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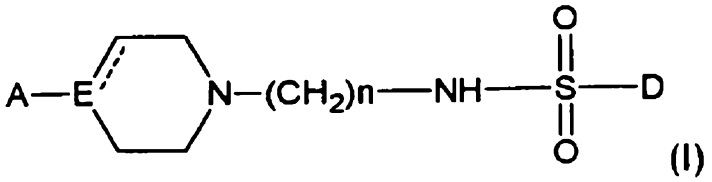

(I)

(57) Abstract: Arylsulphonamide derivatives of formula (I) and pharmaceutically acceptable salts thereof. The compounds may be useful for the treatment and/or prevention of disorders of the central nervous system.

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ARYLOSULFONAMIDES FOR THE TREATMENT OF CNS DISEASES

Field of the invention

The present invention relates to novel arylsulphonamides having affinity to dopaminergic, serotoninergic, adrenergic, sigma and serotonine transporter receptors, pharmaceutical compositions containing the same and to the use thereof. The compounds may be useful for the treatment of diseases of the central nervous system, such as schizophrenia, bipolar affective disorder, depression, anxiety disorders, sleep disorders or Alzheimer disease.

State of the art

CNS disorders are considered a global medical problem. A number of people suffering from those diseases constantly grows, particularly in highly developed countries and intensively developing ones. Approximately 20% of population in highly developed societies suffers from CNS disorders. In addition a cost of treatment of such disorders represents nearly 35% of total expenses spent for treatment of all medical diseases in seven countries considered as the biggest pharmaceutical markets.

Among all psychiatric diseases, schizophrenia, bipolar disorder, depression, anxiety, sleep disorders and addictions are the major ones. The main neurologic disorders are Alzheimer's disease, Parkinson's disease, epilepsy and different pain disorders.

Antipsychotic drugs, which are main treatment of schizophrenia, are divided into two main classes on the basis of their liability to induce neurological side effects after long-term treatment. Typical antipsychotic drugs, such as chlorpromazine and haloperidol, induce after repeated administration various extrapyramidal side effects (EPS) including Parkinson-like symptoms and tardive dyskinesia. Repeated treatment with so called atypical antipsychotic drugs, such as clozapine, risperidone, olanzapine, quetiapine, ziprasidone and aripiprazole, is associated with a lower incidence of neurological side effects. Typical antipsychotics reduce positive symptoms but do not reduce negative symptoms and cognitive dysfunctions. Plasma prolactin levels are increased in humans, and there is a gain in bodyweight potentially leading to the development of metabolic syndrome. Atypical antipsychotic drugs effectively reduce positive symptoms and also to some extent negative symptoms and cognitive disturbances producing less serious EPS. Atypical antipsychotic drugs differ in their propensity to elevate plasma prolactin levels in humans. Typical antipsychotic drugs block dopamine D2 receptors in the mesolimbic and nigrostriatal system. This mechanism is responsible for the antipsychotic effect (reduction of positive symptoms) as well as induction of EPS. Clinical support for the

dopamine hypothesis of antipsychotic drug action was provided by PET findings of high dopamine D2 receptor occupancy in the striatum of patients responding to different antipsychotic drug treatments. Patients with a good response show dopamine D2 receptor occupancy of more than 65% (Nord and Farde 2010). The occurrence of EPS seems to be related to a higher occupancy of dopamine D2 receptors (above 80%). Atypical antipsychotics, also called second generation antipsychotic drugs, have clinical approvals for the treatment of psychosis and mania. Each drug has a unique pharmacodynamic and pharmacokinetic profile. Some of atypical antipsychotic drugs have additional antidepressant, anxiolytic or hypnotic profile (Schwartz and Stahl 2011). Atypical antipsychotic drugs have in common a potent serotonin 5-HT2A receptor antagonism in relation to a weaker dopamine D2 receptor antagonism. This pharmacodynamic property is the basis of "atypicality" (Meltzer 1989). Antagonism of 5-HT2A receptors likely allows more dopamine activity and neurotransmission to occur in the nigrostriatal system to avoid EPS. The same mechanism may allow small improvement in negative symptoms, and 5-HT2 antagonism in the tuberoinfundibular pathway may help to avoid hyperprolactinemia (Schwartz and Stahl 2011).

The atypical antipsychotics have not fulfilled the initial expectations of improved negative symptoms and cognitive dysfunctions in schizophrenia. Therefore, more molecular targets are presently under investigation for the development of new drugs for the treatment of schizophrenia (Gray and Roth 2007; Schizophrenia Research Forum 2007).

Dopaminergic D3 receptors are localized in limbic cortex and thus a preferential blockade of these receptors offers locally selective antidopaminergic activity. This results in increased effectiveness in reducing positive symptoms of schizophrenia sparing the blockade of extrapyramidal system and therefore reduces the risk of the main side effect such as pseudoparkinson's syndrome. Moreover, several preclinical data suggests that D3 dopamine receptor antagonism is more efficient in reducing the negative symptoms of schizophrenia and improves working memory.

Agonism or partial agonism of 5-HT1A receptors is considered a possible mechanism associated with the activity of some atypical antipsychotics such as aripiprazole and ziprasidone. It is assumed that stimulation of 5-HT1A receptors takes part in the antipsychotic effect in combination with D2 receptor blockade, especially in the safety profile of drug as well as is beneficial in fighting mood and cognitive symptoms of schizophrenia (Kim D., Building a Better Antipsychotic: Receptor Targets for the

Treatment of Multiple Symptom Dimensions of Schizophrenia, Neurotherapeutics, 6(1), 78-85, 2009).

Serotoninergic receptors type 5-HT6 are exclusively localized in the central nervous system (CNS). Both the localization of the 5-HT6 receptors in limbic and cortical brain areas and relatively potent affinity and antagonistic activity of several antipsychotics (clozapine, olanzapine, sertindole) and antidepressants (mianserin, amitryptiline) at 5-HT6 receptors are suggestive of a potential role in pathophysiology and treatment of CNS disorders. Recent data in the literature indicate that blockade of 5-HT6 receptors may be implicated in a pro-cognitive effect due to the increase in cholinergic transmission, in antidepressant activity due to the increase in noradrenergic and dopaminergic one, as well as in an anxiolytic effect. It is evident that the 5-HT6 receptor has emerged as a very interesting molecular target and antagonists of that receptor may serve as potential drugs in treatment of disorders characterized by cognitive impairments, such as Alzheimer's disease, schizophrenia, depression, anxiety (Liu K. i Robichaud A., 5-HT6 Antagonists as Potential Treatment for Cognitive Dysfunction, 2009; Wesołowska A. i Nikiforuk A., Effects of the brain-penetrant and selective 5-HT6 receptor antagonist SB-399885 in animal models of anxiety and depression, 2007). Moreover, 5-HT6 receptor antagonists have been demonstrated to be active in reduction of food intake and body weight by clinically approved mechanism that is consistent with an enhancement of satiety. Hence, several compounds with 5-HT6 receptor antagonistic activity are currently being clinically evaluated for the treatment of obesity (Heal D. et al., Selective 5-HT6 receptor ligands: progress in the development of a novel pharmacological approach to the treatment of obesity and related metabolic disorders, 2008).

Intensive research conducted since 1993 indicates that serotoninergic 5-HT7 receptors may play some role in the control of circadian rhythms, sleep, thermoregulation, cognitive processes, pain and migraine, as well as in neuronal excitability. Potent affinity and antagonistic activity of several antipsychotic and antidepressant drugs at 5-HT7 receptors suggest a potential role of these receptors in the pathophysiology of many neuropsychiatric disorders. Taking account of the behavioral data presented in the literature, it has been established that selective 5-HT7 receptor antagonists produce antidepressant and anxiolytic activity in rats and mice (Wesołowska A. et al., Effect of the selective 5-HT7 receptor antagonist SB-269970 in animal models of anxiety and depression, 2006). Using mouse models of antipsychotic activity, Galici et al. showed that a selective 5-HT7 receptor antagonist SB-269970 may also evoke

antipsychotic-like effects (Galici R. et al., Effects of SB-269970, a 5-HT7 receptor antagonist, in mouse models predictive of antipsychotic-like activity, 2008).

Serotoninergic 5-HT2C and histaminergic H1 receptors localized in hypothalamus play an important role in food intake regulation. Blockade of both types of these receptors produced by antipsychotic drugs is most closely correlated with an increased risk of weight gain and diabetes. On the other hand, blockade of 5-HT2C receptors, mostly localized in cortical areas and in the hippocampus, striatum, septal nuclei, thalamic and midbrain nuclei, may produce profitable antidepressant and pro-cognitive effects. In the substantia nigra, 5-HT2C receptors are co-localised with GABA, indicating that they yield indirect control of dopaminergic transmission. Consequently, the blockade of 5-HT2C receptors, together with the 5-HT2A receptor one, would potentiate the D2 receptor-mediated tonic inhibitory control of dopaminergic projection, with protective effect against extrapyramidal symptoms (Kim D., Building a Better Antipsychotic: Receptor Targets for the Treatment of Multiple Symptom Dimensions of Schizophrenia, 2009). Histaminergic H1 receptor blockade produced by antipsychotic drugs may be implicated in sedative effect that is clinically profitable in controlling arousal accompanies the acute phase of psychosis. It seems that simultaneous reduction in affinity of new molecule for both types of these receptors may be an element that protects against excessive body weight. However, the total elimination of affinity for these receptors may not be necessary because of certain benefits of blockade of 5-HT2C and H1 receptors.

Blockade of alpha1 adrenergic receptors, despite potential peripheral adverse effects involving hypotension, may cause some central nervous system benefits involving decrease in the risk of extrapyramidal side effects caused be antipsychotics. This may be associated with interaction between noradrenergic and serotoninergic neurons (Horacek J. et al., Mechanism of Action of Atypical Antipsychotic Drugs and the Neurobiology of Schizophrenia, CNS Drugs, 20(5), 389-409, 2006).

Blockade of alpha2 adrenergic receptors potentiates antidepressants-induced increase of extracellular monoamines. This may suggest that substances inhibiting monoamine transporters and simultaneously blocking alpha2 adrenergic receptors may be potent and fast acting new antidepressants. Moreover, alpha2 antagonists potentiate acetylcholine secretion in the frontal cortex and may improve cognitive functions, what may provide additional advantages both in antidepressant therapy and antipsychotic therapy (especially improvement in negative symptoms). Blockade of alpha2 adrenergic receptors may also counteract sexual dysfunctions caused by serotonin reuptake

inhibitors (Millan M., Dual- and Triple-Acting Agents for Treating Core and Co-morbid Symptoms of Major Depression: Novel Concepts, New Drugs, 2009). Alpha2 antagonists may also be beneficial in reducing extrapyramidal symptoms caused by blockade of D2 receptors in the striatum.

Sigma receptors are a separate group of CNS receptors; however their physiological role is still unknown. It has been shown that some psychotomimetic substances like phencyclidine, metamphetamine, heroin or dextrometorphan are potent sigma receptor agonist. On the other hand, a classic antipsychotic drug, haloperidol, is a strong antagonist of sigma receptors, what may be important for its antipsychotic potential. It has been established that selective sigma receptor agonists may produce antidepressant effect (Cobos E. et al., Pharmacology and Therapeutic Potential of Sigma Receptor Ligands, 2008). The above findings provide evidence that sigma receptors affinity may contribute to the overall beneficial pharmacological profile of a new psychotropic drug.

Because of important role of cholinergic system in the cognitive processes, current research is focused on substances which can directly or indirectly potentiate the activity of cholinergic system. This includes substances which are agonists of selected subtypes of nicotinic or muscarinic receptors and antagonists of 5-HT6 receptors. On the other hand, potential procognitive effects evoked by interaction with the above receptors may be masked by cholinolytic activity. Thus, in the scope of interest are substances free of antagonistic properties against cholinergic receptors. Moreover this strategy allows elimination of many undesired peripheral autonomic effects like constipations, dry mouth or tachycardia (Miamoto S., Treatments for schizophrenia: a critical review of pharmacology and mechanisms of action of antipsychotic drugs, 2005). In addition, it has been found that M3 muscarinic receptors are engaged in the control of insulin secretion, and their activation stimulates pancreas to secrete insulin. Hence, it can be expected that M3 receptors blockade may be unfavorable in terms of the risk of development of type II diabetes in patients treated with second generation antipsychotics (ex. olanzapine, clozapine, quetiapine). Recent research is focused on substances free of this undesired effect (Silvestre J. i Prous J., Research on adverse drug events. I. Muscarinic M3 receptor binding affinity could predict the risk of antipsychotics to induce type 2 diabetes, 2005).

Another serious side effects caused by antipsychotic drugs, e.g. sertindole, ziprasidone, are cardiac arrhythmias associated with delayed repolarization of cardiomyocytes. This condition appears on electrocardiograms (ECG) as prolonged corrected QT interval (QTc), what is most often evoked by substances which block hERG potassium channels.

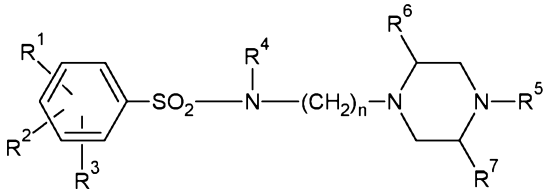
To prevent introduction to the developmental pipelines drugs with pro-arrhythmic potential, at a very early stage of research new substances are screened in vitro for their potency to block hERG potassium channels, using electrophysiological methods (Recanatni M., QT Prolongation Through hERG K+ Channel Blockade: Current Knowledge and Strategies for the Early Prediction During Drug Development, 2005).

Despite the advances that have been made in the development of antidepressants, there are clearly still unmet clinical needs with respect to both efficacy and side effects. These needs range from efficacy in treatment resistant patients (about 30%) to improved onset, to reductions in side effects such as sexual dysfunction, gastrointestinal events, sedation, weight gain. There are multiple approaches to improve current pharmacological means of modulating biogenic amines neurotransmission by either combining mechanisms or alternatively selectively stimulating/blocking receptor subtypes that may trigger improved efficacy or fewer side effects. One of them is combination therapies that maintain the benefits associated with selective serotonin reuptake inhibitors (SSRIs) (blockers of serotonin transporter) but attempt to either improve efficacy or reduce side effects by adding additional mechanism involving blockade of 5-HT2A or 5-HT2C receptors (Millan M., Dual- and Triple-Acting Agents for Treating Core and Co-morbid Symptoms of Major Depression: Novel Concepts, New Drugs, Neurotherapeutics, 6(1), 53-77, 2009). 5-HT2A receptor antagonists administered alone may produce antidepressant activity and also co-administered with SSRIs augment their antidepressant effects. The mechanism for this interaction may be a further increase in extracellular serotonin levels produced when SSRIs are given with 5-HT2A antagonists. Moreover, blockade of 5-HT2A receptors is part of the pharmacological profile of antidepressant drugs such as mianserin and mirtazapine. Presynaptic 5-HT1A receptors are associated with the risk for depressive behavior and their blockade augments the effects of SSRIs. Postsynaptic 5-HT1A receptors are essential for producing the antidepressant effects of 5-HT1A receptor agonists and possibly SSRIs. Thus partial agonism of 5-HT1A receptors is a preferred feature for new molecules the more that this mechanism occurs in approved anxiolytic buspirone and antidepressant/anxiolytic tandospirone.

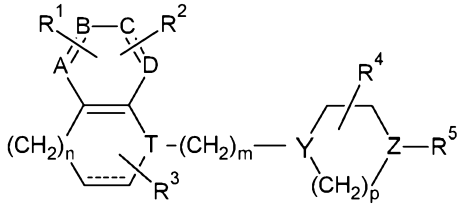
Although introduction of new psychotropic drugs (among others narcoleptics, antidepressants, benzodiazepines, acetylocholinesterase inhibitors) since 50-thies of the XX century was an unquestioned breakthrough, therapy of neuropsychiatric disorders is still far from satisfactory both because of limited efficacy and wide spectrum of side effects evoked by available drugs. These disadvantages are a challenge for modern

pharmacotherapy and there is a continuous effort to search for new, more effective psychotropic drugs.

Arylsulphonamide derivatives potentially useful for treating cardiovascular diseases, such as angina pectoris, cerebral circulation disorder and thrombosis, were described in the publication of European patent application EP0330065A. Disclosed compounds had aromatic ring, for instance phenyl, naphthyl or pyridil, bound to piperazine ring.

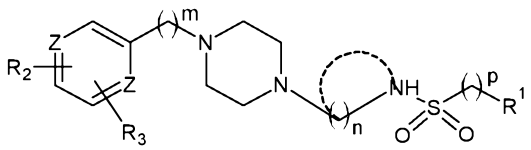


Publication of International patent application WO98/43956 discloses 1,4-disubstituted cyclic amines of the following formula wherein cyclic amine can be linked to bicyclic system.

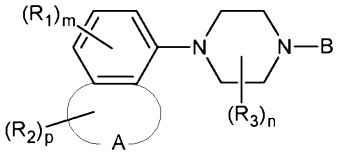


Derivatives mentioned above were described as having antagonistic activity toward serotoninergic receptors and featuring absent or very low affinity toward alpha adrenergic receptors.

In the publication of International patent application WO2004/069794 arylsulphonamide derivatives of the following formula were described as 5-HT1A receptor agonists, having very high activity and selectivity and low or absent cross-reactivity with other receptors.

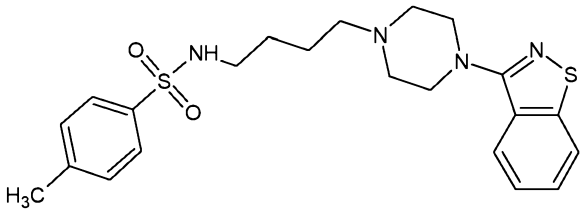


The publication of European patent application EP190472A discloses compounds having antipsychotic activity of the general formula presented below.



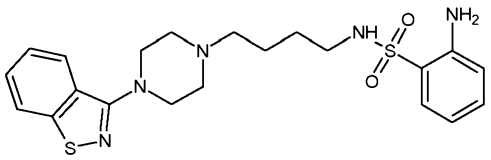
Derivatives of cyclic amines, including derivatives having arylsulphonamide moieties were described in scientific papers as well.

In publication of Ishizumi K. et al. Chem. Pharm. Bull. 43 (12), 2139-2151, 1995, directed to research on structure-activity relationship for succinimide derivatives, a compound of the following structure was disclosed:



The compound was proposed as a structural modification of another compound, N-[4-[4(1,2-benzoxazol-3-yl)-1-piperazinyl]butyl]-1,2-cis-cyclohexanedicarboxyimide (Perospiron, SM-9018), showing high affinity toward 5-HT2 and D2 receptors. Reportedly, replacement of succinimide with 4-methylbenzenesulphonamide moiety resulted however in decrease of affinity toward receptors mentioned above, in particular toward D2 receptor.

Similarly as in the publication mentioned above, also article of Navas F. et al., Bioorg. Med. Chem. 6 (1998), 811-823 related to structure-activity relationship research. A compound of the following formula was disclosed:



It was found that replacement of amide group with sulphonamide moiety as in the disclosed compound resulted in considerable decrease of affinity toward serotoninergic 5-HT1A and dopaminergic D2 receptors.

Publication of Forbes I.T. et al., Bioorg. Med. Chem.Lett. 10(2000) 1803-1806 disclosed indolopiperidine derivatives having antagonistic activity toward chemokine receptor CCR2B, potentially useful for the treatment of diseases of inflammatory origin, such as atherosclerosis and rheumatoid arthritis. Among tested derivatives 3,4-dichloro-N-{[4-

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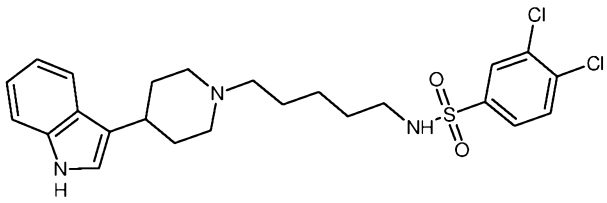
(1H-indol-3-yl)piperidin-1-yl]pentyl}benzensulphonamide of the following formula was disclosed:



However, the above publication did not suggest that this compound could possess activity toward therapeutic targets related to treatment of diseases of central nervous system.

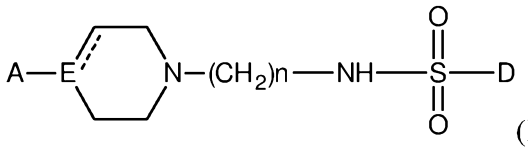
Extended affinity of N-{4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl}benzene-sulphonamide toward 5-HT_{1A}, 5-HT_{2A}, 5-HT_6, 5-HT_7, α_1 and dopaminergic D_2 receptors was disclosed by R. Bugno et al., in the poster "Examination of 5-HT_6 receptor affinity in the group of arylsulfonamide derivatives" published on May 10, 2010 during The Seventh Multidiscliplinary Conference on Drug Research, May 9–12, 2010, Zakopane, Poland.

Aim of the invention

The aim of the present invention is to provide novel compounds potentially useful for the treatment of diseases of the central nervous system. A further aim of the invention is to provide novel compounds useful for the treatment of diseases of central nervous system having higher effectiveness compared to currently used medicaments. Yet further aim of the present invention is to provide novel compounds useful for the treatment of diseases of the central nervous system, which could allow to eliminate or minimize adverse effects associated with currently used therapies.

Disclosure of the invention

According to a first aspect of the present invention there is provided compounds of the general formula (I)



(I)

and pharmaceutically acceptable salts thereof,

wherein

E represents C;

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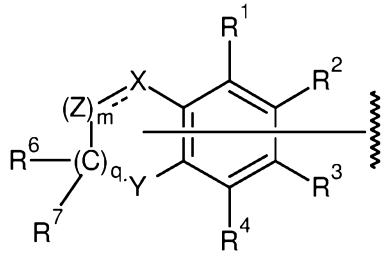
represents double bond;

n represents an integer from 2 to 6, inclusive;

A represents a 9- or 10-membered bicyclic group, consisting of benzene ring fused with 5- or 6-membered heterocyclic ring, which group is linked to E through one of its carbon atoms and has the following formula (A):



(A)

wherein

X represents CR^5, $C(R^5)_2$, NH or O;

Z represents CR^5, $C(R^5)_2$, N;

R^5 represents hydrogen atom, halogen atom or C_1-C_4-alkyl;

Y represents NH, O or S;

each of R^1, R^2, R^3 and R^4 independently represents hydrogen atom or halogen atom;

each of R^6 and R^7 independently represents hydrogen atom, halogen atom, C_1-C_4-alkyl;

or R^6 and R^7 together form carbonyl group =O;

wherein one of R^1, R^2, R^3, R^4, R^5, R^6 or R^7 is replaced by a bond to E;

represents single bond or double bond;

m is 0 or 1;

q is 0 or 1;

wherein at least one of q and m is 1;

D represents a group selected from:

- unsubstituted phenyl or phenyl substituted with one or more substituents independently selected from the group consisting of branched C_1-C_4-alkyl; straight C_1-C_4-alkyl in ortho or meta position with respect to sulphonamide group; C_1-C_3-alkyloxy; halogeno-C_1-C_3-alkyl; halogeno-C_1-C_3-alkyloxy; halogen atom; -CN; -OH; and phenyl;
- unsubstituted naphthyl or naphthyl substituted with one or more substituents independently selected from the group consisting of C_1-C_4-alkyl; C_1-C_3-alkyloxy; halogeno-C_1-C_3-alkyl; halogen atom; -CN; -OH; and phenyl;
- 5-membered aromatic heterocyclic group having 1 to 3 heteroatoms independently selected from the group consisting of N, O, S, the group being

unsubstituted or substituted with one or more substituents independently selected from the group consisting of C_1-C_4-alkyl; C_1-C_3-alkyloxy; halogeno-C_1-C_3-alkyl; halogen atom; -CN; -OH; and phenyl;

- bicyclic group consisting of benzene or pyridine ring fused with 5-membered aromatic or non-aromatic heterocyclic ring having 1 to 3 heteroatoms independently selected from the group consisting of N, O, S, which group is unsubstituted or substituted with one or more substituents independently selected from the group consisting of C_1-C_4-alkyl; C_1-C_3-alkyloxy; halogeno-C_1-C_3-alkyl; halogen atom; =O; -CN; -OH; and phenyl;
- bicyclic group consisting of benzene or pyridine ring fused with 6-membered non-aromatic heterocyclic ring having from 1 to 3 heteroatoms independently selected from the group consisting of N, O, S, which group is unsubstituted or substituted with one or more substituents independently selected from the group consisting of C1-C4-alkyl; C1-C3-alkyloxy; halogeno-C1-C3-alkyl; halogen atom; =O; -CN; -OH; and phenyl.

According to a second aspect of the present invention there is provided a pharmaceutical composition comprising a compound of formula (I) as defined in the first aspect above as an active ingredient in combination with pharmaceutically acceptable carrier(s) and/or excipient(s).

According to a third aspect of the present invention there is provided use of a compound of formula (I) as defined in the first aspect above in the treatment and/or prevention of disorders of the central nervous system related to dopaminergic and/or serotoninergic and/or noradrenergic transmission.

According to a fourth aspect of the present invention there is provided a method of treatment and/or prevention of disorders of the central nervous system related to serotoninergic and dopaminergic transmission in mammals, comprising administration of a pharmaceutically effective amount of a compound of formula (I) as defined in the first aspect above or a pharmaceutical composition as defined in the second aspect above.

According to a fifth aspect of the present invention there is provided use of a compound of formula (I) as defined in the first aspect above, or a pharmaceutical composition as defined in the

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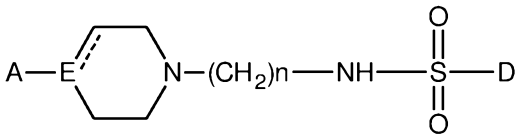
second aspect above, for the manufacture of a medicament for the treatment and/or prevention of disorders of the central nervous system related to dopaminergic and/or serotoninergic and/or noradrenergic transmission.

The present invention relates to novel arylsulphonamide compounds having the structure represented by the general formula (I)



(I)

and pharmaceutically acceptable salts thereof,

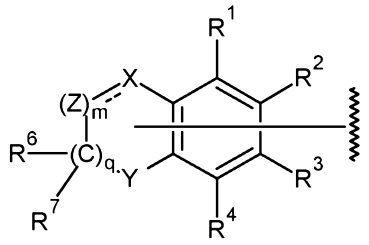
wherein:

E represents N, C or CH;

----- represents single bond or double bond;

n represents an integer from 2 to 6, inclusive;

A represents a 9- or 10-membered bicyclic group, consisting of benzene ring fused with a 5- or 6-membered heterocyclic ring, which group is linked to E through one of its carbon atoms and has the following formula (A):



(A)

wherein

X represents CR^5, $C(R^5)_2$, NH or O;

Z represents CR^5, $C(R^5)_2$, or N;

R^5 represents hydrogen atom, halogen atom or C_1-C_4-alkyl;

Y represents NH, O or S;

each of R^1, R^2, R^3, and R^4 independently represents hydrogen atom or halogen atom;

each of $R^6$and R^7 independently represents hydrogen atom, halogen atom or C_1-C_4-alkyl;

or R^6 and R^7 together form =O;

----- represents single bond or double bond;

m is 0 or 1;

q is 0 or 1;

wherein at least one of q and m is 1;

D is selected from:

- unsubstituted phenyl or phenyl substituted with one or more substituents independently selected from the group consisting of branched C_1-C_4-alkyl, straight C_1-C_4-alkyl in ortho or meta position with respect to sulphonamide

group, C_1-C_3-alkyloxy, halogeno-C_1-C_3-alkyl, halogeno-C_1-C_3-alkyloxy, halogen atom, -CN, -OH, and phenyl;

- unsubstituted naphthyl or naphthyl substituted with one or more substituents independently selected from the group consisting of C_1-C_4-alkyl, C_1-C_3-alkyloxy, halogeno-C_1-C_3-alkyl, halogen atom, -CN, -OH, and phenyl;

- a 5-membered aromatic heterocyclic group having 1 to 3 heteroatoms independently selected from the group consisting of N, O and S, which is unsubstituted or substituted with one or more substituents independently selected from the group consisting of C_1-C_4-alkyl, C_1-C_3-alkyloxy, halogeno-C_1-C_3-alkyl, halogen atom, -CN, -OH, and phenyl;

- a bicyclic group consisting of a ring selected from benzene and pyridine fused with a 5-membered aromatic or non-aromatic heterocyclic ring having 1 to 3 heteroatoms independently selected from the group consisting of N, O, S, said bicyclic group being unsubstituted or substituted with one or more substituent independently selected from the group consisting of C_1-C_4-alkyl, C_1-C_3-alkyloxy, halogeno-C_1-C_3-alkyl, halogen atom, =O, -CN, -OH, and phenyl;

- a bicyclic group consisting of a ring selected from benzene and pyridine fused with a 6-membered non-aromatic heterocyclic ring having 1 to 3 heteroatoms independently selected from the group consisting of N, O, and S, said bicyclic group being unsubstituted or substituted with one or more substituents independently selected from the group consisting of C_1-C_4-alkyl, C_1-C_3-alkyloxy, halogeno-C_1-C_3-alkyl, halogen atom, =O, -CN, -OH, and phenyl;

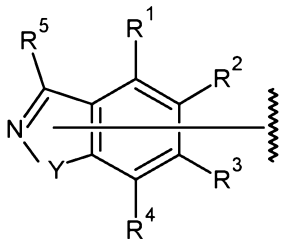
with the proviso that 3,4-dichloro-N-{[4-(1*H*-indol-3-yl)piperidin-1-yl]pentyl}benzene-sulphonamide and N-{4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl}benzene-sulphonamide are excluded.

In one embodiment of the compounds of the present invention group A is linked to E through carbon atom of benzene ring.

In an alternative embodiment of the compounds of the present invention group A is linked to E through carbon atom of heterocyclic ring.

It will be appreciated by a person skilled in the art that respective substituent R^1, R^2, R^3, R^4, R^5, R^6 or R^7 at the carbon atom through which group A is linked to E is absent and is replaced by a bond.

According to one of the variants, compounds of the present invention have the formula (I), wherein in group A ----- represents double bond, q is 0, X represents C(R^5), and Z represents N. In these compounds A corresponds to the following general formula (A1), wherein Y, R^1, R^2, R^3, R^4 and R^5 have the same meanings as defined above, and which is specific variant of the formula (A):

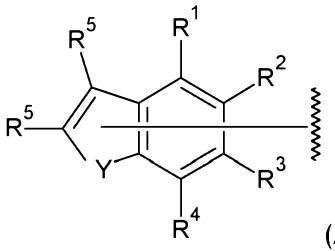


(A1)

Group of formula (A1) may be linked to E through carbon atom of phenyl ring or through carbon atom of 5-membered heterocyclic ring.

Preferably, in the above variant (A1) represents 1,2-benzothiazol-3-yl or 1,2-benzoxazol-3-yl, which may be optionally substituted with halogen atom.

Further variant of the compounds of the present invention are compounds of formula (I), wherein in group A ----- represents double bond, q is 0, X represents C(R^5), and Z represents C(R^5). In these compounds A corresponds to the following general formula (A2), wherein Y, R^1, R^2, R^3, R^4 and R^5 have meanings as defined above, and which is specific variant of the formula (A)



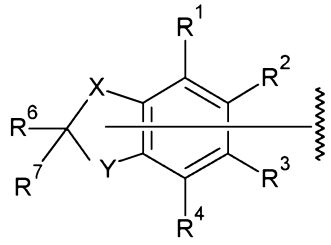
(A2)

Group of formula (A2) may be linked to E through carbon atom of phenyl ring or through carbon atom of 5-membered heteroaromatic ring.

Preferably, in the above variant (A2) represents 1*H*-indol-3-yl, 2-(C_1-C_4-alkyl)-1*H*-indol-3-yl or 1*H*-indol-4-yl, which may be optionally substituted with halogen atom.

Another variant of the compounds of the present invention are compounds of formula (I), wherein in group A ----- represents single bond, and m is 0. In these compounds A

corresponds to the following general formula (A3), wherein X, Y, R^1, R^2, R^3, R^4, R^6 and R^7 have the meanings as defined above, and which is specific variant of the formula (A):

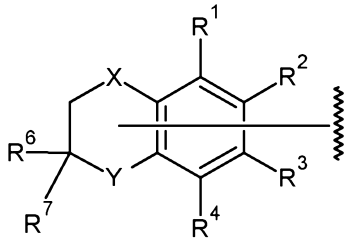


(A3),

Group of formula (A3) may be linked to E through carbon atom of phenyl ring or through carbon atom of heterocyclic ring.

Preferably, in the above variant (A3) represents 2-oxo-2,3-dihydro-1*H*-benzimidazol-4-yl, 2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl, 2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl, 2-oxo-2,3-dihydro-1*H*-indol-4-yl, 2,2-dimethyl-2,3-dihydro-1*H*-indol-4-yl, 2,2-dimethyl-1,3-benzodioxol-4-yl, or 2,2-difluoro-1,3-benzodioxol-4-yl.

Yet another variant of the compounds of the present invention are compounds of formula (I), wherein in group A ----- represents single bond, m is 1, q is 1, and Z represents CH_2. In these compounds A corresponds to the following general formula (A4), wherein X, Y, R^1, R^2, R^3, R^4, R^6 and R^7 have the meanings as defined above, and which is specific variant of the formula (A):



(A4),

Group of formula (A4) may be linked to E through carbon atom of phenyl ring or through carbon atom of 6-membered heterocyclic ring.

Preferably, in the above variant (A4) represents 1,4-benzodioxan-5-yl or 3-okso-3,4-dihydro-2H-1,4-benzoxazin-8-yl.

One of further embodiments of the compounds of the present invention are compounds of formula (I), wherein E represents nitrogen atom. It will be therefore obvious that in such a case ----- in formula (I) will represent single bond.

Another embodiment of compounds of the present invention are compounds of formula (I), wherein E represents CH. It will be therefore obvious that in such a case ⎓ in formula (I) will represent single bond.

Further embodiment of the compounds of the present invention are compounds (I), wherein E represents C, and thus ⎓ in formula (I) represents double bond.

Another sub-group of compounds of the invention are compounds of formula (I) wherein D represents phenyl. Phenyl may be unsubstituted or substituted as defined for substituent D above, for example with one or more substituent independently selected the group consisting of straight C_1-C_4-alkyl in position ortho or meta with respect to sulphonamide group, halogen atom, -CN, -OH, and phenyl;

Yet another sub-group of the compounds of the invention are compounds of formula (I), wherein D represents naphthyl. Naphthyl may be linked to sulphur atom of sulphonamide moiety in position 1 (alpha) or 2 (beta) of naphthyl ring. Naphthyl may be unsubstituted or substituted, as defined for substituent D above, for example with halogen atom.

Yet another group of compounds of the present invention are compounds of formula (I), wherein D represents a 5-membered aromatic heterocyclic group having 1 to 3 heteroatoms independently selected from the group consisting of N, O and S. Preferred aromatic heterocyclic group is thienyl, that is heteroatom represents sulphur atom. 5-Membered aromatic heterocyclic group may be unsubstituted or substituted as defined for substituent D above.

