catalyst, e.g. tetrakis(triphenylphosphine) palladium(0) (see, e.g. 5 Tetrahedron, 2003, 59(34), 6545 and Bioorg. Med. Chem. 1999, 7(5), 665). By choosing a special Stille isomer (e.g. cis- or trans-isobutenyl tributyl stannate), the corresponding cis- or trans alkyl phenyl pyrrolidine can be prepared selectively.

10 Alternatively, the 1-alkenyl-(hetero)aromatic compound (IX) can be synthesized by a Wittig reaction of aryl aldehyde with a Wittig reagent such as $\text{PPh}_3=\text{CHR}$ (R is H, or C_1 - C_3 -alkyl). Conditions for the Wittig reaction are well known in the art and are, e.g. discussed in Jerry March, Advanced Organic Chemistry, John Wiley, 3rd edition, page 845 ff.

15 Advantageously, the 1-(hetero)alkenyl-aromatic compound (IX) further carries a nitro group or another halogeno substituent ($\text{X} = \text{NO}_2$ or halogen). In this case, the subsequent reaction steps can be carried out as outlined in route A or B. If $\text{X} = \text{H}$, the A ring may be first nitrated as described in scheme 2, step (v) and then subjected to the reaction of scheme 2, step (vi) and scheme 1, route A; or ring A may be halogenated and 20 then subjected to the procedure of route B.

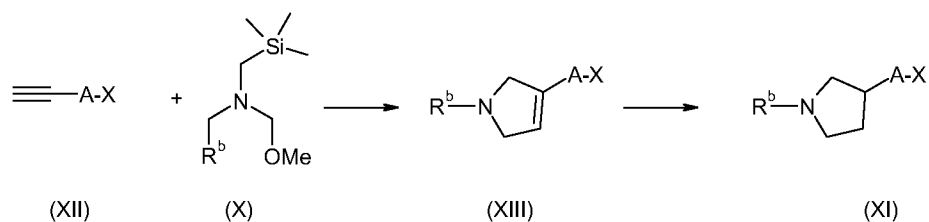
The group CH_2R^b of the precursor amine advantageously corresponds either to the desired group R^1 of the final compound I or is alternatively a cleavable group, such as 25 benzyl, which can be removed to give the N-unsubstituted pyrrolidine. The latter can subsequently be functionalized as described above (see route A).

The synthesis of hetarylpyrrolidines is e.g. described in Chem. Pharm. Bull., 1985, 33, 2762-66; J. Heterocyclic Chemistry, 1996, 1995-2005; J. Heterocyclic Chemistry, 2001, 30 38, 1039-1044; Tetrahedron Letters, 1992, 33, 44, 6607-10; Heterocycles, 1998, 48, 12, 2535-2541 for A being pyridylene. The synthesis of vinyl-substituted thiophene and thiazol is e.g. described in Bioorg. Med. Chem. 1999, 7(5), 665.

5.1.2

35

Scheme 4:



- Phenylpyrrolidines can also be prepared by a [3+2] dipolar cycloaddition of a non-stabilized azomethine ylid to a 1-alkynylbenzene (XII) (see, e.g., Tetrahedron 1996, 52, 59). The resulting pyrroline (XIII) or the final product (I') is then hydrogenated to the corresponding pyrrolidine (XI). If the hydrogenation is carried out under chiral conditions, e.g. by using chiral catalysts, the enantiomerically pure phenylpyrrolidine compounds can be obtained. Chiral hydrogenation catalysts are well known in the art.
- The subsequent conversion to the desired sulfonamide can be carried out as described in route A or B.

5.1.3

- Alternatively, hetarylpyrrolidinyl compounds can be prepared from hetaryl halides which are subjected to a Pd-mediated cross coupling with an organozinc pyrrolidine compound. This process is described in further detail below in route F. In this alternative, too, the hetaryl halide advantageously carries a nitro group. In this case, the conversion to the desired sulfonamides can be carried out as described in route A. Alternatively, the hetaryl halide carries a halogen atom. In this case, the conversion to the desired sulfonamides can be achieved as described in route B.

5.1.4

- Compounds I, wherein n is 1, G is CH₂, A is 1,3-bound arylene or hetarylene and E is NH, can be prepared in a similar way compared to the 1,4-bound compound from a 3-aminoaryl or hetaryl-pyrrolidine which is reacted with an appropriate sulfonyl chloride. Advantageously, the N-atom of the pyrrolidine ring is protected by a urathane-based protective group, like carbomethoxy (-COOCH₃), benzyloxycarbonyl (cbz) and tert-butyloxycarbonyl (boc). This group may be replaced by the desired substituent R¹ by treating the compound with an acid, such as hydrochloric acid, thus removing the acid group, and then introducing the desired substituent as described in route A.

- The 3-aminoaryl or hetaryl-pyrrolidine may be prepared by way of a Heck reaction where a protected pyrroline is reacted with 1-iodo-3-nitrobenzene or the corresponding pyridine (2-iodo-4-nitropyridine or 3-iodo-5-nitropyridine) under typical Heck conditions.

Catalytic hydrogenation of the pyrroline double bond and reduction of the nitro group according to the procedure described in scheme 2 yields the desired product.

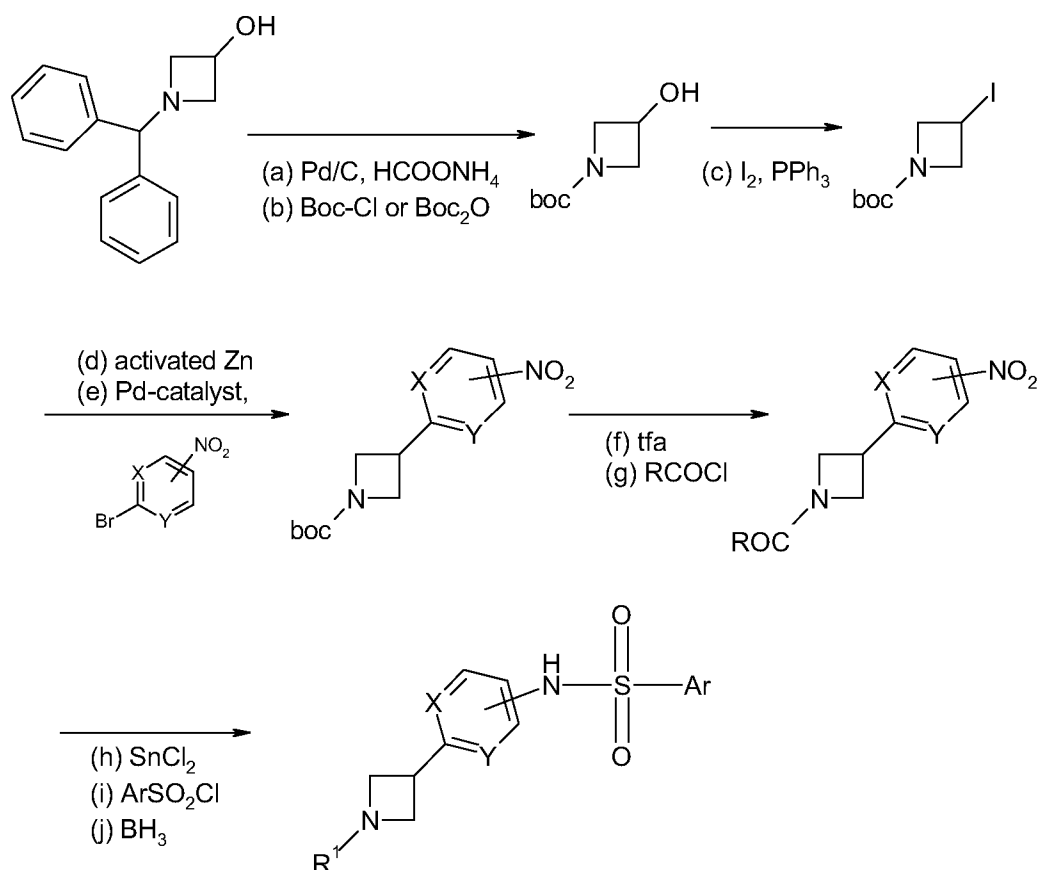
- 5 The N-protected pyrroline can be obtained by reacting commercially available pyrroline with the desired protective group, e.g. with chloromethylfumarate, benzylchloride, Cbz-anhydride or Boc-anhydride.

10 The pyrroline may be synthesized in a metathesis reaction of N-protected diallylamine in the presence of a metathesis catalyst, e.g. a Grubbs catalyst.

5.2 Synthesis of N-(azetidin-3-yl)-sulfonamides

Compounds I, wherein n is 0 (azetidine compounds) can be synthesized as follows:

15 Scheme 5:



In scheme 5, Ar and R¹ are as defined above. X and Y are, independently of each other, CH or N.

Starting from 1-benzhydryl-azetidin-3-ol, Pd-mediated deprotection of the amine (Tetrahedron 2002, 58, 9865-9870), carbamate formation and subsequent halogenation generate an intermediate that undergoes Zn insertion (Tetrahedron 1987, 43, 2203-2212; J. Org. Chem. 1988, 53, 2390-2392). The thus obtained organozinc species can
5 react with an appropriate 2-halo-nitro-ring (Synlett 1998, 4, 379-380; J. Am. Chem. Soc. 2003, 125, 12527-12530) to give the nitro-aryl-azetidine core. If one utilizes a 2-halo-halo-ring, there is also the possibility to realize the direct coupling between the aryl-azetidine halide and the appropriate sulfonamides (Org. Lett. 2000, 2, 1101-1104; J. Am. Chem. Soc. 2002, 124, 6043-6048; Org. Lett. 2003, 5, 4373-4376; Tetrahedron
10 Lett. 2003, 44, 3385-3386). The amine may be regenerated by cleavage of the carbamate (e.g. with trifluoroacetic acid in the case of a Boc carbamate) and subsequently converted into an amide by reaction with the appropriate acyl chloride. The nitro group can be reduced to the amine via tin chloride or catalytic hydrogenation (e.g. Pd-C) and then converted to the desired sulfonamide by reaction with the appropriate sulfonyl
15 chloride in the presence of a base such as pyridine. Ultimate reduction of the amide via hydroboration furnishes the final compounds.

Of course, the reaction also applies to compounds wherein the (hetero)aromatic ring bound to the azetidine group is a 5-membered heterocyclic radical, e.g. thienyl.

20

5.3 Synthesis of N-(piperidin-3-yl)-sulfonamides

Further to the above-described syntheses (routes A, B and C), compounds I, wherein n is 2 and E is NR⁵ (piperidin-3-yl sulfonamides) may be prepared by starting from commercially available 3-aryl or 3-hetaryl piperidines. These starting compounds may then
25 be converted into the amino-substituted or halogenated derivative and then be subjected to the synthetic path of route A or B.

A skilled person will readily appreciate that compounds of the formula I can also be
30 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 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
35 a palladium catalyst in terms of a Buchwald-Hartwig reaction.

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 solvent employed. Alternatively, the activation energy which is required for the reaction
40 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 Loupy (Ed.), Wiley-VCH 2002.

5

The sulfonylchlorides $\text{Cl-SO}_2\text{-Ar}$ 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 $\text{Cl-SO}_2\text{-Ar}$, 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 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, phosphorous 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-NH_2 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 $\text{C}_6\text{H}_5\text{-CH}_2\text{-S-Ar}$ 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.

30 The acid addition salts of compounds I 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.

35

The compounds according to the invention of the formula I have a surprisingly high affinity for 5HT_6 receptors. Compounds of formula I, wherein A is 1,3-phenylene, 2,4-pyridylene or 3,5-pyridylene and in particular 1,3-phenylene, are furthermore highly selective dopamine 5HT_6 receptor ligands which, because of their low affinity for other receptors such as D_1 receptors, D_5 receptors, D_4 receptors, $\alpha 1$ -adrenergic and/or $\alpha 2$ -

40

adrenergic receptors, muscarinic receptors, histamine receptors, opiate receptors and, in particular, dopamine D₂ receptors, give rise to fewer side-effects than other, less selective 5HT₆ ligands. Compounds of formula I, wherein A is 1,4-phenylene, show a high affinity for 5HT₆ receptors and optionally also for dopamine D₃ receptors. Because
5 of their low affinity for other receptors such as D₁ receptors, D₅ receptors, D₄ receptors, α 1-adrenergic and/or α 2-adrenergic receptors, muscarinic receptors, histamine receptors, opiate receptors and, in particular, dopamine D₂ receptors, they give rise to fewer side-effects than other, less selective compounds, such as classic neuroleptics, which are D₂ receptor antagonists.

10

The compound of the invention can be a dopamine 5HT₆ receptor agonist, including partial agonistic activity, or a dopamine 5HT₆ receptor antagonist, including inverse agonist activity.

15 The high affinity of the compounds according to the invention for 5HT₆ receptors is reflected in very low in-vitro receptor binding constants ($K_i(5HT_6)$ 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 ³H-LSD can, for example, be used in receptor binding studies for determining binding affinities to 5-HT₆ receptors and [¹²⁵I]-iodosulpride for determining
20 binding affinities to dopamine D₃ receptors.

The D₃/D₂ selectivity of the compounds according to the invention which also have a high affinity for dopamine D₃ receptors, i.e. the ratio $K_i(D_2)/K_i(D_3)$ of the receptor binding constants, is as a rule at least 25, preferably at least 50, even better at least 100. The
25 displacement of [³H]SCH23390 or [¹²⁵I] spiperone can be used, for example, for carrying out receptor binding studies on D₁, D₂ and D₄ receptors.

Because of their binding profile, the compounds can be used for treating diseases which respond to 5HT₆ receptor ligands and optionally to dopamine D₃ receptor ligands
30 (or which are susceptible to treatment with a 5HT₆ receptor ligand, and optionally with a dopamine D₃ receptor ligand), i.e. they are effective for treating those medical disorders or diseases in which exerting an influence on (modulating) the 5HT₆ receptors, and optionally on (modulating) the dopamine D₃ receptors, leads to an improvement in the clinical picture or to the disease being cured. Examples of these diseases are dis-
35 orders or diseases of the central nervous system.

Disorders or diseases of the central nervous system are understood as meaning disorders which affect the spinal cord and, in particular, the brain. Within the meaning of the invention, the term "disorder" denotes disturbances and/or anomalies which are as
40 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 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 disorders which respond to a modulation of the 5HT₆ receptor. They include cognitive dysfunctions, such as a deficit in memory, cognition and learning, in particular associated with Alzheimer's disease, age-related cognitive decline and mild cognitive impairment, attention deficit disorder/hyperactivity syndrome, personality disorders, such as schizophrenia, in particular cognitive deficits related with schizophrenia, affective disorders such as depression, anxiety and obsessive compulsive disorders, motion or motor disorders such as Parkinson's disease and epilepsy, migraine, sleep disorders (including disturbances of the Circadian rhythm), feeding disorders, such as anorexia and bulimia, certain gastrointestinal disorders such as Irritable Bowl Syndrome, diseases associated with neurodegeneration, such as stroke, spinal or head trauma and head injuries, such as hydrocephalus, drug addiction and obesity.

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.

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.

Compounds of formula I having a high affinity for the 5HT₆ receptor as well as for the dopamine D₃ receptor can be advantageously used for treating disorders, preferably

CNS disorders, having both a dopaminergic and a serotonergic impact. While the 5HT₆ receptor is more related to cognitive functions, the dopamine D₃ receptor is associated with positive symptoms, such as delusion, hallucination, disorganized thinking, disorganized speaking, disorganized, agitated or catatonic behaviour, and negative
5 symptoms, such as depletion of feelings, impairment of the language, loss of motivation, loss of vitality, attention deficits and social retreat. Thus, compounds of formula I having a high affinity for the 5HT₆ receptor as well as for the dopamine D₃ receptor can be advantageously used for treating disorders, such as Alzheimer's disease and in particular schizophrenia, which are characterized by cognitive dysfunctions as well as
10 by positive and negative symptoms.

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 5HT₆ receptors.

15 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 5HT₆ receptors.

20 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
25 which already exist.

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,
30 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, distracted-
35 ness, 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,
40

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.

- 5 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
10 treatment, for example within the context of a maintenance therapy.

The compounds according to the invention are preferentially suitable for treating diseases of the central nervous system, more preferably for treating cognitive dysfunctions and in particular, for treating cognitive dysfunctions associated with schizophrenia
15 or Alzheimer's disease.

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
20 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
25 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
30 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
35 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,
40 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, suppositories or vaginal medicinal forms, semisolid medicinal forms, such as ointments, 5 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. Implanted release devices can also be used for administering inhibitors according to the 10 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 or liquid materials which serve as vehicles, carriers or medium for the active com- 15 pound.

Suitable excipients are listed in the specialist medicinal monographs. In addition, the formulations can comprise pharmaceutically acceptable carriers or customary auxiliary substances, such as glidants; wetting agents; emulsifying and suspending agents; pre- 20 servatives; 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 ointments, creams or oils; silicone derivatives; spreading auxiliaries; stabilizers; steri- 25 lants; 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, Kosmetik und angrenzende Gebiete [Encyclopedia of auxiliary substances for pharmacy, 30 cosmetics and related fields], 4th edition, Aulendorf: ECV-Editio-Kantor-Verlag, 1996.

It has further been found that disorders having both a dopaminergic and a serotonergic impact can also be treated by the combined use of a dopamine D₃ receptor ligand and a 5HT₆ receptor ligand. This combination surprisingly shows no adverse effects. 35

Accordingly, a further aspect of the invention relates to a pharmaceutical composition comprising at least one compound having an affinity for the dopamine D₃ receptor and at least one compound having an affinity for the 5HT₆ receptor and optionally at least one physiologically acceptable carrier and/or auxiliary substance. 40

The invention also relates to the use of at least one compound having an affinity for the dopamine D₃ receptor together with at least one compound having an affinity for the 5HT₆ receptor or of the pharmaceutical composition as defined above for preparing a medicament for the treatment of a disease of the central nervous system.

5

The compounds to be used according to the invention or in the above composition having an affinity for the dopamine D₃ receptor preferably have no or no significant activity for the 5HT₆ receptors and vice versa. Preferably, the compound having an affinity for the dopamine D₃ receptor has a binding constant K_i to the dopamine D₃ receptor of at most 150 nM and the compound having an affinity for the 5HT₆ receptor has a binding constant K_i to the 5HT₆ receptor of at most 150 nM. More preferably, the compound having an affinity for the dopamine D₃ receptor has a selectivity for the D₃ dopamine receptor versus the 5HT₆ receptor K_i(5HT₆)/K_i(D₃) of at least 10, more preferably at least 25, and in particular at least 50 and the compound having an affinity for the 5HT₆ dopamine receptor has a selectivity for the 5HT₆ receptor versus the dopamine D₃ receptor K_i(D₃)/K_i(5HT₆) of at least 10, more preferably at least 25, and in particular at least 50.

Compounds having an affinity for the dopamine D₃ receptor are widely known and are for example described in following publications:

WO 2006/058753, WO 2006/040176, WO 2006/040177, WO 2006/040178, WO 2006/040179, WO 2006/0040180, WO 2006/008592, WO 2006/015842, WO 2005/058328, WO 2004/89905, WO 2004/108706, WO 2004/080981, WO 2004/069830, WO 01/72306, WO 00/67847, WO 00/42038, WO 99/09015, WO 99/02503, WO 97/25324, WO 96/002519, the contents of which are hereby fully incorporated by reference.

Preferred compounds having an affinity for the dopamine D₃ receptor are dopamine D₃ receptor antagonists.

30

Compounds having an affinity for the dopamine 5HT₆ receptor are also well known and are for example described in following publications:

WO 2006/081322, WO 2005/040124, WO 2003/080580, WO 2002/032863, WO 00/05225, WO 98/27081 and S.-H. Zhao et al., Bioorganic and Medicinal Chemistry Letters 2007, the contents of which are hereby fully incorporated by reference.

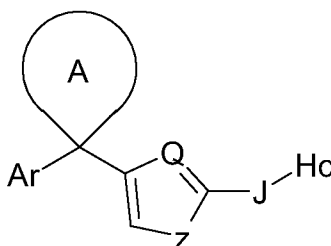
35

Preferred compounds having an affinity for the dopamine 5HT₆ receptor are dopamine 5HT₆ receptor antagonists.

Surprisingly, the combination of compound having an affinity for the dopamine D₃ receptor and at least one compound having an affinity for the 5HT₆ receptor does not have any adverse effects. This can be proved by the assay (microdialysis study) described in the examples. In particular, the binding affinity to the one or other receptor is not reduced.

It has further been found that treating disorders which have both a dopaminergic and a serotonergic impact can also be effected by using compounds which have an affinity for both the D₃ dopamine receptor and the 5HT₆ receptor.