Another sub-group of the compounds of the present invention are compounds of formula (I), wherein D represents a bicyclic group consisting of benzene ring fused with 5-membered aromatic heterocyclic ring having 1 to 3 heteroatoms independently selected from the group consisting of N, O, and S. This bicyclic group may be unsubstituted or substituted as defined above for substituent D, for instance with halogen atom and/or C_1-C_4-alkyl. Preferably, bicyclic group is selected from the group consisting of 1-benzothiophen-3-yl, 1-benzothiophen-2-yl, 1-benzofuran-2-yl, 1-benzofuran-3-yl, 1*H*-benzimidazol-2-yl, 1*H*-indol-2-yl, 1*H*-indol-5-yl, 1*H*-indol-6-yl, 1*H*-indazol-7-yl, 1*H*-indazol-6-yl, 1,2-benzoxazol-5-yl, 1,3-benzoxazol-4-yl, 1,3-benzothiazol-4-yl, and 1,3-benzothiazol-5-yl.

Further sub-group of thecompounds of the present invention are compounds of formula (I), wherein D represents bicyclic group consisting of pyridine ring fused with 5-membered heterocyclic aromatic ring having 1 to 3 heteroatoms independently selected

from the group consisting of of N, O, and S. This bicyclic group may be unsubstituted or substituted as defined above for substituent D, for instance with halogen atom and/or C_1-C_4-alkyl. Preferably, bicyclic group is selected from the group consisting of imidazo[1,2-*a*]-pyridin-3-yl and 1*H*-pyrrolo[2,3-*b*]-pyridin-3-yl.

Yet another sub-group of the compounds of the present invention are compounds of formula (I), wherein D represents bicyclic group consisting of benzene ring fused with a 5-membered non-aromatic heterocyclic ring having 1 to 3 heteroatoms independently selected from the group consisting of N, O, and S. This bicyclic group may be unsubstituted or substituted as defined above for substituent D. Preferred bicyclic group is selected from the group consisting of 2,3-dihydro-1-benzofuran-5-yl, 2-oxo-2,3-dihydro-1,3-benzoxazol-6-yl, 2-oxo-1,3-dihydro-2*H*-indol-5-yl and 1,3-benzodioxol-5-yl.

Yet another sub-group of the compounds of the present invention are compounds of formula (I), wherein D represents bicyclic group consisting of benzene ring, fused with 6-membered non-aromatic heterocyclic ring having from 1 to 3 heteroatoms independently selected from the group consisting of N, O, and S. This bicyclic group may be unsubstituted or substituted as defined above for substituent D. Preferred bicyclic group is 2,3-dihydro-1,4-benzodioxine-6-yl.

Further sub-group of the compounds of the present invention are compounds of formula (I), wherein A represents group of formula (A2) linked to E through carbon atom of heterocyclic ring; E represents CH; and D represents phenyl substituted with one or more halogen atoms.

Another sub-group of the compounds of the present invention are compounds of formula (I), wherein A represents group of formula (A1) wherein Y represents O linked to E through carbon atom of heterocyclic ring; E represents N; and D represents unsubstituted phenyl or phenyl substituted with one or more substituents independently selected from the group as defined for formula (I).

Another sub-group of the compounds of the present invention are compounds of formula (I), wherein n is 2.

Further sub-group of compounds of the present invention are compounds of formula (I), wherein n is 3.

Further sub-group of the compounds of the present invention are compounds of formula (I), wherein n is 4.

The following specific compounds of formula (I) of the invention can be mentioned:

1) N-(4-(4-(1,2-benzothiazol-3-yl)piperazin-1-yl)butyl)naphthalene-1-sulphonamide,

2) N-(4-(4-(1,2-benzothiazol-3-yl)piperazin-1-yl)butyl)naphthalene-2-sulphonamide,

3) N-(4-(4-(1,2-benzothiazol-3-yl)piperazin-1-yl)butyl)-3-methylbenzenesulphonamide,

4) N-(4-(4-(1,2-benzothiazol-3-yl)piperazin-1-yl)butyl)-2-oxo-3H-1,3-benzoxazole-6-sulphonamide,

5) N-(3-(4-(1,2-benzothiazol-3-yl)piperazin-1-yl)propyl)naphthalene-1-sulphonamide,

6) N-(3-(4-(1,2-benzothiazol-3-yl)piperazin-1-yl)propyl)naphthalene-2-sulphonamide,

7) N-(3-(4-(1,2-benzothiazol-3-yl)piperazin-1-yl)propyl)-3-methylbenzenesulphonamide,

8) N-(3-(4-(1,2-benzothiazol-3-yl)piperazin-1-yl)propyl)-2-oxo-3H-1,3-benzoxazole-6-sulphonamide,

9) N-(2-(4-(1,2-benzothiazol-3-yl)piperazin-1-yl)ethyl)naphthalene-1-sulphonamide,

10) N-(2-(4-(1,2-benzothiazol-3-yl)piperazin-1-yl)ethyl)naphthalene-2-sulphonamide,

11) N-(2-(4-(1,2-benzothiazol-3-yl)piperazin-1-yl)ethyl)-3-methylbenzenesulphonamide,

12) N-(2-(4-(1,2-benzothiazol-3-yl)piperazin-1-yl)ethyl)-2-oxo-3H-1,3-benzoxazole-6-sulphonamide,

13) N-(4-(4-(1,2-benzoxazol-3-yl)piperazin-1-yl)butyl)naphthalene-1-sulphonamide,

14) N-(4-(4-(1,2-benzoxazol-3-yl)piperazin-1-yl)butyl)naphthalene-2-sulphonamide,

15) N-(4-(4-(1,2-benzoxazol-3-yl)piperazin-1-yl)butyl)-3-methylbenzenesulphonamide,

16) N-(4-(4-(1,2-benzoxazol-3-yl)piperazin-1-yl)butyl)-2-oxo-3H-1,3-benzoxazole-6-sulphonamide,

17) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]naphthalene-1-sulphonamide,

18) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]naphthalene-2-sulphonamide,

19) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-3-methylbenzenesulphonamide,

20) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]naphthalene-1-sulphonamide,

21) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]naphthalene-2-sulphonamide,

22) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-3-methylbenzene-sulphonamide,

23) N-[2-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]ethyl]naphthalene-1-sulphonamide,

24) N-[2-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]ethyl]naphthalene-2-sulphonamide,

25) N-[2-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]ethyl]-3-methylbenzene-sulphonamide,

26) N-{4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl}naphthalene-2-sulphonamide,

27) N-{4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl}benzenesulphonamide,

28) 3-fluoro-*N*-{4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl}benzenesulphonamide,

29) 3,4-difluoro-*N*-{4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl}benzenesulphonamide,

30) N-{4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl}-imidazo[1,2-a]pyridine-3-sulphonamide,

31) N-{4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl}-1H-pyrrolo[2,3-b]pyridine-3-sulphonamide,

32) N-{4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl}-1-benzothiophene-3-sulphonamide,

33) N-{4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl}-1-benzothiophene-2-sulphonamide,

34) N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}naphthalene-1-sulphonamide,

35) N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}naphthalene-2-sulphonamide,

36) 4-fluoro-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide,

37) 3-fluoro-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide,

38) 4-chloro-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide

39) 3-chloro-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide,

40) 3-methyl-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}-benzenesulphonamide,

41) 3-hydroxy-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}-benzenesulphonamide,

42) 4-methoxy-*N*-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}-benzenesulphonamide

43) N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}naphthalene-1-sulphonamide,

44) N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}naphthalene-2-sulphonamide,

45) 4-fluoro-N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}-benzenesulphonamide,

46) 3-fluoro-N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}-benzenesulphonamide,

47) 4-chloro-N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}-benzenesulphonamide,

48) 3-chloro-N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}-benzenesulphonamide,

49) 3-hydroxy-*N*-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}-benzenesulphonamide,

50) N-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}naphthalene-1-sulphonamide,

51) N-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}naphthalene-2-sulphonamide,

52) N-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}-4-fluorobenzene-sulphonamide,

53) 3-fluoro-N-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}benzene-sulphonamide,

54) 4-chloro-N-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}benzene-sulphonamide,

55) 3-chloro-N-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}benzene-sulphonamide,

56) 3-methyl-N-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}-benzenesulphonamide,

57) 3-hydroxy-N-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}-benzenesulphonamide,

58) 4-chloro-N-{4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]-butyl}benzenesulphonamide,

59) 7-chloro-N-{4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl}naphthalene-2-sulphonamide,

60) 7-chloro-N-{3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl}naphthalene-2-sulphonamide,

61) 6-chloro-N-{4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl}naphthalene-2-sulphonamide,

62) 6-chloro-N-{3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl}naphthalene-2-sulphonamide,

63) 3-chloro-4-fluoro-N-{4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl}benzene-sulphonamide,

64) 3-chloro-4-fluoro-N-{3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl}benzene-sulphonamide,

65) 5-fluoro-3-methyl-N-{4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl}-1-benzo-thiophene-2-sulphonamide,

66) 5-fluoro-3-methyl-N-{3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl}-1-benzo-thiophene-2-sulphonamide,

67) 5-chloro- N-{4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl}-1-benzothiophene-2-sulphonamide,

68) 5-chloro-N-{3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl}-1-benzothiophene-2-sulphonamide,

69) 3-chloro-N-{4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl}benzenesulphonamide,

70) 3-chloro-N-{3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl}benzenesulphonamide,

71) 3-fluoro-N-{4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl}benzenesulphonamide,

72) 3-fluoro-N-{3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl}benzenesulphonamide,

73) 3-cyano-N-{4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl}benzenesulphonamide,

74) 3-cyano-N-{3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl}benzenesulphonamide,

75) N-{4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl}-imidazo[1,2-a]pyridine-3-sulphonamide,

76) N-{3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl}-imidazo[1,2-a]pyridine-3-sulphonamide,

77) 7-chloro-N-{4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl}naphthalene-2-sulphonamide,

78) 7-chloro-N-{3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl}naphthalene-2-sulphonamide,

79) 6-chloro-N-{4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl}naphthalene-2-sulphonamide,

80) 6-chloro-N-{3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl}naphthalene-2-sulphonamide,

81) 5-fluoro-3-methyl-N-{4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl}-1-benzo-thiophene-2-sulphonamide,

82) 5-fluoro-3-methyl-N-{3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl}-1-benzo-thiophene-2-sulphonamide,

83) 5-chloro-N-{4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl}-1-benzothiophene-2-sulphonamide,

84) 5-chloro-N-{3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl}-1-benzothiophene-2-sulphonamide,

85) 3-chloro-N-{4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl}benzenesulphonamide,

86) 3-chloro-N-{3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl}benzenesulphonamide,

87) 3-fluoro-N-{4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl}benzenesulphonamide,

88) 3-fluoro-N-{3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl}benzenesulphonamide,

89) N-{4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl}-1H-pyrrolo[2,3-b]pyridine-3-sulphonamide,

90) N-{3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl}-1H-pyrrolo[2,3-b]pyridine-3-sulphonamide,

91) 3-trifluoromethyl-N-{4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl}benzene-sulphonamide

92) 3-trifluoromethyl-N-{3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl}benzene-sulphonamide,

93) 3,4-dichloro-N-{4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl}benzene-sulphonamide,

94) 3,4-dichloro-N-{3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl}benzene-sulphonamide,

95) 7-chloro-N-{4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl}naphthalene-2-sulphonamide,

96) 7-chloro-N-{3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl}naphthalene-2-sulphonamide,

97) 6-chloro-N-{4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl}naphthalene-2-sulphonamide,

98) 6-chloro-N-{3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl}naphthalene-2-sulphonamide,

99) N-{4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl}-1*H*-benzimidazole-2-sulphonamide,

100) N-{3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl}-1*H*-benzimidazole-2-sulphonamide,

101) 5-fluoro-3-methyl- N-{4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl}-1-benzothiophene-2-sulphonamide,

102) 5-fluoro-3-methyl- N-{3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl}-1-benzothiophene-2-sulphonamide,

103) 5-chloro- N-{4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl}-1-benzo-thiophene-2-sulphonamide,

104) 5-chloro- N-{3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl}-1-benzo-thiophene-2-sulphonamide,

105) 3-chloro-N-{4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl}benzene-sulphonamide,

106) 3-chloro-N-{3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl}benzene-sulphonamide,

107) 3-fluoro-N-{4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl}benzene-sulphonamide,

108) 3-fluoro-N-{3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl}benzene-sulphonamide,

109) 3-bromo-N-{4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl}benzene-sulphonamide,

110) 3-bromo-N-{3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl}benzene-sulphonamide,

111) 4-phenyl-N-{4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl}benzene-sulphonamide,

112) 4-phenyl-N-{3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl}benzene-sulphonamide,

113) 3-chloro-N-{4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl}benzenesulphonamide,

114) 3-chloro-N-{3-[4-(1H-indol-4-yl)piperazin-1-yl]propyl}benzenesulphonamide,

115) N-{4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl}-1,3-benzothiazole-4-sulphonamide,

116) N-{3-[4-(1H-indol-4-yl)piperazin-1-yl]propyl}-1,3-benzothiazole-4-sulphonamide,

117) 7-chloro-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}-naphthalene-2-sulphonamide,

118) 7-chloro-N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}-naphthalene-2-sulphonamide,

119) 6-chloro-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}-naphthalene-2-sulphonamide,

120) 6-chloro-N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}-naphthalene-2-sulphonamide,

121) 5-fluoro-3-methyl-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}-1-benzothiophene-2-sulphonamide,

122) 5-fluoro-3-methyl-N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]-propyl}-1-benzothiophene-2-sulphonamide,

123) 5-chloro- N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}-1-benzothiophene-2-sulphonamide,

124) 5-chloro- N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}-1-benzothiophene-2-sulphonamide,

125) N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}-1H-indazole-7-sulphonamide,

126) N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}-1H-indazole-7-sulphonamide,

127) 7-chloro-N-{4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]-butyl}naphthalene-2-sulphonamide,

128) 7-chloro-N-{3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]-propyl}naphthalene-2-sulphonamide,

129) 6-chloro-N-{4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]-butyl}naphthalene-2-sulphonamide,

130) 6-chloro-N-{3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]-propyl}naphthalene-2-sulphonamide,

131) 5-fluoro-3-methyl-N-{4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}-1-benzothiophene-2-sulphonamide,

132) 5-fluoro-3-methyl-N-{3-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}-1-benzothiophene-2-sulphonamide,

133) 5-chloro-N-{4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]-butyl}-1-benzothiophene-2-sulphonamide,

134) 5-chloro-N-{3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]-propyl}-1-benzothiophene-2-sulphonamide,

135) N-{4-[4-(5-chloro-2-methyl-1*H*-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}-1H-indazole-7-sulphonamide,

136) N-{3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}-1H-indazole-7-sulphonamide,

137) 3-chloro-N-{4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]-butyl}benzenesulphonamide,

138) 3-chloro-N-{3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]-propyl}benzenesulphonamide,

139) 3-fluoro-N-{4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]-butyl}benzenesulphonamide,

140) 3-fluoro-N-{3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]-propyl}benzenesulphonamide,

141) 4-tert-butyl-N-{4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]-butyl}benzenesulphonamide,

142) 4-tert-butyl-N-{3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]-propyl}benzenesulphonamide,

143) 7-chloro-N-{4-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl)piperazin-1-yl]butyl}-naphthalene-2-sulphonamide,

144) 7-chloro-N-{3-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl)piperazin-1-yl]propyl}-naphthalene-2-sulphonamide,

145) 6-chloro-N-{4-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl)piperazin-1-yl]butyl}-naphthalene-2-sulphonamide,

146) 6-chloro-N-{3-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl)piperazin-1-yl]propyl}-naphthalene-2-sulphonamide,

147) 5-fluoro-3-methyl-N-{4-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl)piperazin-1-yl]-butyl}-1-benzothiophene-2-sulphonamide,

148) 5-fluoro-3-methyl-N-{3-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl)piperazin-1-yl]-propyl}-1-benzothiophene-2-sulphonamide,

149) 5-chloro-N-{4-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl)piperazin-1-yl]butyl}-1-benzothiophene-2-sulphonamide,

150) 5-chloro-N-{3-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl)piperazin-1-yl]propyl}-1-benzothiophene-2-sulphonamide,

151) N-{4-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl)piperazin-1-yl]butyl}-1,2-benzoxazole-5-sulphonamide,

152) N-{3-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl)piperazin-1-yl]propyl}-1,2-benzoxazole-5-sulphonamide,

153) 3-chloro-N-{4-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl)piperazin-1-yl]butyl}-benzenesulphonamide,

154) 3-chloro-N-{3-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl)piperazin-1-yl]propyl}-benzenesulphonamide,

155) 4-trifluoromethyl-N-{4-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl)piperazin-1-yl]-butyl}benzenesulphonamide,

156) 4-trifluoromethyl-N-{3-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl)piperazin-1-yl]-propyl}benzenesulphonamide,

157) 3-hydroxy-N-{4-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl)piperazin-1-yl]butyl}-benzenesulphonamide,

158) 3-hydroxy-N-{3-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-4-yl)piperazin-1-yl]propyl}-benzenesulphonamide,

159) 7-chloro-N-{4-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]butyl}-naphthalene-2-sulphonamide,

160) 7-chloro-N-{3-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]propyl}-naphthalene-2-sulphonamide,

161) 6-chloro-N-{4-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]butyl}-naphthalene-2-sulphonamide,

162) 6-chloro-N-{3-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]propyl}-naphthalene-2-sulphonamide,

163) 5-fluoro-3-methyl-N-{4-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]-butyl}-1-benzothiophene-2-sulphonamide,

164) 5-fluoro-3-methyl-N-{3-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]-propyl}-1-benzothiophene-2-sulphonamide,

165) 5-chloro-3-methyl-N-{4-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]-butyl}-1-benzothiophene-2-sulphonamide,

166) 5-chloro-3-methyl-N-{3-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]-propyl}-1-benzothiophene-2-sulphonamide,

167) 5-chloro-N-{4-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]butyl}-1-benzothiophene-2-sulphonamide,

168) 5-chloro-N-{3-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]propyl}-1-benzothiophene-2-sulphonamide,

169) N-{4-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]butyl}-1,3-benzoxazole-4-sulphonamide,

170) N-{3-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]propyl}-1,3-benzoxazole-4-sulphonamide,

171) 4-cyano-N-{4-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]butyl}-benzenesulphonamide,

172) 4-cyano-N-{3-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]propyl}-benzenesulphonamide,

173) 3-chloro-N-{4-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]butyl}-benzenesulphonamide,

174) 3-chloro-N-{3-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]propyl}-benzenesulphonamide,

175) 3-fluoro-N-{4-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]butyl}-benzenesulphonamide,

176) 3-fluoro-N-{3-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)piperazin-1-yl]propyl}-benzenesulphonamide,

177) 7-chloro-N-{4-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]butyl}-naphthalene-2-sulphonamide,

178) 7-chloro-N-{3-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]propyl}-naphthalene-2-sulphonamide,

179) 6-chloro-N-{4-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]butyl}-naphthalene-2-sulphonamide,

180) 6-chloro-N-{3-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]propyl}-naphthalene-2-sulphonamide,

181) 5-fluoro-3-methyl-N-{4-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]-butyl}-1-benzothiophene-2-sulphonamide,

182) 5-fluoro-3-methyl-N-{3-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]-propyl}-1-benzothiophene-2-sulphonamide,

183) 5-chloro-N-{4-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]butyl}-1-benzothiophene-2-sulphonamide,

184) 5-chloro-N-{3-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]propyl}-1-benzothiophene-2-sulphonamide,

185) N-{4-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]butyl}-1-benzo-thiophene-2-sulphonamide,

186) N-{3-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]propyl}-1-benzo-thiophene-2-sulphonamide,

187) N-{4-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]butyl}-2,3-dihydro-1-benzofurane-5-sulphonamide,

188) N-{3-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]propyl}-2,3-dihydro-1-benzofurane-5-sulphonamide,

189) 4-bromo-N-{4-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]butyl}-benzenesulphonamide,

190) 4-bromo-N-{3-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]propyl}-benzenesulphonamide,

191) 3-chloro-N-{4-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]butyl}-benzenesulphonamide,

192) 3-chloro-N-{3-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]propyl}-benzenesulphonamide,

193) 3-fluoro-N-{4-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]butyl}-benzenesulphonamide,

194) 3-fluoro-N-{3-[4-(2-oxo-2,3-dihydro-1,3-benzoxazol-7-yl)piperazin-1-yl]propyl}-benzenesulphonamide,

195) N-{4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl}-5-chlorothiophene-2-sulphonamide,

196) N-{3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl}-5-chlorothiophene-2-sulphonamide,

197) 7-chloro-N-{4-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl}-naphthalene-2-sulphonamide,

198) 7-chloro-N-{3-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]propyl}-naphthalene-2-sulphonamide,

199) 6-chloro-N-{4-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl}-naphthalene-2-sulphonamide,

200) 6-chloro-N-{3-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]propyl}-naphthalene-2-sulphonamide,

201) 5-fluoro-3-methyl-N-{4-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl}-1-benzothiophene-2-sulphonamide,

202) 5-fluoro-3-methyl-N-{3-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]propyl}-1-benzothiophene-2-sulphonamide,

203) 5-chloro-N-{4-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl}-1-benzothiophene-2-sulphonamide,

204) 5-chloro-N-{3-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]propyl}-1-benzothiophene-2-sulphonamide,

205) N-{4-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl}-1-benzothiophene-3-sulphonamide,

206) N-{3-[4-(3-oxo-3,4-dihydro-2*H*-1,4-benzoksazyn-8-ylo)piperazyn-1-yl]propyl}-1-benzothiophene-3-sulphonamide,

207) N-{4-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl}-1,3-benzodioxole-5-sulphonamide,

208) N-{3-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]propyl}-1,3-benzodioxole-5-sulphonamide,

209) 3-chloro-N-{4-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl}-benzenesulphonamide,

210) 3-chloro-N-{3-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]propyl}-benzenesulphonamide,

211) 3-fluoro-N-{4-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl}-benzenesulphonamide,

212) 3-fluoro-N-{3-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]propyl}-benzenesulphonamide,

213) 4-isopropyl-N-{4-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]-butyl}benzenesulphonamide,

214) 4-isopropyl-N-{3-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]-propyl}benzenesulphonamide,

215) N-{4-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl}thiophene-2-sulphonamide,

216) N-{3-[4-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-8-yl)piperazin-1-yl]propyl}thiophene-2-sulphonamide,

217) N-{4-[4-(2,2-difluoro-1,3-benzodioxol-4-yl)piperazin-1-yl]butyl}-naphthalene-2-sulphonamide,

218) N-{3-[4-(2,2-difluoro-1,3-benzodioxol-4-yl)piperazin-1-yl]propyl}-naphthalene-2-sulphonamide,

219) N-{4-[4-(2,2-difluoro-1,3-benzodioxol-4-yl)piperazin-1-yl]butyl}-naphthalene-1-sulphonamide,

220) N-{3-[4-(2,2-difluoro-1,3-benzodioxol-4-yl)piperazin-1-yl]propyl}-naphthalene-1-sulphonamide,

221) 3-fluoro-N-{4-[4-(2,2-difluoro-1,3-benzodioxol-4-yl)piperazin-1-yl]butyl}benzene-sulphonamide,

222) 3-fluoro-N-{3-[4-(2,2-difluoro-1,3-benzodioxol-4-ylo)piperazyn-1-yl]propyl}-benzenesulphonamide,

223) 3-chloro-N-{4-[4-(2,2-difluoro-1,3-benzodioxol-4-yl)piperazin-1-yl]butyl}benzene-sulphonamide,

224) 3-chloro-N-{3-[4-(2,2-difluoro-1,3-benzodioxol-4-yl)piperazin-1-yl]propyl}benzene-sulphonamide,

225) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-4-fluorobenzenesulphonamide,

226) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-3,4-difluorobenzene-sulphonamide,

227) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-4-chlorobenzenesulphonamide,

228) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-3,4-dichlorobenzene-sulphonamide,

229) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-4-bromobenzenesulphonamide,
230) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-3-bromobenzenesulphonamide,
231) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-3-hydroxybenzene-sulphonamide,
232) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-3-methoxybenzene-sulphonamide,
233) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-4-tert-butylbenzene-sulphonamide,
234) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-4-(trifluoromethyl)benzene-sulphonamide,
235) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-3-(trifluoromethyl)benzene-sulphonamide,
236) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-4-(trifluoromethoxy)benzene-sulphonamide,
237) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-4-phenylbenzenesulphonamide,
238) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]thiophene-2-sulphonamide,
239) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]benzothiophene-2-sulphonamide,
240) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]benzothiophene-3-sulphonamide,
241) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-6-chlorobenzothiophene-2-sulphonamide,
242) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-2,3-dihydrobenzofuran-5-sulphonamide,
243) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-1,3-benzothiazole-4-sulphonamide,
244) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-1H-indazole-6-sulphonamide,
245) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-1,3-benzodioxole-5-sulphonamide,
246) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]imidazo[1,2-a]pyridine-3-sulphonamide,
247) N-[4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butyl]-1H-pyrrolo[2,3-b]pyridine-3-sulphonamide,
248) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-4-fluorobenzene-sulphonamide,

249) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-3,4-difluorobenzene-sulphonamide,

250) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-4-chlorobenzene-sulphonamide,

251) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-3,4-dichlorobenzene-sulphonamide,

252) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-4-bromobenzene-sulphonamide,

253) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-3-bromobenzene-sulphonamide,

254) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-3-hydroxybenzene-sulphonamide,

255) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-3-methoxybenzene-sulphonamide,

256) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-4-tert-butylbenzene-sulphonamide,

257) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-4-(trifluoromethyl)-benzenesulphonamide,

258) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-3-(trifluoromethyl)-benzenesulphonamide,

259) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-4-(trifluoromethoxy)-benzenesulphonamide,

260) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-4-phenylbenzene-sulphonamide,

261) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]thiophene-2-sulphonamide,

262) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]benzothiophene-2-sulphonamide,

263)N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]benzothiophene-3-sulphonamide,

264) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-6-chlorobenzothiophene-2-sulphonamide,

265) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-2,3-dihydrobenzofuran-5-sulphonamide,

266) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-1,2-benzoxazole-5-sulphonamide,

267) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-1,3-benzothiazole-4-sulphonamide,
268) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-1H-indazole-6-sulphonamide,
269) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-1,3-benzodioxole-5-sulphonamide,
270) N-[3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propyl]-1H-pyrrolo[2,3-b]pyridine-3-sulphonamide,
271) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-4-fluorobenzenesulphonamide,
272) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-3,4-difluorobenzene-sulphonamide,
273) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-4-chlorobenzenesulphonamide,
274) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-4-bromobenzenesulphonamide,
275) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-3-bromobenzenesulphonamide,
276) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-3-chloro-4-fluorobenzene-sulphonamide,
277) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-3-hydroxybenzenesulphonamide,
278) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-3-methoxybenzene-sulphonamide,
279) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-4-tert-butylbenzene-sulphonamide,
280) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-4-(trifluoromethyl)benzene-sulphonamide,
281) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-4-(trifluoromethoxy)benzene-sulphonamide,
282) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-3-cyanobenzenesulphonamide,
283) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-4-phenylbenzenesulphonamide,
284) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]thiophene-2-sulphonamide,
285) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-5-chloro-thiophene-2-sulphonamide,
286) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]benzothiophene-2-sulphonamide,
287) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]benzothiophene-3-sulphonamide,
288) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-6-chlorobenzothiophene-2-sulphonamide,
289) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-2,3-dihydrobenzofuran-5-sulphonamide,

290) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-1,3-benzothiazole-4-sulphonamide,

291) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-1H-indazole-6-sulphonamide,

292) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]-1,3-benzodioxole-5-sulphonamide,

293) N-[4-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]butyl]imidazo[1,2-a]pyridine-3-sulphonamide,

294) 4-fluoro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide,

295) 3,4-difluoro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide,

296) 4-chloro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide,

297) 3,4-dichloro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide,

298) 4-bromo-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide,

299) 3-chloro-4-fluoro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-benzenesulphonamide,

300) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-3-methoxybenzene-sulphonamide,

301) 4-tert-butyl-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide,

302) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-4-(trifluoromethyl)-benzenesulphonamide,

303) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-3-(trifluoromethyl)-benzenesulphonamide,

304) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-4-(trifluoromethoxy)-benzenesulphonamide,

305) 4-cyano-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide,

306) 3-cyano-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide,

307) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]thiophene-3-sulphonamide,

308) 5-chloro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]thiophene-2-sulphonamide,

309) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-2,5-dimethyl-thiophene-3-sulphonamide,

310) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-1-methyl-indole-4-sulphonamide,

311) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-1-methyl-indole-6-sulphonamide,

312) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzothiophene-2-sulphonamide,

313) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzothiophene-3-sulphonamide,

314) 6-chloro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzothiophene-2-sulphonamide,

315) 5-chloro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-3-methylbenzo-thiophene-2-sulphonamide,

316) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzofuran-2-sulphonamide,

317) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-2,3-dihydrobenzofuran-5-sulphonamide,

318) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-1,3-benzothiazole-4-sulphonamide,

319) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-1H-indazole-6-sulphonamide,

320) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-1,3-benzodioxole-5-sulphonamide,

321) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-2,3-dihydro-1,4-benzodioxine-6-sulphonamide,

322) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]imidazo[1,2-a]pyridine-3-sulphonamide,

323) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-1H-pyrrolo[2,3-b]-pyridine-3-sulphonamide,

324) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-2-oxo-indoline-5-sulphonamide,

325) N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]thiophene-2-sulphonamide,

326) 4-fluoro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide,

327) 3,4-difluoro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide,

328) 4-chloro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide,

329) 3,4-dichloro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide,

330) 4-bromo-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide,

331) 3-chloro-4-fluoro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-benzenesulphonamide,

332) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-3-methoxybenzene-sulphonamide,

333) 4-tert-butyl-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide,

334) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-4-(trifluoromethyl)-benzenesulphonamide,

335) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-3-(trifluoromethyl)-benzenesulphonamide,

336) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-4-(trifluoromethoxy)-benzenesulphonamide,

337) 4-cyano-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide,

338) 3-cyano-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide,

339) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]thiophene-2-sulphonamide,

340) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]thiophene-3-sulphonamide,

341) 5-chloro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]thiophene-2-sulphonamide,

342) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-2,5-dimethyl-thiophene-3-sulphonamide,

343) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-1-methyl-indole-4-sulphonamide,

344) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-1-methyl-indole-5-sulphonamide,

345) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzothiophene-2-sulphonamide,

346) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzothiophene-3-sulphonamide,

347) 6-chloro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzothiophene-2-sulphonamide,

348) 5-chloro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-3-methyl-benzothiophene-2-sulphonamide,

349) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzofuran-2-sulphonamide,

350) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-2,3-dihydrobenzofuran-5-sulphonamide,

351) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-1,3-benzothiazole-4-sulphonamide,

352) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-1H-indazole-6-sulphonamide,

353) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-2-oxo-3H-1,3-benzoxazole-6-sulphonamide,

354) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-1,3-benzodioxole-5-sulphonamide,

355) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-2,3-dihydro-1,4-benzodioxine-6-sulphonamide,

356) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]imidazo[1,2-a]pyridine-3-sulphonamide,

357) N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-1H-pyrrolo[2,3-b]-pyridine-2-sulphonamide,

358) 6-chloro-N-[4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl]naphthalene-2-sulphonamide,

359) 4-fluoro-N-[4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl]benzenesulphonamide,

360) N-[4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl]-4-(trifluoromethyl)benzene-sulphonamide,

361) N-[4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl]-3-(trifluoromethyl)benzene-sulphonamide,

362) 3-cyano-N-[4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl]benzenesulphonamide,

363) 6-chloro-N-[4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl]benzothiophene-2-sulphonamide,

364) 5-fluoro-N-[4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl]-3-methylbenzothiophene-2-sulphonamide,

365) N-[4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl]-1,3-benzodioxole-5-sulphonamide,

366) N-[3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl]naphthalene-1-sulphonamide,

367) N-[3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl]naphthalene-2-sulphonamide,

368) N-[3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl]-4-fluorobenzenesulphonamide,

369) N-[3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl]-3,4-difluorobenzene-sulphonamide,

370) N-[3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl]-4-chlorobenzenesulphonamide,

371) N-[3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl]-4-bromobenzenesulphonamide,

372) N-[3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl]-3-bromobenzenesulphonamide,

373) N-[3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl]-3-chloro-4-fluorobenzene-sulphonamide,

374) N-[3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl]-4-tert-butyl-benzene-sulphonamide,

375) N-[3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl]-4-(trifluoromethyl)benzene-sulphonamide,

376) N-[3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl]-3-cyanobenzenesulphonamide,

377) N-[3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl]-4-phenylbenzenesulphonamide,

378) N-[3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl]-2,3-dihydrobenzofuran-5-sulphonamide,

379) N-[3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propyl]-1,3-benzothiazole-4-sulphonamide,

380) N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]naphthalene-1-sulphonamide,

381) N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]naphthalene-2-sulphonamide,

382) 6-chloro-N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-naphthalene-2-sulphonamide,

383) N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-3-fluorobenzene-sulphonamide,

384) N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-3,4-difluoro-benzenesulphonamide,

385) 3-chloro-N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]benzene-sulphonamide,

386) 3-bromo-N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]benzene-sulphonamide,

387) 3-chloro-N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-4-fluoro-benzenesulphonamide,

388) N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-3-hydroxy-benzenesulphonamide,

389) N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-3-methoxy-benzenesulphonamide,

390) N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-3-methyl-benzenesulphonamide,

391) N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-4-phenyl-benzenesulphonamide,

392) N-[4-[4-(2,3-dihydro-1,4-benzodioxin-8-yl)piperazin-1-yl]butyl]thiophene-2-sulphonamide,

393) 5-chloro-N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]thiophene-2-sulphonamide,

394) N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]benzothiophene-2-sulphonamide,

395) N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]benzothiophene-3-sulphonamide,

396) 6-chloro-N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-benzothiophene-2-sulphonamide,

397) N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-1H-indazole-6-sulphonamide,

398) N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-2-oxo-3H-1,3-benzoxazole-6-sulphonamide,

399) N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-1,3-benzodioxole-5-sulphonamide,

400) N-[3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]naphthalene-1-sulphonamide,

401) N-[3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]naphthalene-2-sulphonamide,

402) 6-chloro-N-[3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]-naphthalene-2-sulphonamide,

403) N-[3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]-4-fluoro-benzenesulphonamide,

404) N-[3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]-3-fluoro-benzenesulphonamide,

405) N-[3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]-3,4-difluoro-benzenesulphonamide,

406) 3-chloro-N-[3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]-benzenesulphonamide,

407) 4-bromo-N-[3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]-benzenesulphonamide,

408) 3-bromo-N-[3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]-benzenesulphonamide,

409) N-[3-[4-(2,3-dihydro-1,4-benzodioxin-8-yl)piperazin-1-yl]propyl]-3-methyl-benzenesulphonamide,

410) N-[3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]-4-phenyl-benzenesulphonamide,

411) N-[3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]benzothiophene-3-sulphonamide,

412) N-[3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]-2,3-dihydro-benzofuran-5-sulphonamide,

413) N-[4-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]butyl]naphthalene-1-sulphonamide,

414) N-[4-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]butyl]naphthalene-2-sulphonamide,

415) 4-fluoro-N-[4-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]butyl]-benzenesulphonamide,

416) 4-chloro-N-[4-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]butyl]-benzenesulphonamide,

417) 3-methyl-N-[4-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]butyl]-benzenesulphonamide,

418) N-[3-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]propyl]naphthalene-1-sulphonamide,

419) N-[3-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]propyl]naphthalene-2-sulphonamide,

420) 4-chloro-N-[3-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]propyl]-benzenesulphonamide,

421) 3-methyl-N-[3-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]propyl]-benzenesulphonamide,

422) N-[4-[4-(3-oxo-4H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl]naphthalene-2-sulphonamide,

423) 4-fluoro-N-[4-[4-(3-oxo-4H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl]benzene-sulphonamide,

424) N-[4-[4-(3-oxo-4H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl]-4-(trifluoromethyl)-benzenesulphonamide,

425) N-[4-[4-(3-oxo-4H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl]-3-(trifluoromethyl)-benzenesulphonamide,

426) 5-chloro-N-[4-[4-(3-oxo-4H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl]thiophene-2-sulphonamide,

427) N-[4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-naphthalene-1-sulphonamide,

428) N-[4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-naphthalene-2-sulphonamide,

429) N-[4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-4-fluorobenzenesulphonamide

430) N-[4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-3-hydroxybenzenesulphonamide,

431) N-[4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-3-methylbenzenesulphonamide,

432) N-[4-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]naphthalene-2-sulphonamide,

433) 3-fluoro-N-[4-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-benzenesulphonamide,

434) N-[4-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-3-hydroxy-benzenesulphonamide,

435) N-[4-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-3-methyl-benzenesulphonamide,

436) 3-fluoro-N-[3-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-benzenesulphonamide,

437) N-[3-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-3-hydroxy-benzenesulphonamide,

438) N-[2-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]naphthalene-2-sulphonamide,

439) 3-fluoro-N-[2-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-benzenesulphonamide,

440) N-[2-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-3-methyl-benzenesulphonamide,

441) N-[3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-naphthalene-1-sulphonamide,

442) N-[3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-naphthalene-2-sulphonamide,

443) N-[3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-4-fluorobenzenesulphonamide,

444) 4-chloro-N-[3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]-propyl]benzenesulphonamide,

445) N-[3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-3-hydroxybenzenesulphonamide,

446) N-[3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-3-methylbenzenesulphonamide,

447) N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-naphthalene-1-sulphonamide,

448) N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-naphthalene-2-sulphonamide,

449) N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-4-fluorobenzenesulphonamide,

450) N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-3-fluorobenzenesulphonamide,

451) 4-chloro-N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]-ethyl]benzenesulphonamide,

452) 3-chloro-N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]-ethyl]benzenesulphonamide,

453) N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-3-hydroxybenzenesulphonamide,

454) N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-3-methylbenzenesulphonamide,

and pharmaceutically acceptable salts thereof.

Arylsulphonamide derivatives of the above formula (I) exhibit affinity to receptors which are recognized therapeutical targets in the treatment of CNS disorders, such as

dopaminergic, in particular D2 and D3, serotoninergic, in particular 5-HT1A, 5-HT2A, 5-HT6, 5-HT7, adrenergic, in particular α1 and α2C, sigma and serotonine transporter receptors and do not exhibit or have low affinity toward biological targets associated with adverse effects, such as potassium channel hERG, muscarinic receptors, histaminergic receptors and serotoninergic receptor 5-HT2C. Due to such a broad pharmacological profile, the compounds of the invention may be useful in medicine as medicaments, for the treatment and/or prevention of the central nervous system disorders such as schizophrenia, schizoaffective disorders, schizophreniform disorders, delusional syndromes and other psychotic conditions related and not related to taking psychoactive substances, affective disorder, bipolar disorder, mania, depression, anxiety disorders of various aetiology, stress reactions, conciousness disorders, coma, delirium of alcoholic or other aetiology, aggression, psychomotor agitation and other conduct disorders, sleep disorders of various aetiology, withdrawal syndromes of various aetiology, addiction, pain syndromes of various aetiology, intoxication with psychoactive substances, cerebral circulatory disorders of various aetiology, psychosomatic disorders of various aetiology, conversion disorders, dissociative disorders, urination disorders, autism and other developmental disorders, including nocturia, stuttering, tics, cognitive disorders of various types, such as Alzheimer's disease, psychopatological symptoms and neurological disorders in the course of other diseases of the central and peripheral nervous systems.

Thus, the subject of the present invention are the compounds of formula (I) as defined above, for use as a medicament.

In the treatment of central nervous system disorders compound of formula (I) may be administered in the form of a pharmaceutical composition or preparation containing it.

Thus, the subject of the present invention is also the pharmaceutical composition containing a compound or compounds of formula (I) as defined above as an active substance, in combination with pharmaceutically acceptable carrier(s) and/or excipient(s).

The subject of the invention is also a use of arylsulphonamide derivatives of the above formula (I) for the treatment of disorders of central nervous system.

The invention relates also to a method for the treatment of disorders of the central nervous system in mammals, including humans, comprising administration of a therapeutically effective amount of the compound of above formula (I) or the

pharmaceutical composition containing the compound of formula (I) as defined above as an active substance.

Terms used in the description of the present invention have the following meanings.

Unless otherwise indicated, the term „C_1-C_4-alkyl" relates to a saturated, straight or branched hydrocarbon group, having indicated number of carbon atoms. Specific examples of groups encompassed by this term are methyl, ethyl, n-propyl, isopropyl, n-butyl, tert-butyl, and sec-butyl.

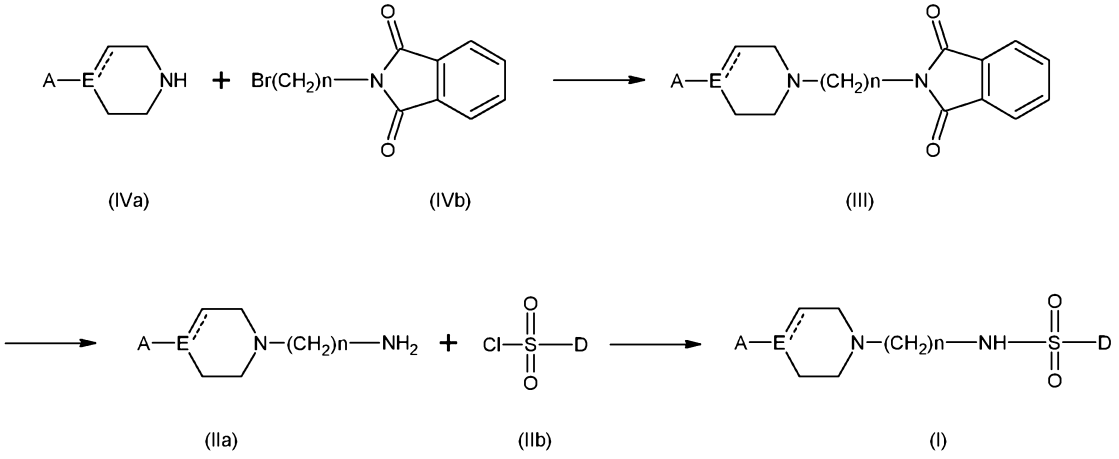
The term „C_1-C_3-alkyloxy" relates to a -O-C_1-C_3-alkyl group, wherein C_1-C_3-alkyl represents saturated hydrocarbon group having indicated number of carbon atoms, and which is a straight- or branched-chain. Specific examples of groups encompassed by this term are methoxy, ethoxy, n-propoxy, and iso-propoxy.

The term „halogen atom" relates to a substituent selected from F, Cl, Br and I.

The term „halogeno-C_1-C_3-alkyl" relates to a saturated, straight or branched hydrocarbon group, having indicated number of carbon atoms and in which one carbon atom may be substituted with from 1-3 halogen atoms, depending on the number of carbon atoms bonded to it. Halogen atom has the meaning as defined above. Particularly preferred example of a group encompassed by this term is trifluoromethyl group -CF_3.

The term "halogeno- C_1-C_3-alkyloxy" relates to a -O-C_1-C_3-halogenoalkyl group, wherein C_1-C_3-halogenoalkyl means saturated, straight or branched hydrocarbon group having indicated number of carbon atoms and in which one carbon atom may be substituted with 1-3 halogen atoms, depending on the number of carbon atoms bonded to it. Halogen atom has the meaning as defined above. Particularly preferred example of a group encompassed by his term is trifluoromethoxy group -O-CF_3.

The compounds of formula (I) can be prepared in a process presented in the following scheme:



(IVa) (IVb) (III)

(IIa) (IIb) (I)

In the first step compound (IVa), for example as hydrochloride, is reacted with appropriate 2-(bromoalkyl)-1*H*-isoindoline-1,3(2*H*)-dione (IVb) in a solvent, such as N,N-dimethylformamide or acetonitrile, in the presence of a base at room temperature or at elevated temperature, to give a compound of formula (III). Then imide (III) is hydrolysed using 40% aqueous methylamine solution at room temperature, to obtain amine derivative (IIa). Compound (IIa) is reacted with appropriate arylsulphonyl chloride (IIb), for example in methylene chloride in the presence of triethylamine, at room temperature, to give arylsulphonamide derivative (I) of the invention.

Starting compounds of formulas (IVa) and (IVb) are either well known or commercially available, or can be prepared from commercially available starting materials by adapting and applying known methods, such as described in publication of Hallett D.J. et al., J. Org. Chem. 2000, 65, 4984-4993.

Preparation of exemplary starting compounds of formula (III) is described in detail in the experimental part.

Since the compounds of formula (I) have alkaline character (contain at least one tertiary amine group), they can form acid addition salts.

Salts with acids can be pharmaceutically acceptable, especially when they are intended to be an active ingredient in pharmaceutical composition. The present invention relates also to salts of the compounds of formula (I) with acids other than pharmaceutically acceptable ones, which may be useful for example as intermediates suitable for purification of the compounds of the invention. In practice, it is often desirable to isolate first the compound from a reaction mixture in the form of a salt which is not pharmaceutically acceptable to purify the compound, and then convert the salt into

free base by treatment with alkaline agent and to isolate, and optionally convert into the salt again.

Acid addition salts can be formed with inorganic (mineral) or organic acids. In particular, hydrochloric, hydrobromic, hydroiodic, phosphoric, sulphuric, nitric, carbonic, succinic, maleic, formic, acetic, propionic, fumaric, citric, tartaric, lactic, benzoic, salicylic, glutamic, aspargic, p-toluenesulphonic, benzenesulphonic, methanesulphonic, ethanesulphonic, naphthalenesulphonic such as 2-naphthalene-sulphonic, pamoic, xinafoic or hexanoic acids can be mentioned as examples of acids.

Acid addition salt can be prepared in a simple manner by reaction of the compound of formula (I) with suitable inorganic or organic acid, optionally in suitable solvent, such as organic solvent, to form a salt that is usually isolated, for example by crystallization and filtration. For example, compounds in the form of a free base can be converted into corresponding hydrochloride salts by reaction of a compound in a solution, for example in methanol, with stoichiometric amount of hydrochloric acid or with solution of hydrochloric acid in methanol, ethanol or diethyl ether, followed by evaporation of solvent(s).

The term „disorders of the central nervous system" should be understood as including disorders selected from schizophrenia, schizoaffective disorders, schizophreniform disorders, delusional syndromes and other psychotic conditions related and not related to taking psychoactive substances, affective disorder, bipolar disorder, mania, depression, anxiety disorders of various aetiology, stress reactions, conciousness disorders, coma, delirium of alcoholic and other aetiology, aggression, psychomotor agitation and other conduct disorders, sleep disorders of various aetiology, withdrawal syndromes of various aetiology, addiction, pain syndromes of various aetiology, intoxication with psychoactive substances, cerebral circulatory disorders of various aetiology, psychosomatic disorders of various aetiology, conversion disorders, dissociative disorders, urination disorders, autism and other developmental disorders, including nocturia, stuttering, and tics, cognitive disorders of various types, like Alzheimer's disease, psychopatological symptoms and neurological disorders in the course of other diseases of the central and peripheral nervous systems are.

In the treatment of the disorders mentioned above, compounds of formula (I) of the present invention can be administered as a chemical compound, but usually will be applied in the form of a pharmaceutical compositions containing the compound of the

present invention or its pharmaceutically acceptable salt as defined above as an active ingredient in combination with pharmaceutically acceptable carrier(s) and/or excipient(s).

In the treatment of the above mentioned disorders the pharmaceutical compositions of the invention can be delivered by any route of administration, preferably oral or parenteral, and will have the form of a preparation for use in medicine, depending on the intended route of administration.

Compositions for oral administration may have the form of solid or liquid preparations. Solid preparations may be in the form, for example, tablets or capsules prepared in conventional manner using pharmaceutically acceptable inactive ingredients, such as binding agents (e.g. pregelatinized maize starch, polyvinylpyrrolidone or hydroxypropylmethylcellulose); fillers (e.g. lactose, sucrose, carboxymethylcellulose, microcrystalline cellulose or calcium hydrogen phosphate) lubricants (e.g. magnesium stearate, talc or silica); disintegrants (e.g. crospovidone, maize starch or sodium starch glycolate); wetting agents (e.g. sodium lauryl sulfate). The tablets may be coated using methods well known in the art with conventional coatings, delaying /controlling release coatings or enteric coatings. Liquid preparations for oral administration may have the form of *e.g.* solutions, syrups or suspensions, or may be prepared from a dry product suitable for reconstitution with water or other suitable carrier *ex tempore*. Such liquid preparations may be prepared by conventional methods with pharmaceutically acceptable inactive ingredients, such as suspending agents (e.g. sorbitol syrup, cellulose derivatives or hydrogenated edible fats), emulsifying agents (e.g. lecithin or acacia gum), non-aqueous matrix components (e.g. almond oil, oils esters, ethyl alcohol or fractionated vegetable oils) and preservatives (e.g. methyl or propyl p-hydroxybenzoates or sorbic acid). The preparations may also contain suitable buffering systems, flavouring and aroma agents, colourants and sweeteners.

Preparations for oral administration can be formulated according to methods well known to those skilled in the art to afford a controlled release of the active compound.

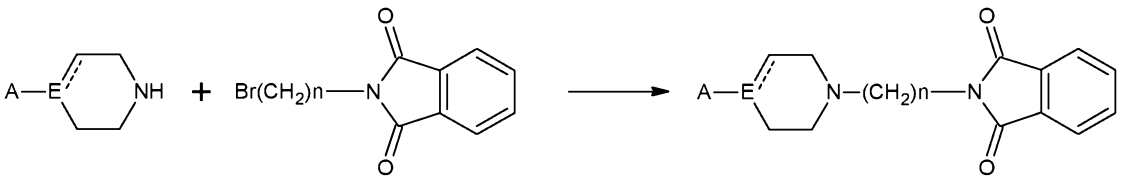
The parenteral route of administration comprises administration by intramuscular and intravenous injections and intravenous continuous infusions. Compositions for parenteral administration may be in the form of a dosage unit, e.g. in ampoules or in multidose containers with the addition of a preservative. The compositions may be in the form of suspensions, solutions or emulsions in oily or aqueous media, and may

contain pharmaceutically acceptable excipients, such as suspending agents, stabilizing and/or dispersing agents. Alternatively, the active ingredient may be in the form of a powder for reconstitution *ex tempore* in a suitable carrier, e.g. sterile pyrogen-free water.

Method of treatment using compounds of this invention will be based on administration of a therapeutically effective amount of the compound of the invention, preferably in the form of a pharmaceutical composition, to a subject in need of such a treatment.

The proposed dose of the compounds of the invention will be comprised in the range from 1 to about 1000 mg per day, in a single dose or in divided doses. It will be apparent to those skilled in the art that selection of a dose required to achieve the desired biological effect will depend on several factors, such as the type of specific compound, the indication, route of administration, age and condition of a patient and the exact dose will be finally determined at the discretion of attending physician.

Example 1. Preparation of starting materials of the general formula (III):



(IVa) (IVb) (III)

a) General procedure for compounds wherein in formula (IVa) ----- represents single bond

A mixture of 10 mmol of compound (IVa) as hydrochloride and 10 mmol of compound (IVb), 30 mmol of potassium carbonate, small crystal of potassium iodide and 20 ml of N,N-dimethylformamide was stirred at room temperature until disappearance of starting materials (TLC monitoring). Usually, the reaction was carried out for 2 days. The reaction mixture was subsequently poured into 50 ml of water, and precipitate thus formed was isolated by filtration. For purification, crude product was suspended in 20 ml of methanol, then the solid was filtered off and dried to constant weight.

Alternatively (for **III-8**), the reaction was carried out in acetonitrile, after completion of the reaction the solvent was evaporated and product was purified by column chromatography on silica gel using chloroform/methanol 95:5 as eluent.

Structures of products were confirmed by mass spectrometry.

According to the above procedure the following compounds were prepared:

2-(4-(4-(1,2-benzothiazol-3-yl)piperazin-1-yl)butyl)-1H-isoindole-1,3(2H)-dione (**III-1**), reaction in N,N-dimethylformamide, MS: 421[M+H$^+$], yield: 87%;

2-(3-(4-(1,2-benzothiazol-3-yl)piperazin-1-yl)propyl)-1H-isoindole-1,3(2H)-dione (**III-2**), reaction in N,N-dimethylformamide, MS: 407[M+H$^+$], yield: 77%;

2-(2-(4-(1,2-benzothiazol-3-yl)piperazin-1-yl)ethyl)-1H-isoindole-1,3(2H)-dione (**III-3**), reaction in N,N-dimethylformamide, MS: 393[M+H$^+$], yield: 37%;

2-(4-(4-(1,2-benzoxazol-3-yl)piperazin-1-yl)butyl)-1H-isoindole-1,3(2H)-dione (**III-4**), reaction in N,N-dimethylformamide, MS: 405[M+H$^+$], yield: 75%;

2-(4-(4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl)butyl)-1H-isoindole-1,3(2H)-dione (**III-5**), reaction in N,N-dimethylformamide, MS: 422[M+H$^+$], yield: 71%;

2-(3-(4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl)propyl)-1H-isoindole-1,3(2H)-dione (**III-6**), reaction in N,N-dimethylformamide, MS: 408[M+H$^+$], yield: 55%;

2-{2-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperydyn-1-yl]ethyl}-1H-isoindole-1,3(2H)-dione (**III-7**), reaction in N,N-dimethylformamide, MS: 394[M+H$^+$], yield: 47%;

2-{4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl}-1*H*-isoindole-1,3(2H)-dione (**III-8**) , reaction in acetonitrile, MS: 403[M+H$^+$], yield: 71%.

2-(3-(4-(1,2-benzoxazol-3-yl)piperazin-1-yl)propyl)-1H-isoindole-1,3(2H)-dione (**III-13**), reaction in N,N-dimethylformamide, MS: 391[M+H$^+$], yield: 77%;

2-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-1H-isoindole-1,3(2H)-dione (**III-14**), reaction in N,N-dimethylformamide, MS: 422[M+H$^+$], yield: 73%;

2-[3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]-1H-isoindole-1,3(2H)-dione (**III-15**), reaction in N,N-dimethylformamide, MS: 408[M+H$^+$], yield: 68%;

2-[4-[4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-4-yl)piperazin-1-yl]butyl]-1H-isoindole-1,3(2H)-dione (**III-16**), reaction in N,N-dimethylformamide, MS: 420[M+H$^+$], yield: 70%;

2-[3-[4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-4-yl)piperazin-1-yl]propyl]-1H-isoindole-1,3(2H)-dione (**III-17**), reaction in N,N-dimethylformamide, MS: 406[M+H$^+$], yield: 72%;

2-{4-[4-(3-oxo-3,4-dihydro-2*H*-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl}-1*H*-isoindole-1,3(2*H*)-dione (**III-18**), reaction in N,N-dimethylformamide, MS: 435[M+H$^+$], yield: 79%;

b) General procedure for compounds wherein in formula (IVa) ----- represents double bond:

b1) General procedure for starting compounds (IVa) easily soluble in N,N-dimethylformamide:

A mixture of 5.6 mmol of compound (IVa) and 5.6 mmol of compound (IVb), 12 mmol of N,N-diisopropylethylamine, and 20 ml of N,N-dimethylformamide was stirred at room temperature until disappearance of starting materials (TLC monitoring). Usually, the reaction was carried out for 2.5 days. Then to the mixture 100 ml of water was added and the whole was left for 1 hour. Subsequently, 20 ml of methanol was added to the resulting mixture and after heating, it was refluxed for 20 minutes. Precipitated product was isolated by filtration and dried to the constant weight. Structure of the product was confirmed by mass spectrometry.

The following compounds were prepared according to the above procedure:

2-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2*H*)-yl]butyl}-1*H*-isoindole-1,3(2H)-dione (**III-9**) MS: 434[M+H$^+$], yield: 57%;

2-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2*H*)-yl]propyl}-1*H*-isoindole-1,3(2H)-dione (**III-10**) MS: 420[M+H$^+$], yield: 45%;

2-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2*H*)-yl]ethyl}-1*H*-isoindole-1,3(2H)-dione (**III-11**) MS: 406[M+H$^+$], yield: 30%.

2-{4-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydropyridin-1(2*H*)-yl]butyl}-1*H*-isoindole-1,3(2H)-dione (**III-19**) MS: 418[M+H$^+$], yield: 79%;

2-{3-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydropyridin-1(2*H*)-yl]propyl}-1*H*-isoindole-1,3(2H)-dione (**III-20**) MS: 404[M+H$^+$], yield: 84%;
2-{2-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydropyridin-1(2*H*)-yl]ethyl}-1*H*-isoindole-1,3(2H)-dione (**III-21**) MS: 390[M+H$^+$], yield: 77%.

b2) General procedure for starting compounds (IVa) poorly soluble in acetonitrile:

A mixture of 13 mmol of compound (IVa) and 13 mmol of compound (IVb), 13 mmol N,N-diisopropylethylamine, catalytic amount of potassium iodide and 300 ml of mixture of N,N-dimethylformamide and acetonitrile 1:1 was stirred at 70°C for 3 days. Then the reaction mixture was concentrated under reduced pressure and the residue was purified

using column chromatography on silica gel using methylene chloride : methanol = 9:1 as eluent. Structure of the product was confirmed by mass spectrometry.

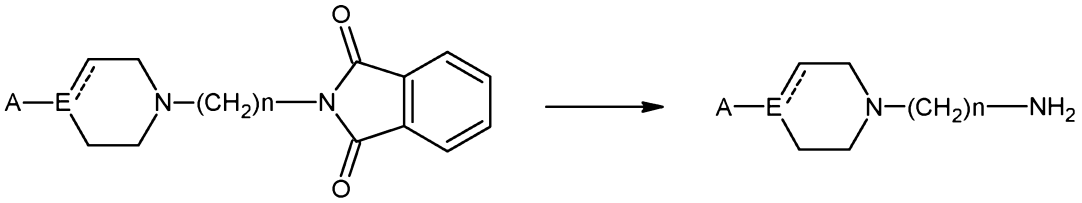
According to the above procedure, the following compounds were prepared:

2-{4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2*H*)-yl]butyl}-1*H*-isoindole-1,3(2H)-dione (**III-12**) MS: 448[M+H$^+$], yield: 36%.

2-{3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2*H*)-yl]propyl}-1*H*-isoindole-1,3(2H)-dione (**III-22**) MS: 404[M+H$^+$], yield: 40%.

2-{2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2*H*)-yl]ethyl}-1*H*-isoindole-1,3(2H)-dione (**III-23**) MS: 390[M+H$^+$], yield: 47%.

Example 2. General procedure for the preparation of starting materials of general formula (IIa) by hydrolysis of imide (III):



(III) (IIa)

a) General procedure for compounds wherein in formula (III) ----- represents single bond.

A mixture of 6 mmol of compound (III) and 30 ml of 40% aqueous solution of methylamine was stirred at room temperature for 3 days. To the resulting solution 30 ml of 20% aqueous solution of sodium hydroxide was added and the whole was stirred for 1,5 hours. Then 4 g of sodium chloride was added and the solution was extracted with methylene chloride (2×30 ml). Organic layer was washed with water (2×30 ml), and then dried over anhydrous magnesium sulphate. Product was obtained by evaporation of methylene chloride from dry solution. If necessary, the product was purified using column chromatography on silica gel, with chloroform/methanol 95:5 as eluent. Structure of the product was confirmed by mass spectrometry.

According to the above procedure the following compounds were prepared:

4-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]butan-1-amine (**IIa-1**) from compound **(III-1)**

MS: 291[M+H$^+$], yield: 81%;

3-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]propan-1-amine (**IIa-2**) from compound **(III-2)**

MS: 277[M+H$^+$], yield: 78%;

2-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]ethan-1-amine (**IIa-3**) from compound **(III-3)**

MS: 263[M+H$^+$], yield: 71%;

4-(4-(1,2-benzoxazol-3-yl)piperazin-1-yl)butan-1-amine (**IIa-4**) from compound **(III-4)**

MS: 275[M+H$^+$], yield: 88%;

4-(4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl)butan-1-amine (**IIa-5**) from compound **(III-5)** MS: 292[M+H$^+$], yield: 82%;

3-(4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl)propan-1-amine (**IIa-6**) from compound **(III-7)** MS: 278[M+H$^+$], yield: 86%;

2-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]ethan-1-amine (**IIa-7**) from compound **(III-7)** MS: 264[M+H$^+$], yield: 74%;

4-[4-(1*H*-indol-4-yl)piperazin-1-yl]butan-1-amine (**IIa-8**) from compound **(III-8)** MS: 273[M+H$^+$], yield: 67%.

3-[4-(1,2-benzoxazol-3-yl)piperazin-1-yl]propan-1-amine (**IIa-13**) from compound **(III-13)** MS: 261[M+H$^+$], yield: 77%.

4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butan-1-amine (**IIa-14**) from compound **(III-14)** MS: 292[M+H$^+$], yield: 83%.

3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propan-1-amine (**IIa-15**) from compound **(III-15)** MS: 278[M+H$^+$], yield: 85%.

4-[4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-4-yl)piperazin-1-yl]butan-1-amine (**IIa-16**) from compound **(III-16)** MS: 290[M+H$^+$], yield: 70%.

3-[4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-4-yl)piperazin-1-yl]propan-1-amine (**IIa-17**) from compound **(III-17)** MS: 276[M+H$^+$], yield: 74%.

4-[4-(3-oxo-3,4-dihydro-2*H*-1,4-benzoxazin-8-yl)piperazin-1-yl]butan-1-amine (**IIa-18**) from compound **(III-18)** MS: 305[M+H$^+$], yield: 90%.

b) General procedure for compounds wherein in formula (III) ----- represents double bond.

1,7 Mmol of compound (III) was suspended in 40 ml of 40% aqueous solution of methylamine and stirred at room temperature for 16 hours. Then methylamine was evaporated and resulting precipitate was filtered off. Precipitate was washed with water and dried to the constant weight.

Structure of the product was confirmed by mass spectrometry.

According to the above procedure, the following compounds were prepared:

4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butan-1-amine (**IIa-9**) from compound (**III-9**) MS: 304[M+H$^+$], yield: 85%;

3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propan-1-amine (**IIa-10**) from compound (**III-10**) MS: 290[M+H$^+$], yield: 66%;

2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethan-1-amine (**IIa-11**) from compound (**III-11**) MS: 276[M+H$^+$], yield: 65%;

4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butan-1-amine (**IIa-12**) from compound (**III-12**) MS: 318[M+H$^+$], yield: 80%.

4-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl-1-amine (**IIa-19**) from compound (**III-19**) MS: 288[M+H$^+$], yield: 62%;

3-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl-1-amine (**IIa-20**) from compound (**III-20**) MS: 274[M+H$^+$], yield: 60%;

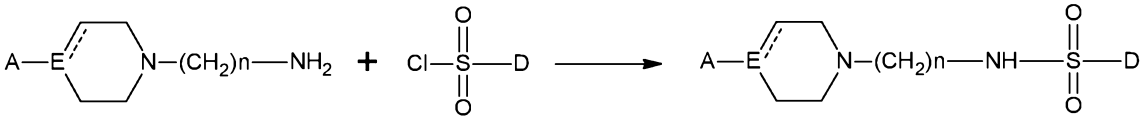
2-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl-1-amine (**IIa-21**) from compound (**III-21**) MS: 260[M+H$^+$], yield: 67%.

3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl-1-amine (**IIa-22**) from compound (**III-22**) MS: 304[M+H$^+$], yield: 66%.

2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl-1-amine (**IIa-23**) from compound (**III-23**) MS: 290[M+H$^+$], yield: 60%.

Example 3. General procedure for the preparation of compounds (I) of the invention:

Compounds of the invention were prepared according to the following scheme.



(IIa) (IIb) (I)

a) General procedure for compounds wherein in formula (IIa) ----- represents single bond.

0.5 ml Of triethylamine and then 0,5 mmol of suitable arylsulphonyl chloride (**IIb**) were added to the solution of 0,5 mmol of amine (**IIa**) in 10 ml of methylene chloride at 10°C. Upon dissolution of chloride (IIb) the reaction mixture was left at room temperature for 3 hours, then the solvent and excess of triethylamine were evaporated. Precipitate thus formed was dissolved in 10 ml of methylene chloride and washed subsequently with 5% solution of sodium hydrogen carbonate (10 ml) and water (10 ml). Organic layer was dried over anhydrous magnesium sulphate, and the solvent was evaporated. Crude sulphonamides were usually purified by crystallization (from methanol), and some of them using column chromatography on silica gel using chloroform : methanol = 9:1 as eluent.

Structure of prepared compounds was confirmed by MS data, and purity by HPLC analysis. For selected compounds structure identification was confirmed by ^{1}H-NMR analysis.

Following the general procedure described above and starting from appropriate amine (IIa) and arylsulphonyl chloride (IIb), the following compounds were obtained.

Compound 1.

N-(4-(4-(1,2-Benzothiazol-3-yl)piperazin-1-yl)butyl)naphthalene-1-sulphonamide

The title compound was prepared starting from amine (IIa-1) and naphthalene-1-sulphonyl chloride. Yield: 62%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 8.66 (d, 1H, *J* = 8.5 Hz), 8.21 (d, 1H, *J* = 8.1 Hz), 8.13-7.98 (m, 4H), 7.74-7.64 (m, 3H), 7.55 (t, 1H, *J* = 6.9 Hz), 7.42 (t, 1H, *J* = 8.4 Hz), 3.09-3.00 (m, 2H), 2.85-2.78 (m, 4H), 2.42-2.32 (m, 4H), 2.16-2.05 (m, 2H), 1.21-1.32 (m, 4H). MS: 481[M+H$^+$].

Compound 2.

N-(4-(4-(1,2-Benzothiazol-3-yl)piperazin-1-yl)butyl)naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-1) and naphthalene-2-sulphonyl chloride. Yield: 60%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 8.42 (s, 1H), 8.16-8.11 (m, 2H), 8.06-7.98 (m, 3H), 7.81 (d, 1H, *J* = 8.7 Hz), 7.74 (t, 1H, *J* = 6.0 Hz), 7.66-7.62 (m, 1H), 7.54 (t, 1H, *J* = 7.2 Hz), 7.42 (t, 1H, *J* = 7.2 Hz), 2.84-2.78 (m, 4H), 2.48-2.4 (m, 6H), 2.26-2.18 (m, 2H), 1.36-1.41 (m, 4H). MS: 481[M+H$^+$].

Compound 3.

N-(4-(4-(1,2-Benzothiazol-3-yl)piperazin-1-yl)butyl)-3-methylbenzenesulphonamide

The title compound was prepared starting from amine (IIa-1) and 3-methylbenzene-sulphonyl chloride. Yield: 51%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 8.05 (d, 2H, *J* = 7.2 Hz), 7.60-7.41 (m, 6H), 3.40-3.35 (m, 4H), 2.72-2.79 (m, 2H), 2.50-2.48 (m, 4H), 2.38 (s, 3H), 2.28-2.26 (m, 2H), 1.36-1.44 (m, 4H). MS: 445[M+H$^+$].

Compound 4.

N-(4-(4-(1,2-Benzothiazol-3-yl)piperazin-1-yl)butyl)-2-oxo-3*H*-1,3-benzoxazole-6-sulphonamide

The title compound was prepared starting from amine (IIa-1) and 2-oxo-3H-1,3-benzoxazole-6-sulphonyl chloride. Yield: 47%. MS: 488[M+H$^+$].

Compound 5.

N-(3-(4-(1,2-Benzothiazol-3-yl)piperazin-1-yl)propyl)naphthalene-1-sulphonamide

The title compound was prepared starting from amine (IIa-2) and naphthalene-1-sulphonyl chloride. Yield: 53%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 8.66 (d, 1H, *J* = 8.4 Hz), 8.21 (d, 1H, *J* = 8.1 Hz), 8.14-7.96 (m, 3H), 7.74-7.61 (m, 3H), 7.53 (t, 1H, *J* = 6.9 Hz), 7.41 (t, 1H, *J* = 7.2) Hz), 3.31-3.25 (m, 4H), 2.81-2.88 (m, 2H), 2.29-2.25 (m, 4H), 2.14 (t, 2H, *J* = 7.2 Hz), 1.44 (quintet, 2H, *J* = 6.9 Hz). MS: 467[M+H$^+$].

Compound 6.

N-(3-(4-(1,2-Benzothiazol-3-yl)piperazin-1-yl)propyl)naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-2) and naphthalene-2-sulphonyl chloride. Yield: 56%. ^{1}H-NMR (300 MHz, CD_3OD): δ 8.44 (s, 1H), 8.10-8.05 (m, 2H), 8.00-7.85 (m, 4H), 7.70-7.61 (m, 2H), 7.53 (t, 1H, *J* = 6.9 Hz), 7.42 (t, 1H, *J* = 7.2 Hz), 3.46-3.43 (m, 4H), 3.00 (t, 2H, *J* = 6.9 Hz), 2.61-2.58 (m, 4H), 2.46 (t, 2H, *J* = 7.2 Hz), 1.69 (quintet, 2H, *J* = 6.9 Hz). MS: 467[M+H$^+$].

Compound 7.

N-(3-(4-(1,2-Benzothiazol-3-yl)piperazin-1-yl)propyl)-3-methylbenzenesulphonamide

The title compound was prepared starting from amine (IIa-2) and 3-methyl-benzenesulphonyl chloride. Yield: 49%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 8.03 (t, 2H, *J* = 7.2 Hz), 7.60-7.39 (m, 6H), 3.39-3.35 (m, 4H), 2.76-2.82 (m, 2H), 2.50-2.46 (m, 4H), 2.38 (s, 3H), 2.30 (t, 2H, *J* = 7.2 Hz), 1.54 (quintet, 2H, *J* = 6.9 Hz). MS: 431[M+H$^+$].

Compound 8.

N-(3-(4-(1,2-Benzothiazol-3-yl)piperazin-1-yl)propyl)-2-oxo-3*H*-1,3-benzoxazole-6-sulphonamide

The title compound was prepared starting from amine (IIa-2) and 2-oxo-3H-1,3-benzoxazole-6-sulphonyl chloride. Yield: 31%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.88-7.79 (m, 1H), 7.62 (s, 1H), 7.47 (t, 1H, *J* = 7.4 Hz), 7.35 (t, 1H, *J* = 7.4 Hz), 7.24 (t, 1H, *J* = 8.2 Hz), 6.75 (t, 1H, *J* = 8.2 Hz), 6.59-6.49 (m, 1H), 5,62-5.55 (m, 2H), 3.57-3.52 (m, 4H), 3.09 (t, 2H, *J* = 5.9 Hz), 2.66-2.61 (m, 4H), 2.51 (t, 2H, *J* = 5.9 Hz), 1.69 (quintet, 2H, *J* = 5.9 Hz). MS: 474[M+H$^+$].