Accordingly, the invention further relates to the use of at least one compound which has an affinity for both the D₃ dopamine receptor and the 5HT₆ receptor for preparing a medicament for the treatment of a disease of the central nervous system, excepting compounds of the formula



15

where

Ar is a substituted or unsubstituted aryl or hetaryl ring;

A is a 3- to 7-membered substituted or unsubstituted cycloalkyl or heterocyclyl ring;

Hc is a substituted or unsubstituted nitrogen-containing heterocyclyl or heteroaryl ring;

20

Q is C-K or N, where K is H, lower alkyl, halogen or cyano;

Z is O, S or NR, where R is H or lower alkyl;

J is a chain havin from 0 to 8 units selected from unsubstituted or substituted methylene; NR⁸, O and S, where R⁸ is H or unsubstituted or substituted lower alkyl,

25

cycloalkyl, heterocyclyl, aralkyl, heteroaralkyl, aryl or hetaryl.

Preferably, the compound has a combined dopamine D₃/5HT₆ antagonistic activity.

The invention also relates to the use of at least one compound which is a D₃ dopamine receptor antagonist and also has an affinity for the 5HT₆ receptor for preparing a medicament for the treatment of a disease of the central nervous system.

30

Preferably, the compound has a 5HT₆ receptor antagonistic activity. Preferably, the compound has a combined dopamine D₃/5HT₆ antagonistic activity.

Compounds having these "mixed" affinities are for example the compounds described
5 in WO 2006/040182.

Among the compounds of the formula I described in WO 2006/040182, preference is given to compounds wherein

- R¹ is H, n is 1, A is optionally substituted 1,4-phenylene, E is NH and Ar is phenyl
10 carrying in the 4-position (relative to the 1-position of the SO₂ group) a substituent R^a and optionally 1 or 2 further substituents R^a, where the substituent R^a bound in the 4-position is preferably a radical R^{ab} and is in particular selected from isopropyl or fluorinated isopropyl, such as 1-methyl-2-fluoro-1-ethyl, 1-methyl-2,2-difluoro-1-ethyl or 1-methyl-2,2,2-trifluoro-1-ethyl; or
- 15 - R¹ is not H and is in particular n-propyl, n is 0, A is optionally substituted 1,4-phenylene and Ar is phenyl carrying in the 4-position (relative to the 1-position of the SO₂ group) a substituent R^a and optionally 1 or 2 further substituents R^a; or
- R¹ is not H and is in particular n-propyl, n is 1, A is optionally substituted 1,2-phenylene and Ar is phenyl carrying at least one substituent R^a.

20

More preferred compounds are those described as compounds I herein, preference being given to the compounds described herein as preferred.

- In particular, in the compounds of the invention having a mixed activity, R¹ is not H.
25 Preferably, R¹ is selected from C₁-C₄-alkyl, in particular methyl, ethyl or particularly propyl, fluorinated C₁-C₄-alkyl, in particular 3-fluoropropyl or 2-fluoropropyl, C₃-C₄-alkenyl, in particular allyl, cyclopropylmethyl or benzyl. Particularly preferably R¹ is propyl.

- 30 G is preferably CH₂ and n is preferably 1.

A is preferably 1,4-phenylene, in particular unsubstituted 1,4-phenylene.

E is preferably NH.

35

Ar is preferably a group (A) or (F).

R^a is preferably halogen, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl, C₁-C₄-alkoxy, fluorinated C₁-C₄-alkoxy or a 5- or 6-membered unsaturated or saturated heterocyclic ring. R^b and R^c are preferably selected from H, halogen and C₁-C₄-haloalkoxy.

- 5 R^d is preferably halogen, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl or a 5- or 6-membered heteroaryl ring which is unsubstituted or carries one substituent selected from C₁-C₄-alkyl and fluorinated C₁-C₄-alkyl. Preferred 6-membered hetaryl rings contain one or two nitrogen atoms (particularly preferred being pyridyl and pyrimidyl) and in particular one nitrogen atom. Preferred 5-membered hetaryl rings contain one nitrogen atom and
10 optionally one or two further heteroatoms selected from N, O and S.

k is preferably 0 or in particular 1.

- The compound having a "mixed" affinity for both the dopamine D₃ receptor and the
15 5HT₆ receptor preferably has a binding constant K_i to the dopamine D₃ receptor of at most 150 nM and to the 5HT₆ receptor of at most 150 nM. More preferably, the compound having an affinity for the dopamine D₃ receptor and the 5HT₆ receptor has a binding constant K_i to the dopamine D₃ receptor of at most 100 nM and to the 5HT₆ receptor of at most 100 nM. Even more preferably, the compound having an affinity for
20 the dopamine D₃ receptor and the 5HT₆ receptor has a binding constant K_i to the dopamine D₃ receptor of at most 50 nM and to the 5HT₆ receptor of at most 50 nM.

- Disorders having both a dopaminergic and a serotonergic impact are disorders which respond to the modulation of the dopamine D₃ receptor and the 5HT₆ receptor. Disorders having both a dopaminergic and a serotonergic impact are in particular cognitive
25 dysfunctions and specifically cognitive dysfunctions associated with Alzheimer's disease and schizophrenia.

- 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 the intermediates

a. Preparation of sulfonyl chlorides

10

a.1 3-Bromo-4-trifluoromethoxy-benzenesulfonyl chloride

15

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.

20

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

b. Preparation of 3-(3-aminophenyl)-pyrrolidines

25

b.1 1-(Methoxycarbonyl)-3-(3-aminophenyl)-pyrrolidine

b.1.1 1-(Methoxycarbonyl)-pyrroline

30

In a 5 l flask fitted with a mechanical stirrer and a thermocouple, were charged 500g of powdered potassium carbonate, 2.5 l of dichloromethane, and stirring was started. The resulting suspension was cooled to 0 °C. 300 g of diallylamine, were charged slowly. There was a slight exotherm. Subsequently, 292.95 g of methylchloroformate in 500 ml of CH₂Cl₂ were charged to an addition funnel and the solution was slowly added to the amine over a period of 1 hour. Temperature was kept below 10 °C. Then, the reaction mixture was allowed to warm to r.t. over night. After filtering the reaction mixture through a pad of celite, the filter cake was washed with dichloromethane. The dichloromethane solution was washed with water and dried over MgSO₄. Concentration under vacuum yielded the product in the form of a yellow oil. Further purification was accomplished by vacuum distillation. At about 10 –12 mm of Hg, three fractions were

35

collected at 50 – 61 °C, 61 – 85 °C, and 85 – 90 °C. The 2nd and 3rd fractions were identified via NMR to be the desired N-protected diallylamine.

5 The obtained N-carbomethoxy diallyl amine (400 g) was dissolved in 1.5 l of dichloromethane purged with nitrogen for 10 minutes by bubbling nitrogen through the stirred solution. In a 5 l flask fitted with a mechanical stirrer and an addition funnel, was charged the Grubb's catalyst (bis(tricyclohexylphosphine)styrylrutheniumdichloride (3 g, 3.9 mmol) under a steady purge. Dichloromethane was added and the resultant dark solution was stirred at r.t. with nitrogen bubbling for 10 minutes. The N-carbomethoxy
10 diallyl amine solution was added to the catalyst solution over a period of 2 hours. When the addition was complete, the solution was stirred at r.t. for 2.5 days. Then, the reaction mixture was concentrated to an oil, which was subsequently purified by vacuum distillation. The desired product was obtained as a clear colorless liquid boiling at about 90 °C (10 mm of Hg) The NMR was consistent with the expected structure.

15

¹H-NMR (CDCl₃): δ [ppm] 5.8-5.75 (m, 2H); 4.1 (m, 2H), 4.13 (m, 2H); 3.72 (s, 3H)

b.1.2 1-(Methoxycarbonyl)-3-(3-aminophenyl)-pyrrolidine

20 A 3-necked flask was flushed with nitrogen for 10 minutes. Palladium acetate and tri-*o*-tolyl phosphine were charged to the flask under a gentle purge of nitrogen. Anhydrous dimethyl formamide was pre-purged with nitrogen by bubbling nitrogen through it for several minutes, and was then charged to the Pd(OAc)₂ catalyst and phosphine, with a nitrogen purge going through the flask. Subsequently, diisopropylethyl amine, the pyr-
25 roline obtained in example b.1.1, 1-iodo-3-nitrobenzene, and silver(II) carbonate were also charged to the flask. The reaction mixture was stirred and heated under nitrogen to 100 °C for 6 hours. After about 9 hours, the reaction was complete (t.l.c. analysis). After the reaction mixture had cooled to r.t. over night, it was quenched with 10% sodium carbonate and extracted with MTBE (methyl tert-butyl ether) three times. The
30 combined organic phases were dried over MgSO₄ and concentrated. The excess olefin was removed by vacuum distillation. The dark residue was dissolved in MTBE, loaded on a silica column and chromatographed with MTBE:heptane, gradient from 1:9 to 2:8.

2.05 g of the eluted pyrroline product was then slurried in portions in 95 ml of methanol
35 and hydrogenated using 0.14 g of Wilkinson's catalyst (RhCl(PPh₃)₃; 2 mol%) at r.t. and 40 psi of hydrogen pressure to yield 1-(methoxycarbonyl)-3-(3-nitrophenyl)-pyrrolidine.

The product was then subjected to an acidic treatment (HCl in methanol, TFA) to yield
40 the title compound.

CI-MS: 221.2 [M+H]⁺

c. Preparation of enantiomerically pure precursors

c.1 (S)- and (R)-1-Benzyl-3-(3-nitrophenyl)-pyrrolidine

3-Nitrostyrene was reacted with 2.5 mole equivalents of benzyl methoxymethyl trimethylsilylmethyl amine in dichloromethane in the presence of trifluoroacetic acid.

To 54 g of the hydrochloride of racemic 1-benzyl-3-(3-nitrophenyl)-pyrrolidine (48 of free base) dissolved in ethanol was added 1 molar equivalent of L-tartric acid. The precipitated tartrate was isolated and recrystallized 4 times in methanol. The thus purified salt was isolated, dissolved and converted into the free pyrrolidine. 24.9 g of (S)-1-benzyl-3-(3-nitrophenyl)-pyrrolidine having >99%ee were obtained.

The combined filtrates of the above resolution process were concentrated, neutralized and subjected to the above treatment, however using D-tartric acid instead of the L-form. 17.5 g of (R)-1-benzyl-3-(3-nitrophenyl)-pyrrolidine having >99%ee were obtained.

II. Preparation of the compounds I

EXAMPLE 1

3-Trifluoromethoxy-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide and its hydrochloride

1.1 (S)-2-Phenyl-succinic acid dimethyl ester

5 g of (S)-2-phenyl succinic acid (25.75 mmol) were dissolved in 50 ml of methanol. At 4°C, 4.7 ml of thionyl chloride (64.37 mmol) were added dropwise. The reaction mixture was stirred at room temperature for 2h, the solvents were evaporated under reduced pressure. The residue that remained was dissolved in diethyl ether, washed once with saturated aqueous NaHCO₃ solution, reextracted with diethyl ether, and the combined organic layers dried over magnesium sulfate, filtered, and evaporated to dryness to yield 5.8 g of the desired product.

ESI-MS: 223.1 [M+H]⁺

1.2 (S)-2-Phenyl-butane-1,4-diol

2.54 g of lithium aluminium hydride (66.95 mmol) were suspended under ice cooling in 25 ml of tetrahydrofuran. 5.8 g of (S)-2-phenyl succinic acid dimethyl ester (25.75 mmol) dissolved in 25 ml of tetrahydrofuran were added slowly at 5-10°C. Stirring was continued for 15 minutes and then 15 ml of tetrahydrofuran/water (1:1) were added dropwise. The suspension was adjusted to pH 3-4 with conc. hydrochloric acid, filtered and the filter washed with dichloromethane. The filtrate was evaporated to dryness, taken up in diethylether, washed with saturated sodium hydrogen carbonate solution, reextracted with diethylether, and the combined organic layers dried over magnesium sulfate, filtered, and the solvent evaporated under reduced pressure to yield 4.2 g of the diol.

ESI-MS: 189.1 [M+Na]⁺

¹H-NMR (CDCl₃): δ [ppm] 7.25-7.4 (m, 2H), 7.15-7.3 (m, 3H), 4.2-4.35 (m, 2H), 3.2 (m, 1H), 3.1 (m, 1H), 2.1-2.3 (m, 3H).

1.3 Methanesulfonic acid (S)-4-methanesulfonyloxy-3-phenyl-butyl ester

4.19 g of (S)-2-phenyl-butane-1,4-diol (25.21 mmol) were dissolved in 50 ml of dichloromethane. 10.53 ml of triethylamine (75.6 mmol) were added, and, under ice cooling, 5 ml of methansulfonyl chloride (64.34 mmol). Stirring was continued for 15 minutes and then 40 ml of water were added. The organic phase was separated, and the aqueous phase extracted with dichloromethane. The combined organic layers were dried over magnesium sulfate, filtered, and the solvent evaporated under reduced pressure to yield 8.37 g of the product.

1.4 (S)-3-phenyl-1-propyl-pyrrolidine

2.0 g of methanesulfonic acid (S)-4-methanesulfonyloxy-3-phenyl-butyl ester (5.51 mmol) were dissolved in 5 ml of n-propylamine (60.82 mmol). The reaction mixture was stirred for 15 h at room temperature, diethyl ether added, the organic phase washed twice with water. The aqueous phase was reextracted once with diethylether, the organic layers combined, dried over magnesium sulfate, filtered, and the solvent evaporated under reduced pressure to yield 1.09 g of the product.

ESI-MS: 190.1 [M+H]⁺

1.5 (S)-3-(4-Nitro-phenyl)-1-propyl-pyrrolidine

0.3 g of (S)-3-phenyl-1-propyl-pyrrolidine (1.48 mmol) was dissolved in 2 ml of conc. sulphuric acid under argon and ice cooling. 165.16 mg of potassium nitrate (1.63 mmol) were added in small portions. The reaction mixture was stirred for 15 minutes under ice cooling, for 15 h at room temperature, and poured onto crushed ice. The aqueous solu-

tion was made alkaline with 25 % sodium hydroxide, extracted three times with diethyl ether, the aqueous phase reextracted once with diethylether, the organic layers combined, dried over magnesium sulfate, filtered, and the solvent evaporated under reduced pressure to yield 0.326 g of a brownish oil. A second reaction yielded another
5 0.919 g of the desired product.

ESI-MS: 235.1 [M+H]⁺

¹H-NMR (CDCl₃): δ [ppm] 8.15 (d, 2H), 7.45 (d, 2H), 3.4-3.5 (m, 1H), 2.9-3.0 (m, 1H), 2.75 (m, 1H), 2.3-2.6 (m, 4H), 1.8-1.9 (m, 1H), 1.5-1.65 (m, 3H), 0.95 (m, 3H).

10 1.6 (S)-3-(4-Amino-phenyl)-1-propyl-pyrrolidine

0.907 g of (S)-3-(4-nitro-phenyl)-1-propyl-pyrrolidine (3.59 mmol) were dissolved in 20 ml of methanol, 7.0 g of tin dichloride (31.02 mmol) added, and the reaction mixture stirred under reflux for 1 h. The methanol was evaporated, 60 ml of 1 N sodium hydroxide and dichloromethane added, and the phases separated after extensive stirring. The
15 aqueous phase was extracted twice with dichloromethane, the organic layers combined, dried over magnesium sulfate, filtered, and the solvent evaporated under reduced pressure to yield 0.744 g of the crude amino compound. ESI-MS:

205.2 [M+H]⁺

20 ¹H-NMR (DMSO-d₆): δ [ppm] 6.9 (d, 2H), 6.45 (d, 2H), 4.7 (s, broad, 2H), 3.1 (m, 1H), 2.85 (m, 1H), 2.65 (m, 1H), 2.55 (m, 1H), 2.25-2.45 (m, 3H), 2.1 (m, 1H), 1.65 (m, 1H), 1.4-1.5 (m, 2H), 0.85 (m, 3H).

25 1.7 3-Trifluoromethoxy-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide and its hydrochloride

0.4 g of (S)-3-(4-amino-phenyl)-1-propyl-pyrrolidine (1.96 mmol) and 0.455 g of commercially available 3-trifluoromethoxy-phenylsulfonyl chloride (1.86 mmol) were dissolved in 15 ml of tetrahydrofuran. 0.82 ml of triethylamine (5.87 mmol) were added
30 and the reaction mixture stirred for 15 h at room temperature. The solvents were evaporated under reduced pressure, the residue treated with water and adjusted to an alkaline pH with sodium hydroxide solution. The aqueous layer was extracted three times with diethyl ether, the organic layers combined, dried over magnesium sulfate, filtered, and the solvent evaporated under reduced pressure. The crude product was
35 purified with silica gel chromatography with ethyl acetate/methanol (2.5-3%) as eluent, yielding 0.225 g of the purified product.

ESI-MS: 429.15 [M+H]⁺

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 7.7 (d, 1H), 7.55 (s, 1H), 7.5 (t, 1H), 7.4 (d, 1H), 7.15 (d, 2H), 6.95 (d, 2H), 5.3 (bs, 1H), 3.3 (m, 1H), 3.05 (m, 1H), 2.85 (m, 1H), 2.65 (m, 1H), 2.5 (m, 1H), 2.45 (m, 2H), 2.3 (m, 1H), 1.8 (m, 1H), 1.55 (m, 2H), 0.9 (t, 3H).

- 5 This material was dissolved in 15 ml of diethyl ether and 1 ml of dichloromethane, 0.61 ml of 1 N HCl in diethyl ether added, and after formation of a precipitate, the suspension evaporated under reduced pressure to yield 0.235 g of a white precipitate.

EXAMPLE 2

- 10 4-Bromo-3-fluoro-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide

0.289 g of the desired product were obtained following the same synthetic procedure as described for 3-trifluoromethoxy-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide using commercially available 4-bromo-3-fluoro-benzene-sulfonylchloride.

15

ESI-MS: 441.0 / 443.0 [M+H]⁺

¹H-NMR (CDCl₃): δ [ppm] 7.65 (m, 1H), 7.5 (m, 1H), 7.4 (m, 1H), 7.15 (d, 2H), 7.0 (d, 2H), 3.3 (m, 1H), 3.0 (m, 1H), 2.8 (m, 1H), 2.65 (m, 1H), 2.35-2.5 (m, 3H), 2.3 (m, 1H), 1.8 (m, 1H), 1.5 (m, 2H), 0.9 (m, 3H).

20

EXAMPLE 3

4-Bromo-3,6-difluoro-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide

- 0.131 g of the desired product were obtained following the same synthetic procedure as described for 3-trifluoromethoxy-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide using commercially available 4-bromo-3,6-difluoro-benzenesulfonylchloride.

25

ESI-MS: 459.0 / 461.0 [M+H]⁺

- ¹H-NMR (CDCl₃): δ [ppm] 7.55 (m, 1H), 7.4 (m, 1H), 7.15 (d, 2H), 7.0 (d, 2H), 4.7 (s, very broad, 2H), 3.3 (m, 1H), 3.0 (m, 1H), 2.85 (m, 1H), 2.7 (m, 1H), 2.4-2.6 (m, 3H), 2.25 (m, 1H), 1.8 (m, 1H), 1.55 (m, 2H), 0.85 (m, 3H).

30

EXAMPLE 4

3-Trifluoromethyl-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide

35

0.11 g of the desired product were obtained following the same synthetic procedure as described for 3-trifluoromethoxy-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide using commercially available 3-trifluoromethyl-benzenesulfonylchloride.

- 40 ESI-MS: 427.2 [M+H]⁺

EXAMPLE 5

3,4-Difluoro-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide hydrochloride

ESI-MS: 381.2 [M+H]⁺

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 11.25 (bd, 1H), 10.55 (m, 1H), 7.85 (t, 1H), 7.65 (m, 2H), 7.3 (d, 1H), 7.25 (d, 1H), 7.1 (m, 2H), 3.2-3.8 (m, 5H), 2.9-3.15 (m, 2H), 2.3 (m, 1H), 1.95 (m, 1H), 1.7 (m, 2H), 0.9 (t, 3H).

EXAMPLE 6

N-(3-Pyrrolidin-3-yl-phenyl)-3-trifluoromethoxy-benzenesulfonamide

6.1 3-[3-(3-Trifluoromethoxy-benzenesulfonylamino)-phenyl]-pyrrolidine-1-carboxylic acid methyl ester

This compound was obtained following the same synthetic procedure as described for 3-trifluoromethoxy-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide by reacting 1-(Methoxycarbonyl)-3-(3-aminophenyl)-pyrrolidine as obtained in example b.1 with commercially available 3-trifluoromethoxy-benzenesulfonyl chloride.

ESI-MS: 445.1 [M+H]⁺

6.2 N-(3-Pyrrolidin-3-yl-phenyl)-3-trifluoromethoxy-benzenesulfonamide

3-[3-(3-Trifluoromethoxy-benzenesulfonylamino)-phenyl]-pyrrolidine-1-carboxylic acid methyl ester (0.105 g; 0.24 mmol) were dissolved in 2.5 ml ethanol and 0.9 ml of concentrated HCl were added. The reaction mixture was heated in a microwave system (CEM) at 90-150°C for several hours until consumption of starting material. The mixture was then concentrated in vacuo and the acidic aqueous phase extracted twice with diethylether. The aqueous phase was adjusted to pH 9 with 1 N aqueous NaOH, extracted three times with diethylether, and the combined organic layers dried over sodium sulfate, filtered and the solvent evaporated to dryness to yield 45 mg of the product.

ESI-MS: 387.15 [M+H]⁺

EXAMPLE 7

N-((S)-3-Pyrrolidin-3-yl-phenyl)-3-trifluoromethoxy-benzene sulfonamide

7.1 (S)-1-Benzyl-3-(3-amino-phenyl)-pyrrolidine

(S)-1-Benzyl-3-(3-nitro-phenyl)-pyrrolidine (1 g, 3.54 mmol) was dissolved in methanol, 4.5 g of stannous dichloride (19.94 mmol) were added and the reaction mixture was stirred for 1.5 h under refluxing conditions. When the starting material was consumed, the solvent was evaporated under reduced pressure and the residue treated with a mixture of 1 N aqueous NaOH/ethyl acetate and filtered over celite. Phases were separated, the aqueous phase was extracted with ethyl acetate and the combined organic layers were dried over magnesium sulfate, filtered and evaporated to dryness to yield 0.75 g of a yellowish oil.

7.2 N-[3-((S)-1-Benzyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethoxy-benzene sulfonamide

(S)-1-Benzyl-3-(3-amino-phenyl)-pyrrolidine (0.4 g, 1.59 mmol) and commercially available 3-trifluoromethoxy-benzene sulfonylchloride (0.39 g, 1.5 mmol) were dissolved in 30 ml tetrahydrofuran. 0.66 ml of triethylamine (3.75 mmol) were added and the mixture was stirred for 16 h at room temperature. The solvent was evaporated under reduced pressure and the residue was treated with water/diethylether. After adjusting the aqueous phase to alkaline pH with 1 N aqueous NaOH, the aqueous layer was extracted with diethylether and the combined organic layers dried over magnesium sulfate, filtered and evaporated. The product was purified via silica gel chromatography using an Isco Companion semi-automated chromatography system to yield 0.512 g of the desired compound.

ESI-MS: 477.1 [M+H]⁺

7.3 N-((S)-3-Pyrrolidin-3-yl-phenyl)-3-trifluoromethoxy-benzenesulfonamide

N-[3-((S)-1-Benzyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethoxy-benzene sulfonamide (0.5 g, 1.05 mmol) was dissolved in glacial acetic acid and 10% Pd on charcoal was added under a nitrogen atmosphere. The reaction mixture was then hydrogenated for 5 h at 70°C. Subsequently, the catalyst was removed by filtration over celite. The filtrate was concentrated under reduced pressure. The residue was treated with water and the pH adjusted to alkaline pH with 1 N aqueous NaOH. The aqueous layer was extracted twice with ethyl acetate and once with dichloromethane and the combined organic layers were dried over magnesium sulfate, filtered and evaporated. The remaining white solid was triturated with 10 ml diethylether, and the precipitate was filtered and dried to yield 0.18 g of the title compound.

ESI-MS: 387.0 [M+H]⁺

¹H-NMR (DMSO): δ [ppm] 7.75 (d, 1H), 7.6 (m, 2H), 7.5 (d, 1H), 7.0 (t, 1H), 6.85 (s, 1H), 6.8 (d, 1H), 6.7 (d, 1H), 3.3 (m, 1H), 3.0-3.2 (m, 3H), 2.7 (m, 1H), 2.1 (m, 1H), 1.7 (m, 1H).

5

EXAMPLE 8

N-[4-Methoxy-3-(1-propyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethoxy-benzenesulfonamide

10 8.1 1-[3-(2-Methoxy-phenyl)-pyrrolidin-1-yl]-propan-1-one

Commercially available 3-(2-methoxy-phenyl)-pyrrolidin (1.64 g, 9.25 mmol) was dissolved in 50 ml tetrahydrofuran, 1.873 g triethylamine (18.51 mmol) were added, and after cooling to 0-5°C, 1.325 g propionic acid anhydride (10.18 mmol), dissolved in
15 some tetrahydrofurane, was added dropwise. After stirring for 30 minutes, the starting material was consumed, and 2 ml of 7 N ammonia in methanol were added. After stirring at room temperature for 10 minutes, the solvents were evaporated under reduced pressure, the residue was treated with diethylether, washed once with saturated aqueous sodium bicarbonate, dried over magnesium sulfate, filtered, and the solvent was
20 evaporated again to yield 2.2 g of the desired product.

ESI-MS: 234.1 [M+H]⁺

25 8.2 1-[3-(2-Methoxy-5-nitro-phenyl)-pyrrolidin-1-yl]-propan-1-one

1-[3-(2-Methoxy-phenyl)-pyrrolidin-1-yl]-propan-1-one (0.7 g; 3 mmol) were dissolved in 10 ml of nitromethane. At -5°C to -10°C, a mixture of 0.290 g nitric acid, 0.5 g water and 5.52 g sulphuric acid were added within 25 minutes, and the reaction mixture was stirred for another 1 h at low temperature and 16 h at room temperature. Ice was
30 added, the reaction mixture was adjusted to alkaline pH with 50% aqueous NaOH, and the aqueous phase was extracted twice with diethylether. The organic layers were combined, dried over magnesium sulfate, filtered and the solvent was evaporated under reduced pressure to yield 0.85 g of the desired product as a mixture of isomers and small amounts of the dinitro derivative which was used in the next reaction without further
35 purification.

ESI-MS: 279.1 [M+H]⁺

40 8.3 1-[3-(2-Methoxy-5-amino-phenyl)-pyrrolidin-1-yl]-propan-1-one

1-[3-(2-Methoxy-5-nitro-phenyl)-pyrrolidin-1-yl]-propan-1-one (0.85 g; 3.05 mmol) were dissolved in 50 ml methanol. 3.65 g of stannous dichloride (16.18 mmol) were added and the reaction mixture was stirred for 2 h under refluxing conditions. When the starting material was consumed, the solvent was evaporated under reduced pressure and the residue was treated with a mixture of 1 N aqueous NaOH/ethyl acetate and filtered. Phases were separated, the aqueous phase was extracted with ethyl acetate and the combined organic layers were dried over magnesium sulfate, filtered and evaporated to dryness to yield 0.44 g of crude product which was used in the next reaction without further purification.

10

ESI-MS: 249.1 [M+H]⁺

15

8.4 N-[4-Methoxy-3-(1-propionyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethoxy-benzenesulfonamide

1-[3-(2-Methoxy-5-amino-phenyl)-pyrrolidin-1-yl]-propan-1-one (0.44 g, 1.77 mmol) and commercially available 3-trifluoromethoxy-benzene sulfonylchloride (0.23 g, 0.89 mmol) were reacted as described above, to yield, after purification via silica gel chromatography using a ISCO Companion instrument, 0.198 g of the desired compound.

20

ESI-MS: 473.1 [M+H]⁺

25

8.5 N-[4-Methoxy-3-(1-propyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethoxy-benzenesulfonamide

N-[4-Methoxy-3-(1-propionyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethoxy-benzenesulfonamide (0.19 g, 0.4 mmol) were dissolved in 15 ml tetrahydrofuran and 2 ml 1 M borane-tetrahydrofuran complex in tetrahydrofuran was added dropwise. The reaction mixture was heated to reflux for 30 minutes, 2 ml of 2 N aqueous hydrochloric acid was added and the mixture was refluxed again for 3 h. After stirring for 16 h at room temperature, the solvent was evaporated, the residue was treated with water and the pH was adjusted to alkaline pH with 1 N aqueous NaOH. The aqueous layer was extracted twice with diethylether, the combined organic layers were dried over magnesium sulfate, filtered and the solvent was evaporated. The crude product was chromatographed on a Chromabond column using 0-5% dichloromethane/methanol as eluent, to yield 0.077 mg of the title compound.

35

ESI-MS: 459.1 [M+H]⁺

¹H-NMR (CDCl₃): δ [ppm] 7.65 (d, 1H), 7.5 (s, 1H), 7.45 (t, 1H), 7.35 (d, 1H), 6.95 (d, 1H), 6.85 (s, 1H), 6.7 (d, 1H), 6.5 (s, broad, 1H), 3.8 (s, 3H), 3.6 (m, 1H), 2.9 (m, 1H), 2.75 (m, 1H), 2.65 (m, 1H), 2.3-2.5 (several m, 3H), 2.15 (m, 1H), 1.65 (m, 1H), 1.5 (m, 2H), 0.9 (t, 3H).

5

EXAMPLE 9

5-Chloro-3-methyl-benzo[b]thiophene-2-sulfonic acid (3-azetidin-3-yl-phenyl)-amide

Following the same procedure as described in Example 1.7, tert-butyl 3-(3-aminophenyl)azetidine-1-carboxylate (100 mg, 0.40 mmol) was coupled with 5-chloro-3-methylbenzo[b]thiophene-2-sulfonyl chloride (118 mg, 0.42 mmol) to give tert-butyl 3-(3-(5-chloro-3-methylbenzo[b]thiophene-2-sulfonamido)phenyl)azetidine-1-carboxylate (140 mg, 71%).

ESI-MS: 437.0 [M+H]⁺

15

tert-Butyl 3-(3-(5-chloro-3-methylbenzo[b]thiophene-2-sulfonamido)phenyl)azetidine-1-carboxylate (140 mg, 0.28 mmol) was stirred in formic acid (3 ml) at 0°C for 3 h. The solution was concentrated, dissolved in water, concentrated HCl added and the solution concentrated by lyophilisation to give the title compound (113 mg, 93 %) as a white foam.

20

ESI-MS: 393.0 [M+H]⁺

The compounds of Examples 10 to 32 were prepared by following the same procedure.

25 EXAMPLE 10

N-(3-Azetidin-3-yl-phenyl)-3-(2-methyl-thiazol-4-yl)-benzenesulfonamide

ESI-MS: 386.1 [M+H]⁺

EXAMPLE 1130

N-(4-Azetidin-3-yl-phenyl)-3-trifluoromethyl-benzenesulfonamide

ESI-MS: 357.1 [M+H]⁺

EXAMPLE 12

Thiophene-2-sulfonic acid (3-azetidin-3-yl-phenyl)-amide

35

ESI-MS: 294.9 [M+H]⁺

¹H NMR (400 MHz, DMSO) : δ (ppm) 3.82 (m, 2H), 3.92 (m, 1H), 4.04 (m, 2H), 6.87 (d, 1H), 6.91 (d, 1H), 6.95 (s, 1H), 7.00 (t, 1H), 7.13 (t, 1H), 7.41 (d, 1H), 7.68 (d, 1H).

EXAMPLE 13

N-(3-Azetidin-3-yl-phenyl)-3,5-bis-trifluoromethyl-benzenesulfonamide

ESI-MS: 425.0 [M+H]⁺

5 ¹H NMR (400 MHz, DMSO) : δ (ppm) 3.93 (m, 3H), 4.15 (m, 2H), 6.71 (d, 1H), 6.78 (d, 1H), 6.87 (s, 1H), 7.04 (t, 1H), 8.17 (s, 1H), 8.20 (s, 1H).

EXAMPLE 14

N-(3-Azetidin-3-yl-phenyl)-2,5-dimethoxy-benzenesulfonamide

ESI-MS: 349.0 [M+H]⁺

10 ¹H NMR (400 MHz, DMSO) : δ (ppm) 3.78 (m, 2H), 3.70 (m, 3H), 3.91 (m, 3H), 6.94 (t, 2H), 7.02 (s, 1H), 7.09 (m, 1H), 7.11 (d, 1H), 7.17 (t, 1H), 7.23 (d, 1H).

EXAMPLE 15

N-(3-Azetidin-3-yl-phenyl)-3-fluoro-benzenesulfonamide

15 ESI-MS: 306.9 [M+H]⁺

¹H NMR (400 MHz, DMSO) : δ (ppm) 3.81 (m, 2H), 3.91 (m, 1H), 4.04 (m, 2H), 6.87 (d, 1H), 6.94 (s, 1H), 7.12 (t, 1H), 7.36 (t, 1H), 7.47 (d, 1H), 7.49 (m, 1H), 7.56 (m, 1H).

EXAMPLE 16

20 2,5-Dichloro-thiophene-3-sulfonic acid (3-azetidin-3-yl-phenyl)-amide

ESI-MS: 362.9 [M+H]⁺

¹H NMR (400 MHz, DMSO) : δ (ppm) 3.93 (m, 3H), 4.14 (m, 2H), 6.71 (d, 1H), 6.81 (d, 1H), 6.85 (s, 1H), 7.06 (t, 1H), 7.10 (s, 1H).

25 EXAMPLE 17

N-(3-Azetidin-3-yl-phenyl)-3-chloro-benzenesulfonamide

ESI-MS: 322.9 [M+H]⁺

¹H NMR (400 MHz, DMSO) : δ (ppm) 3.86 (m, 2H), 3.94 (m, 1H), 4.07 (m, 2H), 6.87 (t, 2H), 6.94 (s, 1H), 7.13 (t, 1H), 7.52 (t, 1H), 7.57 (d, 1H), 7.72 (m, 2H).

30

EXAMPLE 18

N-(3-Azetidin-3-yl-phenyl)-3,5-dichloro-benzenesulfonamide

ESI-MS: 356.9 [M+H]⁺

35 ¹H NMR (400 MHz, DMSO) : δ (ppm) 3.90 (m, 3H), 4.11 (m, 2H), 6.66 (d, 1H), 6.76 (d, 1H), 6.82 (s, 1H), 7.03 (t, 1H), 7.62 (m, 2H).

EXAMPLE 19

N-(3-Azetidin-3-yl-phenyl)-3-methyl-benzenesulfonamide

ESI-MS: 303.0 [M+H]⁺

- 5 ¹H NMR (400 MHz, DMSO) : δ (ppm) 2.31 (s, 3H), 3.78 (m, 2H), 3.93 (m, 3H), 6.93 (d, 1H), 6.96 (d, 1H), 7.00 (s, 1H), 7.17 (t, 1H), 7.38 (m, 2H), 7.54 (m, 1H), 7.57 (s, 1H).

EXAMPLE 20

N-(3-Azetidin-3-yl-phenyl)-5-bromo-2-methoxy-benzenesulfonamide

- 10 ESI-MS: 399.0 [M+H]⁺

¹H NMR (400 MHz, DMSO) : δ (ppm) 3.78 (m, 2H), 3.85 (s, 3H), 3.91 (m, 3H), 6.95 (d, 1H), 6.97 (d, 1H), 7.02 (s, 1H), 7.13 (d, 1H), 7.18 (t, 1H), 7.71 (d, 1H), 7.80 (s, 1H).

EXAMPLE 21

- 15 5-Benzenesulfonyl-thiophene-2-sulfonic acid (3-azetidin-3-yl-phenyl)-amide

ESI-MS: 435.0 [M+H]⁺

¹H NMR (400 MHz, DMSO) : δ (ppm) 3.91 (m, 3H), 4.14 (m, 2H), 6.66 (d, 1H), 6.80 (s, 1H), 6.81 (d, 1H), 7.00 (d, 1H), 7.18 (t, 1H), 7.71 (d, 1H), 7.80 (s, 1H).

- 20 EXAMPLE 22

N-(3-Azetidin-3-yl-phenyl)-2-methoxy-5-methyl-benzenesulfonamide

ESI-MS: 333.0 [M+H]⁺

- 25 ¹H NMR (400 MHz, DMSO) : δ (ppm) 1.78 (m, 3H), 2.20 (s, 3H), 3.81 (m, 3H), 4.14 (m, 2H), 6.75 (d, 1H), 6.80 (s, 1H), 6.81 (d, 1H), 7.00 (d, 1H), 7.18 (t, 1H), 7.71 (d, 1H), 7.80 (s, 1H).

EXAMPLE 23

5-(2-Methylsulfanyl-pyrimidin-4-yl)-thiophene-2-sulfonic acid (3-azetidin-3-yl-phenyl)-amide

- 30 ESI-MS: 417.1 [M-H]⁺

¹H NMR (400 MHz, DMSO) : δ (ppm) 3.85 (s, 3H), 3.91 (m, 3H), 4.10 (m, 2H), 6.70 (d, 1H), 6.89 (m, 2H), 7.04 (d, 1H), 7.36 (d, 1H), 7.58 (d, 1H), 7.83 (s, 1H), 8.58 (m, 1H).

EXAMPLE 24

- 35 N-(3-Azetidin-3-yl-phenyl)-3-cyano-benzenesulfonamide

ESI-MS: 313.9 [M+H]⁺

EXAMPLE 25

N-(3-Azetidin-3-yl-phenyl)-3-methoxy-benzenesulfonamide

5 ESI-MS: 319.0 [M+H]⁺

EXAMPLE 26

5-Chloro-3-methyl-benzo[b]thiophene-2-sulfonic acid (4-azetidin-3-yl-phenyl)-amide

10 ESI-MS: 393.3 [M+H]⁺

EXAMPLE 27

N-(4-Azetidin-3-yl-phenyl)-4-fluoro-3-oxazol-4-yl-benzenesulfonamide ESI-MS: 374.1 [M+H]⁺

15 EXAMPLE 28

N-(4-Azetidin-3-yl-phenyl)-4-fluoro-3-oxazol-5-yl-benzenesulfonamide

ESI-MS: 374.1 [M+H]⁺

EXAMPLE 29

20 N-(3-Azetidin-3-yl-phenyl)-3-difluoromethoxy-benzenesulfonamide

ESI-MS: 355.1 [M+H]⁺

EXAMPLE 30

N-(4-Azetidin-3-yl-phenyl)-3-difluoromethoxy-benzenesulfonamide

25 ESI-MS: 355.1 [M+H]⁺

EXAMPLE 31

N-(3-Azetidin-3-yl-phenyl)-3-trifluoromethyl-benzenesulfonamide

30 ESI-MS: 357.1 [M+H]⁺

EXAMPLE 32

N-(3-Azetidin-3-yl-phenyl)-3-trifluoromethoxy-benzenesulfonamide

ESI-MS: 373.1 [M+H]⁺

35

EXAMPLE 33

5-Chloro-3-methyl-benzo[b]thiophene-2-sulfonic acid (4-azetidin-3-yl-phenyl)-methyl-amide

tert-Butyl 3-(4-(5-chloro-3-methylbenzo[b]thiophene-2-sulfonamido)phenyl)azetidine-1-carboxylate (216 mg, 0.44 mmol) was stirred in THF (5 ml) and NaH (25 mg, 0.53 mmol) was added. After stirring at r.t. for 15 min, methyl iodide (0.028 ml, 0.44 mmol) was added and stirring was continued for 116 h. The solution was concentrated in vacuo, dissolved in water (pH 11) and extracted with EtOAc. The organic extracts were dried (MgSO₄), filtered and concentrated to give tert-butyl 3-(4-(5-chloro-N,3-dimethylbenzo[b]thiophene-2-sulfonamido)phenyl)azetidine-1-carboxylate (= starting compound methylated at the amido-N) (185 mg, 83 %).

ESI-MS: 508.1 [M+H]⁺

tert-Butyl 3-(4-(5-chloro-N,3-dimethylbenzo[b]thiophene-2-sulfonamido)phenyl)azetidine-1-carboxylate (185 mg, 0.36 mmol) was stirred in formic acid (3 ml) at 0°C for 3.5 h. The solution was concentrated, dissolved in water, concentrated HCl was added and the solution was concentrated by lyophilisation to give the title compound (144 mg, 87 %) as a white foam.

ESI-MS: 408.1 [M+H]⁺

EXAMPLE 34

3-((S)-2,2-Difluoro-1-methyl-ethyl)-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide

Following the same procedure as described in Example 1.7, (S)-3-(4-amino-phenyl)-1-propyl-pyrrolidine was coupled with (S)-3-(1,1-difluoropropan-2-yl)benzene-1-sulfonyl chloride to give the title compound.

ESI-MS: 424.1 [M+H]⁺

The compounds of Examples 35 to 58 were prepared by following the same procedure.

EXAMPLE 35

5-Isoxazol-5-yl-thiophene-2-sulfonic acid [4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-amide

ESI-MS: 418.1 [M+H]⁺

EXAMPLE 36

5-Isoxazol-3-yl-thiophene-2-sulfonic acid [4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-amide

ESI-MS: 418.1 [M+H]⁺

EXAMPLE 37

5-Oxazol-5-yl-thiophene-2-sulfonic acid [4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-amide

ESI-MS: 418.1 [M+H]⁺

5 EXAMPLE 38

3-((S)-2-Methyl-pyrrolidin-1-yl)-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide

ESI-MS: 428.1 [M+H]⁺

10 EXAMPLE 39

Thiophene-2-sulfonic acid [4-(1-propyl-azetidin-3-yl)-phenyl]-amide

Following the same procedure as described in Example 1.7, 4-(1-propylazetidin-3-yl)aniline was coupled with thiophene-2-sulfonyl chloride to give the title compound.