Compound 9.

N-(2-(4-(1,2-Benzothiazol-3-yl)piperazin-1-yl)ethyl)naphthalene-1-sulphonamide

The title compound was prepared starting from amine (IIa-3) and naphthalene-1-sulphonyl chloride. Yield: 51%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.68 (d, 1H, *J* = 8.5 Hz), 8.29 (d, 1H, *J* = 7.4 Hz), 8.08 (d, 1H, *J* = 8.2 Hz), 7.95 (d, 1H, *J* = 8.2 Hz), 7.82-7.68 (m, 3H), 7.62-7.54 (m, 2H), 7.46 (t, 1H, *J* = 6.9 Hz), 7.33 (t, 1H, *J* = 6.9) Hz), 3.33-3.27 (m, 4H), 3.03-2.97 (m, 2H), 2.37-2.30 (m, 6H). MS: 453[M+H$^+$].

Compound 10.

N-(2-(4-(1,2-Benzothiazol-3-yl)piperazin-1-yl)ethyl)naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-3) and naphthalene-2-sulphonyl chloride. Yield: 51%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.47 (s, 1H), 8.00-7.79 (m, 6H), 7.68-7.59 (m, 2H), 7.46 (t, 1H, *J* = 6.9 Hz), 7.33 (t, 1H, *J* = 6.9) Hz), 5.39 (s, 1H), 3.47-3.43 (m, 4H), 3.11-3.04 (m, 2H), 2.52-2.44 (m, 6H). MS: 453[M+H$^+$].

Compound 11.

N-(2-(4-(1,2-Benzothiazol-3-yl)piperazin-1-yl)ethyl)-3-methylbenzenesulphonamide

The title compound was prepared starting from amine (IIa-3) and 3-methyl-benzenesulphonyl chloride. Yield: 49%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.86-7.79 (m, 2H), 7.72-7.66 (m, 2H), 7.49-7.31 (m, 4H), 5.28 (s, 1H), 3.48-3.43 (m, 4H), 3.08-3.01 (m, 2H), 2.53-2.46 (m, 6H), 2.43 (s, 3H); MS: 417[M+H$^+$].

Compound 12.

N-(2-(4-(1,2-Benzothiazol-3-yl)piperazin-1-yl)ethyl)-2-oxo-3*H*-1,3-benzoxazole-6-sulphonamide

The title compound was prepared starting from amine (IIa-3) and 2-oxo-3*H*-1,3-benzoxazole-6-sulphonyl chloride. Yield: 41%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 8.02 (t, 2H, *J* = 8.2 Hz), 7.62-7.51 (m, 3H), 7.45-7.38 (m, 3H), 3.37-3.24 (m, 4H), 2.93-2.85 (m, 2H), 2.52-2.47 (m, 4H), 2.39 (t, 2H, *J* = 6.7 Hz). MS: 460[M+H$^+$].

Compound 13.

N-(4-(4-(1,2-Benzoxazol-3-yl)piperazin-1-yl)butyl)naphthalene-1-sulphonamide

The title compound was prepared starting from amine (IIa-4) and naphthalene-1-sulphonyl chloride. Yield: 64%. MS: 465[M+H$^+$].

Compound 14.

N-(4-(4-(1,2-Benzoxazol-3-yl)piperazin-1-yl)butyl)naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-4) and naphthalene-2-sulphonyl chloride. Yield: 67%. MS: 465[M+H$^+$].

Compound 15.

N-(4-(4-(1,2-Benzoxazol-3-yl)piperazin-1-yl)butyl)-3-methylbenzenesulphonamide

The title compound was prepared starting from amine (IIa-4) and 3-methylbenzene-sulphonyl chloride. Yield: 59%. MS: 429[M+H$^+$].

Compound 16.

N-(4-(4-(1,2-Benzoxazol-3-yl)piperazin-1-yl)butyl)-2-oxo-3*H*-1,3-benzoxazole-6-sulphonamide

The title compound was prepared starting from amine (IIa-4) and 2-oxo-3*H*-1,3-benzoxazole-6-sulphonyl chloride. Yield: 71%. MS: 472[M+H$^+$].

Compound 17.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]naphthalene-1-sulphonamide

The title compound was prepared starting from amine (IIa-5) and naphthalene-1-sulphonyl chloride. Yield: 52%. MS: 483[M+H$^+$].

Compound 18.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-5) and naphthalene-2-sulphonyl chloride. Yield: 44%. MS: 483[M+H$^+$].

Compound 19.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-3-methylbenzene-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 3-methylbenzene-sulphonyl chloride. Yield: 65%. ^{1}H-NMR (300 MHz, $CDCl_3$-d_6): δ 7.96-7.91 (m, 1H), 7.69-

7.65 (m, 2H), 7.40-7.35 (m, 2H), 7.24 (d, 1H, J = 9.0 Hz), 7.05 (t, 1H, J = 9 Hz), 3.13-2.96 (m, 4H), 2.41-2.34 (m, 5H), 2.31-2.04 (m, 7H), 1.60-1.58 (m, 4H). MS: 446[M+H$^+$].

Compound 20.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]naphthalene-1-sulphonamide

The title compound was prepared starting from amine (IIa-6) and naphthalene-1-sulphonyl chloride. Yield: 45%. ^{1}H-NMR (300 MHz, $CDCl_3$-d_6): δ 8.75-8.70 (m, 1H), 8.28-8.24 (m, 1H), 8.09-8.03 (m, 1H), 7.89-7.83 (m, 1H), 7.68-7.52 (m, 3H), 7.29-7.24 (m, 2H), 7.13-6.98 (m, 1H), 3.32-3.14 (m, 5H), 2.66 (t, 2H, J =6.0 Hz), 2.46-2.17 (m, 6H), 1.78 (quintet, 2H, J = 6.0 Hz). MS: 468[M+H$^+$].

Compound 21.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-6) and naphthalene-2-sulphonyl chloride. Yield: 37%. ^{1}H-NMR (300 MHz, $CDCl_3$-d_6): δ 8.44 (s, 1H), 7.99-7.83 (m, 5H), 7.67-7.57 (m, 2H), 7.27-7.23 (m, 1H), 7.11 (t, 1H, J = 8.9 Hz), 3.14 (t, 3H, J = 5.3 Hz), 3.03-3.02 (m, 2H), 2.47 (t, 2H, J = 5.6 Hz), 2.19-2.05 (m, 6H), 1.66 (quintet, 2H, J = 5.6 Hz). MS: 468[M+H$^+$].

Compound 22.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-3-methylbenzene-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 3-methylbenzene-sulphonyl chloride. Yield: 55%. MS: 432[M+H$^+$].

Compound 23.

N-[2-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]ethyl]naphthalene-1-sulphonamide

The title compound was prepared starting from amine (IIa-7) and naphthalene-1-sulphonyl chloride. Yield: 58%. ^{1}H-NMR (300 MHz, $CDCl_3$-d_6): δ 8.74-8.68 (m, 1H), 8.32-8.27 (m, 1H), 8.09-8.04 (m, 1H), 7.95-7.85 (m, 1H), 7.74-7.51 (m, 3H), 7.29-7.24 (m, 2H), 7.09 (t, 1H, J = 9.0 Hz), 5.57-5.30 (m, 1H), 2.98-2.85 (m, 3H), 2.48-2.40 (m, 2H), 2.29-2.22 (m, 2H), 2.00 (t, 2H, J = 11.5 Hz), 1.84-1.67 (m, 4H). MS: 454[M+H$^+$].

Compound 24.

N-[2-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]ethyl]naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-7) and naphthalene-2-sulphonyl chloride. Yield: 33%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 10.54 (s, 1H), 8.50 (s, 1H), 8.20-8.03 (m, 4H), 7.88 (d, 2H, J = 6.6 Hz), 7.75-7.72 (m, 3H), 7.34 (t, 1H, J = 9.2 Hz), 3.65-3.57 (m, 2H), 3.46-3.37 (m, 1H), 3.26-3.10 (m, 6H), 2.26-2.17 (m, 4H). MS: 454[M+H$^+$].

Compound 25.

N-[2-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]ethyl]-3-methylbenzene-sulphonamide

The title compound was prepared starting from amine (IIa-7) and 3-methylbenzene-sulphonyl chloride. Yield: 41%. ^{1}H-NMR (300 MHz, $CDCl_3$-d_6): δ 7.71-7.66 (m, 3H), 7.64-7.38 (m, 2H), 7.36-7.26 (m, 1H), 7.08 (t, 1H, J = 9 Hz), 5.27 (s, 1H), 3.08-2.98 (m, 3H), 2.77-2.73 (m, 2H), 2.48-2.42 (m, 5H), 2.16-2.07 (m, 2H), 2.03-1.96 (m, 4H). MS: 418[M+H$^+$].

Compound 26.

N-{4-[4-(1H-Indol-4-yl)piperazin-1-yl]butyl}naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-8) and naphthalene-2-sulphonyl chloride. Yield: 68%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.42 (s, 1H), 8.32 (s, 1H), 7.96-7.82 (m, 4H), 7.64-7.52 (m, 2H), 7.16-7.06 (m, 4H), 6.64-6.58 (m, 1H), 6.58-6.44 (t, 1H, *J* = 2.3 Hz), 3.38-3.26 (m, 4H), 3.06-2.98 (m, 2H), 2.74-2.64 (m, 4H), 2.46-2.38 (m, 2H), 1.68-1.54 (m, 4H). MS: 463[M+H$^+$].

Compound 27.

N-{4-[4-(1H-Indol-4-yl)piperazin-1-yl]butyl}benzenesulphonamide

The title compound was prepared starting from amine (IIa-8) and benzenesulphonyl chloride. Yield: 50%. ^{1}H-NMR (300 MHz, aceton-d_6): δ 10.2 (bs, 1H), 7.91-7.86 (m, 2H), 7.64-7.54 (m, 3H), 7.23 (t, 1H, *J* = 2.8 Hz), 7.10-6.98 (m, 2H), 6.54-6.48 (m, 2H), 3.28-3.20 (m 4H), 3.00-2.94 (m, 2H), 2.78-2.64 (m, 4H), 2.50-2.42 (m, 2H), 1.66-1.52 (4H).

MS: 413 [M+H$^+$].

Compound 28.

3-Fluoro-*N*-{4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl}benzenesulphonamide

The title compound was prepared starting from amine (IIa-8) and 3-fluorobenzene-sulphonyl chloride. Yield: 61%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.30 (s, 1H), 7.90-7.84 (m, 1H), 7.68-7.62 (m, 1H), 7.58-7.52 (m, 2H), 7.48-7.38 (m, 2H), 7.21-7.18 (m, 2H), 6.66-

6.60 (m, 2H), 6.54-6.48 (m, 1H), 3.38-3.30 (m, 4H), 3.06-2.98 (m, 2H), 2.80-2.42 (m, 4H), 2.50-2.48 (m, 2H), 1.68-1.60 (m, 4H). MS: 431 [M+H$^+$].

Compound 29.

3,4-Difluoro-*N*-{4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl}benzenesulphonamide

The title compound was prepared starting from amine (IIa-8) and 3,4-difluorobenzene-sulphonyl chloride Yield: 48%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.26 (s, 1H), 7.72-7.69 (m, 1H), 7.68-7.60 (m, 1H), 7.29-7.20 (m, 2H), 7.18-7.06 (m, 2H), 6.64-6.60 (dd, 1H, *J* = 1.2 Hz and 6.9 Hz), 6.54-6.50 (m, 1H), 3.38-3.30 (m, 4H), 3.06-2.98 (m, 2H), 2.82-2.74 (m, 4H), 2.52-2.44 (m, 2H), 1.70-1.60 (m, 4H). MS: 449[M+H$^+$]

Compound 30.

N-{4-[4-(1H-Indol-4-yl)piperazin-1-yl]butyl}-imidazo[1,2-a]pyridine-3-sulphonamide

The title compound was prepared starting from amine (IIa-8) and imidazo[1,2-a]-pyridine-3-sulphonyl chloride. Yield: 52%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.68-8.62 (m, 1H), 8.24 (s, 1H), 8.12 (s, 1H), 7.74-7.70 (m, 1H), 7.40-7.34 (m, 1H), 7.18-7.08 (m, 3H), 6.98-6.90 (m, 1H), 6.68-6.62 (dd, 1H, *J* = 1.2 and 6.9 Hz), 6.56-6.50 (m, 1H), 3.42-3.32 (m, 4H), 3.02-2.98 (m, 2H), 2.82-2.72 (m, 4H), 2.52-2.46 (m, 2H), 1.68-1.58 (m, 4H). MS: 453[M+H$^+$].

Compound 31.

N-{4-[4-(1H-Indol-4-yl)piperazin-1-yl]butyl}-1*H*-pyrrolo[2,3-*b*]pyridine-3-sulphonamide

The title compound was prepared starting from amine (IIa-8) and 1*H*-pyrrolo-[2,3-*b*]-pyridine-3-sulphonyl chloride. Yield: 73%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 10.6 (bs, 1H), 8.38 (dd, 1H, *J* = 1.7 and 4 Hz), 8.30 (dd, 1H, *J* = 1.5 and 7.9 Hz), 8.22 (s, 1H), 7.86 (s, 1H), 7.22-7.08 (m, 4H), 6.62-6.60 (dd, 1H, *J* = 1.2 and 6.9 Hz), 6.50 (t, 1H, *J* = 2.3 Hz), 3.32-3.24 (m, 4H), 3.08-2.98 (m, 2H), 2.70-2.64 (m, 4H), 2.46-2.38 (m, 2H), 1.68-1.58 (m, 4H). MS: 453[M+H$^+$].

Compound 32.

N-{4-[4-(1H-Indol-4-yl)piperazin-1-yl]butyl}-1-benzothiophene-3-sulphonamide

The title compound was prepared starting from amine (IIa-8) and 1-benzo-thiophene-3-sulphonyl chloride. Yield: 81%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.29-8.22 (m, 2H), 8.18 (s, 1H), 7.90-7.84 (m, 1H), 7.46-7.40 (m, 2H), 7.18-7.06 (m, 3H), 6.68-6.62 (dd, 1H, J = 1.2 and 6.9 Hz), 6.52 (m, 1H), 3.38-3.32 (m, 4H), 3.06-3.00 (m, 2H), 2.78-2.68 (m, 4H), 2.46-2.40 (m, 2H), 1.60-1.52 (m, 4H). MS: 469[M+H$^+$].

Compound 33.

N-{4-[4-(1H-Indol-4-yl)piperazin-1-yl]butyl}-1-benzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-8) and 1-benzothiophene-2-sulphonyl chloride. Yield: 78%. MS: 469[M+H$^+$].

Compound 61.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-6-chloro-naphthalene-2-sulphonamide, hydrochloride

The title compound was prepared starting from amine (IIa-1) and 6-chloro-naphthalene-2-sulphonyl chloride. Yield: 87%. MS: 515[M+H$^+$].

Compound 62.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-6-chloro-naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-2) and 6-chloro-naphthalene-2-sulphonyl chloride. Yield: 67%. MS: 501[M+H$^+$].

Compound 63.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-3-chloro-4-fluorobenzene-sulphonamide

The title compound was prepared starting from amine (IIa-1) and 3-chloro-4-fluoro-benzenesulphonyl chloride. Yield: 80%. MS: 483[M+H$^+$].

Compound 64.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-3-chloro-4-fluorobenzene-sulphonamide

The title compound was prepared starting from amine (IIa-2) and 3-chloro-4-fluoro-benzenesulphonyl chloride. Yield: 76%. MS: 469[M+H$^+$].

Compound 65.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-5-fluoro-3-methylbenzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-1) and 5-fluoro-3-methyl-benzothiophene-2-sulphonyl chloride. Yield: 94%. MS: 519[M+H$^+$].

Compound 66.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-5-fluoro-3-methylbenzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-2) and 5-fluoro-3-methyl-benzothiophene-2-sulphonyl chloride. Yield: 94%. MS: 505[M+H$^+$].

Compound 69.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-3-chlorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-1) and 3-chloro-benzenesulphonyl chloride. Yield: 79%. MS: 465[M+H$^+$].

Compound 70.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-3-chlorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-2) and 3-chloro-benzenesulphonyl chloride. Yield: 80%. MS: 451[M+H$^+$].

Compound 71.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-3-fluorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-1) and 3-fluoro-benzenesulphonyl chloride. Yield: 81%. MS: 449[M+H$^+$].

Compound 72.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-3-fluorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-2) and 3-fluorobenzene-sulphonyl chloride. Yield: 79%. MS: 435[M+H$^+$].

Compound 73.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-3-cyanobenzenesulphonamide

The title compound was prepared starting from amine (IIa-1) and 3-cyanobenzene-sulphonyl chloride. Yield: 85%. MS: 456[M+H$^+$].

Compound 74.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-3-cyanobenzenesulphonamide

The title compound was prepared starting from amine (IIa-2) and 3-cyanobenzene-sulphonyl chloride. Yield: 91%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 8.03 (dd, 2H, *J* = 8.0 Hz, *J* = 3.6 Hz), 7.79 (d, 2H, *J* = 6.4 Hz), 7.74 (br. s, 1H), 7.26 (d, 2H, *J* = 8.7 Hz), 7.54 (t, 1H,

J = 7.2 Hz), 7.41 (t, 1H, *J* = 7.2 Hz), 3.38 (br. s, 4H), 2.84-2.78 (m, 2H), 2.49 (br. s, 4H), 2.31 (br.s, 2H), 1.57 (br. s, 2H). MS: 442[M+H$^+$].

Compound 76.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]imidazo[1,2-a]pyridine-3-sulphonamide

The title compound was prepared starting from amine (IIa-2) and imidazo[1,2-a]-pyridine-3-sulphonyl chloride. Yield: 63%. MS: 457[M+H$^+$].

Compound 79.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-6-chloro-naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-4) and 6-chloro-naphthalene-2-sulphonyl chloride. Yield: 78%. MS: 499[M+H$^+$].

Compound 80.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]-6-chloro-naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-13) and 6-chloro-naphthalene-2-sulphonyl chloride. Yield: 78%. MS: 485[M+H$^+$].

Compound 81.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-5-fluoro-3-methylbenzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-4) and 5-fluoro-3-methylbenzothiophene-2-sulphonyl chloride. Yield: 92%. MS: 503[M+H$^+$].

Compound 82.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]-5-fluoro-3-methylbenzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-13) and 5-fluoro-3-methyl-benzothiophene-2-sulphonyl chloride. Yield: 51%. MS: 489[M+H$^+$].

Compound 85.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-3-chlorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-4) and 3-chlorobenzene-sulphonyl chloride. Yield: 76%. MS: 449[M+H$^+$].

Compound 86.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]-3-chlorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-13) and 3-chlorobenzene-sulphonyl chloride. Yield: 72%. MS: 435[M+H$^+$].

Compound 87.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-3-fluorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-4) and 3-fluorobenzene-sulphonyl chloride. Yield: 81%. MS: 433[M+H$^+$].

Compound 89.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-1H-pyrrolo[2,3-b]pyridine-3-sulphonamide

The title compound was prepared starting from amine (IIa-4) and 1H-pyrrolo-[2,3-b]-pyridine-3-sulphonyl chloride. Yield: 65%. MS: 455[M+H$^+$].

Compound 91.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-3-(trifluoromethyl)benzene-sulphonamide

The title compound was prepared starting from amine (IIa-4) and 3-(trifluoromethyl)-benzenesulphonyl chloride. Yield: 90%. MS: 483[M+H$^+$].

Compound 92.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]-3-(trifluoromethyl)benzene-sulphonamide

The title compound was prepared starting from amine (IIa-13) and 3-(trifluoromethyl)-benzenesulphonyl chloride. Yield: 58%. MS: 469[M+H$^+$].

Compound 93.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-3,4-dichlorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-4) and 3,4-dichloro-benzenesulphonyl chloride. Yield: 78%. MS: 483[M+H$^+$].

Compound 94.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]-3,4-dichlorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-13) and 3,4-dichloro-benzenesulphonyl chloride. Yield: 61%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 7.96 (d, 1H, *J* = 2.1 Hz), 7.91-7.87 (m, 1H), 7.85-7.80 (m, 1H), 7.74 (d, 1H, *J* = 8.2 Hz), 7.37 (d, 1H, *J* = 7.4 Hz), 7.26 (d, 1H, *J* = 7.7 Hz), 7.12 (t, 1H, *J* = 7.5 Hz), 7.00 (t, 1H, *J* = 7.7 Hz), 3.55 (br. s, 4H), 2.86-2.78 (m, 2H), 2.38 (br. s, 4H), 2.85 (t, 2H, *J* = 6.9 Hz), 1.60-1.48 (m, 2H). MS: 469[M+H$^+$].

Compound 97.

6-Chloro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 6-chloro-naphthalene-2-sulphonyl chloride. Yield: 67%. MS: 516[M+H$^+$].

Compound 98.

6-Chloro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 6-chloro-naphthalene-2-sulphonyl chloride. Yield: 76%. MS: 503[M+H$^+$].

Compound 101.

5-Fluoro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-3-methylbenzo-thiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 5-fluoro-3-methyl-benzothiophene-2-sulphonyl chloride. Yield: 51%. MS: 520[M+H$^+$].

Compound 102.

5-Fluoro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-3-methylbenzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 5-fluoro-3-methyl-benzothiophene-2-sulphonyl chloride. Yield: 91%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 8.18 (br. s, 1H), 8.07 (dd, 1H, *J* = 8.7 Hz, *J* = 5.1 Hz), 7.93 (dd, 1H, *J* = 8.7 Hz, *J* = 5.1 Hz), 7.78 (dd, 1H, *J* = 9.7 Hz, *J* = 2.3 Hz), 7.66 (dd, 1H, *J* = 9.2 Hz, *J* = 2.3 Hz), 7.39 (td, 1H, *J* = 9.0 Hz, *J* = 2.6 Hz), 7.25 (td, 1H, *J* = 9.5 Hz, *J* = 2.3 Hz), 3.10-2.98 (m, 1H), 2.95 (t, 2H, *J* = 6.3 Hz), 2.82-2.73 (m, 2H), 2.59 (s, 3H), 2.26 (t, 2H, *J* = 7.2 Hz), 2.00-1.85 (m, 4H), 1.76-1.60 (m, 2H), 1.60-1.50 (m, 2H). MS: 506[M+H$^+$].

Compound 105.

3-Chloro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 3-chlorobenzene-sulphonyl chloride. Yield: 71%. MS: 466[M+H$^+$].

Compound 106.

3-Chloro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 3-chlorobenzene-sulphonyl chloride. Yield: 66%. MS: 453[M+H$^+$].

Compound 107.

3-Fluoro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 3-fluorobenzene-sulphonyl chloride. Yield: 68%. MS: 450[M+H$^+$].

Compound 108.

3-Fluoro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide, hydrochloride

The title compound was prepared starting from amine (IIa-6) and 3-fluorobenzene-sulphonyl chloride. Yield: 63%. ^{1}H-NMR (300 MHz, DMSO-d_6), hydrochloride: δ 10.40 (br. s, 1H), 8.15 (dd, 1H, *J* = 8.7 Hz, *J* = 5.4 Hz), 7.96 (t, 1H, *J* = 5.9), 7.73-7.49 (m, 4H), 7.33 (td, 1H, *J* = 9.2 Hz, *J* = 2.3 Hz), 3.61-3.50 (m, 2H), 3.50-3.41 (m, 1H), 3.17-2.99 (m, 4H), 2.89-2.80 (m, 2H), 2.34-2.14 (m, 4H), 1.95-1.81 (m, 4H). MS: 436[M+H$^+$].

Compound 109.

3-Bromo-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 3-bromobenzene-sulphonyl chloride. Yield: 72%. MS: 510[M+H$^+$].

Compound 110.

3-Bromo-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 3-bromobenzene-sulphonyl chloride. Yield: 59%. MS: 497[M+H$^+$].

Compound 111.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-4-phenylbenzene-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 4-phenylbenzene-sulphonyl chloride. Yield: 80%. MS: 508[M+H$^+$].

Compound 112.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-4-phenylbenzene-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 4-phenylbenzene-sulphonyl chloride. Yield: 53%. MS: 494[M+H$^+$].

Compound 113.

N-[4-[4-(1H-Indol-4-yl)piperazin-1-yl]butyl]-3-chlorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-8) and 3-chlorobenzene-sulphonyl chloride. Yield: 71%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.23 (s, 1H), 7.84 (t, 1H, J = 1.8 Hz), 7.74 (dt, 1H, J = 1.3 and 7.9 Hz), 7.52-7.46 (m, 1H), 7.40 (m, 1H, J = 7.7 Hz), 7.16-7.08 (m, 3H), 6.64 (dd, 1H, J = 1.3 and 6.9 Hz), 6.52 (t, 1H, J = 2.3 Hz), 3.36-3.28 (m, 4H), 3.04-2.96 (m, 2H), 2.76-2.68 (m, 4H), 2.50-2.46 (m, 2H), 1.66-1.60 (m, 4H). MS: 447[M+H$^+$].

Compound 165.

5-Chloro-3-methyl-N-[4-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]butyl]-1-benzothiophene-2-sulfonamid

The title compound was prepared starting from amine (IIa-16) and 5-chloro-3-methyl-1-benzothiophene-2-sulphonyl chloride. Yield: 55%. MS: 534[M+H$^+$].

Compound 173.

3-Chloro-N-[4-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-16) and 3-chlorobenzene-sulphonyl chloride. Yield: 61%. MS: 464[M+H$^+$].

Compound 174.

3-Chloro-N-[3-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]propyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-17) and 3-chlorobenzene-sulphonyl chloride. Yield: 53%. MS: 450[M+H$^+$].

Compound 175.

3-Fluoro-N-[4-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-16) and 3-fluorobenzene-sulphonyl chloride. Yield: 71%. MS: 448[M+H$^+$].

Compound 176.

3-Fluoro-N-[3-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]propyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-17) and 3-fluorobenzene-sulphonyl chloride. Yield: 62%. MS: 434[M+H$^+$].

Compound 195.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-5-chloro-thiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-1) and 5-chloro-thiophene-2-sulphonyl chloride. Yield: 76%. MS: 471[M+H$^+$].

Compound 196.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-5-chloro-thiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-2) and 5-chloro-thiophene-2-sulphonyl chloride. Yield: 76%. MS: 457[M+H$^+$].

Compound 209.

3-Chloro-N-[4-[4-(3-oxo-4H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-18) and 3-chlorobenzene-sulphonyl chloride. Yield: 81%. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.39 (s, 1H), 7.38 (t, 1H, J = 1.7 Hz), 7.72 (dt, 1H, J = 1.3 and 7.7 Hz), 7.52-7.48 (m, 1H), 7.42 (t, 1H, J = 7.7 Hz), 6.91 (t, 1H, J = 7.7 Hz), 6.70 (dd, 1H, J = 1.5 and 8.2 Hz), 6.52 (dd, 1H, J = 1.3 and 7.9

Hz), 3.22-3.10 (m, 4H), 3.02-2.92 (m, 2H), 2.72-2.64 (m, 4H), 2.48-2.38 (m, 2H), 1.68-1.58 (m, 4H). MS: 479[M+H$^+$].

Compound 211.

3-Fluoro-N-[4-[4-(3-oxo-4H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-18) and 3-fluorobenzene-sulphonyl chloride. Yield: 82%. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.40 (s, 1H), 7.66-7.62 (m, 1H), 7.58-7.52 (m, 1H), 7.50-7.42 (m, 1H), 7.28-7.20 (m, 1H), 6.91 (t, 1H, J = 7.9 Hz), 6.67 (dd, 1H, J = 8.2 and 1.2 Hz), 6.52 (dd, 1H, J = 7.7 and 1.2 Hz), 4.60 (s, 2H), 3.22-3.12 (m, 4H), 3.02-2.94 (m, 2H), 2.74-2.64 (m, 4H), 2.48-2.40 (m, 2H), 1.68-1.58 (m, 4H). MS: 463[M+H$^+$].

Compound 225.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-4-fluorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-1) and 4-fluorobenzene-sulphonyl chloride. Yield: 90%. MS: 449[M+H$^+$].

Compound 226.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-3,4-difluorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-1) and 3,4-difluorobenzene-sulphonyl chloride. Yield: 80%. MS: 467[M+H$^+$].

Compound 227.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-4-chlorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-1) and 4-chlorobenzene-sulphonyl chloride. Yield: 84%. MS: 465[M+H$^+$].

Compound 228.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-3,4-dichlorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-1) and 3,4-dichlorobenzene-sulphonyl chloride. Yield: 82%. MS: 499[M+H$^+$].

Compound 229.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-4-bromobenzenesulphonamide

The title compound was prepared starting from amine (IIa-1) and 4-bromobenzene-sulphonyl chloride. Yield: 81%. MS: 509[M+H$^+$].

Compound 230.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-3-bromobenzenesulphonamide

The title compound was prepared starting from amine (IIa-1) and 3-bromobenzene-sulphonyl chloride. Yield: 77%. MS: 509[M+H$^+$].

Compound 231.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-3-hydroxybenzenesulphonamide

The title compound was prepared starting from amine (IIa-1) and 3-hydroxybenzene-sulphonyl chloride. Yield: 41%. MS: 447[M+H$^+$].

Compound 232.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-3-methoxybenzenesulphonamide

The title compound was prepared starting from amine (IIa-1) and 3-methoxybenzene-sulphonyl chloride. Yield: 76%. MS: 461[M+H$^+$].

Compound 233.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-4-tert-butyl-benzenesulphonamide

The title compound was prepared starting from amine (IIa-1) and 4-tert-butyl-benzene-sulphonyl chloride. Yield: 65%. MS: 487[M+H$^+$].

Compound 234.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-4-(trifluoromethyl)benzene-sulphonamide

The title compound was prepared starting from amine (IIa-1) and 4-trifluoromethyl-benzenesulphonyl chloride. Yield: 82%. MS: 499[M+H$^+$].

Compound 235.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-3-(trifluoromethyl)benzene-sulphonamide

The title compound was prepared starting from amine (IIa-1) and 3-trifluoromethyl-benzenesulphonyl chloride. Yield: 79%. MS: 499[M+H$^+$].

Compound 236.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-4-(trifluoromethoxy)benzene-sulphonamide

The title compound was prepared starting from amine (IIa-1) and 4-trifluoromethoxy-benzenesulphonyl chloride. Yield: 71%. MS: 515[M+H$^+$].

Compound 237.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-4-phenylbenzenesulphonamide

The title compound was prepared starting from amine (IIa-1) and 4-phenylbenzene-sulphonyl chloride. Yield: 94%. MS: 507[M+H$^+$].

Compound 238.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]thiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-1) and thiophene-2-sulphonyl chloride. Yield: 88%. MS: 437[M+H$^+$].

Compound 239.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]benzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-1) and benzothiophene-2-sulphonyl chloride. Yield: 71%. MS: 487[M+H$^+$].

Compound 240.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]benzothiophene-3-sulphonamide

The title compound was prepared starting from amine (IIa-1) and benzothiophene-3-sulphonyl chloride. Yield: 66%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 8.43 (s, 1H), 8.19 (d, 1H, *J* = 7.0 Hz), 8.09 (d, 1H, *J* = 7.0 Hz), 8.02 (t, 2H, *J* = 8.7 Hz), 7.92 (t, 1H, *J* = 5.4 Hz), 7.57-7.39 (m, 4H), 3.36-3.31 (m, 4H), 2.88-2.81 (m, 2H), 2.42-2.36 (m, 4H), 2.14 (t, 2H, *J* = 6.4 Hz), 1.34-1.27 (m, 4H). MS: 487[M+H$^+$].

Compound 241.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-6-chlorobenzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-1) and 6-chlorobenzo-thiophene-2-sulphonyl chloride. Yield: 93%. MS: 521[M+H$^+$].

Compound 242.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-2,3-dihydrobenzofuran-5-sulphonamide

The title compound was prepared starting from amine (IIa-1) and 2,3-dihydro-benzofuran-5-sulphonyl chloride. Yield: 78%. MS: 473[M+H$^+$].

Compound 243.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-1,3-benzothiazole-4-sulphonamide

The title compound was prepared starting from amine (IIa-1) and 1,3-benzothiazole-4-sulphonyl chloride. Yield: 72%. MS: 488[M+H$^+$].

Compound 244.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-1H-indazole-6-sulphonamide

The title compound was prepared starting from amine (IIa-1) and 1H-indazole-6-sulphonyl chloride. Yield: 56%. MS: 471[M+H$^+$].

Compound 245.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-1,3-benzodioxole-5-sulphonamide

The title compound was prepared starting from amine (IIa-1) and 1,3-benzodioxole-5-sulphonyl chloride. Yield: 80%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 8.03 (dd, 2H, *J* = 8.2 Hz, *J* = 3,6 Hz), 7.57-7.39 (m, 3H), 7.31 (d, 1H, *J* = 8.2 Hz), 7.23 (s, 1H), 7.06 (d, 1H, *J* = 8.2 Hz), 6.56 (s, 2H), 3.40 (br.s, 4H), 2.77-2.71 (m, 2H), 2.53 (br. s, 4H), 2.28 (br. s, 2H), 1.39 (br. s, 4H). MS: 475[M+H$^+$].

Compound 246.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]imidazo[1,2-a]pyridine-3-sulphonamide

The title compound was prepared starting from amine (IIa-1) and imidazo[1,2-a]-pyridine-3-sulphonyl chloride. Yield: 60%. MS: 471[M+H$^+$].

Compound 247.

N-[4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl]-1H-pyrrolo[2,3-b]pyridine-3-sulphonamide

The title compound was prepared starting from amine (IIa-1) and 1H-pyrrolo-[2,3-b]-pyridine-3-sulphonyl chloride. Yield: 65%. MS: 471[M+H$^+$].

Compound 248.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-4-fluorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-2) and 4-fluorobenzene-sulphonyl chloride. Yield: 75%. MS: 435[M+H$^+$].

Compound 249.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-3,4-difluorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-2) and 3,4-difluorobenzene-sulphonyl chloride. Yield: 89%. MS: 453[M+H$^+$].

Compound 250.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-4-chlorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-2) and 4-chlorobenzene-sulphonyl chloride. Yield: 90%. MS: 452[M+H$^+$].

Compound 251.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-3,4-dichlorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-2) and 3,4-dichlorobenzene-sulphonyl chloride. Yield: 87%. MS: 485[M+H$^+$].

Compound 252.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-4-bromobenzenesulphonamide

The title compound was prepared starting from amine (IIa-2) and 4-bromobenzene-sulphonyl chloride. Yield: 92%. MS: 495[M+H$^+$].

Compound 253.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-3-bromobenzenesulphonamide

The title compound was prepared starting from amine (IIa-2) and 3-bromobenzene-sulphonyl chloride. Yield: 88%. MS: 495[M+H$^+$].

Compound 254.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-3-hydroxybenzenesulphonamide

The title compound was prepared starting from amine (IIa-2) and 3-hydroxybenzene-sulphonyl chloride. Yield: 45%. MS: 433[M+H$^+$].