15 ESI-MS: 337.0 [M+H]⁺

¹H NMR (400 MHz, DMSO) : δ (ppm) 0.88 (t, 3H), 1.45 (m, 2H), 3.11 (m, 2H), 3.97 (m, 3H), 4.22 (m, 1H), 4.35 (m, 1H), 7.11 (m, 3H), 7.29 (m, 2H), 7.54 (m, 1H), 7.84 (m, 1H).

EXAMPLE 40

20 2,5-Dichloro-N-[4-(1-propyl-azetidin-3-yl)-phenyl]-benzenesulfonamide

ESI-MS: 400.8 [M+H]⁺

EXAMPLE 41

N-[4-(1-Propyl-azetidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide

25 ESI-MS: 400.8 [M+H]⁺

EXAMPLE 42

N-[4-(1-Propyl-azetidin-3-yl)-phenyl]-3,5-bis-trifluoromethyl-benzenesulfonamide

ESI-MS: 467.1 [M+H]⁺

30

EXAMPLE 43

2,5-Dimethyl-N-[4-(1-propyl-azetidin-3-yl)-phenyl]-benzenesulfonamide

ESI-MS: 359.1 [M+H]⁺

35 EXAMPLE 44

3-Chloro-4-fluoro-N-[4-(1-propyl-azetidin-3-yl)-phenyl]-benzenesulfonamide

ESI-MS: 383.0 [M+H]⁺

EXAMPLE 45

3-Fluoro-N-[4-(1-propyl-azetidin-3-yl)-phenyl]-benzenesulfonamide ESI- ESI-MS: 349.0
[M+H]⁺ 349.1

5 EXAMPLE 46

2,5-Dichloro-thiophene-3-sulfonic acid [4-(1-propyl-azetidin-3-yl)-phenyl]-amide
ESI-MS: 404.9 [M+H]⁺

EXAMPLE 47

10 5-Chloro-thiophene-2-sulfonic acid [4-(1-propyl-azetidin-3-yl)-phenyl]-amide
ESI-MS: 370.9 [M+H]⁺

EXAMPLE 48

15 3-Chloro-N-[4-(1-propyl-azetidin-3-yl)-phenyl]-benzenesulfonamide
ESI-MS: 365.1[M+H]⁺

EXAMPLE 49

3,5-Dichloro-N-[4-(1-propyl-azetidin-3-yl)-phenyl]-benzenesulfonamide
ESI-MS: 400.8 [M+H]⁺
20

EXAMPLE 50

3-Methyl-N-[4-(1-propyl-azetidin-3-yl)-phenyl]-benzenesulfonamide
ESI-MS: 345.1 [M+H]⁺

25 EXAMPLE 51

2,3-Dichloro-N-[4-(1-propyl-azetidin-3-yl)-phenyl]-benzenesulfonamide
ESI-MS: 400.8 [M+H]⁺

EXAMPLE 52

30 3-Bromo-N-[4-(1-propyl-azetidin-3-yl)-phenyl]-benzenesulfonamide
ESI-MS: 410.9 [M+H]⁺

EXAMPLE 53

5-Isoxazol-3-yl-thiophene-2-sulfonic acid [4-(1-propyl-azetidin-3-yl)-phenyl]-amide
35 ESI-MS: 404.0 [M+H]⁺

EXAMPLE 54

3,4-Difluoro-N-[4-(1-propyl-azetidin-3-yl)-phenyl]-benzenesulfonamide ESI-MS: 367.0 [M+H]⁺

5 EXAMPLE 55

3-Cyano-N-[4-(1-propyl-azetidin-3-yl)-phenyl]-benzenesulfonamide
ESI-MS: 356.3 [M+H]⁺

EXAMPLE 56

10 4-Fluoro-3-oxazol-4-yl-N-[4-(1-propyl-azetidin-3-yl)-phenyl]-benzenesulfonamide
ESI-MS: 416.1 [M+H]⁺

EXAMPLE 57

4-Fluoro-3-oxazol-4-yl-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide
15 ESI-MS: 430.1 [M+H]⁺

EXAMPLE 58

4-Fluoro-3-oxazol-5-yl-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide
ESI-MS: 430.1 [M+H]⁺

20

EXAMPLE 59

5-Bromo-thiophene-2-sulfonic acid [4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-amide hydrochloride

25 59.1 (S)-2-Phenyl-succinic acid dimethyl ester

5 g of (S)-2-phenyl succinic acid (25.75 mmol) were dissolved in 50 ml of methanol. At 4°C, 4.7 ml of thionyl chloride (64.37 mmol) were added dropwise. The reaction mixture was stirred at room temperature for 2h, the solvents were evaporated under reduced
30 pressure. The residue that remained was dissolved in diethyl ether, washed once with saturated aqueous NaHCO₃ solution, reextracted with diethyl ether, and the combined organic layers dried over magnesium sulfate, filtered, and evaporated to dryness to yield 5.8 g of the desired product. ESI-MS: 223.1 [M+H]⁺

35 59.2 (S)-2-Phenyl-butane-1,4-diol

2.54 g of lithium aluminium hydride (66.95 mmol) were suspended under ice cooling in 25 ml of tetrahydrofuran. 5.8 g of (S)-2-phenyl succinic acid dimethyl ester (25.75

mmol) dissolved in 25 ml of tetrahydrofuran were added slowly at 5-10°C. Stirring was continued for 15 minutes and then 15 ml of tetrahydrofuran/water (1:1) were added dropwise. The suspension was adjusted to pH 3-4 with conc. hydrochloric acid, filtered and the filter washed with dichloromethane. The filtrate was evaporated to dryness, taken up in diethylether, washed with saturated sodium hydrogen carbonate solution, reextracted with diethylether, and the combined organic layers dried over magnesium sulfate, filtered, and the solvent evaporated under reduced pressure to yield 4.2 g of the diol.

ESI-MS: 189.1 [M+Na]⁺

¹H-NMR (CDCl₃): δ [ppm] 7.25-7.4 (m, 2H), 7.15-7.3 (m, 3H), 4.2-4.35 (m, 2H), 3.2 (m, 1H), 3.1 (m, 1H), 2.1-2.3 (m, 3H).

59.3 Methanesulfonic acid (S)-4-methanesulfonyloxy-3-phenyl-butyl ester

4.19 g of (S)-2-phenyl-butane-1,4-diol (25.21 mmol) were dissolved in 50 ml of dichloromethane. 10.53 ml of triethylamine (75.6 mmol) were added, and, under ice cooling, 5 ml of methansulfonyl chloride (64.34 mmol). Stirring was continued for 15 minutes and then 40 ml of water were added. The organic phase was separated, and the aqueous phase extracted with dichloromethane. The combined organic layers were dried over magnesium sulfate, filtered, and the solvent evaporated under reduced pressure to yield 8.37 g of the product.

59.4 (S)-3-phenyl-1-propyl-pyrrolidine

2.0 g of methanesulfonic acid (S)-4-methanesulfonyloxy-3-phenyl-butyl ester (5.51 mmol) were dissolved in 5 ml of n-propylamine (60.82 mmol). The reaction mixture was stirred for 15 h at room temperature, diethyl ether added, the organic phase washed twice with water. The aqueous phase was reextracted once with diethylether, the organic layers combined, dried over magnesium sulfate, filtered, and the solvent evaporated under reduced pressure to yield 1.09 g of the product.

ESI-MS: 190.1 [M+H]⁺

59.5 (S)-3-(4-Nitro-phenyl)-1-propyl-pyrrolidine

0.3 g of (S)-3-phenyl-1-propyl-pyrrolidine (1.48 mmol) was dissolved in 2 ml of conc. sulphuric acid under argon and ice cooling. 165.16 mg of potassium nitrate (1.63 mmol) were added in small portions. The reaction mixture was stirred for 15 minutes under ice cooling, for 15 h at room temperature, and poured onto crushed ice. The aqueous solution was made alkaline with 25 % sodium hydroxide, extracted three times with diethyl

ether, the aqueous phase reextracted once with diethylether, the organic layers combined, dried over magnesium sulfate, filtered, and the solvent evaporated under reduced pressure to yield 0.326 g of a brownish oil. A second reaction yielded another 0.919 g of the desired product.

5 ESI-MS: 235.1 [M+H]⁺

¹H-NMR (CDCl₃): δ [ppm] 8.15 (d, 2H), 7.45 (d, 2H), 3.4-3.5 (m, 1H), 2.9-3.0 (m, 1H), 2.75 (m, 1H), 2.3-2.6 (m, 4H), 1.8-1.9 (m, 1H), 1.5-1.65 (m, 3H), 0.95 (m, 3H).

59.6 (S)-3-(4-Amino-phenyl)-1-propyl-pyrrolidine

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0.907 g of (S)-3-(4-nitro-phenyl)-1-propyl-pyrrolidine (3.59 mmol) were dissolved in 20 ml of methanol, 7.0 g of tin dichloride (31.02 mmol) added, and the reaction mixture stirred under reflux for 1 h. The methanol was evaporated, 60 ml of 1 N sodium hydroxide and dichloromethane added, and the phases separated after extensive stirring. The aqueous phase was extracted twice with dichloromethane, the organic layers combined, dried over magnesium sulfate, filtered, and the solvent evaporated under reduced pressure to yield 0.744 g of the crude amino compound.

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ESI-MS:

205.2 [M+H]⁺

¹H-NMR (DMSO-d₆): δ [ppm] 6.9 (d, 2H), 6.45 (d, 2H), 4.7 (s, broad, 2H), 3.1 (m, 1H), 2.85 (m, 1H), 2.65 (m, 1H), 2.55 (m, 1H), 2.25-2.45 (m, 3H), 2.1 (m, 1H), 1.65 (m, 1H), 1.4-1.5 (m, 2H), 0.85 (m, 3H).

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59.7 5-Bromo-thiophene-2-sulfonic acid [4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-amide hydrochloride

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400 mg g of (S)-3-(4-amino-phenyl)-1-propyl-pyrrolidine hydrochloride (1.66 mmol) and 435 mg of (0.33 mmol) of 5-bromothiophene-2-sulfonyl chloride (1.66 mmol) were dissolved in 15 ml of tetrahydrofuran. 1.2 ml of triethylamine (8.3 mmol) were added and the reaction mixture was stirred for 15 h at room temperature. The solvents were evaporated under reduced pressure, the residue was treated with water and adjusted to an alkaline pH with sodium hydroxide solution. The aqueous layer was extracted three times with diethyl ether, the organic layers were combined, dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure. The crude product was purified with silica gel chromatography with ethyl dichloromethane/methanol (0-6%) as eluent, yielding 45 mg of the purified product. This material was dissolved in 10 ml of diethyl ether and 0.055 ml of 1 N HCl in diethyl ether were

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added, and after formation of a precipitate, the suspension was evaporated under reduced pressure to yield 50 mg of a white precipitate.

ESI-MS: 431.0 [M+H]⁺

¹H-NMR (DMSO): δ [ppm] 11.2 and 11.0 (2 s, broad, 1H), 10.65 (m, 1H), 7.2-7.4 (several m, 4H), 7.1 (m, 2H), 3.0-3.8 (several m, 7H), 2.3 (m, 1H), 1.85-2.0 (m, 1H), 1.7 (m, 2H), 0.9 (m, 3H).

EXAMPLE 60

5-Propyl-thiophene-2-sulfonic acid [4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-amide

The title product was obtained following the same synthetic procedure as described in Example 59 using 5-propyl-thiophene-2-sulfonylchloride which itself was prepared from commercially available 2-propyl-thiophene through reaction with chlorosulfonic acid.

ESI-MS: 393.1 [M+H]⁺

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 7.3 (d, 1H), 7.2 (d, 2H), 7.05 (d, 2H), 6.65 (d, 1H), 3.35 (m, 1H), 3.1 (m, 1H), 2.9 (m, 1H), 2.75 (m, 3H), 2.5 (m, 3H), 2.3 (m, 1H), 1.85 (m, 1H), 1.5-1.7 (m, 4H), 0.9 (m, 6H).

EXAMPLE 61

3-Bromo-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-4-trifluoromethoxy-benzenesulfonamide hydrochloride

The title product was obtained following the same synthetic procedure as described in Example 59 using commercially available 3-bromo-4-trifluoromethoxy-benzenesulfonylchloride.

ESI-MS: 507.05/509.05 [M+H]⁺

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 11.1-11.4 (broad, 1H), 10.6 (broad, 1H), 8.15 (s, 1H); 7.9 (d, 1H), 7.7 (d, 1H), 7.35 (d, 1H), 7.3 (d, 1H), 7.1 (d, 2H), 3.2-3.8 (several m, 4H), 2.95-3.15 (several m, 3H), 2.8 (m, 1H), 1.95 (m, 1H), 1.7 (m, 2H), 0.9 (t, 3H).

EXAMPLE 62

5-Chloro-thiophene-2-sulfonic acid [4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-amide

The title product was obtained following the same synthetic procedure as in Example 59 using commercially available 5-chloro-thiophene-2-sulfonylchloride.

ESI-MS: 385.0 [M+H]⁺

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 7.25 (d, 1H), 7.2 (d, 2H), 7.0 (d, 2H), 6.8 (d, 1H), 5.1 (bs, 1H), 3.3 (m, 1H), 3.05 (m, 1H), 2.85 (m, 1H), 2.7 (m, 1H), 2.4-2.6 (several m, 3H), 2.3 (m, 1H), 1.8 (m, 1H), 1.55 (m, 2H), 0.9 (t, 3H).

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EXAMPLE 63

N-(3-Piperidin-3-yl-phenyl)-3-trifluoromethoxy-benzenesulfonamide hydrochloride

10 ESI-MS: 401.0 [M+H]⁺

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.55 (broad, 1H), 9.35 (broad, 1H), 9.2 (broad, 1H), 7.8 (d, 1H), 7.7 (m, 1H), 7.65 (m, 2H), 7.2 (t, 1H), 7.0 (m, 3H), 3.25 (m, 1H), 3.2 (m, 1H), 2.8-3.0 (m, 3H), 1.7-1.9 (m, 3H), 1.5-1.65 (m, 1H).

15 EXAMPLE 64

3-Cyano-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide hydrochloride

The title product was obtained following the same synthetic procedure as described in Example 59 using commercially available 3-cyanobenzenesulfonylchloride.

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ESI-MS: 370.4 [M+H]⁺

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.8 (broad, 2H), 8.2 (s, 1H), 8.1 (d, 1H), 8.05 (d, 1H), 7.8 (t, 1H), 7.25 (d, 2H), 7.1 (d, 2H), 3.0-3.8 (several m, 7H), 2.3 (m, 1H), 1.95 (m, 1H), 1.7 (m, 2H), 0.9 (t, 3H).

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EXAMPLE 65

N-[3-((S)-1-Benzyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzene sulfonamide

The title product was obtained following the same synthetic procedure as described in Example 59 using commercially available 3-trifluoromethyl-benzene sulfonylchloride.

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ESI-MS: 461.1 [M+H]⁺

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 8.0 (s (1H), 7.9 (d, 1H), 7.75 (d, 1H), 7.55 (t, 1H), 7.2-7.4 (several m, 6H), 7.15 (m, 1H), 7.05 (d, 1H), 6.95 (s, 1H), 6.9 (d, 1H), 3.65 (s, 2H), 3.25 (m, 1H), 2.95 (m, 1H), 2.75 (m, 2H), 2.45 (m, 1H), 2.25 (m, 1H), 1.75 (m, 1H),

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EXAMPLE 66

5-Pyridin-2-yl-thiophene-2-sulfonic acid [4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-amide hydrochloride

The title product was obtained following the same synthetic procedure as described in
5 Example 59 using commercially available 5-Pyridin-2-yl-thiophene-2-sulfonylchloride.

ESI-MS: 428.1 [M+H]⁺

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.8-11.2 (broad, 1H), 10.6 (m, 1H), 8.55 (d, 1H), 8.0 (d, 1H), 7.9 (t, 1H), 7.8 (d, 1H), 7.6 (d, 1H), 7.3-7.4 (m, 2H), 7.3 (d, 1H), 7.15
10 (m, 2H), 3.8 (m, 1H), 3.65 (m, 1H), 3.6 (m, 1H), 3.3-3.5 (m, 1H), 3.25 (m, 1H), 3.0-3.15 (m, 2H), 2.35 (m, 1H), 2.0 (m, 1H), 1.7 (m, 2H), 0.9 (t, 3H).

EXAMPLE 67

15 N-[3-((S)-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzene sulfonamide

A solution of N-[3-((S)-1-benzyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzene sulfonamid (620 mg, 1.34 mmol) (Example 65) in methanol (30 ml) was hydrogenated using the ThalesNano H-Cube® hydrogenation reactor employing a 10% palladium on charcoal catalyst cartridge. After concentration of the solution under reduced pressure, the
20 crude product was purified with silica gel chromatography with ethyl acetate/methanol (1:1; 0:1) as eluent, yielding 328 mg of the purified product.

ESI-MS: 371.0 [M+H]⁺

¹H-NMR (MeOD, 400 MHz): δ [ppm] 7.9 (m, 2H), 7.7 (m, 1H), 7.55 (m, 1H), 7.0 (m, 25 1H), 6.7-6.85 (m, 3H), 3.2-3.3 (m, 2H), 3.05-3.15 (m, 2H), 3.0 (m, 1H), 2.7 (m, 1H), 2.1 (m, 1H), 1.7 (m, 1H).

EXAMPLE 68

30 5-Pyridin-2-yl-thiophene-2-sulfonic acid [4-((S)-1-allyl-pyrrolidin-3-yl)-phenyl]-amide hydrochloride

The title product was obtained following the same synthetic procedure as described for 5-bromo-thiophene-2-sulfonic acid [4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-amide
35 hydrochloride (Example 59) using commercially available 5-pyridin-2-yl-thiophene-2-sulfonylchloride and 4-((S)-1-allyl-pyrrolidin-3-yl)-phenylamine.

ESI-MS: 426.1 [M+H]⁺

EXAMPLE 69

5-Pyridin-2-yl-thiophene-2-sulfonic acid ((S)-4-pyrrolidin-3-yl-phenyl)-amide hydrochloride

5

36 mg of Pd₂(dba)₃ (0.04 mmol) and 24 mg of 1,4-bis-(diphenylphosphino)-butane (0.06 mmol) were dissolved in 10 ml of tetrahydrofuran. After stirring for 20 min, 5-pyridin-2-yl-thiophene-2-sulfonic acid [4-((S)-1-allyl-pyrrolidin-3-yl)-phenyl]-amide (235 mg, 0.55 mmol) (Example 68) and 2-mercapto-benzoic acid (160 mg, 1.04 mmol) were added, each as a solution in 3 ml of tetrahydrofuran. The reaction mixture was stirred for 20 h at room temperature. The solvents were evaporated under reduced pressure, the residue was dissolved in ethyl acetate and extracted with 0.5 N HCl. The aqueous phase was adjusted to an alkaline pH with sodium hydroxide solution and then extracted three times with dichloromethane. The organic layers were combined, dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure. The crude product was purified by chromatography (Chromabond-C18) with H₂O/acetonitrile (95:5; 0:100; 95:5)/0.1% acetic acid as eluent. To a solution of the so obtained oil in 2-propanol HCl in diethylether was added. The solid formed was filtered and dried in a vacuum oven to obtain 8 mg of the title compound.

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ESI-MS: 386.0 [M+H]⁺

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 8.5 (d, 1H), 7.95 (d, 1H), 7.85 (t, 1H), 7.7 (d, 1H), 7.4 (d, 1H), 7.3 (m, 1H), 7.1 (d, 2H), 7.0 (d, 2H), 3.4 (m, 1H), 3.2-3.3 (m, 2H), 3.1 (m, 1H), 2.85 (m, 1H), 2.2 (m, 1H), 1.7-1.85 (m, 1H).

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EXAMPLE 70

3-Bromo-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide

The title product was obtained following the same synthetic procedure as described in Example 59 using commercially available 3-bromo-benzenesulfonylchloride.

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ESI-MS: 423.0/425.0 [M+H]⁺

EXAMPLE 71

35 N-[4-((S)-1-Propyl-pyrrolidin-3-yl)-phenyl]-3-pyrrolidin-1-yl-benzenesulfonamide

0.4 g of 3-Bromo-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide (0.94 mmol), 0.156 ml pyrrolidin (1.89 mmol), 160 mg sodium tert-butanolate ((1.66 mmol) and 540 mg sodium sulfate were dissolved in 15 ml of tetrahydrofuran and heated to 50°C. 120 mg of 2,2'-bis(diphenylphosphino)-1,1'-binaphthalene (0.19 mmol) and 85

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mg tri(dibenzylidenacetone)dipalladium(0) (0.09 mmol) were added and the reaction stirred for 4 h under reflux. After workup, the partially converted starting material was reacted again under the same reaction conditions until completion. The solvents were evaporated under reduced pressure, the residue was treated with dichloromethane and water, the organic layer was dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure. The crude product was purified with silica gel chromatography with dichloromethane/methanol (0-20%) as eluent using a semi-automated ISCO companion instrument, yielding 0.309 g of the purified product.

ESI-MS: 414.1 [M+H]⁺

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 7.2 (m, 1H), 7.15 (d, 2H), 7.0 (m, 3H), 6.8 (s, 1H), 6.65 (d, 1H), 3.3 (m, 1H), 3.2 (m, 4H), 3.0 (m, 1H), 2.8 (m, 1H), 2.6 (m, 1H), 2.3-2.5 (several m, 3H), 2.25 (m, 1H), 2.0 (m, 4H), 1.75 (m, 1H), 1.5 (m, 2H), 0.9 (t, 3H).

EXAMPLE 72

3-(2-Methyl-pyrrolidin-1-yl)-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide hydrochloride

0.023 g of the desired product were obtained following the same synthetic procedure as described in Example 71.

ESI-MS: 428.2 / 443.0 [M+H]⁺

¹H-NMR (DMSO-d₆): δ [ppm] 10.8-11.2 (broad, 1H), 10.2 (m, 1H), 7.2-7.35 (several m, 3H), 7.1 (m, 2H), 6.95 (d, 1H), 6.8 (s, 1H), 6.7 (d, 1H), 2.9-3.9 (several m, 8H), 2.3 (m, 1H), 1.8-2.1 (several m, 4H), 1.6-1.75 (several m, 3H), 1.0 (d, 3H), 0.9 (t, 3H).

EXAMPLE 73

5-Pyrazol-1-yl-thiophene-2-sulfonic acid [4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-amide hydrochloride

0.2 g of 5-bromo-thiophene-2-sulfonic acid [4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-amide (0.47 mmol), 0.038 g pyrazole (0.56 mmol), 0.005 g Cu₂O (0.03 mmol), 0.015 g of salicylaloxim (0.11 mmol) and 0.3 g of cesium carbonate (0.93 mmol) were dissolved in 3 ml acetonitrile and heated in a microwave instrument (CEM) at 120°C for 4 h. The reaction mixture was filtered over celite, the filtrate was evaporated under reduced pressure, the residue was treated with dichloromethane and water, and the organic layer were washed with saturated aqueous sodium chloride. The organic phase was evaporated under reduced pressure and the crude product was purified with preparative HPLC yielding 0.02 g of the purified product.

ESI-MS: 417.1 [M+H]⁺

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.65-11.0 (broad, 1H), 10.55 (s, 1H), 8.55 (s, 1H), 7.8 (s, 1H), 7.5 (s, 1H), 7.35 (d, 2H), 7.3 (m, 1H), 7.15 (d, 2H), 6.6 (s, 1H), 2.9-3.85 (several m, 7H), 2.3-2.4 (m, 1H), 1.85-2.1 (m, 1H), 1.6-1.75 (m, 2H), 0.9 (t, 3H).

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EXAMPLE 74

4,5-Dichloro-thiophene-2-sulfonic acid [4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-amide hydrochloride

- 10 The title product was obtained following the same synthetic procedure as described in Example 59 using commercially available 4,5-dichloro-thiophene-2-sulfonylchloride.

ESI-MS: 419/421 [M+H]⁺

- 15 ¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.9-11.2 (broad, 1H), 10.8 (s, 1H), 7.7 (s, 1H), 7.4 (d, 1H), 7.3 (d, 1H), 7.2 (d, 2H), 3.8 (m, 1H), 3.2-3.7 (several m, 3H), 2.95-3.2 (m, 3H), 2.35 (m, 1H), 1.9-2.1 (m, 1H), 1.6-1.8 (m, 2H), 0.9 (t, 3H).

EXAMPLE 75

- 20 5-[1,2,3]Thiadiazol-4-yl-thiophene-2-sulfonic acid [4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-amide hydrochloride

The title product was obtained following the same synthetic procedure as described in Example 59 using commercially available 5-[1,2,3]Thiadiazol-4-yl-thiophene-2-sulfonylchloride.

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ESI-MS: 435.1 [M+H]⁺

- ¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.55-10.85 (broad, 1H), 10.6 (s, 1H), 9.7 (s, 1H), 7.8 (d, 1H), 7.65 (d, 1H), 7.3-7.4 (m, 2H), 7.2 (d, 2H), 3.2-3.8 (several m, 4H), 2.95-3.2 (m, 3H), 2.35 (m, 1H), 1.85-2.1 (m, 1H), 1.6-1.75 (m, 2H), 0.9 (t, 3H).

30

EXAMPLE 76

5-Trifluoromethyl-thiophene-2-sulfonic acid [4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-amide hydrochloride

- 35 5-trifluoromethyl-thiophene-2-sulfonylchloride was prepared from commercially available 2-trifluoromethyl-thiophene through reaction with chlorosulfonic acid in dichloromethane and subsequent silica gel chromatography (¹H-NMR of the sulfonylchloride (CDCl₃, 400 MHz): δ [ppm] 7.9 (1H, d), 7.5 (1H, d)).

ESI-MS: 419.1 [M+H]⁺

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.8-11.1 (broad, 2H), 7.8 (d, 1H), 7.65 (d, 1H), 7.25-7.4 (m, broad, 2H), 7.1-7.2 (d, 2H), 3.2-3.9 (several m, 4H), 2.9-3.2 (m, 3H), 2.35 (m, 1H), 1.85-2.1 (m, 1H), 1.6-1.8 (m, 2H), 0.95 (t, 3H).

5 EXAMPLE 77

N-[3-((S)-1-Methyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide hydrochloride

10 The product was obtained after reductive amination of N-[3-((S)-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide (of Example 67) with formaldehyde and sodium triacetoxy borohydride in dichloromethane in the presence of acetic acid.

ESI-MS: 385.0 [M+H]⁺

15 ¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.5-11.0 (broad, 2H), 7.9-8.1 (m, 3H), 7.8 (m, 1H), 7.25 (m, 1H), 7.1 (m, 1H), 7.1. (s, 1H), 6.95 (d, 1H), 3.0-3.8 (m, 5H), 2.85 (s, 3H), 2.3 (m, 1H), 1.85-2.05 (m, 1H).

EXAMPLE 78

20 5-(2-Methyl-thiazol-4-yl)-thiophene-2-sulfonic acid [4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-amide

The title product was obtained following the same synthetic procedure as described in Example 59 using commercially available 5-(2-Methyl-thiazol-4-yl)-thiophene-2-sulfonylchloride.

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ESI-MS: 448.1 [M+H]⁺

30 ¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 9.7-11.0 (broad, 1H), 8.0 (s, 1H), 7.5 (d, 1H), 7.45 (d, 1H), 7.2 (d, 2H), 7.1 (d, 2H), 3.25 (m, 1H), 2.84 (m, 1H), 2.7 (s, 3H), 2.6-2.7 (m, 2H), 2.3-2.5 (m, 3H), 2.1-2.2 (m, 1H), 1.6-1.7 (m, 1H), 1.4-1.5 (m, 2H), 0.8-0.9 (t, 3H).

EXAMPLE 79

N-[3-((S)-pyrrolidin-3-yl)-phenyl]-2-fluoro-5-trifluoromethyl-benzenesulfonamide

35 The product was prepared as described for the synthesis of N-[3-((S)-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide (Example 67). Deprotection of the N-benzyl derivative was achieved through hydrogenation in the H-cubeTM.

ESI-MS: 389.1 [M+H]⁺

EXAMPLE 80

N-[3-((S)-pyrrolidin-3-yl)-phenyl]-3-fluoro-5-trifluoromethyl-benzenesulfonamide

- 5 The product was prepared as described for the synthesis of N-[3-((S)-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide (Example 67). Deprotection of the N-benzyl derivative was achieved through hydrogenation in the H-cube™.

ESI-MS: 389.0 [M+H]⁺

- 10 ¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 7.8 (s, 1H), 7.7-7.8 (m, 2H), 6.95 (t, 1H), 6.8 (s, 1H), 6.75 (d, 1H), 6.6 (d, 1H), 5.8 (very broad, 2H), 3.45 (m, 1H), 3.3 (m, 1H), 3.1-3.25 (m, 2H), 2.85 (m, 1H), 2.2 (m, 1H), 1.75 (m, 1H).

EXAMPLE 81

- 15 N-[3-((S)-pyrrolidin-3-yl)-phenyl]-4-fluoro-5-trifluoromethyl-benzenesulfonamide

The product was prepared as described for the synthesis of N-[3-((S)-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide (Example 67). Deprotection of the N-benzyl derivative was achieved through hydrogenation in the H-cube™.

20

ESI-MS: 389.0 [M+H]⁺

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 8.05 (m, 1H), 8.0 (m, 1H), 7.6 (t, 1H), 7.0 (m, 2H), 6.85 (s, 1H), 6.8 (d, 1H), 6.7 (d, 1H), 5.8 (very broad, 2H), 3.4 (m, 1H), 3.2 (m, 2H), 3.1 (m, 1H), 2.85 (m, 1H), 2.2 (m, 1H), 1.75 (m, 1H).

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EXAMPLE 82

N-[3-((S)-pyrrolidin-3-yl)-phenyl]-2-methoxy-5-trifluoromethyl-benzenesulfonamide

- 30 The product was prepared as described for the synthesis of N-[3-((S)-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide (Example 67). Deprotection of the N-benzyl derivative was achieved through hydrogenation in the H-cube™.

ESI-MS: 401.1 [M+H]⁺

- 35 ¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 8.0 (s, 1H), 7.9 (m, 1H), 7.35 (d, 1H), 7.1 (m, 1H), 7.0 (m, 1H), 6.85-6.95 (m, 2H), 3.9 (s, 3H), 3.0-3.4 (several m, 4H), 2.65 (m, 1H), 2.1 (m, 1H), 1.6 (m, 1H).

EXAMPLE 83

3,5-Dibromo-4-(2-fluoro-ethoxy)-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide

5 The corresponding sulfonylchloride was prepared from commercially available 2,6-dibromophenol via reaction with 1-bromo-2-fluoro-ethane and cesium carbonate and subsequent formation of the sulfonylchloride through reaction with chloro sulfonic acid (¹H-NMR (CDCl₃, 400 MHz) of 3,5-dibromo-4(2-fluoro-ethoxy)phenylsulfonylchloride: δ [ppm] 8.2 (s, 2H), 4.9 (m, 1H), 4.8 (m, 1H), 4.45 (m, 1H), 4.4 (m, 1H)).

10 ESI-MS: 565.0 [M+H]⁺

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 7.85 (s, 2H), 7.2 (d, 2H), 7.0 (d, 2H), 4.85 (m, 1H), 4.7 (m, 1H), 4.35 (m, 1H), 4.25 (m, 1H), 3.35 (m, 1H), 3.1 (m, 1H), 2.9 (m, 1H), 2.8 (m, 1H), 2.45-2.6 (m, 3H), 2.3 (m, 1H), 1.85 (m, 1H), 1.6 (m, 2H), 0.95 (t, 3H).

15 EXAMPLE 84

3-difluoromethoxy-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide hydrochloride

20 The title product was obtained following the same synthetic procedure as in Example 59 using commercially available 3-difluoromethoxy-benzenesulfonylchloride.

ESI-MS: 411.5 [M+H]⁺

25 ¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.2-11.1 (very broad, 2H), 7.65 (m, 2H), 7.5 (s, 1H), 7.45 (m, 1H), 7.25 (m, 2H), 7.1 (m, 2H), 3.1-3.8 (m, 5H), 3.1 (m, 2H), 2.3 (m, 1H), 1.9-2.0 (m, 1H), 1.6-1.75 (m, 2H), 0.9 (t, 3H).

EXAMPLE 85

5-bromo-2,4-difluoro-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide

30 The title product was obtained following the same synthetic procedure as described in Example 59 using commercially available 5-bromo-2,4-difluoro-benzenesulfonylchloride.

ESI-MS: 459.0/461.0 [M+H]⁺

35 ¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.9 (very broad), 8.1 (t, 1H), 7.75 (t, 1H), 7.3 (d, 2H), 7.1 (d, 2H), 3.15-3.8 (m, 5H), 3.1 (m, 2H), 2.35 (m, 1H), 1.9-2.0 (m, 1H), 1.6-1.75 (m, 2H), 0.9 (t, 3H).

EXAMPLE 86

3-Bromo-2,4-difluoro-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide hydrochloride

The title product was obtained following the same synthetic procedure as described in Example 59 using commercially available 3-bromo-2,4-difluoro-benzenesulfonylchloride.

ESI-MS: 459.4/461.4 [M+H]⁺

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.9 (very broad), 7.9 (q, 1H), 7.45 (t, 1H), 7.3 (d, 2H), 7.1 (d, 2H), 3.15-3.8 (m, 5H), 3.1 (m, 2H), 2.3 (m, 1H), 1.9-2.0 (m, 1H), 1.6-1.75 (m, 2H), 0.9 (t, 3H).

EXAMPLE 87

N-[4-((S)-1-Propyl-pyrrolidin-3-yl)-phenyl]-3,5-bis-trifluoromethyl-benzenesulfonamide hydrochloride

The title product was obtained following the same synthetic procedure as described in Example 59 using commercially available 3,5-bis-trifluoromethoxy-benzenesulfonylchloride.

ESI-MS: 481.1 [M+H]⁺

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.8 (very broad), 8.5 (s, 1H), 8.25 (s, 2H), 7.3 (d, 2H), 7.1 (d, 2H), 3.15-3.7 (m, 5H), 3.1 (m, 2H), 2.3 (m, 1H), 1.9-2.0 (m, 1H), 1.6-1.75 (m, 2H), 0.9 (t, 3H).

EXAMPLE 88

3-Bromo-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-5-trifluoromethyl-benzenesulfonamide hydrochloride

The title product was obtained following the same synthetic procedure as described in Example 59 using commercially available 3-bromo-5-trifluoromethyl-benzenesulfonylchloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.7 (very broad), 8.3 (s, 1H), 8.15 (s, 1H), 7.95 (s, 1H), 7.3 (d, 2H), 7.1 (d, 2H), 3.15-3.7 (m, 5H), 3.1 (m, 2H), 2.25-2.4 (m, 1H), 1.85-2.05 (m, 1H), 1.6-1.75 (m, 2H), 0.9 (t, 3H).

EXAMPLE 89

N-[4-((S)-1-Propyl-pyrrolidin-3-yl)-phenyl]-2,5-bis-trifluoromethyl-benzenesulfonamide hydrochloride

The title product was obtained following the same synthetic procedure as described in Example 59 using commercially available 2,5-bis-trifluoromethyl-benzenesulfonylchloride.

5

ESI-MS: 481.1 [M+H]⁺

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.5-11.0 (very broad), 8.35 (s, 1H), 8.25 (s, 2H), 7.3 (broad, 2H), 7.1 (d, 2H), 3.2-3.8 (m, 4H), 2.9-3.1 (m, 3H), 2.25-2.4 (m, 1H), 1.8-2.05 (m, 1H), 1.6-1.75 (m, 2H), 0.9 (t, 3H).

10

EXAMPLE 90

5-Methyl-thiophene-2-sulfonic acid [4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-amide hydrochloride

15 The title product was obtained following the same synthetic procedure as described in Example 59 using commercially available 5-methyl-thiophene-2-sulfonylchloride.

ESI-MS: 365.1 [M+H]⁺

20 ¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 11.1-11.2 (very broad), 10.85-11.0 (very broad), 10.4 (m, 1H), 7.4 (d, 1H), 7.3 (d, 1H), 7.25 (d, 1H), 7.1 (d, 2H), 6.8 (s, 1H), 3.2-3.8 (m, 4H), 2.95-3.2 (m, 3H), 2.45 (s, 3H), 2.25-2.4 (m, 1H), 1.85-2.1 (m, 1H), 1.6-1.75 (m, 2H), 0.9 (t, 3H).

EXAMPLE 91

25 2-Methoxy-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-5-trifluoromethyl-benzenesulfonamide

The title product was obtained following the same synthetic procedure as described in Example 59 using commercially available 2-methoxy-5-trifluoromethyl-benzenesulfonylchloride.

30

ESI-MS: 443.1 [M+H]⁺

35 ¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.9 (very broad), 10.25 (very broad), 7.95 (m, 2H), 7.4 (d, 1H), 7.3 (d, 2H), 7.1 (d, 2H), 3.95 (s, 3H), 2.9-3.8 (several m, 7H), 2.25-2.35 (m, 1H), 1.8-2.0 (m, 1H), 1.6-1.75 (m, 2H), 0.9 (t, 3H).

EXAMPLE 92

N-((R)-3-Pyrrolidin-3-yl-phenyl)-3-trifluoromethyl-benzenesulfonamide

The product was prepared as described for the synthesis of N-[3-((S)-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide (Example 67). Deprotection of the N-benzyl derivative was achieved through hydrogenation in the H-cube™.

5 ESI-MS: 371.1 [M+H]⁺

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 8.0 (m, 2H), 7.85 (d, 1H), 7.7 (m, 1H), 7.0 (t, 1H), 6.85 (s, 1H), 6.8 (d, 1H), 6.7 (d, 1H), 3.35 (m, 1H), 3.0-3.2 (m, 3H), 2.75 (m, 1H), 2.05-2.2 (m, 1H), 1.6-1.75 (m, 1H).

10 EXAMPLE 93

3-(2-Methyl-thiazol-4-yl)-N-((S)-3-pyrrolidin-3-yl-phenyl)-benzenesulfonamide

The product was prepared as described for the synthesis of N-[3-((S)-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide (Example 67). Deprotection of the N-benzyl derivative was achieved through hydrogenation with ammoniumformate and 10% Pd/C.

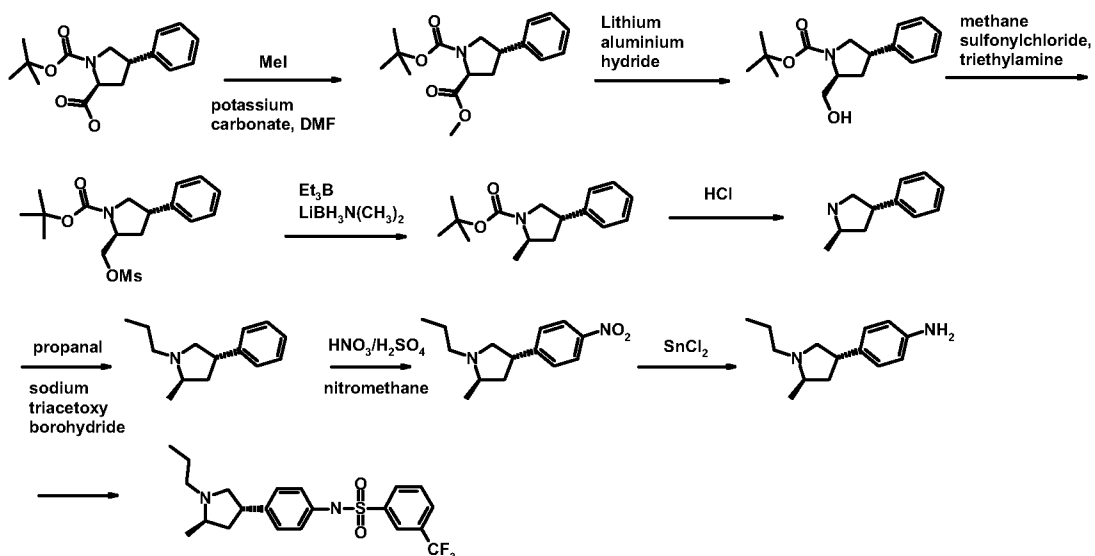
ESI-MS: 400.1 [M+H]⁺

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 8.4 (s, 1H), 8.1 (d, 1H), 8.0 (s, 1H), 7.65 (d, 1H), 7.55 (t, 1H), 7.1 (t, 1H), 7.0 (s, 1H), 6.8-6.9 (m, 2), 3.2 (m, 1H), 2.85-3.1 (m, 3H), 2.7 (s, 3H), 2.55 (m, 1H), 2.0-2.1 (m, 1H), 1.5-1.65 (m, 1H).

EXAMPLE 94

25 N-[4-((3S,5R)-5-Methyl-1-propyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide hydrochloride

The product was prepared via the following intermediates:



94.1 (2S,4S)-4-Phenyl-pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester

- 5 4.48 g of commercially available (2S,4S)-Boc-4-phenyl-pyrrolidine-2-carboxylic acid (15.37 mmol) were dissolved in 50 ml dimethylformamide. 2.59 g of potassium carbonate (18.76 mmol) and 2.66 g of methyl iodide (18.76 mmol) were added and the reaction was stirred for 48 h at room temperature. Standard work-up with ethyl acetate yielded 5.3 of the product.

10

ESI-MS: 206.1 (-Boc), 250.1 (-tBu) [M+H]⁺

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 7.2-7.35 (m, 5H), 4.4-4.55 (m, 1H), 3.9-4.1 (m, 1H), 3.75 (s, 3H), 3.55 (m, 1H), 3.4 (m, 1H), 2.35 (m, 2H), 1.45 (m, 9H).