Compound 255.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-3-methoxybenzenesulphonamide

The title compound was prepared starting from amine (IIa-2) and 3-methoxybenzene-sulphonyl chloride. Yield: 79%. MS: 447[M+H$^+$].

Compound 256.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-4-tert-butylbenzenesulphonamide

The title compound was prepared starting from amine (IIa-2) and 4-tert-butyl-benzene-sulphonyl chloride. Yield: 93%. MS: 473[M+H$^+$].

Compound 257.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-4-(trifluoromethyl)benzene-sulphonamide

The title compound was prepared starting from amine (IIa-2) and 4-(trifluoromethyl)-benzenesulphonyl chloride. Yield: 85%. MS: 485[M+H$^+$].

Compound 258.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-3-(trifluoromethyl)benzene-sulphonamide

The title compound was prepared starting from amine (IIa-2) and 3-(trifluoromethyl)-benzenesulphonyl chloride. Yield: 90%. MS: 485[M+H$^+$].

Compound 259.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-4-(trifluoromethoxy)benzene-sulphonamide

The title compound was prepared starting from amine (IIa-2) and 4-(trifluoromethoxy)-benzenesulphonyl chloride. Yield: 76%. MS: 501[M+H$^+$].

Compound 260.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-4-phenylbenzenesulphonamide

The title compound was prepared starting from amine (IIa-2) and 4-phenylbenzene-sulphonyl chloride. Yield: 93%. MS: 493[M+H$^+$].

Compound 261.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]thiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-2) and thiophene-2-sulphonyl chloride. Yield: 86%. MS: 423[M+H$^+$].

Compound 262.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]benzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-2) and benzothiophene-2-sulphonyl chloride. Yield: 73%. MS: 473[M+H$^+$].

Compound 263.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]benzothiophene-3-sulphonamide

The title compound was prepared starting from amine (IIa-2) and benzothiophene-3-sulphonyl chloride. Yield: 77%. MS: 473[M+H$^+$].

Compound 264.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-6-chlorobenzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-2) and 6-chloro-benzothiophene-2-sulphonyl chloride. Yield: 86%. MS: 507[M+H$^+$].

Compound 265.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-2,3-dihydrobenzofuran-5-sulphonamide

The title compound was prepared starting from amine (IIa-2) and 2,3-dihydro-benzofuran-5-sulphonyl chloride. Yield: 92%. MS: 459[M+H$^+$].

Compound 266.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-1,2-benzoxazole-5-sulphonamide

The title compound was prepared starting from amine (IIa-2) and 1,2-benzoxazole-5-sulphonyl chloride. Yield: 75%. MS: 458[M+H$^+$].

Compound 267.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-1,3-benzothiazole-4-sulphonamide

The title compound was prepared starting from amine (IIa-2) and 1,3-benzothiazole-4-sulphonyl chloride. Yield: 83%. MS: 474[M+H$^+$].

Compound 268.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-1H-indazole-6-sulphonamide

The title compound was prepared starting from amine (IIa-2) and 1H-indazole-6-sulphonyl chloride. Yield: 57%. MS: 457[M+H$^+$].

Compound 269.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-1,3-benzodioxole-5-sulphonamide

The title compound was prepared starting from amine (IIa-2) and 1,3-benzodioxole-5-sulphonyl chloride. Yield: 84%. MS: 461[M+H$^+$].

Compound 270.

N-[3-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]propyl]-1H-pyrrolo[2,3-b]pyridine-3-sulphonamide

The title compound was prepared starting from amine (IIa-2) and 1H-pyrrolo-[2,3-b]-pyridine-3-sulphonyl chloride. Yield: 68%. MS: 457[M+H$^+$].

Compound 271.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-4-fluorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-4) and 4-fluorobenzene-sulphonyl chloride. Yield: 89%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 7.86-7.81 (m, 2H), 7.64 (t, 1H, *J* = 5.9 Hz), 7.48-7.35 (m, 3H), 7.26 (d, 1H, *J* = 7.7 Hz), 7.13 (t, 1H, *J* = 7.4 Hz), 6.99 (t, 1H, *J* = 7.7 Hz), 3.56 (br. s, 4H), 2.79-2.72 (m, 2H), 2.41 (br. s, 4H), 2.23 (br. s, 2H), 1.37 (br. s, 4H). MS: 433[M+H$^+$].

Compound 272.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-3,4-difluorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-4) and 3,4-difluorobenzene-sulphonyl chloride. Yield: 84%. MS: 451[M+H$^+$].

Compound 273.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-4-chlorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-4) and 4-chlorobenzene-sulphonyl chloride. Yield: 93%. MS: 449[M+H$^+$].

Compound 274.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-4-bromobenzenesulphonamide

The title compound was prepared starting from amine (IIa-4) and 4-bromobenzene-sulphonyl chloride. Yield: 91%. MS: 493[M+H$^+$].

Compound 275.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-3-bromobenzenesulphonamide

The title compound was prepared starting from amine (IIa-4) and 3-bromobenzene-sulphonyl chloride. Yield: 71%. MS: 493[M+H$^+$].

Compound 276.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-3-chloro-4-fluorobenzene-sulphonamide

The title compound was prepared starting from amine (IIa-4) and 3-chloro-4-fluoro-benzenesulphonyl chloride. Yield: 83%. MS: 467[M+H$^+$].

Compound 277.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-3-hydroxybenzenesulphonamide

The title compound was prepared starting from amine (IIa-4) and 3-hydroxy-benzenesulphonyl chloride. Yield: 38%. MS: 431[M+H$^+$].

Compound 278.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-3-methoxybenzenesulphonamide

The title compound was prepared starting from amine (IIa-4) and 3-methoxy-benzenesulphonyl chloride. Yield: 89%. MS: 445[M+H$^+$].

Compound 279.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-4-tert-butylbenzenesulphonamide, hydrochloride

The title compound was prepared starting from amine (IIa-4) and 4-tert-butyl-benzenesulphonyl chloride. Yield: 80%. MS: 471[M+H$^+$].

Compound 280.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-4-(trifluoromethyl)benzene-sulphonamide

The title compound was prepared starting from amine (IIa-4) and 4-(trifluoromethyl)-benzenesulphonyl chloride. Yield: 74%. MS: 483[M+H$^+$].

Compound 281.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-4-(trifluoromethoxy)benzene-sulphonamide

The title compound was prepared starting from amine (IIa-4) and 4-(trifluoromethoxy)-benzenesulphonyl chloride. Yield: 72%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 7.93-7.88 (m, 2H), 7.76 (t, 1H, *J* = 5.6 Hz), 7.58 (d, 2H, *J* = 9.0 Hz), 7.37 (d, 1H, *J* = 7.4 Hz), 7.26 (d, 1H, *J* = 7.6 Hz), 7.13 (d, 1H, *J* = 7.4 Hz), 7.00 (d, 1H, *J* = 7.5 Hz), 3.54 (br. s, 4H), 2.82-2.77 (m, 2H), 2.40 (br. s, 4H), 2.22 (br. s, 2H), 1.37 (br. s, 4H). MS: 499[M+H$^+$].

Compound 282.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-3-cyanobenzenesulphonamide

The title compound was prepared starting from amine (IIa-4) and 3-cyanobenzene-sulphonyl chloride. Yield: 87%. MS: 440[M+H$^+$].

Compound 283.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-4-phenylbenzenesulphonamide

The title compound was prepared starting from amine (IIa-4) and 4-phenylbenzene-sulphonyl chloride. Yield: 90%. MS: 491[M+H$^+$].

Compound 284.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]thiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-4) and thiophene-2-sulphonyl chloride. Yield: 83%. MS: 421[M+H$^+$].

Compound 285.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-5-chloro-thiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-4) and 5-chloro-thiophene-2-sulphonyl chloride. Yield: 77%. MS: 455[M+H$^+$].

Compound 286.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]benzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-4) and benzothiophene-2-sulphonyl chloride. Yield: 79%. MS: 471[M+H$^+$].

Compound 287.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]benzothiophene-3-sulphonamide

The title compound was prepared starting from amine (IIa-4) and benzothiophene-3-sulphonyl chloride. Yield: 75%. MS: 471[M+H$^+$].

Compound 288.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-6-chlorobenzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-4) and 6-chlorobenzo-thiophene-2-sulphonyl chloride. Yield: 69%. MS: 505[M+H$^+$].

Compound 289.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-2,3-dihydrobenzofuran-5-sulphonamide

The title compound was prepared starting from amine (IIa-4) and 2,3-dihydro-benzofuran-5-sulphonyl chloride. Yield: 80%. MS: 457[M+H$^+$].

Compound 290.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-1,3-benzothiazole-4-sulphonamide

The title compound was prepared starting from amine (IIa-4) and 1,3-benzothiazole-4-sulphonyl chloride. Yield: 72%. MS: 472[M+H$^+$].

Compound 291.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-1H-indazole-6-sulphonamide

The title compound was prepared starting from amine (IIa-4) and 1H-indazole-6-sulphonyl chloride. Yield: 74%. MS: 455[M+H$^+$].

Compound 292.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]-1,3-benzodioxole-5-sulphonamide

The title compound was prepared starting from amine (IIa-4) and 1,3-benzodioxole-5-sulphonyl chloride. Yield: 88%. MS: 459[M+H$^+$].

Compound 293.

N-[4-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]butyl]imidazo[1,2-a]pyridine-3-sulphonamide

The title compound was prepared starting from amine (IIa-4) and imidazo[1,2-a]-pyridine-3-sulphonyl chloride. Yield: 64%. MS: 455[M+H$^+$].

Compound 294.

4-Fluoro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 4-fluorobenzene-sulphonyl chloride. Yield: 79%. MS: 450[M+H$^+$].

Compound 295.

3,4-Difluoro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 3,4-difluoro-benzenesulphonyl chloride. Yield: 70%. MS: 468[M+H$^+$].

Compound 296.

4-Chloro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 4-chlorobenzene-sulphonyl chloride. Yield: 71%. MS: 466[M+H$^+$].

Compound 297.

3,4-Dichloro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 3,4-dichlorobenzene-sulphonyl chloride. Yield: 65%. MS: 500[M+H$^+$].

Compound 298.

4-Bromo-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 4-bromobenzene-sulphonyl chloride. Yield: 82%. MS: 510[M+H$^+$].

Compound 299.

3-Chloro-4-fluoro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 3-chloro-4-fluoro-benzenesulphonyl chloride. Yield: 70%. MS: 484[M+H$^+$].

Compound 300.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-3-methoxybenzene-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 3-methoxybenzene-sulphonyl chloride. Yield: 68%. MS: 462[M+H$^+$].

Compound 301.

4-tert-Butyl-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 4-tert-butyl-benzene-sulphonyl chloride. Yield: 69%. MS: 488[M+H$^+$].

Compound 302.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-4-(trifluoromethyl)benzene-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 4-(trifluoromethyl)-benzenesulphonyl chloride. Yield: 58%. MS: 500[M+H$^+$].

Compound 303.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-3-(trifluoromethyl)-benzenesulphonamide

The title compound was prepared starting from amine (IIa-5) and 3-(trifluoromethyl)-benzenesulphonyl chloride. Yield: 64%. MS: 500[M+H$^+$].

Compound 304.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-4-(trifluoromethoxy)-benzenesulphonamide

The title compound was prepared starting from amine (IIa-5) and 4-(trifluoromethoxy)-benzenesulphonyl chloride. Yield: 65%. MS: 516[M+H$^+$].

Compound 305.

4-Cyano-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 4-cyanobenzene-sulphonyl chloride. Yield: 76%. MS: 457[M+H$^+$].

Compound 306.

3-Cyano-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 3-cyanobenzene-sulphonyl chloride. Yield: 61%. MS: 457[M+H$^+$].

Compound 307.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]thiophene-3-sulphonamide

The title compound was prepared starting from amine (IIa-5) and thiophene-3-sulphonyl chloride. Yield: 50%. MS: 438[M+H$^+$].

Compound 308.

5-Chloro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]thiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 5-chloro-thiophene-2-sulphonyl chloride. Yield: 51%. MS: 472[M+H$^+$].

Compound 309.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-2,5-dimethyl-thiophene-3-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 2,5-dimethyl-thiophene-3-sulphonyl chloride. Yield: 67%. MS: 466[M+H$^+$].

Compound 310.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-1-methyl-indole-4-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 1-methyl-indole-4-sulphonyl chloride. Yield: 57%. MS: 485[M+H$^+$].

Compound 311.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-1-methyl-indole-6-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 1-methyl-indole-6-sulphonyl chloride. Yield: 78%. MS: 485[M+H$^+$].

Compound 312.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-5) and benzothiophene-2-sulphonyl chloride. Yield: 51%. MS: 488[M+H$^+$].

Compound 313.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzothiophene-3-sulphonamide

The title compound was prepared starting from amine (IIa-5) and benzothiophene-3-sulphonyl chloride. Yield: 62%. MS: 488[M+H$^+$].

Compound 314.

6-Chloro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 6-chloro-benzothiophene-2-sulphonyl chloride. Yield: 53%. MS: 522[M+H$^+$].

Compound 315.

5-Chloro-N-[4-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-3-methylbenzo-thiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 5-chloro-3-methyl-benzothiophene-2-sulphonyl chloride. Yield: 61%. MS: 536[M+H$^+$].

Compound 316.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]benzofuran-2-sulphonamide

The title compound was prepared starting from amine (IIa-5) and benzofuran-2-sulphonyl chloride. Yield: 71%. MS: 472[M+H$^+$].

Compound 317.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-2,3-dihydrobenzofuran-5-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 2,3-dihydro-benzofuran-5-sulphonyl chloride. Yield: 54%. MS: 474[M+H$^+$].

Compound 318.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-1,3-benzothiazole-4-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 1,3-benzothiazole-4-sulphonyl chloride. Yield: 47%. MS: 489[M+H$^+$].

Compound 319.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-1H-indazole-6-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 1H-indazole-6-sulphonyl chloride. Yield: 58%. MS: 472[M+H$^+$].

Compound 320.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-1,3-benzodioxole-5-sulphonamide, hydrochloride

The title compound was prepared starting from amine (IIa-5) and 1,3-benzodioxole-5-sulphonyl chloride. Yield: 65%. MS: 476[M+H$^+$].

Compound 321.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-2,3-dihydro-1,4-benzodioxine-6-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 2,3-dihydro-1,4-benzodioxine-6-sulphonyl chloride. Yield: 78%. MS: 490[M+H$^+$].

Compound 322.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]imidazo[1,2-a]pyridine-3-sulphonamide

The title compound was prepared starting from amine (IIa-5) and imidazo[1,2-a]-pyridine-3-sulphonyl chloride. Yield: 47%. MS: 472[M+H$^+$].

Compound 323.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-1H-pyrrolo[2,3-b]pyridine-3-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 1H-pyrrolo-[2,3-b]-pyridine-3-sulphonyl chloride. Yield: 63%. MS: 472[M+H$^+$].

Compound 324.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]-2-oxo-indoline-5-sulphonamide

The title compound was prepared starting from amine (IIa-5) and 2-oxo-indoline-5-sulphonyl chloride. Yield: 48%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 7.98 (dd, 1H, *J* = 8.7 Hz, *J* = 5.4 Hz), 7.66 (dd, 1H, *J* = 9.0 Hz, *J* = 2.3 Hz), 7.59-7.53 (m, 2H), 7.29-7.17 (m, 2H), 3.35 (s, 2H), 3.18-3.09 (m, 1H), 2.95-2.88 (m, 2H), 2.74 (s, 2H), 2.27 (s, 2H), 2.12-1.95 (m, 6H), 1.86-1.75 (m, 2H), 1.42-1.34 (m, 4H). MS: 487[M+H$^+$].

Compound 325.

N-[4-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]butyl]thiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-5) and thiophene-2-sulphonyl chloride. Yield: 70%. MS: 438[M+H$^+$].

Compound 326.

4-Fluoro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 4-fluorobenzene-sulphonyl chloride. Yield: 56%. MS: 436[M+H$^+$].

Compound 327.

3,4-Difluoro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 3,4-difluorobenzene-sulphonyl chloride. Yield: 69%. MS: 454[M+H$^+$].

Compound 328.

4-Chloro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 4-chlorobenzene-sulphonyl chloride. Yield: 56%. MS: 453[M+H$^+$].

Compound 329.

3,4-Dichloro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 3,4-dichlorobenzene-sulphonyl chloride. Yield: 87%. MS: 486[M+H$^+$].

Compound 330.

4-Bromo-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 4-bromobenzene-sulphonyl chloride. Yield: 48%. MS: 497[M+H$^+$].

Compound 331.

3-Chloro-4-fluoro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 3-chloro-4-fluoro-benzenesulphonyl chloride. Yield: 83%. MS: 471[M+H$^+$].

Compound 332.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-3-methoxybenzene-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 3-methoxybenzene-sulphonyl chloride. Yield: 81%. MS: 448[M+H$^+$].

Compound 333.

4-tert-Butyl-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 4-tert-butyl-benzene-sulphonyl chloride. Yield: 51%. MS: 474[M+H$^+$].

Compound 334.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-4-(trifluoromethyl)-benzenesulphonamide

The title compound was prepared starting from amine (IIa-6) and 4-(trifluoromethyl)-benzenesulphonyl chloride. Yield: 73%. MS: 486[M+H$^+$].

Compound 335.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-3-(trifluoromethyl)-benzenesulphonamide

The title compound was prepared starting from amine (IIa-6) and 3-(trifluoromethyl)-benzenesulphonyl chloride. Yield: 48%. MS: 486[M+H$^+$].

Compound 336.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-4-(trifluoromethoxy)-benzenesulphonamide

The title compound was prepared starting from amine (IIa-6) and 4-(trifluoromethoxy)-benzenesulphonyl chloride. Yield: 53%. MS: 502[M+H$^+$].

Compound 337.

4-Cyano-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 4-cyanobenzene-sulphonyl chloride. Yield: 85%. MS: 443[M+H$^+$].

Compound 338.

3-cyano-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 3-cyanobenzene-sulphonyl chloride. Yield: 84%. MS: 443[M+H$^+$].

Compound 339.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]thiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-6) and thiophene-2-sulphonyl chloride. Yield: 68%. MS: 424[M+H$^+$].

Compound 340.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]thiophene-3-sulphonamide

The title compound was prepared starting from amine (IIa-6) and thiophene-3-sulphonyl chloride. Yield: 66%. MS: 424[M+H$^+$].

Compound 341.

5-Chloro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]thiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 5-chloro-thiophene-2-sulphonyl chloride. Yield: 81%. MS: 459[M+H$^+$].

Compound 342.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-2,5-dimethyl-thiophene-3-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 2,5-dimethyl-thiophene-3-sulphonyl chloride. Yield: 58%. MS: 452[M+H$^+$].

Compound 343.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-1-methyl-indole-4-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 1-methyl-indole-4-sulphonyl chloride. Yield: 62%. MS: 471[M+H$^+$].

Compound 344.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-1-methyl-indole-5-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 1-methyl-indole-5-sulphonyl chloride. Yield: 55%. MS: 471[M+H$^+$].

Compound 345.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-6) and benzothiophene-2-sulphonyl chloride. Yield: 57%. MS: 474[M+H$^+$].

Compound 346.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzothiophene-3-sulphonamide

The title compound was prepared starting from amine (IIa-6) and benzothiophene-3-sulphonyl chloride. Yield: 63%. MS: 474[M+H$^+$].

Compound 347.

6-Chloro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 6-chlorobenzo-thiophene-2-sulphonyl chloride. Yield: 66%. MS: 509[M+H$^+$].

Compound 348.

5-Chloro-N-[3-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-3-methyl-benzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 5-chloro-3-methyl-benzothiophene-2-sulphonyl chloride. Yield: 88%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 8.20 (br. s, 1H), 8.08-8.02 (m, 2H), 7.93 (dd, 1H, *J* = 8.7 Hz, *J* = 5.4 Hz), 7.68 (dd, 1H, *J* = 9.2 Hz, *J* = 2.1 Hz), 7.53 (dd, 1H, *J* = 8.5 Hz, *J* = 2.1 Hz), 7.25 (td, 1H, *J* = 9.0 Hz, *J* = 2.1 Hz), 3.10-3.00 (m, 1H), 2.96 (t, 2H, *J* = 6.7 Hz), 2.77 (br. s, 2H), 2.61 (s, 3H), 2.28 (br. s, 2H), 2.02-1.86 (m, 4H), 1.76-1.64 (m, 2H), 1.60-1.50 (m, 2H). MS: 523[M+H$^+$].

Compound 349.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]benzofuran-2-sulphonamide

The title compound was prepared starting from amine (IIa-6) and benzofuran-2-sulphonyl chloride. Yield: 48%. MS: 458[M+H$^+$].

Compound 350.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-2,3-dihydrobenzofuran-5-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 2,3-dihydro-benzofuran-5-sulphonyl chloride. Yield: 29%. MS: 460[M+H$^+$].

Compound 351.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-1,3-benzothiazole-4-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 1,3-benzothiazole-4-sulphonyl chloride. Yield: 57%. MS: 475[M+H$^+$].

Compound 352.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-1H-indazole-6-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 1H-indazole-6-sulphonyl chloride. Yield: 80%. MS: 458[M+H$^+$].

Compound 353.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-2-oxo-3H-1,3-benzoxazole-6-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 2-oxo-3H-1,3-benzoxazole-6-sulphonyl chloride. Yield: 57%. MS: 475[M+H$^+$].

Compound 354.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-1,3-benzodioxole-5-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 1,3-benzodioxole-5-sulphonyl chloride. Yield: 65%. MS: 462[M+H$^+$].

Compound 355.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-2,3-dihydro-1,4-benzo-dioxine-6-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 2,3-dihydro-1,4-benzodioxine-6-sulphonyl chloride. Yield: 64%. MS: 476[M+H$^+$].

Compound 356.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]imidazo[1,2-a]pyridine-3-sulphonamide

The title compound was prepared starting from amine (IIa-6) and imidazo[1,2-a]-pyridine-3-sulphonyl chloride. Yield: 62%. MS: 458[M+H$^+$].

Compound 357.

N-[3-[4-(6-Fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]propyl]-1H-pyrrolo[2,3-b]pyridine-2-sulphonamide

The title compound was prepared starting from amine (IIa-6) and 1H-pyrrolo-[2,3-b]-pyridine-2-sulphonyl chloride. Yield: 64%. MS: 458[M+H$^+$].

Compound 358.

6-Chloro-N-[4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl]naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-8) and 6-chloro-naphthalene-2-sulphonyl chloride. Yield: 72%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.39 (s, 1H), 8.20 (s, 1H), 7.88-7.82 (m, 3H), 7.78 (d, 1H, J = 8.9 Hz), 7.49 (dd, 1H, J = 2.0 and 8.7 Hz), 7.18-7.14 (m, 2H), 7.13-7.10 (m, 1H), 6.62 (dd, 1H, J = 1.6 and 6.8 Hz), 6.51 (t, 1H, J = 2.3 Hz), 3.35-3.30 (m, 4H), 3.09-3.00 (m, 2H), 2.75-2.70 (m, 4H), 2.49-2.42 (m, 2H), 1.65-1.60 (m, 4H). MS: 497[M+H$^+$].

Compound 359.

4-Fluoro-N-[4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl]benzenesulphonamide

The title compound was prepared starting from amine (IIa-8) and 4-fluorobenzenesulphonyl chloride. Yield: 75%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.22 (s, 1H), 7.90-7.82 (m, 2H), 7.18-7.00 (m, 5H), 6.62 (dd, 1H, J = 1.2 and 7.1 Hz), 6.52 (t, 1H, J = 2.3 Hz), 3.58-3.36 (m, 4H), 3.02-2.96 (m, 2H), 2.78-2.70 (m, 4H), 2.48-2.40 (m, 2H), 1.66-1.58 (m, 4H). MS: 431[M+H$^+$].

Compound 360.

N-[4-[4-(1H-Indol-4-yl)piperazin-1-yl]butyl]-4-(trifluoromethyl)benzenesulphonamide

The title compound was prepared starting from amine (IIa-8) and 4-(trifluoromethyl)-benzenesulphonyl chloride. Yield: 60%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.18 (s, 1H), 8.76 (d, 2H, J = 7.9 Hz), 7.72 (d, 2H, J = 8.2 Hz), 7.18-7.04 (m, 3H), 6.61 (dd, 1H, J = 1.2 and 6.9 Hz), 6.52 (t, 1H, J = 2.3 Hz), 3.36-3.18 (m, 4H), 3.08-2.96 (m, 2H), 2.78-2.70 (m, 4H), 2.48-2.40 (m, 2H), 1.68-1.60 (m, 4H). MS: 481[M+H$^+$].

Compound 361.

N-[4-[4-(1H-Indol-4-yl)piperazin-1-yl]butyl]-3-(trifluoromethyl)benzenesulphonamide

The title compound was prepared starting from amine (IIa-8) and 3-(trifluoromethyl)-benzenesulphonyl chloride. Yield: 75%. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.45 (s, 1H), 8.15-8.00 (m, 2H), 7.82-7.78 (m, 2H), 7.50-7.46 (d, 1H, J = 6.9 Hz), 7.31-7.20 (m, 2H), 6.62-6.58 (m, 1H), 6.52-6.46 (m, 1H), 3.62-3.42 (m, 4H), 3.48-3.40 (m, 2H), 3.38-3.30 (m, 2H), 3.02-2.88 (m, 1H), 2.75-2.60 (m, 2H), 2.50-2.40 (m, 1H), 2.22-2.14 (m, 2H), 1.68-1.54 (m, 2H). MS: 481[M+H$^+$].

Compound 362.

3-Cyano-N-[4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl]benzenesulphonamide

The title compound was prepared starting from amine (IIa-8) and 3-cyanobenzenesulphonyl chloride. Yield: 68%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.32 (s, 1H), 8.12 (t, 1H, J =1.7 Hz), 8.06 (dt, 1H, J = 1.0 and 7.9 Hz), 7.78 (dd, 1H, J = 1.4 and 7.9 Hz), 7.18-7.06 (m, 3H), 6.62 (dd, 1H, J = 1.3 and 6.9 Hz), 6.50 (t, 1H, J = 2.3 Hz), 3.36-3.28 (m, 4H), 3.04-2.96 (m, 2H), 2.80-2.72 (m, 4H), 2.50-2.42 (m, 2H), 1.70-1.60 (m, 4H). MS: 438[M+H$^+$].

Compound 363.

6-Chloro-N-[4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl]benzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-8) and 6-chlorobenzothiophene-2-sulphonyl chloride. Yield: 68%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.26 (s, 1H), 7.80 (d, 1H, J = 1.8 Hz), 7.76 (d, 1H, J = 0.7 Hz), 7.70 (d, 1H, J = 8.4 Hz), 7.38 (dd, 1H, J = 1.6 and 8.7 Hz), 7.18-7.10 (m, 4H), 6.61 (dd, 1H, J = 1.6 and 6.7 Hz), 6.51 (t, 1H, J = 2.3 Hz), 3.40-3.32 (m, 4H), 3.12-3.08 (m, 2H), 2.80-2.72 (m, 4H), 2.50-2.42 (m, 2H), 1.70-1.16 (m, 4H). MS: 503[M+H$^+$].

Compound 364.

5-Fluoro-N-[4-[4-(1H-indol-4-yl)piperazin-1-yl]butyl]-3-methylbenzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-8) and 5-fluoro-3-methylbenzothiophene-2-sulphonyl chloride. Yield: 75%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.24 (s, 1H), 7.78-7.68 (m, 1H), 7.50-7.39 (m, 1H), 7.28-7.20 (m, 1H), 7.16-7.04 (m, 3H), 6.60-6.58 (m, 1H), 6.56-6.50 (m, 1H), 3.38-3.32 (m, 2H), 3.28-3.19 (m, 3H), 3.16-3.10 (m, 1H), 2.78-2.68 (m, 4H), 2.68 (s, 3H), 2.50-2.44 (m, 2H), 1.68-1.60 (m, 4H). MS: 501[M+H$^+$].

Compound 365.

N-[4-[4-(1H-Indol-4-yl)piperazin-1-yl]butyl]-1,3-benzodioxole-5-sulphonamide

The title compound was prepared starting from amine (IIa-8) and 1,3-benzodioxole-5-sulphonyl chloride. Yield: 70%. MS: 378[M+H$^+$].

Compound 371.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]naphthalene-1-sulphonamide

The title compound was prepared starting from amine (IIa-13) and naphthalene-1-sulphonyl chloride. Yield: 87%. MS: 451[M+H$^+$].

Compound 372.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]naphthalene-2-sulphonamide, hydrochloride

The title compound was prepared starting from amine (IIa-13) and naphthalene-2-sulphonyl chloride. Yield: 80%. MS: 451[M+H$^+$].

Compound 373.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]-4-fluorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-13) and 4-fluorobenzene-sulphonyl chloride. Yield: 65%. MS: 419[M+H$^+$].

Compound 374.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]-3,4-difluorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-13) and 3,4-difluorobenzene-sulphonyl chloride. Yield: 70%. MS: 437[M+H$^+$].

Compound 375.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]-4-chlorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-13) and 4-chlorobenzene-sulphonyl chloride. Yield: 70%. MS: 435[M+H$^+$].

Compound 376.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]-4-bromobenzenesulphonamide

The title compound was prepared starting from amine (IIa-13) and 4-bromobenzene-sulphonyl chloride. Yield: 78%. MS: 479[M+H$^+$].

Compound 377.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]-3-bromobenzenesulphonamide

The title compound was prepared starting from amine (IIa-13) and 3-bromobenzene-sulphonyl chloride. Yield: 74%. MS: 479[M+H$^+$].

Compound 378.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]-3-chloro-4-fluorobenzene-sulphonamide

The title compound was prepared starting from amine (IIa-13) and 3-chloro-4-fluoro-benzenesulphonyl chloride. Yield: 60%. MS: 453[M+H$^+$].

Compound 379.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]-4-tert-butyl-benzenesulphonamide

The title compound was prepared starting from amine (IIa-13) and 4-tert-butyl-benzene-sulphonyl chloride. Yield: 59%. MS: 457[M+H$^+$].

Compound 380.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]-4-(trifluoromethyl)benzene-sulphonamide

The title compound was prepared starting from amine (IIa-13) and 4-(trifluoromethyl)-benzenesulphonyl chloride. Yield: 56%. MS: 469[M+H$^+$].

Compound 381.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]-3-cyanobenzenesulphonamide

The title compound was prepared starting from amine (IIa-13) and 3-cyanobenzene-sulphonyl chloride. Yield: 62%. MS: 426[M+H$^+$].

Compound 382.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]-4-phenylbenzenesulphonamide

The title compound was prepared starting from amine (IIa-13) and 4-phenylbenzene-sulphonyl chloride. Yield: 78%. MS: 477[M+H$^+$].

Compound 383.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]-2,3-dihydrobenzofuran-5-sulphonamide

The title compound was prepared starting from amine (IIa-13) and 2,3-dihydro-benzofuran-5-sulphonyl chloride. Yield: 67%. MS: 443[M+H$^+$].

Compound 384.

N-[3-[4-(1,2-Benzoxazol-3-yl)piperazin-1-yl]propyl]-1,3-benzothiazole-4-sulphonamide

The title compound was prepared starting from amine (IIa-13) and 1,3-benzothiazole-4-sulphonyl chloride. Yield: 56%. MS: 458[M+H$^+$].

Compound 385.

N-[4-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]naphthalene-1-sulphonamide

The title compound was prepared starting from amine (IIa-14) and naphthalene-1-sulphonyl chloride. Yield: 81%. MS: 482[M+H$^+$].

Compound 386.

N-[4-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-14) and naphthalene-2-sulphonyl chloride. Yield: 88%. MS: 482[M+H$^+$].

Compound 387.

6-Chloro-N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-14) and 6-chloro-naphthalene-2-sulphonyl chloride. Yield: 74%. MS: 516[M+H$^+$].

Compound 388.

N-[4-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-3-fluorobenzene-sulphonamide

The title compound was prepared starting from amine (IIa-14) and 3-fluorobenzene-sulphonyl chloride. Yield: 70%. MS: 450[M+H$^+$].

Compound 389.

N-[4-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-3,4-difluorobenzene-sulphonamide

The title compound was prepared starting from amine (IIa-14) and 3,4-difluorobenzene-sulphonyl chloride. Yield: 77%. MS: 468[M+H$^+$].

Compound 390.

3-Chloro-N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-14) and 3-chlorobenzene-sulphonyl chloride. Yield: 67%. MS: 466[M+H$^+$].

Compound 391.

3-Bromo-N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-14) and 3-bromobenzene-sulphonyl chloride. Yield: 73%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 7.91 (s, 1H), 7.86-7.78 (m, 3H), 7.55 (t, 1H, *J* = 8.0 Hz), 6.69 (t, 1H, *J* = 8.0 Hz), 6.49-6.41 (m, 2H), 4.21-4.17 (m, 4H), 2.90 (br. s, 4H), 2.81-2.75 (m, 2H), 2.41 (br. s, 4H), 2.21 (br. s, 2H), 1.37 (br. s, 4H). MS: 510[M+H$^+$].

Compound 392.

3-Chloro-N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-4-fluoro-benzenesulphonamide

The title compound was prepared starting from amine (IIa-14) and 3-chloro-4-fluoro-benzenesulphonyl chloride. Yield: 68%. MS: 484[M+H$^+$].

Compound 393.

N-[4-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-3-hydroxybenzene-sulphonamide

The title compound was prepared starting from amine (IIa-14) and 3-hydroxybenzene-sulphonyl chloride. Yield: 45%. MS: 448[M+H$^+$].

Compound 394.

N-[4-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-3-methoxybenzene-sulphonamide

The title compound was prepared starting from amine (IIa-14) and 3-methoxybenzene-sulphonyl chloride. Yield: 70%. MS: 462[M+H$^+$].

Compound 395.

N-[4-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-3-methylbenzene-sulphonamide

The title compound was prepared starting from amine (IIa-14) and 3-methylbenzene-sulphonyl chloride. Yield: 63%. MS: 446[M+H$^+$].

Compound 396.

N-[4-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-4-phenylbenzene-sulphonamide

The title compound was prepared starting from amine (IIa-14) and 4-phenylbenzene-sulphonyl chloride. Yield: 76%. MS: 508[M+H$^+$].

Compound 397.

N-[4-[4-(2,3-Dihydro-1,4-benzodioxin-8-yl)piperazin-1-yl]butyl]thiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-14) and thiophene-2-sulphonyl chloride. Yield: 73%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 7.91 (d, 1H, *J* = 5.1 Hz), 7.85 (t, 1H, *J* = 5.7 Hz), 7.56 (d, 1H, *J* = 3.9 Hz), 7.18-7.15 (m, 1H), 6.69 (t, 1H, *J* = 8.2 Hz), 6.49-6.41 (m, 2H), 4.21-4.17 (m, 4H), 2.92 (br. s, 4H), 2.85-2.82 (m, 2H), 2.48 (br. s, 4H), 2.25 (br. s, 2H), 1.40 (br. s, 4H). MS: 438[M+H$^+$].

Compound 398.

5-Chloro-N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]thiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-14) and 5-chloro-thiophene-2-sulphonyl chloride. Yield: 64%. MS: 472[M+H$^+$].

Compound 399.

N-[4-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]benzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-14) and benzothiophene-2-sulphonyl chloride. Yield: 66%. MS: 488[M+H$^+$].