- 15 94.2 (2S,4S)-2-Hydroxymethyl-4-phenyl-pyrrolidine-1-carboxylic acid tert-butyl ester

4.2 g of (2S,4S)-4-Phenyl-pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester (13.75 mmol) in 30 ml tetrahydrofuran were slowly added to a suspension of 0.27 g of lithium aluminium hydride in 50 ml tetrahydrofuran. Stirring was continued for 5 h
20 at 0-5°C and for 14 h at room temperature. For workup, a mixture of tetrahydrofuran/water (1:1) was slowly added to the reaction mixture at 0°C. The solvent was then evaporated under reduced pressure, water was added and the pH was adjusted to about 5 with 20 % aqueous citric acid. The aqueous phase was extracted four times with ethyl acetate, the organic layers were combined, dried over magnesium sulphate,
25 filtered, and the solvent was removed under reduced pressure to yield 3.85 of product.

ESI-MS: 222.1 (-tBu) [M+H]⁺

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 7.2-7.4 (m, 5H), 4.15 (m, 1H), 3.65-3.8 (m, 3H), 3.35-3.5 (m, 2H), 3.1 (broad, 1H), 2.15 (m, 1H), 2.05 (m, 1H), 1.5 (s, 9H).

30

94.3 (2S,4S)-2-Methanesulfonyloxymethyl-4-phenyl-pyrrolidine-1-carboxylic acid tert-butyl ester

- To 2.5 g of (2S,4S)-2-Hydroxymethyl-4-phenyl-pyrrolidine-1-carboxylic acid tert-butyl ester (9.01 mmol) in 70 ml dichloromethane were added 1.92 g of triethylamine (18.02 mmol) and 1.03 g of methanesulfonylchloride (9.01 mmol), dissolved in 5 ml dichloro-
- 35

methane. The reaction was stirred for 16 h at room temperature and yielded 3.4 g of product after standard workup.

ESI-MS: 300.1 (-tBu) [M+H]⁺

5

94.4 (2R,4S)-2-Methyl-4-phenyl-pyrrolidine-1-carboxylic acid tert-butyl ester

3.4 g of (2S,4S)-2-Methanesulfonyloxymethyl-4-phenyl-pyrrolidine-1-carboxylic acid tert-butyl ester (9.56 mmol) were dissolved in 50 ml tetrahydrofuran. After addition of 10 15.1 ml lithium-dimethylaminoborohydride (14.34 mmol; 1 M in tetrahydrofuran), 1.93 ml triethylborane (1M in tetrahydrofuran) were added and the reaction mixture stirred under reflux for 20 min. Standard workup gave 2.7 g of crude product which was purified via silica gel chromatography using a ISCO Companion instrument, yielding 1.69 g of purified product.

15

ESI-MS: 206.1 (-tBu) [M+H]⁺

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 7.2-7.35 (m, 5H), 3.9-4.0 (m, 1H), 3.7 (m, 1H), 3.5 (m, 1H), 3.15 (m, 1H), 2.3 (d, 3H), 2.15 (m, 1H), 1.9 (m, 1H), 1.4 (s, 9H).

20

94.5 (2R,4S)-2-Methyl-4-phenyl-pyrrolidine

1.68 g of (2R,4S)-2-Methyl-4-phenyl-pyrrolidine-1-carboxylic acid tert-butyl ester (6.42 mmol) were dissolved in 40 ml dichloromethane and 19.2 ml (38.56 mmol) 2N HCl in 25 diethylether dropwise added. After stirring at room temperature for 16 h, the solvents were evaporated, the residue was dissolved in water, the pH was adjusted to pH 9 with aqueous sodium hydroxide, and the aqueous phase was extracted three times with ethyl acetate. The organic phases were combined, dried over magnesium sulphate, filtered and evaporated to dryness under reduced pressure to yield 1.05 g of product.

30

ESI-MS: 162.2 [M+H]⁺

94.6 (2R,4S)-2-Methyl-4-phenyl-1-propyl-pyrrolidine

35 1.05 g of (2R,4S)-2-Methyl-4-phenyl-pyrrolidine (6.51 mmol) were dissolved in 30 ml dichloromethane, 0.58 g of acetic acid, 0.56 g of propionic aldehyde (9.76 mmol) and 2.07 g of sodium triacetoxyborohydride (9.76 mmol) were slowly added in portions.

After stirring at room temperature for 90 min., the solvent was evaporated, water was added and the pH was adjusted to pH 6. The aqueous phase was extracted three times with ethyl acetate, the organic phases were combined, dried over magnesium sulphate, filtered and evaporated to dryness under reduced pressure to yield 1.48 g of product.

5

ESI-MS: 204.1 $[M+H]^+$

Nitration followed by reduction of the nitro group with stannous dichloride and coupling of the aniline with 3-trifluoromethyl-phenyl sulfonyl chloride was performed as already described for other examples to yield 0.088 g of N-[4-((3S,5R)-5-Methyl-1-propyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide hydrochloride.

10

ESI-MS: 427.1 $[M+H]^+$

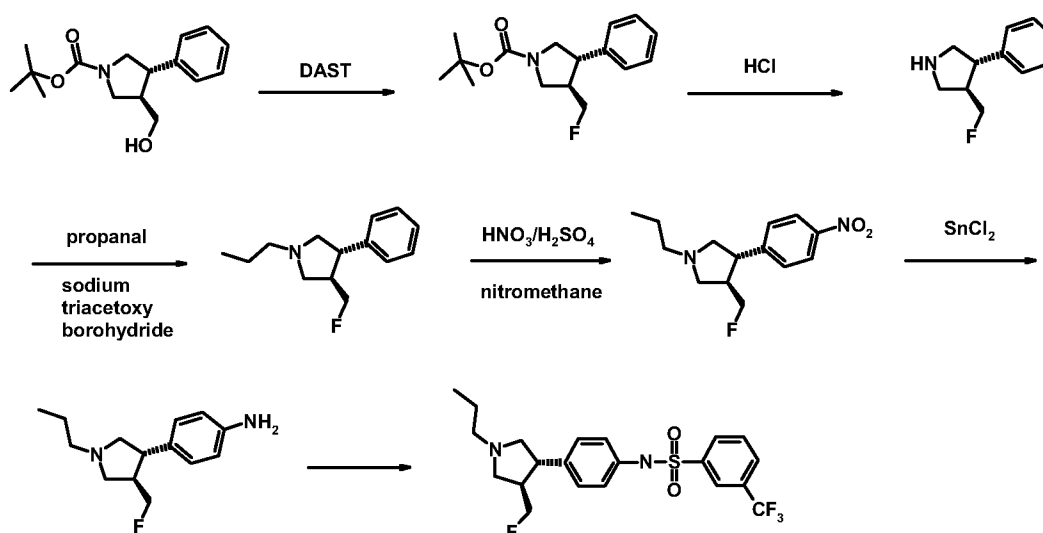
$^1\text{H-NMR}$ (DMSO- d_6 , 400 MHz): δ [ppm] 10.65 (broad, 1H), 10.5 (1H), 7.95-8.1 (m, 3H), 7.8 (t, 1H), 7.25 (d, 2H), 7.15 (d, 2H), 3.8 (m, 1H), 3.65 (m, 1H), 3.5 (m, 1H), 3.25 (m, 1H), 3.0 (m, 1H), 2.95 (m, 1H), 2.2 (m, 1H), 2.1 (m, 1H), 1.7 (m, 2H), 1.4 (d, 3H), 0.9 (t, 3H).

15

EXAMPLE 95

20 N-[4-(trans-4-Fluoromethyl-1-propyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide

The product was prepared via the following intermediates:



25 95.1 trans-3-Fluoromethyl-4-phenyl-pyrrolidine-1-carboxylic acid tert-butyl ester

1.5 g trans-3-hydroxymethyl-4-phenyl-pyrrolidine-1-carboxylic acid tert-butyl ester (5.41 mmol) were dissolved in 20 ml dichloromethane and 1.31 g of diethylaminosulfurtrifluoride (DAST, 8.1 mmol) in 2 ml dichloromethane were added at 0°C. The reaction mixture was stirred for 72 h at room temperature, further dichloromethane and water were added, the organic phase was separated, dried over magnesium sulphate, filtered and evaporated to dryness to yield 1.7 g of a light yellowish oil. The crude product was purified via silica gel chromatography using n-heptane/ethyl acetate (6:4) as eluent to yield 1.08 g product.

ESI-MS: 224.1 (-Boc) [M+H]⁺

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 7.2-7.4 (m, 5H), 4.45 (m, 0.5H), 4.35 (m, 1H), 4.25 (m, 0.5H), 3.9 (m, 1H), 3.8 (m, 1H), 3.3-3.5 (m, 2H), 3.2 (m, 1H), 2.5-2.7 (m, 1H), 1.45 (s, 9H).

95.2 trans-3-Fluoromethyl-4-phenyl-pyrrolidine

ESI-MS: 180.1 [M+H]⁺

95.3 trans-3-Fluoromethyl-4-phenyl-1-propyl-pyrrolidine

20

ESI-MS: 222.1 [M+H]⁺

95.4 trans-3-Fluoromethyl-4-(4-nitro-phenyl)-1-propyl-pyrrolidine

25 ESI-MS: 267.1 [M+H]⁺

95.5 trans-3-Fluoromethyl-4-(4-amino-phenyl)-1-propyl-pyrrolidine

ESI-MS: 237.1 [M+H]⁺

30

Coupling of trans-3-fluoromethyl-4-(4-amino-phenyl)-1-propyl-pyrrolidine with 3-trifluoromethyl-phenyl sulfonyl chloride using methods already described for other examples yielded 0.155 g of N-[4-(trans-4-fluoromethyl-1-propyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide.

35

ESI-MS: 445.1 [M+H]⁺

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.6 (broad, 1H), 8.0-8.1 (m, 2H), 7.95 (s, 1H), 7.8 (t, 1H), 7.25 (d, 2H), 7.05 (d, 2H), 4.4 (m, 1H), 4.3 (m, 1H), 3.3 (m, 1H), 3.2 (m, 1H), 3.1 (m, 1H), 2.9 (m, 2H), 2.75 (m, 2H), 2.55 (m, 1H), 1.5-1.6 (m, 2H), 0.9 (t, 3H).

5 EXAMPLE 96

3-(5-Methyl-[1,3,4]oxadiazol-2-yl)-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide hydrochloride

0.047 g of the desired product were obtained following the same synthetic procedure as described for 3-trifluoromethoxy-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide (Example 1) using commercially available 3-(5-Methyl-[1,3,4]oxadiazol-2-yl)-benzenesulfonylchloride.

ESI-MS: 427.0 [M+H]⁺

15 ¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 8.4 (s, 1H), 8.2 (d, 1H), 7.9 (d, 1H), 7.55 (t, 1H), 7.15 (d, 2H), 7.0 (d, 2H), 3.35 (m, 1H), 3.1 (m, 1H), 2.9 (m, 1H), 2.8 (m, 1H), 2.6 (s, 3H), 2.55 (m, 3H), 2.3 (m, 1H), 1.85 (m, 1H), 1.6 (m, 2H), 0.95 (t, 3H).

EXAMPLE 97

20 3-Fluoro-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide trifluoroacetate

0.0065 g of the desired product were obtained following the same synthetic procedure as described for 3-trifluoromethoxy-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide (Example 1) using commercially available 3-fluoro-benzenesulfonylchloride.

ESI-MS: 363.1 [M+H]⁺

EXAMPLE 98

30 3-Chloro-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide

0.118 g of the desired product were obtained following the same synthetic procedure as described for 3-trifluoromethoxy-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide using commercially available 3-chloro-benzenesulfonylchloride.

35

ESI-MS: 379.1 [M+H]⁺

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 7.75 (s, 1H), 7.6 (d, 1H), 7.5 (d, 1H), 7.35 (t, 1H), 7.15 (d, 2H), 7.0 (d, 2H), 3.3 (m, 1H), 3.0 (m, 1H), 2.8 (m, 1H), 2.7 (m, 1H), 2.4-2.55 (m, 3H), 2.3 (m, 1H), 1.8 (m, 1H), 1.55 (m, 2H), 0.95 (t, 3H).

40

EXAMPLE 99

3-(2-Methyl-thiazol-4-yl)-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide

0.113 g of the desired product were obtained following the same synthetic procedure
5 as described for 3-trifluoromethoxy-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-
benzenesulfonamide (Example 1) using commercially available 3-(2-Methyl-thiazol-4-
yl)-benzenesulfonylchloride.

ESI-MS: 442.0 [M+H]⁺

10 ¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 8.4 (s, 1H), 8.05 (d, 1H), 7.7 (d, 1H), 7.4 (m, 2H),
7.15 (d, 2H), 7.05 (d, 2H), 3.55 (m, 2H), 3.2-3.5 (m, broad, 2H), 2.9-3.0 (m, 3H), 2.7 (s,
3H), 2.35 (m, 1H), 2.0-2.1 (m, 1H), 1.75-1.9 (m, 2H), 0.95 (t, 3H).

EXAMPLE 100

15 N-[4-((S)-1-Allyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide

0.01 g of the desired product were obtained following the same synthetic procedure as
described for 3-trifluoromethoxy-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-
benzenesulfonamide (Example 1) using commercially available 3-trifluoromethyl-
20 benzenesulfonylchloride.

ESI-MS: 411.1 [M+H]⁺

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 7.95 (s, 1H), 7.9 (d, 1H), 7.8 (d, 1H), 7.6 (t, 1H),
7.15 (d, 2H), 6.95 (d, 2H), 5.9 (m, 1H), 5.2 (d, 1H), 5.1 (d, 1H), 3.3 (m, 1H), 3.1-3.2 (m,
25 2H), 3.0 (m, 1H), 2.8 (m, 1H), 2.65 (m, 1H), 2.45 (m, 1H), 2.3 (m, 1H), 1.8 (m, 1H).

EXAMPLE 101

N-((S)-4-Pyrrolidin-3-yl-phenyl)-3-trifluoromethyl-benzenesulfonamide

30 0.071 g of tris-(dibenzylidenacetone)-dipalladium(0) (0.08 mmol) and 0.033 g of 1,3-bis-
(diphenylphosphino)-butane (0.08 mmol) were dissolved in 20 ml tetrahydrofuran and
stirred for 30 min. 0.32 g of N-[4-((S)-1-allyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-
benzenesulfonamide (0.78 mmol), dissolved in 5 ml tetrahydrofuran, were added to
35 the solution, followed by 0.129 g 2-mercaptobenzoic acid (0.84 mmol). The reaction
mixture was stirred at room temperature for 72 h, the solvent was evaporated, and di-
chloromethane and 1 N aqueous hydrochloric acid were added. The aqueous phase
was adjusted to basic pH, extracted with dichloromethane and the combined organic
layers were washed with aqueous sodium chloride solution, dried over sodium sul-
40 phate, filtered and evaporated to dryness under reduced pressure. The crude product

was purified via silica gel chromatography using a ISCO companion instrument to yield 0.01 g of product.

ESI-MS: 371.1 [M+H]⁺

- 5 ¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 8.0 (d, 1H), 7.95 (s, 1H), 7.8 (d, 1H), 7.7 (t, 1H), 6.95 (d, 2H), 6.85 (d, 2H), 3.3 (m, 1H), 3.05-3.2 (m, 2H), 3.0 (m, 1H), 2.7 (m, 1H), 2.1 (m, 1H), 1.7 (m, 1H).

EXAMPLE 102

- 10 4-Fluoro-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide

0.253 g of the desired product were obtained following the same synthetic procedure as described for 3-trifluoromethoxy-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide (Example 1) using commercially available 3-trifluoromethyl-4-fluoro-benzenesulfonylchloride.

ESI-MS: 431.2 [M+H]⁺

- 20 ¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.5 (broad, 1H), 8.1 (m, 1H), 8.05 (d, 1H), 7.75 (t, 1H), 7.25 (d, 2H), 7.05 (d, 2H), 3.2-3.6 (m, 5H), 3.0 (m, 2H), 2.3 (m, 1H), 1.9 (m, 1H), 1.65 (m, 2H), 0.9 (t, 3H).

EXAMPLE 103

- 25 3-Fluoro-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-5-trifluoromethyl-benzenesulfonamide hydrochloride

0.080 g of the desired product were obtained following the same synthetic procedure as described for 3-trifluoromethoxy-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide (Example 1) using commercially available 3-fluoro-5-trifluoromethyl-benzenesulfonylchloride.

ESI-MS: 431.4 [M+H]⁺

- 35 ¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.55 (broad), 8.1 (d, 1H), 7.9 (d, 1H), 7.8 (s, 1H), 7.3 (d, 2H), 7.1 (d, 2H), 3.2-3.6 (m, 5H), 3.1 (m, 2H), 2.3 (m, 1H), 1.95 (m, 1H), 1.7 (m, 2H), 0.9 (t, 3H).

EXAMPLE 104

2-Fluoro-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-5-trifluoromethyl-benzenesulfonamide

0.103 g of the desired product were obtained following the same synthetic procedure as described for 3-trifluoromethoxy-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide (Example 1) using commercially available 2-fluoro-5-trifluoromethyl-benzenesulfonylchloride.

5

ESI-MS: 431.1 [M+H]⁺

¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.7 (very broad, 1H), 8.1 (m, 1H), 8.05 (d, 1H), 7.7 (t, 1H), 7.25 (d, 2H), 7.05 (d, 2H), 3.1-3.6 (m, 5H), 2.9-3.0 (m, 2H), 2.3 (m, 1H), 1.85 (m, 1H), 1.6 (m, 2H), 0.9 (t, 3H).

10

EXAMPLE 105

3-Morpholin-4-yl-N-[4-((S)-1-propyl-pyrrolidin-3-yl)-phenyl]-benzenesulfonamide

0.033 g of the desired product were obtained following the same synthetic procedure as described for N-[4-((S)-1-Propyl-pyrrolidin-3-yl)-phenyl]-3-pyrrolidin-1-yl-benzenesulfonamide (Example 71) using morpholine as amine.

15

ESI-MS: 430.5 [M+H]⁺

¹H-NMR (CDCl₃, 400 MHz): δ [ppm] 7.2-7.35 (m, 2H), 7.1-7.2 (m, 3H), 6.95-7.05 (m, 3H), 3.8 (t, 4H), 3.3 (m, 1H), 3.1 (t, 4H), 3.05 (m, 1H), 2.85 (m, 1H), 2.7 (m, 1H), 2.4-2.6 (m, 3H), 2.3 (m, 1H), 1.8 (m, 1H), 1.55 (m, 2H), 0.95 (t, 3H).

20

EXAMPLE 106

N-[4-(cis-2-Methyl-1-propyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide hydrochloride

25

0.015 g of the product were prepared as described for the synthesis of N-[4-((3S,5R)-5-methyl-1-propyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide (Example 94) from commercially available Boc-cis-3-phenyl-pyrrolidin-2-carboxylic acid:

30

106.1 cis-3-Phenyl-pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester

ESI-MS: 206.1 (-Boc), 250.1 (-tBu) [M+H]⁺

106.2 cis-2-Hydroxymethyl-3-phenyl-pyrrolidine-1-carboxylic acid tert-butyl ester

35

ESI-MS: 222.1 (-tBu) [M+H]⁺

106.3 cis-2-Methanesulfonyloxymethyl-3-phenyl-pyrrolidine-1-carboxylic acid tert-butyl ester

ESI-MS: 256.2 (-Boc), 299.9 (-tBu) [M+H]⁺

5

106.4 cis-2-Methyl-3-phenyl-pyrrolidine-1-carboxylic acid tert-butyl ester

ESI-MS: 206.1 (-tBu) [M+H]⁺

10 106.5 cis-2-Methyl-3-phenyl-pyrrolidine

ESI-MS: 162.1 [M+H]⁺

106.6 cis-2-Methyl-3-phenyl-1-propyl-pyrrolidine

15

ESI-MS: 204.1 [M+H]⁺

106.7 cis-2-Methyl-3-(4-nitro)phenyl-1-propyl-pyrrolidine

20 ESI-MS: 249.1 [M+H]⁺

106.8 cis-2-Methyl-3-(4-amino)phenyl-1-propyl-pyrrolidine

ESI-MS: 219.1 [M+H]⁺

25

Coupling of the aniline with 3-trifluoromethyl-phenyl sulfonyl chloride was performed as already described for other examples to yield 0.015 g of the final product.

ESI-MS: 427.1 [M+H]⁺

30 ¹H-NMR (DMSO-d₆, 400 MHz): δ [ppm] 10.3 (very broad), 8.0 (d, 1H), 7.95 (d, 1H), 7.85 (s, 1H), 7.75 (t, 1H), 7.15 (d, 2H), 7.0 (d, 2H), 3.8 (m, 1H), 3.65 (m, 1H), 3.3-3.6 (m, 2H), 3.1 (m, 1H), 2.9 (m, 1H), 2.2 (m, 2H), 1.65 (m, 2H), 0.85 (t, 3H), 0.7 (d, 3H).

EXAMPLE 107

35 N-[4-((3S,5S)-5-Methyl-1-propyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide hydrochloride

0.053 g of the product were prepared as described for the synthesis of N-[4-((3S,5R)-5-methyl-1-propyl-pyrrolidin-3-yl)-phenyl]-3-trifluoromethyl-benzenesulfonamide (Example 94) from commercially available (2R,4S)-Boc-4-phenyl-pyrrolidin-2-carboxylic acid:

- 5 107.1 (2R,4S)-4-Phenyl-pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester

ESI-MS: 206.0 (-Boc), 250.0 (-tBu) [M+H]⁺

- 10 107.2 (2R,4S)-2-Hydroxymethyl-4-phenyl-pyrrolidine-1-carboxylic acid tert-butyl ester

ESI-MS: 222.1 (-tBu) [M+H]⁺

- 15 107.3 (2R,4S)-2-Methanesulfonyloxymethyl-4-phenyl-pyrrolidine-1-carboxylic acid tert-butyl ester

ESI-MS: 256.1 (-Boc), 300.1 (-tBu) [M+H]⁺

- 20 107.4 (2S,4S)-2-Methyl-4-phenyl-pyrrolidine-1-carboxylic acid tert-butyl ester

ESI-MS: 206.1 (-tBu) [M+H]⁺

- 25 107.5 (2S,4S)-2-Methyl-4-phenyl-pyrrolidine

ESI-MS: 162.1 [M+H]⁺

- 30 107.6 (2R,4S)-2-Methyl-4-phenyl-1-propyl-pyrrolidine

ESI-MS: 204.1 [M+H]⁺

- 35 107.7 (2S,4S)-2-Methyl-4-(4-nitro)phenyl-1-propyl-pyrrolidine

ESI-MS: 249.1 [M+H]⁺

- 107.8 (2S,4S)-Methyl-4-(4-amino)phenyl-1-propyl-pyrrolidine

ESI-MS: 219.1 [M+H]⁺

Coupling of the aniline with 3-trifluoromethyl-phenyl sulfonyl chloride was performed as already described for other examples to yield 0.053 g of the final product.

ESI-MS: 427.1 $[M+H]^+$

- 5 $^1\text{H-NMR}$ (DMSO- d_6 , 400 MHz): δ [ppm] 10.6 (very broad), 8.05 (m, 1H), 8.0 (m, 2H), 7.8 (m, 1H), 7.3 (m, 2H), 7.05 (m, 2H), 3.3-3.6 (m, 4H), 3.2 (broad, 1H), 2.9 (broad, 1H), 2.4 (broad, 1H), 1.75 (broad, 2H), 1.65 (broad, 1H), 1.4 (broad, 3H), 0.9 (broad, 3H).

10

III. Examples of galenic administration forms

A) Tablets

15

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

- 20 40 mg of substance from Example 8
120 mg of corn starch
13.5 mg of gelatin
45 mg of lactose
2.25 mg of Aerosil® (chemically pure silicic acid in submicroscopically fine dispersion)
6.75 mg of potato starch (as a 6% paste)

25

B) Sugar-coated tablets

- 20 mg of substance from Example 8
60 mg of core composition
30 70 mg of saccharification composition

- 35 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.

IV. Biological investigations

- 40 Receptor binding studies:

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.

Human 5HT₆ receptor:

5

Characterization of the compounds of this invention to the human 5-HT₆ receptor in the binding assay and the functional adenylyl cyclase assay

10 The compounds were dissolved in a concentration of 10^{-2} M or 10^{-3} M in DMSO. Further dilutions were performed in incubation buffer.

Binding assays

15 The procedure for the binding assay was based on the method of Monsma et al. (1993) Mol Pharmacol 43: 320-327. The binding reaction was carried out in a total volume of 0.250 ml for 60 min at 37°C. Membranes from HEK-293 cells stably expressing the human 5-HT₆ receptor were incubated with 2 nM ³H-LSD in the presence or absence of various concentrations of test compound for 60 min at 37°C. Non-specific binding was defined with 100 µM Serotonin (5-HT). Assays were performed in duplicate. Bound
20 and free radioligand was separated by filtration and bound radioactivity determined by liquid scintillation counting.

Evaluation:

25 The specific ligand binding to the receptors was defined as the difference between the total binding and the nonspecific binding determined in the presence of an excess of unlabelled 5-HT. The results are expressed as a percent of control specific binding obtained in the presence of compound. The IC₅₀ values (concentration causing a half-maximal inhibition of control specific binding) and Hill coefficients (*nH*) were determined
30 by non-linear regression analysis of the competition curves using Hill equation curve fitting.

The inhibition constants (*K_i*) were calculated from the Cheng Prusoff equation ($K_i = IC_{50}/(1+(L/KD))$, where *L* = concentration of radioligand in the assay, and *KD* = affinity
35 of the radioligand for the receptor).

Functional adenylyl cyclase assay

Membranes of human HeLa cells stably expressing human 5-HT₆ receptors were incubated for 20 min at 37°C in HBSS, 1 mM MgCl₂, 1 mM CaCl₂, 100 µM IBMX, pH 7.4 in

the presence and absence of test compounds. For agonistic effect, compounds were incubated alone. For antagonistic effects inhibition of 0.3 μ M serotonin (5-HT)-induced cAMP increase was determined.

- 5 Evaluation: cAMP accumulation was determined by EIA quantification.

Dopamine D₃ receptor:

- 10 The assay mixture (0.250 ml) was composed of membranes derived from $\sim 10^6$ 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 μ M spiperone (nonspecific binding). Each assay mixture was run in triplicate.

- 15 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 μ M quinolone and 0.1% ascorbic acid (prepared fresh daily). The buffer was adjusted to pH 7.4 with HCl.

- 20 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 [¹²⁵I] iodospiperone 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.

- 25 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. The buffer was adjusted to pH 7.4 with HCl.
- 30

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.
- 35
- 40

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.

5

The results of the receptor binding studies are expressed as receptor binding constants $K_i(5HT_6)$, $K_i(D_3)$ and $K_i(D_2)$, respectively, as herein before described, and given in table 6.

10 In these tests, the compounds according to the invention exhibit very good affinities for the $5HT_6$ receptor (< 50 nM, or < 10 nM, frequently < 5 nM). Some of the compounds, in particular those having as 1,4-phenylene as group A, also exhibit very good affinities for the D_3 receptor (< 50 nM, or < 10 nM, frequently < 5 nM) and bind selectively to the D_3 receptor, as compared to the affinity for the D_2 receptor.

15

The results of the binding tests are given in table 6.

Table 6:

Example	$K_i(5HT_6)^*$ [nM]	$K_i(D_3)^*$ [nM]	$K_i(D_2)/K_i(D_3)$
1	++		
3	++	+++	+++
4	+++	++	+
6	+++		
7	+++		
8	++		
9	+++		
10	+++		
11	+++		
12	++		
13	++		
14	+++		
15	+++		
16	+++		
17	++++		
18	+++		
19	+++		
20	++++		
21	+		

Example	K _i (5HT ₆)* [nM]	K _i (D ₃)* [nM]	K _i (D ₂)/K _i (D ₃)
22	+++		
23	++		
24	+		
25	+++		
26	+++		
31	+++		
32	+++		
34	++		
40	+		
42	+		
43	++		
44	+		
45	++		
46	+		
47	++		
48	++		
49	++		
50	+		
51	+		
52	++		
54	+		
59	+++	+++	+++
60	++	++++	+
61	++	+++	++
62	+++	+++	++++
63	++		
64	+		
65	++		
66	++	++++	+++
67	+++		
69	++	++	+++
70	+++	+++	++
71	+++	++	+
73	++	+++	++
74	+++	++	++

Example	K _i (5HT ₆)* [nM]	K _i (D ₃)* [nM]	K _i (D ₂)/K _i (D ₃)
75	++	++	+
76	+++	+++	+++
77	+++		
78	+++	++++	
86	++	+++	++
90	+++	+++	++++
91	++		
94	++		
95	+++	++	+
97	+++	++	++
98	+++	++	+
99	+++	+	+
100	+++	++	+++
101	++		
102	++	++	++
103	++	+	++
104	++		

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

5 Key:

	K _i (D ₃)* and K _i (5HT ₆)*	K _i (D ₂)/K _i (D ₃)*
+	between 50 and 150 nM	between 10 and 50
++	between 10 and 50 nM	between 50 and 100
+++	between 1 and 10 nM	between 100 and 150
++++	< 1 nM	> 150

Assay for testing the compatibility of dopamine D₃ and 5HT₆ receptor ligands

10 Microdialysis Studies

An increase in cholinergic function is widely believed to improve cognitive performance, an increase of cortical extracellular acetylcholine (ACh) can be regarded as a biochemical marker for potential pro-cognitive effects.

5 Therefore, microdialysis studies in freely moving rats were performed. The effects of 5-HT₆ receptor ligands, selective D₃ ligands or the combination of both principles, on acetylcholine release in the medial prefrontal cortex and in the hippocampus has been investigated: one guide cannula was implanted into the medial prefrontal cortex (AP = 2.5; ML = 0.6; DV = - 0.2) and the second into the hippocampus (AP = -5.5; ML = 4.5; 10 DV = -4.5). 5 to 7 days after surgery, 2 microdialysis probes (CMA/12, 3 mm membrane length) were slowly lowered into the final position. On the day of the experiment, the test compound or its vehicle (2 ml/kg) was administered intraperitoneally. Microdialysate fractions (six 20-min fractions before and six fractions after compound administration) were analyzed for acetylcholine by high performance liquid chromatography in combination with electrochemical detection (for methods see Fox et al., J. Pharmacol. Exp. Ther. 2005, 313, 176 to 190 and detailed description below). 15

5-HT₆ receptor ligands and selective D₃ receptor ligands increased dose-dependently extracellular ACh levels in the medial prefrontal cortex and in the hippocampus. The 20 combination of both 5-HT₆ receptor ligands and D₃ receptor ligands resulted in an at least additive effect of both principles in the medial prefrontal cortex and in the hippocampus, suggesting thus that the combination of both principles may offer a therapeutic benefit in CNS disorders characterized by impaired cognitive functions, including dementia and schizophrenia.

25 Furthermore, mixed D₃/5-HT₆ receptor ligands also increase microdialysate ACh levels in the medial prefrontal cortex and in the hippocampus. Based on dose comparisons, compounds combining D₃/5-HT₆ within the molecule are more potent in increasing cortical cholinergic function than "pure" D₃ receptor antagonists.

30

Microdialysis Experiments

Surgery

35 For pain prophylaxis, Rimadyl® (3 mg/kg, i.p.) was administered before surgery. Individual male Sprague-Dawley rats (290 – 320 g body weight) anesthetized with pentobarbital (60 mg/kg, i.p, Narcoren®, Rhone-Merieux GmbH, France) were mounted in a KOPF stereotaxic frame and two microdialysis guide cannula (CMA/12, Axel Semrau GmbH, Germany) were implanted into selected brain areas of the same animal: one 40 guide cannula was implanted into the medial prefrontal cortex (AP = 2.5; ML = 0.6; DV

= - 0.2) and the second into the hippocampus (AP = -5.5; ML = 4.5; DV = -4.5). The guide cannula were secured with dental cement (Technovit powder, Product No 5071, Technovit polymerization starter fluid, Product No 2060, Kulzer GmbH, Germany) and 4 anchor screws into the skull. The rats were allowed to recover from surgery for 5-7 days. The day before the experiment, each animal was transferred into a system allowing for free movement (CMA/120 Axel Semrau GmbH, Germany, consisting of a plastic bowl, wire attachment, counter-balance arm, swivel assembly connecting in-/outlet of the probe with the perfusion pump). Next, a CMA/12 microdialysis probe (3 mm membrane length) was slowly lowered into the final position. The probe was perfused with Ringer solution (147 mM NaCl, 4.0 mM KCl and 2.4 mM CaCl₂, containing 1 μ M neostigmine), for about one hour (CMA/102 microdialysis pump, Axel Semrau GmbH, Germany; 1.5 μ l/min). The probe was perfused again 24 hours later for at least 1 hour before microdialysate fractions were collected every 20 minutes. Six fractions before and six fractions after the intraperitoneally administration of the test compound or vehicle were analyzed for microdialysate levels of acetylcholine by HPLC with electrochemical detection.

Assay of Microdialysate Acetylcholine Levels

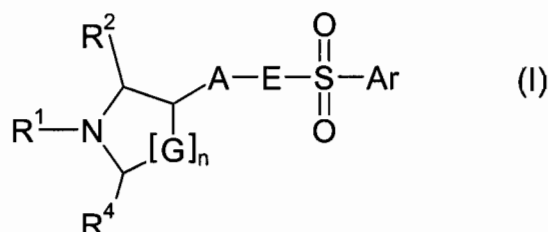
10 μ l of each microdialysate fraction was injected onto a reversed phase column (MF-8908 Acetylcholine SepStik Kit; microbore column, particle size 10 μ m, 530 x 1.0 mm coupled to an immobilized enzyme reactor 50 x 1.0 mm, particle size 10 μ m, containing acetylcholinesterase and choline oxidase; BAS, U.S.A.) using a refrigerated autosampler (HTC PAL twin injector autosampler system, Axel Semrau, Germany). The mobile phase consisted of 50 mmol/l Na₂HPO₄ (pH 8.5) and 5 ml/l Kathon. Flow rate was 0.14 ml/min (Rheos Flux pump, Axel Semrau GmbH, Germany), and the sample run time was less than 15 minutes. Acetylcholine and choline were measured via an electrochemical detector (LC-4C, BAS, U.S.A.) with a platinum working electrode set at + 500 mV versus an Ag/AgCl reference electrode. The system was calibrated by standard solutions (acetylcholine, choline) containing 1 pmol/10 μ l injection. Acetylcholine was identified by its retention time and peak height with an external standard method using chromatography software (Chrom Perfect®, version 4.4.22, Justice Laboratory Software, U.S.A.).

Microdialysis (area under curve 0 - 120 min) data were evaluated for significance using one-way analysis of variance (ANOVA) followed by Dunnett's pair-wise comparison post hoc test using GraphPad Prism v 4.0 software.

We claim:

1. A compound of the formula (I)

5



wherein

10

n is 0, 1 or 2;

G is CH₂ or CHR³;

15

R¹ is H, C₁-C₆-alkyl, C₁-C₆-alkyl substituted by C₃-C₆-cycloalkyl, C₁-C₆-hydroxyalkyl, fluorinated C₁-C₆-alkyl, C₃-C₆-cycloalkyl, fluorinated C₃-C₆-cycloalkyl, C₃-C₆-alkenyl, fluorinated C₃-C₆-alkenyl, formyl, acetyl, propionyl or benzyl;

20

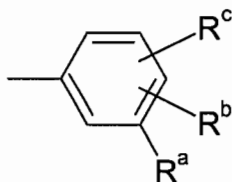
R², R³ and R⁴ are, independently of each other, H, methyl, fluoromethyl, difluoromethyl, or trifluoromethyl;

25

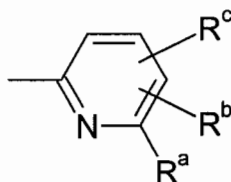
A is 1,4-phenylene or 1,3-phenylene, which is optionally substituted by one, two, three or four substituents selected from halogen, C₁-C₄-alkyl, C₁-C₄-alkoxy, fluorinated C₁-C₄-alkyl and fluorinated C₁-C₄-alkoxy;

E is NR⁵ or CH₂, wherein R⁵ is H or C₁-C₃-alkyl;

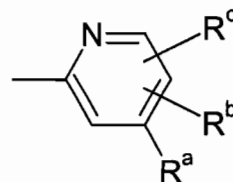
Ar is a radical of the formula A, B, C, D, E, F or G



(A)

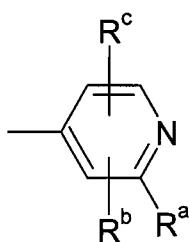


(B)

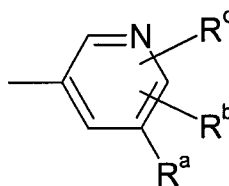


(C)

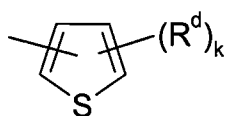
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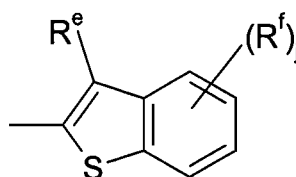
(D)



(E)



(F)



(G)

5 wherein

10 R^a is halogen, hydroxyl, C_1 - C_6 -alkyl, fluorinated C_1 - C_6 -alkyl, C_1 - C_6 -hydroxyalkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, fluorinated C_2 - C_6 -alkenyl, C_3 - C_6 -cycloalkyl, fluorinated C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkoxy, C_1 - C_6 -hydroxyalkoxy, C_1 - C_6 -alkoxy- C_1 - C_6 -alkoxy, fluorinated C_1 - C_6 -alkoxy, C_1 - C_6 -alkylthio, fluorinated C_1 - C_6 -alkylthio, C_1 - C_6 -alkylsulfinyl, fluorinated C_1 - C_6 -alkylsulfinyl, C_1 - C_6 -alkylsulfonyl, fluorinated C_1 - C_6 -alkylsulfonyl, phenylsulfonyl, pyridylsulfonyl, benzyloxy, phenoxy, phenyl, where the phenyl and the pyridyl radical in the 5 last-mentioned radicals may be unsubstituted or may carry 1 to 3 substituents selected from C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl and halogen, CN, nitro, C_1 - C_6 -alkylcarbonyl, fluorinated C_1 - C_6 -alkylcarbonyl, C_1 - C_6 -alkylcarbonylamino, fluorinated C_1 - C_6 -alkylcarbonylamino, carboxy, $NH-C(O)-NR^6R^7$, NR^6R^7 , $NR^6R^7-C_1$ - C_6 -alkylene, $O-NR^6R^7$, where R^6 and R^7 are, independently of each other, H, C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl or C_1 - C_4 -alkoxy or may form, together with N, a 4-, 5- or 6-membered saturated or unsaturated ring, $R^9-CO-NR^6-C_1$ - C_6 -alkylene, where R^6 is as defined above and R^9 is C_1 - C_4 -alkyl or phenyl, where the phenyl radical may be unsubstituted or may carry 1 to 3 substituents selected from C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl and halogen, CH_2 -pyridyl, where the pyridyl radical may be unsubstituted or may carry 1 to 3 substituents selected from C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl and halogen, or is a saturated or unsaturated aromatic or non-aromatic 3- to 7-membered heterocyclic ring comprising as ring members 1, 2, 3 or 4 heteroatoms selected from N, O and S and/or 1, 2 or 3 heteroatom-containing groups selected from NR^8 , where R^8 is H, C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl, C_1 - C_4 -alkylcarbonyl or fluorinated C_1 - C_4 -alkylcarbonyl, SO, SO_2 and CO, and

where the heterocyclic ring may carry 1, 2 or 3 substituents selected from hydroxy, halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl, C₁-C₆-alkoxy, fluorinated C₁-C₆-alkoxy, C₁-C₆-alkylthio, fluorinated C₁-C₆-alkylthio, NR⁶R⁷-C₁-C₆-alkylene, where R⁶ and R⁷ are as defined above, carboxyl and C₁-C₄-alkoxycarbonyl;

R^b and R^c, independently of each other, are H, halogen, CH₃, OCH₃, CH₂F, OCH₂F, CHF₂, OCHF₂, CF₃, OCF₃, CH₂CH₂F, OCH₂CH₂F, CH₂CHF₂, OCH₂CHF₂, CH₂CF₃ or OCH₂CF₃;

R^d is defined like R^a;

R^e is H or is defined like R^a;

R^f is defined like R^a;

k is 0, 1, 2 or 3; and

j is 0, 1, 2, 3 or 4;

with the proviso that R^a is not F, CH₂F, CHF₂, CF₃ or OCF₃ if A is 1,4-phenylene, Ar is a radical of the formula (A) and R^b and R^c are H or halogen;

except compounds, where R¹ is propyl, G is CH₂, n is 1, A is 1,4-phenylene, E is NH, Ar is a radical of formula (F) and R^d is halogen, C₁-C₆-alkyl, C₂-C₆-alkenyl or a 5-membered heteroaromatic ring;

and physiologically tolerated acid addition salts thereof.