Compound 400.

N-[4-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]benzothiophene-3-sulphonamide

The title compound was prepared starting from amine (IIa-14) and benzothiophene-3-sulphonyl chloride. Yield: 68%. MS: 488[M+H$^+$].

Compound 401.

6-Chloro-N-[4-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]benzothiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-14) and 6-chlorobenzo-thiophene-2-sulphonyl chloride. Yield: 70%. MS: 522[M+H$^+$].

Compound 402.

N-[4-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-1H-indazole-6-sulphonamide

The title compound was prepared starting from amine (IIa-14) and 1H-indazole-6-sulphonyl chloride. Yield: 50%. MS: 472[M+H$^+$].

Compound 403.

N-[4-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-2-oxo-3H-1,3-benzoxazole-6-sulphonamide

The title compound was prepared starting from amine (IIa-14) and 2-oxo-3H-1,3-benzoxazole-6-sulphonyl chloride. Yield: 67%. MS: 489[M+H$^+$].

Compound 404.

N-[4-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]butyl]-1,3-benzodioxole-5-sulphonamide

The title compound was prepared starting from amine (IIa-14) and 1,3-benzodioxole-5-sulphonyl chloride. Yield: 68%. MS: 476[M+H$^+$].

Compound 405.

N-[3-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]naphthalene-1-sulphonamide, hydrochloride

The title compound was prepared starting from amine (IIa-15) and naphthalene-1-sulphonyl chloride. Yield: 69%. MS: 468[M+H$^+$].

Compound 406.

N-[3-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]naphthalene-2-sulphonamide, hydrochloride

The title compound was prepared starting from amine (IIa-15) and naphthalene-2-sulphonyl chloride. Yield: 69%. MS: 468[M+H$^+$].

Compound 407.

6-Chloro-N-[3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]naphthalene-2-sulphonamide, hydrochloride

The title compound was prepared starting from amine (IIa-15) and 6-chloro-naphthalene-2-sulphonyl chloride. Yield: 80%. MS: 502[M+H$^+$].

Compound 408.

N-[3-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]-4-fluorobenzene-sulphonamide, hydrochloride

The title compound was prepared starting from amine (IIa-15) and 4-fluorobenzene-sulphonyl chloride. Yield: 68%. MS: 436[M+H$^+$].

Compound 409.

N-[3-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]-3-fluorobenzene-sulphonamide, hydrochloride

The title compound was prepared starting from amine (IIa-15) and 3-fluorobenzene-sulphonyl chloride. Yield: 83%. MS: 436[M+H$^+$].

Compound 410.

N-[3-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]-3,4-difluorobenzene-sulphonamide

The title compound was prepared starting from amine (IIa-15) and 3,4-difluorobenzene-sulphonyl chloride. Yield: 62%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 7.86-7.63 (m, 4H), 6.69 (t, 1H, *J* = 8.2 Hz), 6.51-6.40 (m, 2H), 4.21-4.15 (m, 4H), 2.88 (br. s, 4H), 2.82-2.75 (m, 2H), 2.39 (br. s, 4H), 2.26 (br. s, 2H), 1.51-1.47 (m, 2H). MS: 454[M+H$^+$].

Compound 411.

3-Chloro-N-[3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-15) and 3-chlorobenzene-sulphonyl chloride. Yield: 70%. MS: 452[M+H$^+$].

Compound 412.

4-Bromo-N-[3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]benzene-sulphonamide, hydrochloride

The title compound was prepared starting from amine (IIa-15) and 4-bromobenzene-sulphonyl chloride. Yield: 76%. MS: 496[M+H$^+$].

Compound 413.

3-Bromo-N-[3-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-15) and 3-bromobenzene-sulphonyl chloride. Yield: 70%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 7.93-7.74 (m, 4H), 7.58-7.52 (m, 1H), 6.68 (t, 1H, *J* = 8.2 Hz), 6.49-6.39 (m, 2H), 4.21-4.15 (m, 4H), 2.88 (br. s, 4H), 2.81-2.70 (m, 2H), 2.37 (br. s, 4H), 2.25 (br. s, 2H), 1.54-1.49 (m, 2H). MS: 496[M+H$^+$].

Compound 414.

N-[3-[4-(2,3-Dihydro-1,4-benzodioxin-8-yl)piperazin-1-yl]propyl]-3-methylbenzene-sulphonamide

The title compound was prepared starting from amine (IIa-15) and 3-methylbenzene-sulphonyl chloride. Yield: 78%. MS: 432[M+H$^+$].

Compound 415.

N-[3-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]-4-phenylbenzene-sulphonamide, hydrochloride

The title compound was prepared starting from amine (IIa-15) and 4-phenylbenzene-sulphonyl chloride. Yield: 70%. MS: 494[M+H$^+$].

Compound 416.

N-[3-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]benzothiophene-3-sulphonamide

The title compound was prepared starting from amine (IIa-15) and benzothiophene-3-sulphonyl chloride. Yield: 46%. MS: 474[M+H$^+$].

Compound 417.

N-[3-[4-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]propyl]-2,3-dihydrobenzofuran-5-sulphonamide, hydrochloride

The title compound was prepared starting from amine (IIa-15) and 2,3-dihydro-benzofuran-5-sulphonyl chloride. Yield: 62%. MS: 460[M+H$^+$].

Compound 418.

N-[4-[4-(2-Oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]butyl]naphthalene-1-sulphonamide

The title compound was prepared starting from amine (IIa-16) and naphthalene-1-sulphonyl chloride. Yield: 52%. MS: 480[M+H$^+$].

Compound 419.

N-[4-[4-(2-Oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]butyl]naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-16) and naphthalene-2-sulphonyl chloride. Yield: 76%. MS: 480[M+H$^+$].

Compound 420.

4-Fluoro-N-[4-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-16) and 4-fluorobenzene-sulphonyl chloride. Yield: 64%. MS: 448[M+H$^+$].

Compound 421.

4-Chloro-N-[4-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-16) and 4-chlorobenzene-sulphonyl chloride. Yield: 55%. MS: 464[M+H$^+$].

Compound 422.

3-Methyl-N-[4-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-16) and 3-methylbenzene-sulphonyl chloride. Yield: 71%. MS: 444[M+H$^+$].

Compound 423.

N-[3-[4-(2-Oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]propyl]naphthalene-1-sulphonamide

The title compound was prepared starting from amine (IIa-17) and naphthalene-1-sulphonyl chloride. Yield: 56%. MS: 466[M+H$^+$].

Compound 424.

N-[3-[4-(2-Oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]propyl]naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-17) and naphthalene-2-sulphonyl chloride. Yield: 75%. MS: 466[M+H$^+$].

Compound 425.

4-chloro-N-[3-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]propyl]-benzenesulphonamide

The title compound was prepared starting from amine (IIa-17) and 4-chlorobenzene-sulphonyl chloride. Yield: 65%. MS: 449[M+H$^+$].

Compound 426.

3-Methyl-N-[3-[4-(2-oxo-1,3-dihydrobenzimidazol-4-yl)piperazin-1-yl]propyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-17) and 3-methylbenzene-sulphonyl chloride. Yield: 57%. MS: 430[M+H$^+$].

Compound 427.

N-[4-[4-(3-Oxo-4H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl]naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-18) and naphthalene-2-sulphonyl chloride. Yield: 72%.^{1}H-NMR (300 MHz, $CDCl_3$): 8.40 (s, 1H), 8.39 (s, 1H), 7.96-7.70 (m, 4H), 7.64-7.54 (m, 2H), 6.91 (t, 1H, J = 7.9 Hz), 6.66 (dd, 1H, J = 8.2 and 1.2 Hz), 6.52 (dd, 1H, J = 7.7 and 1.2 Hz), 4.60 (s, 2H), 3.20-3.12 (m, 4H), 3.08-2.98 (m, 2H), 2.70-2.60 (m, 4H), 2.42-2.38 (m, 2H), 1.62-1.54 (m, 4H). MS: 495[M+H$^+$].

Compound 428.

4-Fluoro-N-[4-[4-(3-oxo-4H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-18) and 4-fluorobenzene-sulphonyl chloride. Yield: 80%.^{1}H-NMR (300 MHz, $CDCl_3$): 8.05 (s, 1H), 7.85-7.80 (m, 2H), 7.18-7.06 (m, 2H), 6.82 (t, 1H, J = 7.9 Hz), 6.62 (dd, 1H, J =8.2 and 1.2 Hz), 6.45 (d, 1H, J = 7.7 and 1.2 Hz), 4.60 (m, 2H), 3.20-3.16 (m, 4H), 3.00-2.88 (m, 2H), 2.75-2.60 (m, 4H), 2.47-2.40 (m, 2H), 1.65-1.58 (m, 4H). MS: 463[M+H$^+$].

Compound 429.

N-[4-[4-(3-Oxo-4H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl]-4-(trifluoromethyl)benzene-sulphonamide

The title compound was prepared starting from amine (IIa-18) and 4-(trifluoromethyl)-benzenesulphonyl chloride. Yield: 76%.^{1}H-NMR (300 MHz, $CDCl_3$): .90 (d, 2H, J = 8.2 Hz), 7.70 (d, 2H, J = 8.2 Hz), 6.84 (t, 1H, J = 7.9 Hz), 6.58 (dd, 1H, J = 8.2 and 1.2 Hz), 6.50 (dd, 1H, J = 7.7 and 1.2 Hz), 4.60 (s, 2H), 3.10-3.00 (m, 4H), 2.92-2.88 (m, 2H), 2.62-2.58 (m, 4H), 2.38-2.28 (m, 2H), 1.58-1.50 (m, 4H). MS: 513[M+H$^+$].

Compound 430.

N-[4-[4-(3-Oxo-4H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl]-3-(trifluoromethyl)benzene-sulphonamide

The title compound was prepared starting from amine (IIa-18) and 3-(trifluoromethyl)-benzenesulphonyl chloride. Yield: 65%.^{1}H-NMR (300 MHz, $CDCl_3$): 7.60-7.54 (m, 1H), 7.50-7.42 (m, 1H), 7.28-7.24 (m, 1H), 7.12-6.68 (m, 1H), 7.00-7.68 (m, 1H), 6.62 (d, 1H, J= 6.6 Hz), 6.52 (d, 1H, J= 3.0 Hz), 5.20 (s, 2H), 3.40-3.37 (m, 4H), 3.37-3.30 (m, 1H), 3.04-2.98 (m, 2H), 2.86-2.78 (m, 4H), 2.76-2.70 (m, 1H), 1.68-1.60 (m, 4H). MS: 513[M+H$^+$].

Compound 431.

5-Chloro-N-[4-[4-(3-oxo-4H-1,4-benzoxazin-8-yl)piperazin-1-yl]butyl]thiophene-2-sulphonamide

The title compound was prepared starting from amine (IIa-18) and 5-chloro-thiophene-2-sulphonyl chloride. Yield: 85%.^{1}H-NMR (300 MHz, $CDCl_3$): 8.70 (s, 1H), 7.33 (d, 1H, J= 3.8 Hz), 6.93-6.88 (m, 2H), 6.67 (dd, 1H, J = 8.2 and 1.2 Hz), 6.52 (dd, 1H, J = 7.7 and 1.2 Hz), 4.60 (s, 2H), 3.20-3.12 (m, 4H), 3.08-3.00 (m, 2H), 2.72-2.64 (m, 4H), 2.46-2.40 (m, 2H), 1.68-1.60 (m, 4H). MS: 485[M+H$^+$].

b) General procedure for compounds wherein in formula (IIa) ----- represents double bond.

0.2 Mmol of amine **(IIa)** was dissolved in 5 ml of anhydrous N,N-dimethylformamide, and then 4 mmol of N,N-diisopropylethylamine was added. The mixture was purged with argon, and 0.24 mmol of appropriate arylsulphonyl chloride was subsequently added (**IIb**). After 30 minutes of stirring at room temperature the mixture was poured into about 20 ml of ice water. The mixture was extracted with ethyl acetate or methylene chloride. Organic layer was washed with brine, dried over anhydrous sodium sulphate, and then concentrated under reduced pressure. Crude sulphonamides were usually purified by means of crystallization (from methanol), and some of them using column chromatography on silica gel with using methylene chloride/methanol 20:1 as eluent. Structure of prepared compounds was confirmed by MS data, and purity by HPLC analysis. For selected compounds structure identification was further confirmed by ^{1}H-NMR analysis.

Following the general procedure described above and starting from appropriate compounds amine (IIa) and arylsulphonyl chloride (IIb), the following compounds were obtained.

Compound 34.

N-{4-[4-(5-Chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}naphthalene-1-sulphonamide

The title compound was prepared starting from amine (IIa-9) and naphthalene-1-sulphonyl chloride. Yield: 42%. MS: 494[M+H$^+$].

Compound 35.

N-{4-[4-(5-Chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-9) and naphthalene-2-sulphonyl chloride. Yield: 40%. MS: 494[M+H$^+$].

Compound 36.

4-Fluoro-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide

The title compound was prepared starting from amine (IIa-9) and 4-fluorobenzene-sulphonyl chloride. Yield: 42%. MS: 462[M+H$^+$].

Compound 37.

3-Fluoro-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide

The title compound was prepared starting from amine (IIa-9) and 3-fluorobenzene-sulphonyl chloride. Yield: 60%. MS: 462[M+H$^+$].

Compound 38.

4-Chloro-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide

The title compound was prepared starting from amine (IIa-9) and 4-chlorobenzene-sulphonyl chloride. Yield: 55%. MS: 478[M+H$^+$].

Compound 39.

3-Chloro-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide

The title compound was prepared starting from amine (IIa-9) and 3-chlorobenzene-sulphonyl chloride. Yield: 30%. MS: 478[M+H$^+$].

Compound 40.

3-Methyl-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide

The title compound was prepared starting from amine (IIa-9) and 3-methylbenzene-sulphonyl chloride. Yield: 55%. MS: 458[M+H$^+$].

Compound 41.

3-Hydroxy-*N*-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide

The title compound was prepared starting from amine (IIa-9) and 3-hydroxybenzene-sulphonyl chloride. Yield: 20%. MS: 460[M+H$^+$].

Compound 42.

4-Methoxy-*N*-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide

The title compound was prepared starting from amine (IIa-9) and 4-methoxybenzene-sulphonyl chloride. Yield: 52%. MS: 474[M+H$^+$].

Compound 43.

N-{3-[4-(5-Chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}naphthalene-1-sulphonamide

The title compound was prepared starting from amine (IIa-10) and naphthalene-1-sulphonyl chloride. Yield: 99%. MS: 480[M+H$^+$].

Compound 44.

N-{3-[4-(5-Chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-10) and naphthalene-2-sulphonyl chloride. Yield: 76%. MS: 480[M+H$^+$].

Compound 45.

4-Fluoro-N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}benzene-sulphonamide

The title compound was prepared starting from amine (IIa-10) and 4-fluoro-benzenesulphonyl chloride. Yield: 99%. MS: 448[M+H$^+$].

Compound 46.

3-Fluoro-N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}benzene-sulphonamide

The title compound was prepared starting from amine (IIa-10) and 3-fluorobenzene-sulphonyl chloride. Yield: 98%. MS: 448[M+H$^+$].

Compound 47.

4-Chloro-N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}benzene-sulphonamide

The title compound was prepared starting from amine (IIa-10) and 4-chlorobenzene-sulphonyl chloride. Yield: 72%.

Compound 48.

3-Chloro-N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}-benzenesulphonamide

The title compound was prepared starting from amine (IIa-10) and 3-chlorobenzene-sulphonyl chloride. Yield: 98%. MS: 464[M+H$^+$].

Compound 49.

3-Hydroxy-*N*-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}-benzenesulphonamide

The title compound was prepared starting from amine (IIa-10) and 3-hydroxybenzene-sulphonyl chloride. Yield: 29%. MS: 446[M+H$^+$].

Compound 50.

N-{2-[4-(5-Chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}naphthalene-1-sulphonamide

The title compound was prepared starting from amine (IIa-11) and naphthalene-1-sulphonyl chloride. Yield: 99%. MS: 466[M+H$^+$].

Compound 51.

N-{2-[4-(5-Chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-11) and naphthalene-2-sulphonyl chloride. Yield: 99%. MS: 466[M+H$^+$].

Compound 52.

N-{2-[4-(5-Chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}-4-fluorobenzene-sulphonamide

The title compound was prepared starting from amine (IIa-11) and 4-fluorobenzene-sulphonyl chloride. Yield: 98%. MS: 434[M+H$^+$].

Compound 53.

3-Fluoro-*N*-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}benzene-sulphonamide

The title compound was prepared starting from amine (IIa-11) and 3-fluorobenzene-sulphonyl chloride. Yield: 52%. MS: 434[M+H$^+$].

Compound 54.

4-Chloro-N-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}benzene-sulphonamide

The title compound was prepared starting from amine (IIa-11) and 4-chlorobenzene-sulphonyl chloride. Yield: 98%. MS: 450[M+H$^+$].

Compound 55.

3-Chloro-*N*-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}benzene-sulphonamide

The title compound was prepared starting from amine (IIa-11) and 3-chlorobenzene-sulphonyl chloride. Yield: 89%. MS: 450[M+H$^+$].

Compound 56.

3-Methyl-*N*-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}benzene-sulphonamide

The title compound was prepared starting from amine (IIa-11) and 3-methylbenzene-sulphonyl chloride. Yield: 48%. MS: 430[M+H$^+$].

Compound 57.

3-Hydroxy-*N*-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}-benzenesulphonamide

The title compound was prepared starting from amine (IIa-11) and 3-hydroxybenzene-sulphonyl chloride. Yield: 12%. MS: 432[M+H$^+$].

Compound 58.

4-Chloro-N-{4-[4-(5-chloro-2-methyl-1*H*-indol-3-yl)-3,6-dihydropyridin-1(2*H*)-yl]butyl}-benzenesulphonamide

The title compound was prepared starting from amine (IIa-12) and 4-chlorobenzene-sulphonyl chloride. Yield: 10%. MS: 492[M+H$^+$].

Compound 137.

N-[4-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-3-chloro-benzenesulphonamide

The title compound was prepared starting from amine (IIa-12) and 3-chlorobenzene-sulphonyl chloride. Yield: 95%. MS: 492[M+H$^+$].

Compound 138.

N-[3-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-3-chloro-benzenesulphonamide

The title compound was prepared starting from amine (IIa-22) and 3-chlorobenzene-sulphonyl chloride. Yield: 89%. MS: 478[M+H$^+$].

Compound 139.

N-[4-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-3-fluoro-benzenesulphonamide

The title compound was prepared starting from amine (IIa-12) and 3-fluorobenzene-sulphonyl chloride. Yield: 86%. MS: 476[M+H$^+$].

Compound 140.

N-[3-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-3-fluoro-benzenesulphonamide

The title compound was prepared starting from amine (IIa-22) and 3-fluorobenzene-sulphonyl chloride. Yield: 85%. MS: 462[M+H$^+$].

Compound 141.

N-[4-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-4-tert-butyl-benzenesulphonamide

The title compound was prepared starting from amine (IIa-12) and 4-tert-butyl-benzenesulphonyl chloride. Yield: 67%. MS: 514[M+H$^+$].

Compound 366.

N-[4-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-naphthalene-1-sulphonamide

The title compound was prepared starting from amine (IIa-12) and naphthalene-1-sulphonyl chloride. Yield: 60%. MS: 508[M+H$^+$].

Compound 367.

N-[4-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-12) and naphthalene-2-sulphonyl chloride. Yield: 82%. MS: 508[M+H$^+$].

Compound 368.

N-[4-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-4-fluoro-benzenesulphonamide

The title compound was prepared starting from amine (IIa-12) and 4-fluorobenzene-sulphonyl chloride. Yield: 93%. MS: 376[M+H$^+$].

Compound 369.

N-[4-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-3-hydroxy-benzenesulphonamide

The title compound was prepared starting from amine (IIa-12) and 3-hydroxybenzene-sulphonyl chloride. Yield: 43%. MS: 474[M+H$^+$].

Compound 370.

N-[4-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-3-methyl-benzenesulphonamide

The title compound was prepared starting from amine (IIa-12) and 3-methylbenzene-sulphonyl chloride. Yield: 84%. MS: 472[M+H$^+$].

Compound 432.

N-[4-[4-(5-Fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-19) and naphthalene-2-sulphonyl chloride. Yield: 65%.^{1}H-NMR (300 MHz, $CDCl_3$): 8.40 (s, 1H), 8.20 (s, 1H), 6.98 (t, 1H, J = 3.4 Hz), 6.02 (s, 1H), 3.15-3.10 (m, 2H), 2.98-2.90 (m, 2H), 2.80-2.72 (m, 4H), 2.56-2.52 (m, 2H), 1.65-1.48 (m, 4H). MS: 478[M+H$^+$].

Compound 433.

3-Fluoro-N-[4-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-19) and 3-fluorobenzene-sulphonyl chloride. Yield: 78%.^{1}H-NMR (300 MHz, CD_3OD): 8.01 (q, 1H, J = 4.6 Hz), 7.88 (d, 1H, J = 3.6 Hz), 7.78-7.62 (m, 2H), 7.58-7.48 (m, 2H), 7.38-7.32 (dt, 1H, J = 8.9 and

2.5 Hz), 6.04-5.98 (m, 1H), 3.20-3.18 (m, 2H), 2.92 (t, 2H, J = 6.4 Hz), 2.78 (t, 2H, J = 6.1 Hz), 2.64-2.58 (m, 2H), 2.46 (t, 2H, J = 6.9 Hz), 1.62-1.50 (m, 4H). MS: 446[M+H$^+$].

Compound 434.

N-[4-[4-(5-Fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-3-hydroxybenzene-sulphonamide

The title compound was prepared starting from amine (IIa-19) and 3-hydroxybenzene-sulphonyl chloride. Yield: 67%. MS: 444[M+H$^+$].

Compound 435.

N-[4-[4-(5-Fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-3-methylbenzene-sulphonamide

The title compound was prepared starting from amine (IIa-19) and 3-methylbenzene-sulphonyl chloride. Yield: 76%. ^{1}H-NMR (300 MHz, CD_3OD): 7.54-7.46 (m, 3H), 7.30-7.18 (m, 4H), 6.90 (dt, 1H, J = 8.9 and 2.5 Hz), 6.04-5.98 (m, 1H), 3.38-3.30 (m, 2H), 2.87 (t, 2H, J = 5.9 Hz), 2.80-2.60 (m, 4H), 2.48 (t, 2H, J = 6.6 Hz), 1.58-1.52 (m, 4H). MS: 442[M+H$^+$].

Compound 436.

3-Fluoro-N-[3-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-20) and 3-fluorobenzene-sulphonyl chloride. Yield: 70%. ^{1}H-NMR (300 MHz, CD_3OD): 7.54-7.46 (m, 3H), 7.30-7.18 (m, 4H), 6.90 (dt, 1H, J = 8.9 and 2.5 Hz), 6.04-5.98 (m, 1H), 3.38-3.30 (m, 2H), 2.87 (t, 2H, J = 5.9 Hz), 2.80-2.60 (m, 4H), 2.48 (t, 2H, J = 6.6 Hz), 1.58-1.52 (m, 4H). MS: 432[M+H$^+$].

Compound 437.

N-[3-[4-(5-Fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-3-hydroxybenzene-sulphonamide

The title compound was prepared starting from amine (IIa-20) and 3-hydroxybenzene-sulphonyl chloride. Yield: 62%. MS: 430[M+H$^+$].

Compound 438.

N-[2-[4-(5-Fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-21) and naphthalene-2-sulphonyl chloride. Yield: 54%. MS: 450[M+H$^+$].

Compound 439.

3-Fluoro-N-[2-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]benzene-sulphonamide

The title compound was prepared starting from amine (IIa-21) and 3-fluorobenzene-sulphonyl chloride. Yield: 70%. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.17 (s, 1H), 7.70-7.46 (m, 4H), 7.32-7.20 (m, 3H), 7.00-6.94 (m, 1H), 6.02-5.98 (m, 1H), 3.12 (t, 2H, J = 5.3 Hz), 3.06-3.02 (m, 2H), 2.62-2.48 (m, 4H), 1.76-1.62 (m, 2H). MS: 418[M+H$^+$].

Compound 440.

N-[2-[4-(5-Fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-3-methylbenzene-sulphonamide

The title compound was prepared starting from amine (IIa-21) and 3-methylbenzene-sulphonyl chloride.Yield: 83%. ^{1}H-NMR (300 MHz, CD_3OD): 7.71-7.62 (m, 2H), 7.48-7.40 (m, 3H), 7.32-7.28 (m, 2H), 6.86 (dt, 1H, J = 8.9 and 2.5 Hz), 6.12-6.10 (m, 1H), 3.38 (s, 3H), 3.18-3.14 (m, 2H), 3.10-3.06 (m, 2H), 2.72-2.68 (m, 2H), 2.60-2.54 (m, 2H), 2.38-2.34 (m, 2H). MS: 414[M+H$^+$].

Compound 441.

N-[3-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-naphthalene-1-sulphonamide

The title compound was prepared starting from amine (IIa-22) and naphthalene-1-sulphonyl chloride. Yield: 74%. MS: 494[M+H$^+$].

Compound 442.

N-[3-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-22) and naphthalene-2-sulphonyl chloride. Yield: 67%. MS: 494[M+H$^+$].

Compound 443.

N-[3-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-4-fluorobenzenesulphonamide

The title compound was prepared starting from amine (IIa-22) and 4-fluorobenzene-sulphonyl chloride. Yield: 50%. MS: 462[M+H$^+$].

Compound 444.

4-Chloro-N-[3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-benzenesulphonamide

The title compound was prepared starting from amine (IIa-22) and 4-chlorobenzene-sulphonyl chloride. Yield: 69%. MS: 478[M+H$^+$].

Compound 445.

N-[3-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-3-hydroxy-benzenesulphonamide

The title compound was prepared starting from amine (IIa-22) and 3-hydroxybenzene-sulphonyl chloride. Yield: 40%. MS: 460[M+H$^+$].

Compound 446.

N-[3-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-3-methyl-benzenesulphonamide

The title compound was prepared starting from amine (IIa-22) and 3-methylbenzene-sulphonyl chloride. Yield: 82%. MS: 458[M+H$^+$].

Compound 447.

N-[2-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-naphthalene-1-sulphonamide

The title compound was prepared starting from amine (IIa-23) and naphthalene-1-sulphonyl chloride. Yield: 89%. MS: 480[M+H$^+$].

Compound 448.

N-[2-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-naphthalene-2-sulphonamide

The title compound was prepared starting from amine (IIa-23) and naphthalene-2-sulphonyl chloride. Yield: 61%. MS: 480[M+H$^+$].

Compound 449.

N-[2-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-4-fluoro-benzenesulphonamide

The title compound was prepared starting from amine (IIa-23) and 4-fluorobenzene-sulphonyl chloride. Yield: 45%. MS: 448[M+H$^+$].

Compound 450.

N-[2-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-3-fluoro-benzenesulphonamide

The title compound was prepared starting from amine (IIa-23) and 3-fluorobenzene-sulphonyl chloride. Yield: 56%. MS: 448[M+H$^+$].

Compound 451.

4-Chloro-N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-benzenesulphonamide

The title compound was prepared starting from amine (IIa-23) and 4-chlorobenzene-sulphonyl chloride. Yield: 88%. MS: 464[M+H$^+$].

Compound 452.

3-Chloro-N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-benzenesulphonamide

The title compound was prepared starting from amine (IIa-23) and 3-chlorobenzene-sulphonyl chloride. Yield: 63%. MS: 464[M+H$^+$].

Compound 453.

N-[2-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-3-hydroxy-benzenesulphonamide

The title compound was prepared starting from amine (IIa-23) and 3-hydroxybenzene-sulphonyl chloride. Yield: 46%. MS: 446[M+H$^+$].

Compound 454.

N-[2-[4-(5-Chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-3-methyl-benzenesulphonamide

The title compound was prepared starting from amine (IIa-23) and 3-methylbenzene-sulphonyl chloride. Yield: 51%. MS: 444[M+H$^+$].

Tests *In vitro*

Example 4

In Vitro Pharmacology: Binding Assays

The affinity of compounds of the present invention to dopaminergic, serotoninergic, adrenergic, muscarinic M3, histaminergic H1, sigma and serotonin transporter receptors was tested using the methods as described below, consisting in measuring their binding to these receptors using radioreceptors methods.

The specific ligand binding to the receptors is defined as the difference between the total binding and the nonspecific binding determined in the presence of an excess of unlabelled ligand.

The results are expressed as a percent of control specific binding ((measured specific binding/control specific binding) x 100) and as a percent inhibition of control specific binding (100-((measured specific binding/control specific binding) x 100)) obtained in the presence of the test compounds.The specific ligand binding to the receptor is defined as the difference between total and non-specific binding determined in the presence of an excess of unlabelled ligand. The compounds were tested at a concentration of 1×10^{-6} M, and scintillation counting was the method of detection of ligand binding. Conditions and methodology (by reference to the literature) of *in vitro* tests are given in Table 1 and the tests results for representative compounds are given in Table 2 (dopaminergic receptor D2), in Table 3 (dopaminergic receptor D3), in Table 4 (serotoninergic receptors 5-HT1A and 5-HT2A), in Table 5 (serotoninergic receptors 5-HT6 and 5-HT7), in Table 6 (serotonine transporter (SERT) receptor), in Table 7 (sigma receptor σ), in Table 8 (adrenergic α1 receptor), in Table 9 (adrenergic α2C receptor), in Table 10 (histaminergic H1 receptor), in Table 11 (muscarinic M3 receptor) and in Table 12 (serotoninergic receptor 5-HT2C).

Table 1: Conditions and methodology of *in vitro* tests for binding assays

Assay	Origin	Radioligand	Concentration	Kd	Non Specific	Incubation	Ref.
α_1 (non-selective)	rat cerebral cortex	[^{3}H]prazosin	0.25 nM	0.09 nM	prazosin (0.5 µM)	60 min 22°C	1
α_{2C} *(h)*	human recombinant (CHO cells)	[^{3}H]RX 821002	2 nM	0.95 nM	(-)epinephrine (100 µM)	60 min 22°C	2
D_{2S} *(h)*	human recombinant (HEK-293 cells)	[^{3}H]methyl-spiperone	0.3 nM	0.15 nM	(+)butaclamol (10 µM)	60 min 22°C	3
D_3 *(h)*	human recombinant (CHO cells)	[^{3}H]methyl-spiperone	0.3 nM	0.085 nM	(+)butaclamol (10 µM)	60 min 22°C	4
H_1 *(h)*	human recombinant (HEK-293 cells)	[^{3}H]pyrilamine	1 nM	1.7 nM	pyrilamine (1 µM)	60 min 22°C	5
M_3 *(h)*	human recombinant (CHO cells)	[^{3}H]4-DAMP	0.2 nM	0.5 nM	atropine (1 µM)	60 min 22°C	6
5-HT_{1A} *(h)*	human recombinant (HEK-293 cells)	[^{3}H]8-OH-DPAT	0.3 nM	0.5 nM	8-OH-DPAT (10 µM)	60 min 22°C	7
5-HT_{2A} *(h)*	human recombinant (HEK-293 cells)	[^{3}H]ketanserin	0.5 nM	0.6 nM	ketanserin (1 µM)	60 min 22°C	8
5-HT_{2C} *(h)*	human recombinant (HEK-293 cells)	[^{3}H]mesulergine	1 nM	0.5 nM	RS 102221 (10 µM)	120 min 37°C	9
5-HT_6 *(h)*	human recombinant (CHO cells)	[^{3}H]LSD	2 nM	1.8 nM	serotonin (100 µM)	120 min 37°C	10
5-HT_7 *(h)*	human recombinant (CHO cells)	[^{3}H]LSD	4 nM	2.3 nM	serotonin (10 µM)	120 min 22°C	11
σ (non-selective)	rat cerebral cortex	[^{3}H]DTG	8 nM	29 nM	haloperidol (10 µM)	120 min 22°C	12
SERT *(h)*	human recombinant (CHO cells)	[^{3}H]imipramine	2 nM	1.7 nM	imipramine (10 µM)	60 min 22°C	13

Table 2: Results of dopaminergic receptor D2 affinity test for representative compounds

Cpd.	D2 [%]	Cpd.	D2 [%]	Cpd.	D2 [%]	Cpd.	D2 [%]	Cpd.	D2 [%]	Cpd.	D2 [%]	Cpd.	D2 [%]
1	97	43	100	107	104	249	98	307	88	349	93	406	59
2	98	44	100	108	106	250	97	308	96	350	102	407	58
3	96	45	100	109	100	251	97	309	84	351	101	408	40
4	96	46	100	110	109	252	97	310	96	352	100	409	79
5	96	47	100	111	108	253	99	311	105	353	91	411	40
6	96	48	99	112	103	254	87	312	99	354	83	414	48
7	95	49	99	113	98	255	98	313	101	355	99	415	58
8	98	50	97	137	65	256	97	314	99	356	98	416	59
9	91	51	97	138	40	257	99	315	99	357	99	417	68
10	94	52	99	139	52	258	95	316	98	358	96	418	97
11	89	53	99	140	47	259	93	317	105	359	96	419	93
12	93	54	98	165	64	260	99	318	67	360	99	423	97
13	99	55	98	174	91	261	97	319	109	361	99	424	97
14	99	56	100	176	89	262	98	320	100	362	101	425	91
15	90	57	100	195	99	263	98	321	98	363	99	426	28
16	99	58	97	196	98	264	87	322	96	364	100	427	83
17	98	61	100	209	82	267	100	323	105	365	99	428	78
18	98	62	92	211	81	268	98	324	105	366	54	429	61
19	97	63	99	225	77	269	99	325	96	367	49	430	69
20	98	64	98	226	87	270	74	326	109	368	41	431	68

Cpd.	D2 [%]	Cpd.	D2 [%]	Cpd.	D2 [%]	Cpd.	D2 [%]	Cpd.	D2 [%]	Cpd.	D2 [%]	Cpd.	D2 [%]
21	99	65	99	227	104	273	88	327	89	369	67	435	78
22	96	66	101	228	103	274	96	328	108	370	58	437	57
23	97	69	106	229	101	276	95	329	109	385	75	438	97
24	99	70	99	230	105	282	97	330	108	386	70	439	97
25	96	71	103	231	99	283	99	331	100	387	90	440	44
26	97	72	99	232	92	288	103	332	83	388	50	441	77
27	90	73	102	233	83	289	99	333	92	389	50	442	22
28	98	74	93	234	85	291	99	334	75	390	61	443	22
29	94	76	94	235	103	293	85	335	105	391	76	444	40
30	98	79	99	236	99	294	105	336	97	392	57	445	98
31	38	81	90	237	62	295	95	337	59	393	46	446	44
32	101	85	100	238	87	296	105	338	98	394	72	447	3
33	97	87	87	239	102	297	93	339	96	395	61	449	31
34	99	89	89	240	101	298	99	340	101	396	68	450	15
35	99	91	92	241	100	299	87	341	98	398	73	451	46
36	100	93	98	242	105	300	96	342	106	399	79	452	42
37	100	97	100	243	100	301	96	343	101	400	83	453	48
38	100	98	101	244	105	302	90	344	107	401	84	454	-5
38	101	101	99	245	97	303	108	345	109	402	68		
40	100	102	100	246	98	304	94	346	100	403	85		
41	93	105	107	247	104	305	88	347	103	404	60		
42	74	106	108	248	99	306	106	348	104	405	68		

Table 3: Results of dopaminergic receptor D3 affinity test for representative compounds

Compd.	D3 [%]	Compd.	D3 [%]	Compd.	D3 [%]	Compd.	D3 [%]	Compd.	D3 [%]	Compd.	D3 [%]	Compd.	D3 [%]
1	96	45	100	110	97	251	97	310	97	353	97	414	81
2	100	46	100	111	93	252	98	311	101	354	88	415	76
3	98	47	101	112	98	253	99	312	97	355	97	416	56
4	98	48	97	113	99	254	98	313	99	356	96	417	67
5	98	49	99	137	92	255	82	314	100	357	94	418	99
6	97	50	95	138	57	256	96	315	97	358	99	419	97
7	97	51	87	139	92	257	100	316	95	359	100	420	97
8	97	52	99	140	73	258	97	317	97	360	100	421	94
9	90	53	99	165	89	259	85	318	95	361	98	422	98
10	97	54	98	173	98	260	98	319	90	362	102	423	98
11	91	55	96	174	96	261	98	320	99	363	101	424	98
12	92	56	99	175	87	262	98	321	98	364	100	425	104
13	92	57	98	176	95	263	98	322	93	365	100	426	94
14	97	58	100	195	89	264	65	323	96	366	81	427	104
15	88	61	96	196	97	267	99	324	103	367	87	428	104
16	99	62	63	209	103	268	98	325	95	368	94	429	104
17	93	63	103	211	102	269	100	326	99	369	97	430	101
18	98	64	98	225	76	270	82	327	97	370	91	431	103
19	90	65	74	226	90	273	85	328	99	385	89	434	98
20	96	66	101	227	90	274	91	329	99	386	88	435	95
21	97	69	77	228	92	276	69	330	99	387	93	436	96

Compd.	D3 [%]	Compd.	D3 [%]	Compd.	D3 [%]	Compd.	D3 [%]	Compd.	D3 [%]	Compd.	D3 [%]	Compd.	D3 [%]
22	96	70	101	229	95	282	87	331	100	388	83	437	100
23	93	71	91	230	87	283	101	332	96	389	85	438	98
24	98	72	95	231	97	288	102	333	89	390	81	439	95
25	94	73	94	232	89	289	79	334	96	391	85	440	92
26	98	74	92	233	76	291	85	335	93	392	93	441	72
27	96	76	71	234	91	293	65	336	96	393	92	442	53
28	99	79	96	235	87	294	95	337	79	394	86	443	71
29	98	81	97	236	85	295	98	338	100	395	87	444	74
30	98	85	77	237	85	296	100	339	100	396	86	445	97
31	96	87	77	238	85	297	100	340	101	398	90	446	66
33	101	89	95	239	102	298	98	341	98	399	92	447	-17
34	100	91	70	240	99	299	98	342	99	400	88	449	34
35	101	93	86	241	97	300	96	343	96	401	95	450	39
36	100	97	100	242	89	301	96	344	101	402	89	451	30
37	101	98	104	243	93	302	99	345	100	403	99	452	14
38	100	101	92	244	91	303	97	346	93	404	92	453	56
38	101	102	103	245	97	304	87	347	103	405	62	454	58
40	100	105	88	246	86	305	103	348	102	406	54		
41	100	106	97	247	83	306	99	349	100	407	84		
42	101	107	97	248	100	307	95	350	95	408	70		
43	99	108	98	249	100	308	95	351	103	409	85		
44	98	109	99	250	85	309	90	352	97	411	52		

Table 4. Results of serotoninergic receptors 5-HT1A and 5-HT2A affinity tests for representative compounds

Compd.	5-HT$_{1A}$	5-HT$_{2A}$	Compd.	5-HT$_{1A}$	5-HT$_{2A}$	Compd.	5-HT$_{1A}$	5-HT$_{2A}$	Compd.	5-HT$_{1A}$	5-HT$_{2A}$	Compd.	5-HT$_{1A}$	5-HT$_{2A}$
1	96	99	**62**	46	101	**240**	98	101	**314**	75	102	**386**	96	65
2	99	100	**63**	97	100	**241**	98	101	**315**	70	102	**387**	100	90
3	98	100	**64**	99	101	**242**	92	94	**316**	84	102	**388**	92	19
4	99	99	**65**	100	101	**243**	98	100	**317**	45	98	**389**	118	56
5	99	99	**66**	98	101	**244**	69	96	**318**	96	89	**390**	101	59
6	99	100	**69**	80	92	**245**	99	99	**319**	55	88	**391**	97	68
7	99	100	**70**	99	101	**246**	91	88	**320**	69	101	**392**	100	64
8	100	100	**71**	89	94	**247**	78	88	**321**	78	100	**393**	93	47
9	98	99	**72**	95	94	**248**	97	101	**322**	43	94	**394**	95	71
10	97	99	**74**	99	102	**249**	100	101	**323**	45	96	**395**	75	61
11	99	99	**73**	92	81	**250**	98	92	**324**	56	104	**396**	85	58
12	99	99	**76**	90	81	**251**	99	101	**325**	62	102	**397**	95	13
13	89	100	**79**	84	91	**252**	99	101	**326**	59	96	**398**	107	38
14	88	100	**81**	92	101	**253**	99	101	**327**	67	91	**399**	99	82
15	86	99	**85**	54	88	**254**	94	90	**328**	58	90	**400**	100	66
16	93	100	**87**	41	89	**255**	93	84	**329**	69	91	**401**	103	79
17	84	100	**89**	71	99	**256**	96	102	**330**	67	93	**402**	102	76
18	81	100	**91**	40	95	**257**	99	101	**331**	82	102	**403**	98	64

Compd.	5-HT$_{1A}$	5-HT$_{2A}$	Compd.	5-HT$_{1A}$	5-HT$_{2A}$	Compd.	5-HT$_{1A}$	5-HT$_{2A}$	Compd.	5-HT$_{1A}$	5-HT$_{2A}$	Compd.	5-HT$_{1A}$	5-HT$_{2A}$
19	64	100	**93**	48	90	**258**	100	101	**332**	71	97	**404**	97	55
20	71	100	**97**	75	100	**259**	97	56	**333**	42	99	**405**	97	74
21	77	100	**98**	80	102	**260**	96	102	**334**	86	90	**406**	99	28
22	75	99	**101**	82	100	**261**	98	102	**335**	54	97	**407**	88	50
23	85	100	**102**	92	101	**262**	99	102	**336**	61	100	**408**	101	-50
24	80	100	**105**	41	91	**263**	98	102	**337**	41	102	**409**	81	66
25	92	100	**106**	63	97	**264**	54	105	**338**	80	102	**410**	96	42
26	100	98	**107**	38	95	**267**	98	101	**339**	76	82	**411**	95	4
27	99	62	**108**	48	88	**268**	98	102	**340**	45	104	**413**	88	40
28	100	89	**109**	86	93	**269**	99	101	**341**	74	102	**414**	98	76
29	99	64	**110**	55	99	**270**	75	89	**342**	74	106	**415**	96	25
30	100	67	**111**	39	96	**273**	46	95	**343**	32	105	**416**	101	58
31	82	36	**112**	20	93	**274**	73	97	**344**	42	105	**417**	100	-48
33	100	95	**113**	100	69	**276**	51	87	**345**	45	93	**418**	98	36
34	100	50	**137**	39	47	**282**	50	78	**346**	51	97	**419**	98	52
35	99	60	**138**	54	62	**283**	89	103	**347**	92	101	**423**	99	30
36	97	54	**139**	57	41	**288**	86	95	**348**	36	107	**424**	99	66
37	99	48	**140**	56	68	**289**	68	94	**349**	49	108	**425**	98	25
38	98	46	**165**	70	37	**291**	38	83	**350**	57	95	**426**	79	20
38	100	55	**174**	98	-24	**293**	57	89	**351**	71	103	**427**	84	49

Compd.	5-HT$_{1A}$	5-HT$_{2A}$	Compd.	5-HT$_{1A}$	5-HT$_{2A}$	Compd.	5-HT$_{1A}$	5-HT$_{2A}$	Compd.	5-HT$_{1A}$	5-HT$_{2A}$	Compd.	5-HT$_{1A}$	5-HT$_{2A}$
40	99	49	**176**	97	7	**294**	23	95	**352**	89	101	**428**	90	30
41	77	84	**195**	89	91	**295**	68	99	**353**	48	101	**429**	88	35
42	90	77	**196**	99	102	**296**	34	93	**354**	59	86	**430**	86	87
43	99	36	**209**	92	29	**297**	31	95	**355**	60	103	**431**	101	31
44	94	55	**211**	86	32	**298**	67	100	**356**	95	99	**435**	83	57
45	98	59	**225**	87	84	**299**	45	89	**357**	63	101	**436**	85	56
46	98	57	**226**	90	100	**300**	80	102	**358**	100	99	**437**	24	74
47	98	49	**227**	89	90	**301**	77	101	**359**	100	79	**438**	97	63
48	98	45	**228**	81	91	**302**	50	95	**360**	83	67	**439**	99	83
49	99	88	**229**	92	80	**303**	35	96	**361**	95	49	**440**	76	37
50	99	45	**230**	85	87	**304**	60	76	**362**	91	41	**441**	54	57
51	97	48	**232**	89	100	**305**	58	96	**363**	101	98	**442**	14	61
52	99	88	**231**	97	101	**306**	44	97	**364**	92	89	**443**	59	67
53	100	74	**233**	53	100	**307**	73	99	**365**	90	55	**444**	51	65
54	94	74	**234**	95	92	**308**	81	102	**366**	34	49	**445**	93	78
55	98	53	**235**	86	80	**309**	64	88	**367**	49	51	**446**	73	66
56	99	85	**236**	76	89	**310**	91	99	**368**	-7	64	**447**	42	19
57	99	89	**237**	51	24	**311**	49	105	**369**	62	79	**449**	57	76
58	94	51	**238**	90	95	**312**	86	99	**370**	57	65			
61	94	100	**239**	98	101	**313**	72	101	**385**	103	77			

Table 5. Results of serotoninergic receptors 5-HT6 and 5-HT7 affinity tests for representative compounds

Compd.	5-HT6	5-HT7	Compd.	5-HT6	5-HT7	Compd.	5-HT6	5-HT7	Compd.	5-HT6	5-HT7	Compd.	5-HT6	5-HT7
1	95	96	**62**	69	78	**241**	96	99	**316**	93	97	**389**	19	93
2	97	97	**63**	89	99	**242**	73	101	**317**	78	89	**390**	26	66
3	83	97	**64**	99	99	**243**	73	99	**318**	76	92	**391**	19	92
4	87	97	**65**	97	98	**244**	81	98	**319**	87	90	**392**	7	91
5	84	98	**66**	95	101	**245**	82	98	**320**	82	99	**393**	9	91
6	88	98	**69**	88	96	**246**	49	86	**321**	89	100	**394**	18	98
7	98	97	**70**	99	100	**247**	93	93	**322**	62	95	**395**	-35	83
8	91	97	**71**	76	99	**248**	98	98	**323**	92	93	**396**	31	88
9	22	98	**72**	78	101	**249**	101	100	**324**	78	78	**398**	3	97
10	37	99	**73**	82	91	**250**	73	88	**325**	72	98	**399**	23	96
11	54	99	**74**	95	97	**251**	99	99	**326**	94	94	**400**	9	95
12	80	89	**76**	70	86	**252**	93	99	**327**	99	86	**401**	27	91
13	96	100	**79**	97	97	**253**	101	99	**328**	87	92	**402**	1	100
14	99	99	**81**	98	99	**254**	76	93	**329**	97	95	**403**	-21	95
15	71	100	**85**	77	99	**255**	68	91	**330**	83	90	**404**	4	96
16	94	99	**87**	67	90	**256**	95	100	**331**	97	99	**405**	53	93
17	99	99	**89**	94	98	**257**	94	101	**332**	95	64	**406**	54	92
18	100	98	**91**	83	99	**258**	98	100	**333**	93	92	**407**	37	102

Compd.	5-HT6	5-HT7	Compd.	5-HT6	5-HT7	Compd.	5-HT6	5-HT7	Compd.	5-HT6	5-HT7	Compd.	5-HT6	5-HT7
19	69	100	**93**	92	88	**259**	74	96	**334**	98	85	**408**	35	83
20	85	101	**97**	98	93	**260**	92	100	**335**	93	88	**409**	-9	91
21	93	99	**98**	98	98	**261**	83	100	**336**	92	92	**411**	41	89
22	99	99	**101**	98	98	**262**	93	99	**337**	76	87	**414**	-15	94
23	69	96	**102**	97	97	**263**	96	98	**338**	94	98	**415**	15	92
24	76	95	**105**	87	85	**264**	63	75	**339**	89	89	**416**	55	99
25	71	98	**106**	93	91	**267**	95	100	**340**	72	90	**417**	24	62
26	51	98	**107**	75	91	**268**	93	99	**341**	93	78	**418**	5	89
27	34	92	**108**	86	90	**269**	98	101	**342**	100	96	**419**	12	86
28	98	92	**109**	84	92	**270**	70	82	**343**	77	92	**423**	16	88
29	37	91	**110**	96	91	**273**	74	97	**344**	91	95	**424**	69	95
30	5	96	**111**	95	93	**274**	81	83	**345**	91	91	**425**	5	95
31	18	87	**112**	94	95	**276**	78	87	**346**	95	87	**426**	-4	85
32	23		**113**	74	97	**282**	64	98	**347**	99	100	**427**	36	98
33	42	99	**137**	91	33	**283**	96	99	**348**	96	87	**428**	33	78
34	87	87	**138**	95	52	**288**	98	100	**349**	87	91	**429**	-57	83
35	88	88	**139**	96	56	**289**	78	91	**350**	96	87	**430**	94	84
36	81	90	**140**	92	81	**291**	83	99	**351**	89	94	**431**	35	67
37	80	89	**165**	-16	86	**293**	44	93	**352**	95	100	**435**	58	64
38	86	90	**174**	4	92	**294**	72	94	**353**	58	83	**437**	47	83
38	88	93	**176**	29	80	**295**	93	99	**354**	86	96	**438**	96	92

Compd.	5-HT6	5-HT7	Compd.	5-HT6	5-HT7	Compd.	5-HT6	5-HT7	Compd.	5-HT6	5-HT7	Compd.	5-HT6	5-HT7
40	82	92	**195**	60	98	**296**	83	91	**355**	75	84	**439**	92	78
41	89	76	**196**	92	100	**297**	87	88	**356**	78	99	**440**	86	68
42	96	76	**209**	70	85	**298**	98	100	**357**	94	99	**441**	84	82
43	83	97	**211**	32	81	**299**	84	75	**358**	70	94	**442**	87	61
44	83	97	**225**	74	92	**300**	89	99	**359**	42	95	**443**	92	54
45	90	96	**226**	78	92	**301**	94	98	**360**	67	100	**444**	87	59
46	84	97	**227**	76	94	**302**	72	101	**361**	70	86	**445**	84	98
47	83	98	**228**	87	98	**303**	90	98	**362**	69	88	**446**	96	21
48	91	98	**229**	75	89	**304**	78	93	**363**	84	98	**447**	106	34
49	93	99	**230**	85	101	**305**	78	85	**364**	80	91	**449**	93	81
50	95	95	**231**	95	99	**306**	81	89	**365**	67	95	**450**	96	50
51	94	94	**232**	76	89	**307**	76	85	**366**	98	53	**451**	97	25
52	99	98	**233**	76	93	**308**	83	99	**367**	86	23	**452**	108	41
53	98	99	**234**	62	97	**309**	79	87	**368**	96	42	**453**	107	76
54	97	95	**235**	82	93	**310**	89	89	**369**	99	7	**454**	102	68
55	98	97	**236**	67	91	**311**	99	95	**370**	88	42			
56	99	100	**237**	89	64	**312**	98	97	**385**	10	99			
57	98	102	**238**	74	88	**313**	100	100	**386**	1	82			
58	84	46	**239**	96	98	**314**	100	99	**387**	26	96			
61	96	100	**240**	98	97	**315**	98	98	**388**	-20	90			

Table 6. Results of serotonine transporter (SERT) receptor affinity tests for representative compounds

Compd.	SERT [%]	Compd.	SERT [%]	Compd.	SERT [%]	Compd.	SERT [%]	Compd.	SERT [%]	Compd.	SERT [%]
1	49	**51**	100	**196**	75	**276**	3	**336**	41	**400**	30
2	69	**52**	100	**209**	-1	**282**	12	**337**	35	**401**	-8
3	57	**53**	99	**211**	33	**283**	24	**338**	21	**402**	16
4	26	**54**	99	**225**	-4	**288**	-14	**339**	3	**403**	-9
5	84	**55**	98	**226**	4	**289**	9	**340**	9	**404**	-9
6	95	**56**	99	**227**	2	**291**	8	**341**	8	**405**	-5
7	88	**57**	100	**228**	16	**293**	3	**342**	26	**406**	10
8	63	**58**	78	**229**	9	**294**	-14	**343**	4	**407**	-2
9	29	**61**	55	**230**	13	**295**	16	**344**	31	**408**	-18
10	50	**62**	15	**231**	59	**296**	49	**345**	-10	**409**	2
11	1	**63**	53	**232**	13	**297**	23	**346**	17	**411**	12
12	7	**64**	80	**233**	5	**298**	35	**347**	33	**414**	18
13	7	**65**	57	**234**	32	**299**	14	**348**	6	**415**	-5
14	3	**66**	93	**235**	8	**300**	30	**349**	0	**416**	-4
15	-3	**69**	6	**236**	-15	**301**	45	**350**	-5	**417**	-11
16	-3	**70**	82	**237**	-7	**302**	19	**351**	31	**418**	5
17	44	**71**	41	**238**	13	**303**	9	**352**	56	**419**	-21
18	39	**72**	44	**239**	64	**304**	4	**353**	-1	**423**	25

Compd.	SERT [%]	Compd.	SERT [%]	Compd.	SERT [%]	Compd.	SERT [%]	Compd.	SERT [%]	Compd.	SERT [%]
19	8	**73**	37	**240**	46	**305**	-18	**354**	6	**424**	-3
20	85	**74**	79	**241**	50	**306**	-10	**355**	45	**425**	10
21	46	**76**	15	**242**	12	**307**	-3	**356**	11	**426**	-18
22	44	**79**	3	**243**	63	**308**	28	**357**	41	**427**	13
23	68	**81**	28	**244**	19	**309**	-5	**358**	40	**428**	23
24	53	**85**	2	**245**	38	**310**	57	**359**	33	**429**	22
25	20	**87**	2	**246**	31	**311**	34	**360**	8	**430**	19
26	14	**89**	2	**247**	14	**312**	35	**361**	6	**431**	12
27	-3	**91**	2	**248**	80	**313**	23	**362**	37	**435**	81
28	53	**93**	0	**249**	77	**314**	50	**363**	32	**437**	105
29	12	**97**	61	**250**	23	**315**	68	**364**	35	**438**	97
30	14	**98**	54	**251**	87	**316**	47	**365**	25	**439**	93
31	-2	**101**	47	**252**	94	**317**	-17	**366**	8	**440**	70
33	-4	**102**	38	**253**	79	**318**	45	**367**	4	**441**	1
34	101	**105**	-11	**254**	9	**319**	8	**368**	14	**442**	4
35	99	**106**	2	**255**	29	**320**	13	**369**	29	**443**	-9
36	101	**107**	-12	**256**	93	**321**	61	**370**	30	**444**	44
37	101	**108**	-9	**257**	93	**322**	16	**385**	6	**445**	68
38	101	**109**	15	**258**	80	**323**	41	**386**	-5	**446**	20
38	101	**110**	8	**259**	16	**324**	37	**387**	-14	**447**	23

Compd.	SERT [%]	Compd.	SERT [%]	Compd.	SERT [%]	Compd.	SERT [%]	Compd.	SERT [%]	Compd.	SERT [%]
40	101	111	-14	260	90	325	20	388	-28	449	21
41	94	112	-17	261	60	326	19	389	44	450	54
42	96	113	28	262	87	327	-1	390	-15	451	32
43	100	137	38	263	87	328	7	391	-28	452	18
44	100	138	25	264	-18	329	-2	392	-11	453	23
45	98	139	17	267	91	330	-2	393	-7	454	14
46	102	140	14	268	86	331	31	394	12		
47	101	165	4	269	96	332	18	395	69		
48	101	174	11	270	12	333	5	396	16		
49	101	176	-3	273	22	334	30	398	-7		
50	98	195	-3	274	30	335	-25	399	-22		

Table 7. Results of sigma σ receptor affinity tests for representative compounds

Compd.	σ [%]	Compd.	σ [%]	Compd.	σ [%]	Compd.	σ [%]	Compd.	σ [%]	Compd.	σ [%]]
1	54	22	92	47	53	89	-1	257	57	320	80
2	65	23	82	48	67	97	55	258	61	321	74
3	66	24	80	49	61	98	50	260	41	325	85
4	1	25	76	50	61	101	70	261	57	331	79
5	72	26	99	51	55	102	74	262	51	338	72
6	59	27	78	52	80	113	92	263	49	347	57
7	61	28	84	53	79	174	-16	267	50	352	76
8	17	29	93	54	66	176	-25	268	30	356	70
9	23	30	42	55	79	196	66	269	49	357	64
10	31	33	94	56	78	231	62	283	34	358	84
11	21	34	51	57	75	239	69	288	45	359	85
12	4	35	42	58	34	240	44	295	63	363	96
13	87	36	57	61	46	241	51	298	68	418	6
14	40	37	66	63	54	243	29	300	83	419	-14
15	47	38	46	64	54	245	52	301	73	423	9
16	2	38	57	65	62	248	64	308	86	424	-3
17	83	40	68	66	61	249	68	312	71	425	-3
18	70	43	58	70	64	251	61	313	83	438	79
19	92	44	45	74	34	252	59	314	49	439	80
20	81	45	74	79	37	253	64	315	72	445	67
21	82	46	79	81	59	256	41	316	81		

Table 8. Results of adrenergic α1 receptor affinity tests for representative compounds

Compd.	α1 [%]	Compd.	α1 [%]	Compd.	α1 [%]	Compd.	α1 [%]	Compd.	α1 [%]	Compd.	α1 [%]
1	99	**52**	57	**196**	93	**282**	102	**338**	99	**402**	94
2	97	**53**	61	**209**	90	**283**	92	**339**	108	**403**	98
3	100	**54**	43	**211**	80	**288**	94	**340**	110	**404**	93
4	96	**55**	46	**225**	94	**289**	100	**341**	108	**405**	82
5	98	**56**	61	**226**	94	**291**	99	**342**	103	**406**	77
6	95	**57**	65	**227**	92	**293**	98	**343**	86	**407**	72
7	98	**58**	76	**228**	92	**294**	101	**344**	106	**408**	70
8	94	**61**	94	**229**	96	**295**	96	**345**	102	**409**	81
9	74	**62**	61	**230**	98	**296**	101	**346**	103	**410**	84
10	79	**63**	99	**231**	96	**297**	100	**347**	99	**411**	87
11	85	**64**	93	**232**	94	**298**	103	**348**	90	**413**	90
12	67	**65**	95	**233**	94	**299**	98	**349**	98	**414**	88
13	102	**66**	93	**234**	91	**300**	96	**350**	102	**415**	78
14	102	**69**	94	**235**	95	**301**	96	**351**	97	**416**	81
15	102	**70**	96	**236**	92	**302**	100	**352**	99	**417**	73
16	101	**71**	99	**237**	87	**303**	97	**353**	103	**418**	98
17	100	**72**	93	**238**	103	**304**	101	**354**	103	**419**	86
18	101	**73**	98	**239**	99	**305**	99	**355**	105	**420**	82

Compd.	α1 [%]	Compd.	α1 [%]	Compd.	α1 [%]	Compd.	α1 [%]	Compd.	α1 [%]	Compd.	α1 [%]
19	99	74	94	240	96	306	99	356	101	421	88
20	99	76	95	241	93	307	105	357	99	422	86
21	97	79	88	242	98	308	91	358	88	423	91
22	100	81	96	243	97	309	103	359	97	424	93
23	97	85	98	244	98	310	107	360	93	425	93
24	97	87	98	245	96	311	107	361	98	426	67
25	98	89	98	246	99	312	100	362	96	427	86
26	98	91	99	247	98	313	100	363	92	428	72
27	96	93	97	248	91	314	100	364	87	429	78
28	92	97	98	249	99	315	-13	365	100	430	46
29	99	98	97	250	95	316	90	366	8	431	88
30	96	101	99	251	95	317	99	367	9	435	48
31	101	102	99	252	27	318	98	368	34	437	52
33	100	105	96	253	97	319	94	369	50	438	44
34	81	106	101	254	96	320	98	370	38	439	27
35	70	107	100	255	92	321	98	385	96	440	14
36	84	108	100	256	87	322	103	386	96	441	16
37	82	109	101	257	94	323	103	387	86	442	1
38	77	110	103	258	97	324	103	388	91	443	41
38	84	111	100	259	88	325	95	389	93	444	26

Compd.	α1 [%]	Compd.	α1 [%]	Compd.	α1 [%]	Compd.	α1 [%]	Compd.	α1 [%]	Compd.	α1 [%]
40	86	112	99	260	91	326	101	390	73	445	50
41	87	113	99	261	-90	327	109	391	90	446	29
42	77	137	10	262	95	328	101	392	99	447	1
43	70	138	8	263	90	329	102	393	91	449	12
44	54	139	20	264	53	330	102	394	92	450	-1
45	84	140	17	267	97	331	101	395	92	451	-4
46	78	165	47	268	90	332	107	396	84	452	14
47	68	173	89	269	97	333	106	397	92	453	23
48	71	174	86	270	88	334	105	398	97	454	7
49	84	175	82	273	101	335	101	399	99		
50	50	176	77	274	99	336	107	400	94		
51	40	195	96	276	95	337	93	401	90		

Table 9: Results of adrenergic α2C receptor affinity tests for representative compounds

Compd.	α2C [%]	Compd.	α2C [%]	Compd.	α2C [%]	Compd.	α2C [%]
1	100	35	96	97	100	298	98
2	101	36	92	98	108	300	94
3	99	37	93	101	106	301	98
4	96	38	93	102	101	308	96
5	99	39	98	113	99	312	92
6	93	40	97	174	55	313	100
7	96	43	94	176	44	314	108
8	93	44	86	196	95	315	93
9	98	45	88	231	99	316	94
10	98	46	87	239	105	320	101
11	94	47	92	240	100	321	100
12	83	48	88	241	98	325	93
13	99	49	86	243	96	331	104
14	100	50	97	245	101	338	104
15	98	51	94	248	93	347	110
16	101	52	88	249	98	352	100
17	100	53	87	251	96	356	96
18	100	54	91	252	95	357	94
19	100	55	82	253	102	358	101
20	99	56	90	256	92	359	99
21	98	57	78	257	99	363	101
22	100	58	80	258	98	418	94
23	99	61	101	260	99	419	93
24	99	63	98	261	92	423	69
25	98	64	100	262	94	424	67
26	100	65	104	263	93	425	59
27	100	66	103	267	99	438	94
28	92	70	100	268	99	439	68
29	98	74	92	269	101	445	69
30	99	79	106	283	109		
33	100	81	106	288	109		
34	98	89	98	295	97		

Table 10: Results of histaminergic H1 receptor affinity tests for representative compounds

Compd.	H1 [%]	Compd.	H1 [%]	Compd.	H1 [%]	Compd.	H1 [%]
1	91	**35**	51	**97**	91	**298**	90
2	94	**36**	66	**98**	100	**300**	87
3	94	**37**	56	**101**	97	**301**	88
4	100	**38**	67	**102**	94	**308**	92
5	92	**39**	69	**113**	60	**312**	86
6	93	**40**	56	**174**	25	**313**	90
7	93	**43**	41	**176**	8	**314**	93
8	97	**44**	41	**196**	93	**315**	90
9	77	**45**	62	**231**	97	**316**	85
10	81	**46**	60	**239**	98	**320**	84
11	74	**47**	56	**240**	92	**321**	95
12	79	**48**	57	**241**	97	**325**	83
13	84	**49**	74	**243**	93	**331**	97
14	88	**50**	10	**245**	98	**338**	95
15	84	**51**	17	**248**	97	**347**	98
16	97	**52**	45	**249**	97	**352**	97
17	80	**53**	38	**251**	-220	**356**	80
18	79	**54**	28	**252**	-77	**357**	84
19	79	**55**	18	**253**	98	**358**	74
20	78	**56**	96	**256**	94	**359**	60
21	90	**57**	35	**257**	91	**363**	70
22	88	**58**	75	**258**	97	**418**	55
23	67	**61**	97	**260**	95	**419**	12
24	56	**63**	99	**261**	92	**423**	16
25	62	**64**	98	**262**	95	**424**	28
26	52	**65**	95	**263**	93	**425**	6
27	27	**66**	99	**267**	92	**438**	67
28	57	**70**	97	**268**	95	**439**	18
29	74	**74**	90	**269**	92	**445**	60
30	40	**79**	96	**283**	96		
33	56	**81**	93	**288**	94		
34	67	**89**	85	**295**	95		

Table 11: Results of muscarinic M3 receptor affinity tests for representative compounds

Compd.	M3 [%]	Compd.	M3 [%]	Compd.	M3 [%]	Compd.	M3 [%]
1	13	35	4	97	16	298	19
2	17	36	-3	98	16	300	18
3	13	37	11	101	14	301	18
4	3	38	9	102	18	308	30
5	7	39	11	113	29	312	19
6	-1	40	10	174	15	313	25
7	13	43	-7	176	6	314	13
8	-11	44	11	196	18	315	24
9	-2	45	9	231	11	316	28
10	-2	46	8	239	9	320	24
11	-6	47	3	240	15	321	14
12	-9	48	8	241	4	325	26
13	-1	49	10	243	10	331	10
14	-6	50	10	245	25	338	1
15	-9	51	1	248	13	347	12
16	-1	52	5	249	9	352	12
17	7	53	8	251	8	356	2
18	6	54	8	252	16	357	25
19	9	55	8	253	24	358	17
20	-9	56	3	256	15	359	63
21	2	57	10	257	12	363	15
22	12	58	11	258	15	418	4
23	-2	61	5	260	11	419	-8
24	10	63	11	261	15	423	-1
25	6	64	7	262	19	424	7
26	17	65	8	263	7	425	2
27	46	66	10	267	13	438	15
28	50	70	25	268	14	439	16
29	25	74	17	269	20	445	27
30	66	79	12	283	-4		
33	5	81	6	288	3		
34	9	89	22	295	19		

Table 12: Results of serotoninergic 5-HT2C receptor affinity tests for representative compounds

Cpd.	5-HT2C [%]	Cpd.	5-HT2C [%]	Cpd.	5-HT2C [%]	Cpd.	5-HT2C [%]
1	80	35	30	97	89	298	52
2	89	36	34	98	91	300	49
3	77	37	35	101	80	301	79
4	91	38	31	102	76	308	57
5	81	39	50	113	10	312	80
6	88	40	50	174	0	313	59
7	89	43	67	176	9	314	85
8	90	44	56	196	89	315	78
9	24	45	70	231	87	316	66
10	54	46	73	239	88	320	46
11	40	47	60	240	78	321	65
12	17	48	64	241	96	325	49
13	34	49	92	243	81	331	82
14	51	50	18	245	72	338	76
15	23	51	14	248	84	347	99
16	53	52	36	249	89	352	78
17	62	53	28	251	83	356	83
18	73	54	24	252	84	357	83
19	56	55	26	253	89	358	62
20	75	56	50	256	94	359	12
21	87	57	58	257	83	363	57
22	73	58	21	258	86	418	19
23	44	61	95	260	90	419	7
24	65	63	95	261	87	423	9
25	32	64	v	262	84	424	8
26	19	65	95	263	87	425	24
27	-1	66	86	267	78	438	59
28	6	70	88	268	78	439	41
29	11	74	78	269	92	445	67
30	11	79	72	283	80		
33	27	81	50	288	32		
34	51	89	34	295	51		

Example 5.

In Vitro Pharmacology: Cellular Functional Assays

The results are expressed as a percent of control specific agonist response ((measured specific response/control specific agonist response) x 100) for agonist effect and as a percent inhibition of control specific agonist response (100 - ((measured specific response/control specific agonist response) x 100)) for antagonist effect obtained in the presence of the test compounds. The compounds were tested at the concentration of 1×10^{-6} M.

Conditions and methodology (by reference to the literature) of cellular functional assays are given in Table 13 and the tests results for representative compounds are given in Table 14 (dopaminergic receptor D2), in Table 15 (dopaminergic receptor D3), in Table 16 (serotoninergic receptor 5-HT1A), in Table 17 (serotoninergic receptor 5-HT2A), in Table 18 (serotoninergic receptor 5-HT6), in Table 19 (serotoninergic receptor 5-HT7), in Table 20 (adrenergic α1 receptor), in Table 21 (adrenergic α2C receptor), in Table 22 (histaminergic H1 receptor) and in Table 23 (serotoninergic 5-HT2C receptor). In the Tables ag refers to agonism, and antag to antagonism).