2. A compound of the formula (I) as claimed in claim 1, wherein Ar is a radical of the formulae A, B, C, D or E.

3. A compound of the formula (I) as claimed in claim 1 or 2, wherein

R¹ is H, C₁-C₆-alkyl, C₁-C₆-alkyl substituted by C₃-C₆-cycloalkyl, C₁-C₆-hydroxyalkyl, fluorinated C₁-C₆-alkyl, C₃-C₆-cycloalkyl, fluorinated C₃-C₆-cycloalkyl, C₃-C₆-alkenyl, fluorinated C₃-C₆-alkenyl, formyl, acetyl or propionyl;

Ar is a radical of the formula A, B, C, D or E;

R^a is halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl, C₁-C₆-hydroxyalkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₂-C₆-alkenyl, fluorinated C₂-C₆-alkenyl, C₃-C₆-cycloalkyl, fluorinated C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₁-C₆-hydroxyalkoxy, C₁-C₆-alkoxy-C₁-C₆-alkoxy, fluorinated C₁-C₆-alkoxy, C₁-C₆-alkylthio, fluorinated C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, fluorinated C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl,

fluorinated C₁-C₆-alkylsulfonyl, phenylsulfonyl, benzyloxy, phenoxy, where the phenyl radical in the 3 last-mentioned radicals may be unsubstituted or may carry 1 to 3 substituents selected from C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl and halogen, CN, nitro, C₁-C₆-alkylcarbonyl, fluorinated C₁-C₆-alkylcarbonyl, C₁-C₆-alkylcarbonylamino, fluorinated C₁-C₆-alkylcarbonylamino, carboxy, NH-C(O)-NR⁶R⁷, NR⁶R⁷, NR⁶R⁷-C₁-C₆-alkylene, O-NR⁶R⁷, where R⁶ and R⁷ are, independently of each other, H, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl or C₁-C₄-alkoxy or may form, together with N, a 4-, 5- or 6-membered saturated or unsaturated ring, or is a saturated or unsaturated 3- to 7-membered heterocyclic ring comprising as ring members 1, 2, 3 or 4 heteroatoms selected from N, O and S and/or 1, 2 or 3 heteroatom-containing groups selected from NR⁸, where R⁸ is H, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl, C₁-C₄-alkylcarbonyl or fluorinated C₁-C₄-alkylcarbonyl, SO, SO₂ and CO, and where the heterocyclic ring may carry 1, 2 or 3 substituents selected from hydroxy, halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl and C₁-C₆-alkoxy; and

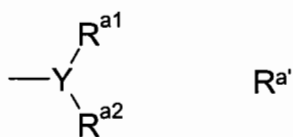
R^b and R^c, independently of each other, are H, halogen, CH₃, OCH₃, CHF₂, OCHF₂, CF₃ or OCF₃;

with the proviso that R^a is not F, CH₂F, CHF₂, CF₃ or OCF₃ if A is 1,4-phenylene and R^b and R^c are H or halogen;

and physiologically tolerated acid addition salts thereof.

4. The compound as claimed in claim 1, where Ar is a radical of the formula (F) or of the formula (G).
5. The compound as claimed in claim 4, where R^d is selected from halogen, hydroxyl, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl, C₁-C₄-alkylsulfonyl, fluorinated C₁-C₄-alkylsulfonyl, phenylsulfonyl, pyridylsulfonyl, phenyl, where the phenyl and the pyridyl radical in the 3 last-mentioned radicals may be unsubstituted or may carry 1 to 3 substituents selected from C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl and halogen, R⁹-CO-NR⁶-C₁-C₂-alkylene, CH₂-pyridyl, where the pyridyl radical may be unsubstituted or may carry 1 to 3 substituents selected from C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl and halogen, and a saturated, partially unsaturated or aromatic 5- or 6-membered heterocyclic ring comprising as ring members 1, 2 or 3 heteroatoms selected from N, O and S and/or 1, 2 or 3 heteroatom-containing groups selected from NR⁸, where R⁸ is H, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl, C₁-C₄-alkylcarbonyl or fluorinated C₁-C₄-alkylcarbonyl, and where the heterocyclic ring may carry 1, 2 or 3 substituents selected from hydroxy, halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl, C₁-C₆-alkoxy, fluorinated C₁-C₆-alkoxy, C₁-C₆-alkylthio, fluorinated C₁-C₆-alkylthio, NR⁶R⁷-C₁-C₆-alkylene, carboxyl and C₁-C₄-alkyoxycarbonyl, where R⁶, R⁷ and R⁹ are as defined in claim 1.

6. The compound as claimed in claim 5, where R^d is selected from halogen, C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl, C_1 - C_4 -alkylsulfonyl, fluorinated C_1 - C_4 -alkylsulfonyl, phenylsulfonyl, where the phenyl radical may be unsubstituted or may carry 1 to 3 substituents selected from C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl and halogen, and a 5- or 6-membered heteroaromatic ring comprising as ring members one nitrogen atom or one group NR^8 , where R^8 is H or C_1 - C_4 -alkyl, and optionally one or two further heteroatoms selected from N, O, S, and where the heteroaromatic ring may carry 1, 2 or 3 substituents selected from halogen, C_1 - C_6 -alkyl, fluorinated C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy, fluorinated C_1 - C_6 -alkoxy, C_1 - C_6 -alkylthio and fluorinated C_1 - C_6 -alkylthio.
7. The compound as claimed in claim 4, where R^e is H, halogen, C_1 - C_4 -alkyl or fluorinated C_1 - C_4 -alkyl, R^f is C_1 - C_4 -alkyl or fluorinated C_1 - C_4 -alkyl and j is 0 or 1.
8. The compound as claimed in any of the preceding claims, wherein n is 0 or 1.
9. The compound as claimed in any of the preceding claims, wherein R^1 is hydrogen, methyl, ethyl, n-propyl, 2-fluoroethyl, 3-fluoropropyl, 3-hydroxypropyl, cyclopropylmethyl, allyl or benzyl.
10. The compound as claimed in claim 9, wherein R^1 is hydrogen, n-propyl or allyl.
11. The compound as claimed in any of the preceding claims, wherein R^2 , R^3 and R^4 are H.
12. The compound as claimed in any of the preceding claims, wherein E is NH.
13. The compound as claimed in any of claims 1 to 3 and 8 to 12, wherein R^a is selected from radicals 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, fluorinated C_1 - C_2 -alkyl and C_1 - C_2 -alkoxy, 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, C_1 - C_2 -alkyl or C_1 - C_2 -alkoxy, wherein one CH_2 moiety may be replaced by O, S, SO, SO_2 or NR^c , wherein R^c is H or C_1 - C_2 -alkyl, and wherein m is 2, 3, 4, 5 or 6.

14. The compound as claimed in any of the preceding claims, wherein the radical R^a is selected from halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl, C₁-C₆-alkoxy, fluorinated C₁-C₆-alkoxy, C₁-C₆-alkylsulfonyl, fluorinated C₁-C₆-alkylsulfonyl, CN, nitro, C₁-C₆-alkylcarbonyl, fluorinated C₁-C₆-alkylcarbonyl, C₁-C₆-alkylcarbonylamino, fluorinated C₁-C₆-alkylcarbonylamino, or a saturated or unsaturated 3- to 7-membered heterocyclic ring comprising as ring members 1, 2, 3 or 4 heteroatoms selected from N, O and S and/or 1, 2 or 3 heteroatom-containing groups selected from NR⁸, where R⁸ is as defined in claim 1, SO, SO₂ and CO, and where the heterocyclic ring may carry 1, 2 or 3 substituents selected from hydroxy, halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl and C₁-C₆-alkoxy.
15. The compound as claimed in any of the preceding claims, wherein the absolute configuration at the carbon atom carrying the group A is (S).
16. The compound as claimed in any of the preceding claims, wherein A is 1,3-phenylene, which is optionally substituted by one or more substituents selected from halogen, C₁-C₄-alkyl, C₁-C₄-alkoxy, fluorinated C₁-C₄-alkyl and fluorinated C₁-C₄-alkoxy.
17. The compound as claimed in claims 1 to 15, wherein A is 1,4-phenylene which is optionally substituted by one or more substituents selected from halogen, C₁-C₄-alkyl, C₁-C₄-alkoxy, fluorinated C₁-C₄-alkyl and fluorinated C₁-C₄-alkoxy.
18. The compound as claimed in claim 17, wherein R^a is C₁-C₆-alkyl, C₁-C₆-hydroxyalkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₂-C₆-alkenyl, fluorinated C₂-C₆-alkenyl, C₃-C₆-cycloalkyl, fluorinated C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₁-C₆-hydroxyalkoxy, C₁-C₆-alkoxy-C₁-C₆-alkoxy, C₁-C₆-alkylthio, fluorinated C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, fluorinated C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, fluorinated C₁-C₆-alkylsulfonyl, phenylsulfonyl, benzyloxy, phenoxy, where the phenyl radical in the 3 last-mentioned radicals may be unsubstituted or may carry 1 to 3 substituents selected from C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl and halogen, CN, nitro, C₁-C₆-alkylcarbonyl, fluorinated C₁-C₆-alkylcarbonyl, C₁-C₆-alkylcarbonylamino, fluorinated C₁-C₆-alkylcarbonylamino, carboxy, NH-C(O)-NR⁶R⁷, NR⁶R⁷, NR⁶R⁷-C₁-C₆-alkylene, O-NR⁶R⁷, where R⁶ and R⁷ are, independently of each other, H, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl or C₁-C₄-alkoxy or may form, together with N, a 4-, 5- or 6-membered saturated or unsaturated ring, or is a saturated or unsaturated 3- to 7-membered heterocyclic ring comprising as ring members 1, 2, 3 or 4 heteroatoms selected from N, O and S and/or 1, 2 or 3 heteroatom-containing groups selected from NR⁸, where R⁸ is as defined in claim 1, SO, SO₂ and CO, and where the heterocyclic ring may carry 1, 2 or 3 substituents selected from hydroxy, halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl and C₁-C₆-alkoxy.
19. The compound as claimed any of the preceding claims, wherein the saturated or unsaturated 3- to 7-membered heterocyclic ring R^a is selected from azetidiny, pyrrolidiny, oxopyrrolidiny, oxo-oxazolidiny, piperidiny, piperaziny, morpholinyl,

thiomorpholinyl, 1-oxothiomorpholinyl, 1,1-dioxothiomorpholinyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, triazolyl, oxadiazolyl, furazanyl, thiadiazolyl, and tetrazolyl, where the heterocyclic radical may be unsubstituted or may carry 1 to 3 substituents selected from halogen, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl, C₁-C₄-alkoxy and hydroxy.

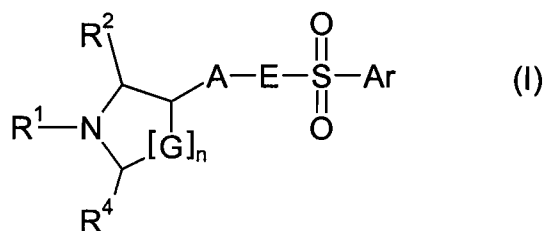
20. The compound as claimed in claim 19, wherein the saturated or unsaturated 3- to 7-membered heterocyclic ring R^a is selected from azetidiny, pyrrolidinyl, oxopyrrolidinyl, oxo-oxazolidinyl, piperidinyl, morpholinyl, furanyl, thienyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl and thiadiazolyl, where the heterocyclic radical may be unsubstituted or may carry 1 to 3 substituents selected from halogen and C₁-C₄-alkyl.

21. The compound as claimed in any of claims 19 or 20, wherein the saturated or unsaturated 3- to 7-membered heterocyclic ring comprises as ring member at least one nitrogen atom or at least one group NR⁸.

22. The compound as claimed in any of claims 1 to 3 and 8 to 21, wherein R^a is selected from halogen, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl, CN, a 5-membered heteroaromatic ring comprising as ring members one nitrogen atom or one group NR⁸, where R⁸ is H or C₁-C₄-alkyl, and optionally one or two further heteroatoms selected from N, O, S, and where the heteroaromatic ring may carry 1, 2 or 3 substituents selected from halogen, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl, C₁-C₄-alkoxy and hydroxy, and a 5- or 6-membered saturated heterocyclic ring bound via a nitrogen atom optionally containing, apart this nitrogen atom one further heteroatom or heteroatom-containing group selected from O and NR⁸, where R⁸ is H or C₁-C₄-alkyl, where the heterocyclic radical may carry 1, 2 or 3 substituents selected from halogen, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl, C₁-C₄-alkoxy and hydroxy.

23. A pharmaceutical composition comprising at least one compound as claimed in any of the preceding claims, optionally together with at least one physiologically acceptable carrier or auxiliary substance.

24. The use of a compound of the formula I



wherein

n is 0, 1 or 2;

G is CH_2 or CHR^3 ;

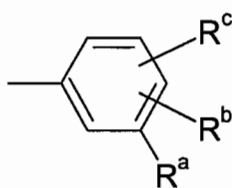
R^1 is H, $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_1\text{-C}_6\text{-alkyl}$ substituted by $\text{C}_3\text{-C}_6\text{-cycloalkyl}$, $\text{C}_1\text{-C}_6\text{-hydroxyalkyl}$, fluorinated $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_3\text{-C}_6\text{-cycloalkyl}$, fluorinated $\text{C}_3\text{-C}_6\text{-cycloalkyl}$, $\text{C}_3\text{-C}_6\text{-alkenyl}$, fluorinated $\text{C}_3\text{-C}_6\text{-alkenyl}$, formyl, acetyl, propionyl or benzyl;

R^2 , R^3 and R^4 are, independently of each other, H, methyl, fluoromethyl, difluoromethyl, or trifluoromethyl;

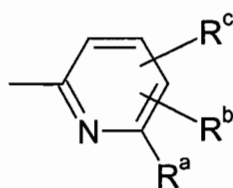
A is 1,4-phenylene or 1,3-phenylene, which is optionally substituted by one, two, three or four substituents selected from halogen, $\text{C}_1\text{-C}_4\text{-alkyl}$, $\text{C}_1\text{-C}_4\text{-alkoxy}$, fluorinated $\text{C}_1\text{-C}_4\text{-alkyl}$ and fluorinated $\text{C}_1\text{-C}_4\text{-alkoxy}$;

E is NR^5 or CH_2 , wherein R^5 is H or $\text{C}_1\text{-C}_3\text{-alkyl}$;

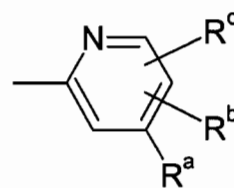
Ar is a radical of the formula A, B, C, D, E, F or G



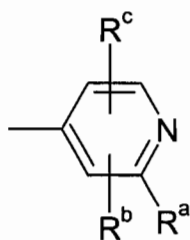
(A)



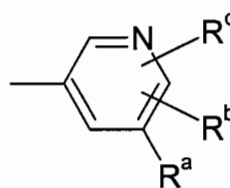
(B)



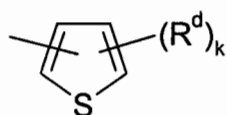
(C)



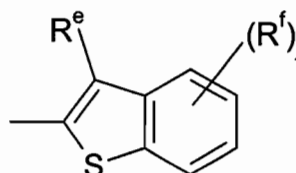
(D)



(E)



(F)



(G)

wherein

R^a is halogen, hydroxyl, C_1 - C_6 -alkyl, fluorinated C_1 - C_6 -alkyl, C_1 - C_6 -hydroxyalkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, fluorinated C_2 - C_6 -alkenyl, C_3 - C_6 -cycloalkyl, fluorinated C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkoxy, C_1 - C_6 -hydroxyalkoxy, C_1 - C_6 -alkoxy- C_1 - C_6 -alkoxy, fluorinated C_1 - C_6 -alkoxy, C_1 - C_6 -alkylthio, fluorinated C_1 - C_6 -alkylthio, C_1 - C_6 -alkylsulfinyl, fluorinated C_1 - C_6 -alkylsulfinyl, C_1 - C_6 -alkylsulfonyl, fluorinated C_1 - C_6 -alkylsulfonyl, phenylsulfonyl, pyridylsulfonyl, benzyloxy, phenoxy, phenyl, where the phenyl and the pyridyl radical in the 5 last-mentioned radicals may be unsubstituted or may carry 1 to 3 substituents selected from C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl and halogen, CN, nitro, C_1 - C_6 -alkylcarbonyl, fluorinated C_1 - C_6 -alkylcarbonyl, C_1 - C_6 -alkylcarbonylamino, fluorinated C_1 - C_6 -alkylcarbonylamino, carboxy, $NH-C(O)-NR^6R^7$, NR^6R^7 , $NR^6R^7-C_1$ - C_6 -alkylene, $O-NR^6R^7$, where R^6 and R^7 are, independently of each other, H, C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl or C_1 - C_4 -alkoxy or may form, together with N, a 4-, 5- or 6-membered saturated or unsaturated ring, $R^9-CO-NR^6-C_1$ - C_6 -alkylene, where R^6 is as defined above and R^9 is C_1 - C_4 -alkyl or phenyl, where the phenyl radical may be unsubstituted or may carry 1 to 3 substituents selected from C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl and halogen, CH_2 -pyridyl, where the pyridyl radical may be unsubstituted or may carry 1 to 3 substituents selected from C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl and halogen, or is a saturated or unsaturated aromatic or non-aromatic 3- to 7-membered heterocyclic ring comprising as ring members 1, 2, 3 or 4 heteroatoms selected from N, O and S and/or 1, 2 or 3 heteroatom-containing groups selected from NR^8 , where R^8 is H, C_1 - C_4 -alkyl, fluorinated C_1 - C_4 -alkyl, C_1 - C_4 -alkylcarbonyl or fluorinated C_1 - C_4 -alkylcarbonyl, SO, SO_2 and CO, and where the heterocyclic ring may carry 1, 2 or 3 substituents selected from hydroxy, halogen, C_1 - C_6 -alkyl, fluorinated C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy, fluorinated C_1 - C_6 -alkoxy, C_1 - C_6 -alkylthio, fluorinated C_1 - C_6 -alkylthio, $NR^6R^7-C_1$ - C_6 -alkylene, where R^6 and R^7 are as defined above, carboxyl and C_1 - C_4 -alkyloxycarbonyl; and

R^b and R^c , independently of each other, are H, halogen, CH_3 , OCH_3 , CH_2F , OCH_2F , CHF_2 , $OCHF_2$, CF_3 , OCF_3 , CH_2CH_2F , OCH_2CH_2F , CH_2CHF_2 , OCH_2CHF_2 , CH_2CF_3 or OCH_2CF_3 ;

R^d is defined like R^a ;

R^e is H or is defined like R^a ;

R^f is defined like R^a ;

k is 0, 1, 2 or 3; and

j is 0, 1, 2, 3 or 4;

and/or of physiologically tolerated acid addition salt thereof,

for preparing a pharmaceutical composition for the treatment of a medical disorder susceptible to treatment with a 5-HT₆ receptor ligand.

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25. The use as claimed in claim 24, wherein in a compound of formula 1

Ar is a radical of the formula A, B, C, D or E;

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R^a is halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl, C₁-C₆-hydroxyalkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₂-C₆-alkenyl, fluorinated C₂-C₆-alkenyl, C₃-C₆-cycloalkyl, fluorinated C₃-C₆-cycloalkyl, C₁-C₆-alkoxy, C₁-C₆-hydroxyalkoxy, C₁-C₆-alkoxy-C₁-C₆-alkoxy, fluorinated C₁-C₆-alkoxy, C₁-C₆-alkylthio, fluorinated C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, fluorinated C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, fluorinated C₁-C₆-alkylsulfonyl, phenylsulfonyl, benzyloxy, phenoxy, where the phenyl radical in the 3 last-mentioned radicals may be unsubstituted or may carry 1 to 3 substituents selected from C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl and halogen, CN, nitro, C₁-C₆-alkylcarbonyl, fluorinated C₁-C₆-alkylcarbonyl, C₁-C₆-alkylcarbonylamino, fluorinated C₁-C₆-alkylcarbonylamino, carboxy, NH-C(O)-NR⁶R⁷, NR⁶R⁷, NR⁶R⁷-C₁-C₆-alkylene, O-NR⁶R⁷, where R⁶ and R⁷ are, independently of each other, H, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl or C₁-C₄-alkoxy or may form, together with N, a 4-, 5- or 6-membered saturated or unsaturated ring, or is a saturated or unsaturated 3- to 7-membered heterocyclic ring comprising as ring members 1, 2, 3 or 4 heteroatoms selected from N, O and S and/or 1, 2 or 3 heteroatom-containing groups selected from NR⁸, where R⁸ is H, C₁-C₄-alkyl, fluorinated C₁-C₄-alkyl, C₁-C₄-alkylcarbonyl or fluorinated C₁-C₄-alkylcarbonyl, SO, SO₂ and CO, and where the heterocyclic ring may carry 1, 2 or 3 substituents selected from hydroxy, halogen, C₁-C₆-alkyl, fluorinated C₁-C₆-alkyl and C₁-C₆-alkoxy; and

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R^b and R^c, independently of each other, are H, halogen, CH₃, OCH₃, CHF₂, OCHF₂, CF₃ or OCF₃.

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26. The use as claimed in claim 24 or 25, wherein a compound of formula I is as defined in any of claims 1 to 22.

27. The use as claimed in any of claims 24 to 26, wherein the medical disorder is a disease of the central nervous system.

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28. The use as claimed in claim 27, for the treatment of cognitive dysfunctions.

29. The use as claimed in claim 28, for the treatment of cognitive dysfunctions associated with Alzheimer's disease and schizophrenia.