Table 13 : Conditions and methodology of *in vitro* tests for cellular functional assays

Assay	Origin	Stimulus	Incubation	Reaction Product	Method of Detection	Ref.
M3 *(h)* (agonist effect)	human recombinant (CHO cells)	none (1 µM acetylcholine for control)	22°C	intracellular $[Ca^{2+}]$	Fluorimetry	14
M3 *(h)* (antagonist effect)	human recombinant (CHO cells)	acetylcholine (10 nM)	22°C	intracellular $[Ca^{2+}]$	Fluorimetry	14
5-HT7 (h) (agonist effect)	human recombinant (CHO cells)	none (10 µM serotonin for control)	45 min 37°C	cAMP	HTRF	15
5-HT7 (h) (antagonist effect)	human recombinant (CHO cells)	serotonin (300 nM)	45 min 37°C	cAMP	HTRF	15
5-HT6 (h) (agonist effect)	human recombinant (CHO cells)	none (10 µM serotonin for control)	45 min 37°C	cAMP	HTRF	16
5-HT6 (h) (antagonist effect)	human recombinant (CHO cells)	serotonin (100 nM)	45 min 37°C	cAMP	HTRF	16
D2S (h) (agonist effect)	human recombinant (HEK-293 cells)	none (3 µM dopamine for control)	28°C	impedance	cellular dielectric spectroscopy	17
D2S (h) (antagonist effect)	human recombinant (HEK-293 cells)	dopamine (30 nM)	28°C	impedance	cellular dielectric spectroscopy	17
5-HT2C (h) (agonist effect)	human recombinant (HEK-293 cells)	none (1 µM serotonin for control)	30 min 37°C	IP1	HTRF	18
5-HT2C (h) (antagonist effect)	human recombinant (HEK-293 cells)	serotonin (10 nM)	30 min 37°C	IP1	HTRF	18
H1 (h) (agonist effect)	human recombinant (HEK-293 cells)	none (10 µM histamine for control)	22°C	intracellular [Ca2+]	Fluorimetry	19
H1 (h) (antagonist effect)	human recombinant (HEK-293 cells)	histamine (300 nM)	22°C	intracellular [Ca2+]	Fluorimetry	19
α_{1A} (h) (agonist effect)	human recombinant (CHO cells)	none (30 nM epinephrine for control)	22°C	intracellular [Ca2+]	Fluorimetry	20

Assay	Origin	Stimulus	Incubation	Reaction Product	Method of Detection	Ref.
α1A (h) (antagonist effect)	human recombinant (CHO cells)	epinephrine (3 nM)	22 °C	intracellular [Ca2+]	Fluorimetry	20
5-HT2A (h) (agonist effect)	human recombinant (HEK-293 cells)	none (100 nM serotonin for control)	30 min 37 °C	IP1	HTRF	18
5-HT2A (h) (antagonist effect)	human recombinant (HEK-293 cells)	serotonin (100 nM)	30 min 37 °C	IP1	HTRF	18
D3 (h) (agonist effect)	human recombinant (CHO cells)	none (300 nM dopamine for control)	10 min 37 °C	cAMP	HTRF	21
D3 (h) (antagonist effect)	human recombinant (CHO cells)	dopamine (10 nM)	10 min 37 °C	cAMP	HTRF	21
5-HT1A (h) (agonist effect)	human recombinant (CHO cells)	none (100 nM 8-OH-DPAT for control)	15 min 22 °C	cAMP	HTRF	22
5-HT1A (h) (antagonist effect)	human recombinant (CHO cells)	8-OH-DPAT (10 nM)	15 min 22 °C	cAMP	HTRF	22
α2C (h) (agonist effect)	human recombinant (CHO cells)	none (1 µM epinephrine for control)	10 min 37 °C	cAMP	HTRF	23
α2C (h) (antagonist effect)	human recombinant (CHO cells)	epinephrine (100 nM)	10 min 37 °C	cAMP	HTRF	23

Table 14: Results of cellular functional assays for dopaminergic D2 receptor for representative compounds

Cpd.	D2-ag [%]	D2-antag. [%]	Cpd.	D2-ag [%]	D2-antag. [%]	Cpd.	D2-ag [%]	D2-antag. [%]	Cpd.	D2-ag [%]	D2-antag. [%]
1	-1	95	**33**	37	98	**51**	10	37	**288**	5	79
2	2	97	**34**	21	66	**53**	5	60	**298**	12	84
7	0	91	**35**	27	65	**56**	42	106	**312**	4	90
8	7	85	**36**	28	92	**57**	10	100	**313**	-5	85
13	2	95	**37**	21	82	**61**	4	77	**314**	9	86
14	4	98	**38**	31	84	**65**	10	74	**331**	4	87
15	2	88	**39**	30	90	**79**	3	77	**338**	3	88
16	4	98	**40**	36	94	**81**	4	73	**352**	12	88
18	-1	98	**43**	20	55	**97**	4	95	**358**	30	84
22	2	99	**44**	16	45	**98**	4	80	**359**	39	96
26	29	99	**45**	20	82	**101**	6	85	**363**	50	94
27	40	100	**46**	23	80	**102**	1	85	**423**	41	96
28	49	105	**47**	26	66	**113**	42	94	**424**	44	97
29	45	99	**48**	22	53	**239**	13	84	**452**	24	53
30	43	97	**49**	11	100	**240**	3	83			
32	35	89	**50**	15	26	**241**	6	82			

Table 15: Results of cellular functional assays for dopaminergic D3 receptor for representative compounds

Compd.	D3-ag [%]	D3-antag. [%]	Compd.	D3-ag [%]	D3-antag. [%]	Compd.	D3-ag [%]	D3-antag. [%]
1	-17	49	**49**	-3	71	**283**	-10	58
2	-15	81	**53**	5	48	**288**	0	72
7	-21	66	**56**	34	45	**298**	-8	99
8	-24	73	**57**	24	41	**312**	10	97
14	-15	92	**61**	4	45	**313**	8	81
18	-27	114	**79**	-9	77	**314**	-30	110
22	-25	81	**81**	-10	76	**331**	-15	114
26	64	-8	**89**	-18	69	**338**	-10	109
28	59	-2	**97**	-23	87	**352**	-18	113
30	52	35	**98**	-10	109	**358**	47	35
33	60	-1	**101**	-18	112	**359**	25	79
36	29	53	**102**	4	83	**363**	65	-3
40	33	59	**113**	39	30	**423**	70	22
45	18		**239**	6	84	**424**	70	18
46	18	48	**240**	8	72			
48	14	54	**241**	7	78			

Table 16: Results of cellular functional assays for serotoninergic 5-HT1A receptor for representative compounds

Compd.	5-HT1A -ag [%]	5-HT1A - antag. [%]	Compd.	5-HT1A -ag [%]	5-HT1A - antag. [%]	Compd.	5-HT1A -ag [%]	5-HT1A - antag. [%]
2	47	18	**38**	94	-33	**61**	75	20
7	59	51	**39**	86	-25	**65**	9	35
8	14	81	**40**	102	-37	**81**	5	22
16	-14	91	**43**	87	-27	**97**	13	38
22	0	99	**44**	90	-29	**102**	1	35
26	67	22	**45**	99	-27	**113**	32	92
27	56	48	**46**	92	-20	**239**	7	58
28	63	27	**47**	90	-31	**240**	9	50
29	71	26	**48**	90	-24	**241**	5	42
30	22	86	**49**	82	7	**358**	22	70
33	63	24	**50**	98	-34	**359**	22	94
34	97	-31	**51**	86	-27	**363**	78	27
35	102	-37	**53**	90	-6	**423**	35	73
36	99	-33	**56**	92	-6	**424**	23	75
37	92	-28	**57**	92	-8	**452**	30	7

Table 17: Results of cellular functional assays for serotoninergic 5-HT2A receptor for representative compounds

Compd.	5-HT2A -ag [%]	5-HT2A -antag. [%]	Compd.	5-HT2A -ag [%]	5-HT2A -antag. [%]
1	0	99	**98**	-2	97
2	2	102	**101**	-1	100
7	0	100	**102**	-2	99
8	-2	99	**239**	-2	94
13	2	100	**240**	-3	93
14	1	100	**241**	-2	99
15	-1	100	**283**	0	99
16	-1	98	**288**	-2	97
18	-1	102	**298**	-1	99
22	-1	102	**312**	-2	98
26	-1	77	**313**	-3	98
33	-1	41	**314**	-2	99
61	0	97	**331**	-1	98
65	-2	98	**338**	-1	100
79	-2	97	**352**	-1	100
81	-1	95	**358**	-1	57
89	-2	94	**363**	-1	62
97	-3	102			

Table 18: Results of cellular functional assays for serotoninergic 5-HT6 receptor for representative compounds

Cpd.	5-HT6 -ag [%]	5-HT6 -antag. [%]	Cpd.	5-HT6 -ag [%]	5-HT6 -antag. [%]	Cpd.	5-HT6 -ag [%]	5-HT6 -antag. [%]
1	1	39	**19**	-1	23	**97**	-2	95
2	2	28	**20**	-2	23	**98**	-2	79
3		22	**21**	-2	39	**101**	-2	103
4	-1	37	**22**	1	82	**102**	-1	82
5		18	**23**	0	1	**239**	0	70
6		26	**24**	2	9	**240**	-2	71
7	1	65	**25**	0	6	**241**	0	69
8	-1	64	**28**	0	53	**283**	0	64
9	0	-4	**36**	1	7	**288**	0	74
10	1	-16	**49**	2	71	**298**	0	89
11	-1	-10	**53**	1	87	**312**	-1	76
12	-1	-2	**56**	2	92	**313**	-3	91
13	1	56	**57**	3	86	**314**	0	91
14	1	69	**61**	-2	72	**331**	-1	98
15	2	21	**65**	-1	81	**338**	0	88
16	0	50	**79**	1	76	**352**	-2	75
17	2	69	**81**	1	88			
18	1	87	**89**	0	83			

Table 19: Results of cellular functional assays for serotoninergic 5-HT7 receptor for representative compounds

Cpd.	5-HT7-ag [%]	5-HT7-antag. [%]	Cpd.	5-HT7-ag [%]	5-HT7-antag. [%]	Cpd.	5-HT7-ag [%]	5-HT7-antag. [%]	Cpd.	5-HT7-ag [%]	5-HT7-antag. [%]
1	-1	97	**17**		95	**40**	-1	30	**240**	-2	98
2	-1	80	**18**	-1	89	**49**	-1	85	**241**	-2	83
3	-2	93	**19**	-1	99	**53**	1	25	**283**	-2	93
4	-1	81	**20**	-1	101	**56**	1	36	**288**	-2	92
5	-1	85	**21**	0	98	**57**	1	91	**298**	-3	98
6	0	66	**22**	-1	100	**61**	-1	78	**312**	-2	97
7	-1	98	**23**	0	88	**65**	-2	91	**313**	-2	100
8	-1	82	**24**	0	99	**79**	-2	97	**314**	-3	95
9	0	48	**25**	-1	97	**81**	-2	98	**331**	-2	102
10	0	85	**26**	14	13	**89**	-2	91	**338**	-3	100
11	0	85	**27**	5	8	**97**	-2	100	**352**	-2	102
12	-1	68	**28**	4	23	**98**	-2	92	**358**	10	28
13	1	95	**29**	5	9	**101**	-2	101	**359**	8	43
14	-1	85	**30**	5	73	**102**	-2	94	**363**	6	24
15	0	96	**33**	19	20	**113**	9	45	**424**	18	43
16	-1	80	**36**	0	16	**239**	-2	81			

Table 20: Results of cellular functional assays for adrenergic α1A receptor for representative compounds

Compd.	α1A -ag [%]	α1A -antag. [%]	Compd.	α1A -ag [%]	α1A -antag. [%]
1	0	100	101	0	100
2	0	100	102	0	100
7	0	100	113	1	100
8	0	100	239	-1	100
13	0	100	240	0	100
14	0	100	241	0	95
16	0	100	283	0	100
18	0	99	288	0	97
22	0	100	298	1	100
26	0	100	312	0	100
27	1	100	313	0	100
30	0	97	314	1	100
33	0	100	331	1	100
61	0	100	338	2	100
65	0	98	352	1	100
81	1	100	359	1	100
89	-1	100	363	0	100
97	0	99	423	16	70
98	0	99	424	39	76

Table 21: Results of cellular functional assays for adrenergic α2C receptor for representative compounds

Compd.	α2C -ag [%]	α2C -antag. [%]	Compd.	α2C -ag [%]	α2C -antag. [%]
1	-9	7	**89**	-10	7
2	-8	30	**97**	-4	36
7	-6	2	**98**	-1	16
8	-16	1	**101**	1	46
13	-7	18	**102**	-7	14
14	-3	12	**113**	13	53
16	-7	9	**239**	3	33
18	-10	28	**240**	13	35
22	-8	12	**241**	-1	14
26	25	53	**283**	2	25
27	3	31	**288**	1	13
28	4	27	**298**	-4	39
30	18	35	**312**	61	39
33	-1	6	**313**	-11	46
36	-2	4	**314**	-2	30
40	-9	9	**331**	-14	7
56	20	4	**338**	-3	9
61	1	18	**352**	-16	16
65	8	20	**358**	28	48
79	7	22	**359**	13	38
81	9	20	**363**	17	42

Table 22: Results of cellular functional assays for histaminergic H1 receptor for representative compounds

Cpd.	H1 -ag [%]	H1 -antag. [%]	Cpd.	H1 -ag [%]	H1 -antag. [%]
1	0	51	**102**	0	48
2	-1	48	**239**	0	54
7	1	70	**240**	0	69
8	1	98	**241**	1	47
56	0	68	**283**	0	41
61	1	76	**288**	0	57
65	0	60	**298**	30	90
79	0	57	**313**	4	47
81	1	38	**314**	5	50
97	3	57	**331**	2	85
98	-1	78	**338**	1	51
101	33	94	**352**	1	60

Table 23: Results of cellular functional assays for serotoninergic 5-HT2C receptor for representative compounds

Cpd.	5-HT2C -ag [%]	5-HT2C -antag. [%]
65	0	18
98	-5	35
241	-4	52

Example 6

Ability to block hERG potassium channels was determined using the electrophysiological method and cloned hERG potassium channels (KCNH2 gene, expressed in CHO cells) as biological material. The effects were evaluated using IonWorksTM Quattro system (MDS-AT).

hERG Test Procedures

hERG current was elicited using a pulse pattern with fixed amplitudes (conditioning pre-pulse: -80 mV for 25 ms; test pulse: +40 mV for 80 ms) from a holding potential of 0 mV. hERG current was measured as a difference between the peak current at 1 ms after the test step to +40 mV and the steady-state current at the end of the step to +40 mV.

Data Analysis

Data acquisition and analyses was performed using the IonWorks QuattroTM system operation software (version 2.0.2; Molecular Devices Corporation, Union City, CA). Data were corrected for leak current.

The hERG block was calculated as: % Block = (1 - I TA / IControl) x 100%, where IControl and ITA were the currents elicited by the test pulse in control and in the presence of a test compound, respectively. Results are presented in Table 24.

Table 24: Results of hERG potassium channels affinity tests for representative compounds

Cpd.	hERG [%]	Cpd.	hERG [%]	Cpd.	hERG [%]	Cpd.	hERG [%]
1	16	**18**	30	**56**	9	**358**	0
2	14	**22**	52	**57**	0	**359**	9
3	17	**30**	-3	**61**	12	**360**	5
5	17	**31**	2	**97**	1	**363**	0
6	13	**36**	2.4	**101**	14	**445**	2
7	14	**50**	6	**113**	16		
14	-1.4	**53**	12	**331**	32		
17	24	**55**	8	**338**	40.5		

Example 7

Guinea-pig ileum test

Ileum was prepared from male guinea-pigs with 300-350 g of body weight, fasted for 24 h before experiment with free access to drinking water. Terminal ileum was dissected and placed into a Krebs solution (NaCl 120 mM, KCl 5.6 mM, $MgCl_2$ 2.2 mM, $CaCl_2$ 2.4 mM, $NaHCO_3$ 19 mM, glucose 10 mM) and 2 cm-long fragments were cut. Each segment of the gut was placed in 30 ml chamber filled with the Krebs solution at 37 C, pH 7.4, with constant oxygenation (O_2/CO_2, 19:1), fixed by the lower end to a glass rod and by the upper end to the force-displacement transducer FDT 10-A (Biopac Systems,

COMMAT, Ltd., Turkey). The preparation was allowed to stabilize in organ baths for 60 min under a resting tension of 0.5 g, washing every 15 min with fresh Krebs solution. All responses were recorded using software Biopac Systems Inc MP-35 Data Acquisition, Turkey.

Stock solutions of test and reference compounds were prepared in concentration 10^{-3} M. About 1 mg of each tested compound was weighed and dissolved in appropriate volume of dimethyl sulfoxide, ethanol or water or in a mixture of them (depending on the solubility). In next step, stock solutions were diluted 10x in water.

The equilibration period a cumulative concentration-response curve was constructed in each tissue for respective agonist - carbachol ($3x10^{-9}$ - $3x10^{-6}$ M) or histamine (10^{-8} - 10^{-5} M) by the method of van Rossum (Ref. 24). Following the first agonist curve, tissues were incubated with one of the concentrations of tested compounds for 15 min and the next cumulative concentration curve to agonist was obtained. Only one concentration of the antagonist was tested in each piece of tissue. Experiments were repeated three to eight times.

After the equilibration period a cumulative concentration-response curve was constructed in each tissue for histamine (10^{-8} - 10^{-5} M) by the method of van Rossum. Following the first histamine curve, tissues were incubated with one of the concentrations of tested compounds for 15 min and the next cumulative concentration curve to histamine was obtained. Only one concentration of the antagonist was tested in each piece of tissue. Experiments were repeated three to seven times.

Concentration-response curves were analysed using GraphPad Prism 4.0 (GraphPad Software Inc., San Diego, CA, USA). Contractile responses to carbachol (in the presence or absence of tested compounds) are expressed as a percentage of maximal carbachol effect (Emax = 100%), reached in the concentration-response curves obtained before incubation with the tested compounds. The data are expressed as the mean ± SEM of at least four separate experiments. The affinity was estimated with the equation pKB = log(concentration ratio-1)-log(molar antagonist concentration), where the concentration ratio is the ratio of equieffective agonist concentrations in the absence and in the presence of the antagonist.

Table 25: Results of Guinea-pig ileum test for representative compounds

Compound	M ant *(pKb)	H ant** (pKb)
1	5.102	6.303
2	5.54	6.34
3	4.74	6.83

* antagonistic activity towards muscarinic receptor

** antagonistic activity towards histaminergic receptor

Results of in vitro tests as described in Examples 4-7 show that compounds of the invention display high affinity for dopamine and serotonin receptors, especially D2, D3, 5-HT1A, 5-HT2A, 5-HT6 and 5-HT7 subtypes, adrenergic alpha2C and alpha1A as well as sigma receptors and serotonin transporter. Most of the tested compounds possess antagonistic profile for all of the receptors they have affinity for, with some of them showing partially agonistic properties for D2 and/or D3 receptors as well as fully or partially agonistic activity towards 5-HT1A receptors. This confirms their potential usefulness in the treatment of diseases connected with disturbances in dopaminergic, serotoninergic and noradrenergic transmission, e.g. psychoses, depression as well as anxiety disorders etc. It should be stressed that some of the compounds possess parallel (simultaneous) affinity for D2, 5-HT6 and 5-HT7 receptors, displaying efficient antagonistic properties for all of them, which particularly differentiates them from the compounds currently used for treatment of abovementioned diseases. Such a pharmacological profile suggests possible efficacy in the treatment of psychoses as well as precognitive and antidepressant activity. In the same time compounds of the invention possess weak affinity for potassium hERG channel and muscarine receptors as well as moderate affinity for H1 and 5-HT2C receptors, what may potentially contribute to reduced side effects such as, arrhythmia, vegetative disorders, weight gain and metabolic disorders, which are frequently caused by many of the currently used drugs for treatment of the abovementioned diseases.

Tests *In vivo*

Example 8

Activity testing in mice

Male CD-1 mice weighing 20-22 g derived from accredited animal facility localized at Medical College of Jagiellonian University, male C57BL/6J mice weighing 20-21 g and male Swiss Albino mice weighing 21-22 g derived from the licensed dealer (Staniszewska; Ilkowice, Poland) were group-housed for 3-4 day period in polycarbonate

Makrolon type 3 cages (dimensions 26.5 x 15 x 42 cm) in an environmentally controlled, experimental room (ambient temperature 22 - 20C ; relative humidity 50-60%; 12:12 light:dark cycle, lights on at 8:00), in groups of 15. Male Wistar rats weighing 205-225 g upon arrival from accredited animal facility Charles River (Sulzfeld, Germany) were group-housed for 6 day period in polycarbonate Makrolon type 3 cages (dimensions 26.5 x 15 x 42 cm) in an environmentally controlled room (ambient temperature 20-22°C; relative humidity 50-60%; 12:12 light:dark cycle, lights on at 8:00), in groups of 4. Standard laboratory food (LSM-B) and filtered water were freely available. Standard laboratory food (Ssniff M-Z) and filtered water were freely available. On the day before experiments the equipment produces “white noise” was turned on for 30 minutes and mice or rats were weighted exact to 1 g. Animals were assigned randomly to treatment groups. All the experiments were performed by two observers unaware of the treatment applied between 9:00 and 14:00 on separate groups of animals. All animals were used only once and were killed immediately after the experiment. All the experimental procedures were approved by the IV Local Bioethics Commission in Warszawa.

d-Amphetamine-induced locomotor hyperactivity

The locomotor activity was recorded with an Opto M3 multi-channel activity monitor (MultiDevice Software v.1.3, Columbus Instruments). The mice were individually placed in plastic cages (22 x 12 x 13 cm) for 30 minutes habituation period, and then the crossings of each channel (ambulation) were counted during 1 h with data recording every 5 minutes. The cages were cleaned up with 70% ethanol after each mouse. Drugs were administered to 10 mice per treatment group. d-Amphetamine was administered 30 minutes before the test. Compound 22 was given 30 minutes before the experiment, and other compounds were given 60 minutes before the experiment.

Table 26: Results of d-amphetamine-induced locomotor hyperactivity test

Compound	MED* [mg/kg]
2	5
7	2
18	2.5
22	2.5
97	2.5

* minimum effective dose [mg of compound/ kg of body weight]

MK-801-induced locomotor hyperactivity

The locomotor activity was recorded according to method described above. Instead of d-Amphetamine, MK-801 was administered 15 min before the test. Compound 22 was given 30 minutes before the experiment.

Table 27: Results of MK-801-induced locomotor hyperactivity test

Compound	MED* [mg/kg]
22	1.25

Tail suspension test in C57BL/6J mice

The testing procedure was based on a method of Steru et al. (The tail suspension test: a new method for screening antidepressants in mice, Psychopharmacology 85, 367-370, 1985). An automated device (Kinder Scientific) was used. Mice were suspended by the tail with tape to an aluminum hook connected to a strain gauge. Mice were positioned such that the base of their tail was aligned with the bottom of the hook. This positioning was found to decrease the propensity for mice to climb their tail during the test. A strain gauge connected to computer software detected any movements by the mouse in order to record the number of times (events) each subject enters into an escape behavior (struggling episodes), the duration of the event, and the average strength of each event during a 6-min test session. The total duration of immobility was calculated as the time the force of the mouse's movements was below a preset threshold. An optimum threshold was determined by comparing manually scored videotapes with automated scores. The following settings were used in all experiments: threshold 0,20 Newtons, off delay 30 msec. Drugs were administered to 7-8 mice per treatment group. Compound 22 was given 30 minutes, while Compound 36 was given 60 minutes before the experiment.

Table 28: Results of tail suspension test in C57BL/6J mice

Compound	MED [mg/kg]
22	0.156
36	0.312

Four-plate test in Swiss mice

The four-plate test (BIOSEB, France) was performed in a cage (25 x 18 x 16 cm) floored by four identical rectangular metal plates (8 x 11 cm) separated from one another by a

gap of 4 mm. The top of the cage was covered by a transparent Perspex lid that prevented escape behaviour. The plates were connected to a device that can generated electric shocks. Following a 15-s habituation period, the animal's motivation to explore a novel environment was suppressed by an electric foot shock (0.8 mA, 0.5 s) every time it moved from one plate to another during a 1-minute test session (Aron et al., Evaluation of a rapid technique for detecting minor tranquilizers, Neuropharmacology 10, 459-469, 1971). This action is referred to as a 'punished crossing', and was followed by a 3 s shock interval, during which the animal could move across plates without receiving a shock. Drugs were administered to 8-10 mice per treatment group. Compound 22 was given 30 minutes, while Compound 36 was given 60 minutes before the experiment.

Table 29: Results of four-plate test in mice

Compound	MED [mg/kg]
22	0.312
36	0.312

Example 9

Activity testing in rats

Drug-naive male Wistar rats (Charles River, Sulzfeld, Germany) weighing 250-400 g were used in all experiments. Rats were housed two per standard plastic cage and kept in a room with constant environmental conditions (21-22°C, relative humidity 60%, a 12:12 light-dark cycle with lights on at 7:00 a.m.). Animals were supplied by the breeder two weeks before the onset of behavioral procedures. During this time, the subjects were weighed and handled several times. Tap water and standard lab chow (Labofeed H, WPIK, Kcynia, Poland) was available ad libitum.

Test compounds

Compounds 22 and 36 ~~and 97~~ were prepared as a suspension in 1% aqueous solution of Tween 80, whereas d-amphetamine and MK-801 were dissolved in distilled water immediately before administration. An injection volume of 10 ml/kg (mice) or 2 ml/kg (rats) was used throughout and all compounds were administered intraperitoneally (i.p.), except d-amphetamine that was given subcutaneously (s.c.).

Statistical analysis

All the data are expressed as the mean ± SEM. The statistical significance of effects was evaluated using separate one-way analysis of variance (ANOVA) with comparison between individual groups by Dunnett's test (when only one drug was given or by the Tukey's test when two drugs were used; $p<0.05$, $p<0.01$ and $p<0.001$ were considered statistically significant. ED_{50} values were calculated using Graph Pad Prism 5 Software.

Apomorphine-induced stereotyped behaviour

All tests were carried out in a sound-attenuated experimental room between 9:00 a.m. and 3:00 p.m. Within 24 h prior to testing, rats were habituated to glass observation cages (25x25x40 cm, WxHxL) with wood chip bedding on the floor for 20 min. On the day of testing, stereotyped behaviour was observed 20 to 25 min. after apomorphine injection (s.c.) as described by Bristow et al. (L-745,870, a subtype selective dopamine D4 receptor antagonist, does not exhibit a neuroleptic-like profile in rodent behavioral tests. J Pharmacol Exp Ther. 1997;283:1256-63) and Feldman et al. (Mixed D2/5-HT2 antagonism differentially affects apomorphine- and amphetamine-induced stereotyped behavior. Pharmacol Biochem Behav. 1997;58:565-72). Rats were injected with apomorphine (0,6 mg/kg) and placed in the observation cages. Views of other rats in the experiment were prohibited. Twenty minutes later, the time spent licking/biting and sniffing downward was recorded by a trained observer for 5 minutes (300 s). Rats were pre-injected i.p. with a test drug 60 min. before the start of the 5-min. test session (the observation period).

The duration of stereotyped sniffing and licking/biting was analyzed with the aid of the Kruskal-Wallis analysis of variance (ANOVA). The Mann-Whitney U test was used for individual post hoc comparisons. P values lower than 0,05 were considered significant.

MK-801-induced stereotyped behaviour

All tests were carried out in a sound-attenuated experimental room between 9:00 a.m. and 3:00 p.m. Within 24 h prior to testing, rats were habituated to glass observation cages (25x25x40 cm, WxHxL) with wood chip bedding on the floor for 20 min. On the day of testing, stereotyped behaviour was observed 15 min. after MK-801 administration. Rats were injected with MK-801 (0.6 mg/kg, i.p.) and placed in the observation cages. Views of other rats in the experiment were prohibited. Fifteen minutes later, the time spent circling / head waving was recorded by a trained observer for 5 min. (300 s). Rats were pre-injected with a test drug 60 min. before the start of the observation period.

The duration of stereotyped circling was analyzed with the aid of the Kruskal-Wallis analysis of variance (ANOVA). The Mann-Whitney U test was used for individual post hoc comparisons. P values lower than 0,05 were considered significant.

2,5-Dimethoxy-4-iodoamphetamine(DOI)-induced head twitches

All tests were carried out in a sound-attenuated experimental room between 9:00 a.m. and 3:00 p.m. as described above for spontaneous head twitches. DOI-induced head twitches were scored as described by Millan et al. (S18327 (1-[2-[4-(6-fluoro-1, 2-benzisoxazol-3-yl)piperid-1-yl]ethyl]3-phenyl imidazolin-2-one), a novel, potential antipsychotic displaying marked antagonist properties at alpha(1)- and alpha(2)-adrenergic receptors: II. Functional profile and a multiparametric comparison with haloperidol, clozapine, and 11 other antipsychotic agents. J Pharmacol Exp Ther 2000;292:54-66). Rats were pre-injected i.p. with a test drug 60 min. before the start of the test session. Fifty five minutes later, rats were injected with DOI (2.5 mg/kg, i.p.) and placed in glass observation cages (25x25x40 cm, WxHxL) with wood chip bedding on the floor. Five minutes later, head twitches were counted for 5 minutes. (300 s) by a trained observer.

Total numbers of head twitches (n/5 min.) were analyzed by means of the Kruskal-Wallis analysis of variance (ANOVA). The Mann-Whitney U test was used for individual post hoc comparisons. P values lower than 0.05 were considered significant but values lower than 0.1 are also reported.

Conditioned avoidance response (CAR)

The effects of a test drug on conditioned response in rats were evaluated using active avoidance responding test. The apparatus consisted of six identical shuttle boxes (PACS-30, Columbus Instruments, USA). Each stainless steel box was 22.8 cm wide, 48.3 cm long and 27.6 cm high and was divided into two equal-sized compartments, separated by a sliding door end equipped with an overhead lights audio generator. An infrared-type beam assembly was used for detecting subject transfers. Each chamber floor was composed of stainless steel grid wired for presentation of a scrambled electric food shock (0,5 mA).

Rats trained to avoid the foot shock were placed in the experimental chambers for a 3 min. habituation period followed by 50 CAR trials presented on a 15-s variable interval (VI) schedule. Each trial consisted of a 10 s warning tone and stimulus light (conditioned stimulus) followed by 10 s electric shock (0.5 mA). If during the initial 10 s of the trial an animal crossed through the sliding door, the tone and light were terminated, no

shock was applied, and the response was considered as "an avoidance response". If the animal crossed through the sliding door after a foot shock was initiated, the response was considered as "an escape response". If the animal did not cross the sliding door the response was considered as "none". If a response was made during an intertrial interval, it was punished with 0.5 s shock (0.5 mA). The PACS-30 software (Columbus) controlled the sessions and counted the number of trials in which a rat avoided the shock, escaped or did not respond. A stable demonstration of >80% of correct avoidance responses after 14-18 training sessions was a criterion for inclusion in subsequent drug tests. On test days, a tested drug was administered i.p. 60 minutes before the start of the test session. Each drug was tested at 3-4 different doses in the same group of eight animals. A 7-day wash-out period was introduced between the subsequent tests. Two CAR sessions were conducted during the wash-out in order to maintain stable conditioned responding. The number of CAR trials during the test and wash-out sessions was reduced to 30.

Avoidances, escapes, and "none" responses were analyzed with the aid of a one-way analysis of variance (ANOVAThe Newman-Keuls test was used for individual post hoc comparisons

Passive avoidance procedure

Potentially impairing effects of test substance on learning and memory function in rats were evaluated using a step-through passive avoidance (PA) test. The apparatus consisted of 6 identical shuttle boxes divided into lighted and dark compartments (220 × 240 × 270 mm) and equipped with grid floors (PACS-30, Columbus Instruments, USA). The two compartments were separated by a sliding door.

In the training session (acquisition), animals were placed in the lighted compartment and allowed to explore it freely for 10 s. The sliding door was then opened, and the step-through latency for a rat to enter the dark compartment was measured. As soon as the rat entered the dark compartment, the door was closed. Three seconds later, an inescapable foot-shock (0.5 mA for 3 s) was delivered through the grid floor with a constant current shock generator. All animals entered the dark compartment within 300 s (a cut-off) and received a foot-shock.

Rats were pre-injected a test drug 60 minutes before the start of the training session.

The test (expression) session was performed 24 h after the training session. The same procedure was used (see above) but no foot-shock was delivered. A step-through latency for animals to enter the dark compartment was measured with a cut-off of 300 s.

Weights and step-trough latencies were analyzed with the aid of a one-way analysis of variance (ANOVA). The Newman-Keuls test was used for individual post hoc comparisons.

Prepulse inhibition (PPI) procedure

The PPI apparatus consisted of eight startle chambers (SR-LAB, San Diego Instruments, San Diego, CA, USA). Each chamber consisted of a Plexiglas cylinder (8,9 cm diameter × 20 cm long) resting on a Plexiglas frame in a sound attenuated, ventilated enclosure. Background noise and acoustic stimuli were presented via a loudspeaker mounted 24 cm above the animal. Startle responses, reflecting the motion of animals in the cylinder following the acoustic stimulus, were detected by a piezoelectric transducer mounted below the frame. The administration of stimuli and response recording were controlled by the SR-LAB software. Test sessions started with a 5-minutes acclimatization period. Throughout the whole session, the chamber light was on, and the background white noise was set at 70 dB. The test session included 3 initial startling stimuli (intensity: 120 dB, duration: 40ms) to accustom the rat to the experimental procedure. The initial stimuli were followed by 60 trials (6 x 10 trials) presented in a random order:

- 10 background trials (B) which involved a presentation of a sham stimulus (intensity: 70 dB, duration: 40 ms),

- two types (2 x 10) of prepulse trials (PP) which included only a prepulse stimuli (84 dB or 90 dB, 20 ms),

- 10 pulse trials (P) which included only a pulse startling stimulus (120 dB, 40 ms),

- two types (2 x 10) of prepulse-and-pulse trials (PP-P) which involved a prepulse (84 dB or 90 dB, 20 ms) followed 100 ms later by a 120-dB pulse stimulus (P).

The average inter-trial interval was 22.5 s (range: 15-30 s). This interval was randomized by the SR-LAB software. Startle responses were measured for 100 ms after the onset of the last trial stimulus. For each type of stimulation, startle amplitudes were averaged across the 10 trials. The magnitude of PPI was calculated as a percent inhibition of the startle amplitude in the pulse trial (treated as 100%) according to the formula: [(startle amplitude in P trials - startle amplitude in PP-P trials) / startle amplitude in P trials] × 100%. Startle responses to the 3 initial stimuli were excluded from the statistical analyses.

Effects of tested compounds on PPI and on amphetamine-induced PPI deficits

Rats were pre-injected with the test drug (60 min.). Each compound was tested in two separate experiments performed over two consecutive days (Experiments 1-2) in separate groups of drug-naive rats. Fifteen minutes before the start of the PPI session, rats were injected with saline (Experiment 1) or amphetamine (Experiment 2).

In Experiment 1, each reference compound, or its vehicle, was given in combination with physiological saline (0.9% NaCl). The purpose of this experiment was to assess effects of the reference drug on basic startle responses and PPI. Results of Experiment 1 determined a range of drug doses tested in Experiment 2. In Experiment 2, the reference drug, or its vehicle, was administered in combination with amphetamine (6 mg/kg, i.p.). The purpose of Experiment 2 was to assess drug's effects on amphetamine-induced PPI deficits.

Startle responses (in manufacturer's arbitrary units), and magnitudes of PPI (%) were analyzed with the aid of a one-way analysis of variance (ANOVA). The Newman-Keuls test was used for individual post hoc comparisons.

Forced swimming test (the Porsolt's test)

The animals were individually subjected to two experimental trials during which they were forced to swim in a cylinder (40 cm high, 18 cm in diameter) filled with warm water (25°C) to a height of 15 cm. A video camera was mounted 50 cm above the cylinder. The first (habituation) and second (test) trial lasted 15 and 5 minutes, respectively. There was a 24-h interval between the trials. The total duration of immobility was measured during the second trial by a trained observer located in a separate room.

Weights and time of immobility were analyzed with the aid of a one-way analysis of variance (ANOVA). The Newman-Keuls test was used for individual post hoc comparisons.

Elevated plus maze test in rats

The testing procedure was based on a method described by Pellow and File (1986). Plus-maze apparatus (an automated device produced by Kinder Scientific) made of durable, high density, non porous black plastic, elevated to a height of 50 cm, consisted of two open arms (50 x 10 cm) and two closed arms (50 x 10 cm, and 30 cm high walls), arranged so that the two arms of each type were opposite each other. Floor of the plus-maze was made of infrared transparent material what means that there are no visible

sensors. The plus-maze was placed in a darkened room, and the center of the apparatus was illuminated with a 25W electric bulb hanging 100 cm above. Plus-maze apparatus was connected to PC software by control chassis. Each rat was gently placed in the center of the plus-maze, facing one of the closed arms, immediately after a 5-min adaptation period in a plastic black box (60 x 60 x 35 cm). During a 5-minutes test period, automated Motor Monitor System recorded the number of entries into the closed and open arms, the time spent in and the distance (cm) covered by a rat in either type of the arms. After each trial the maze was wiped clean. All compounds were administered to 5-8 rats per treatment group. Compounds 22 and 36 were administered 60 minutes before the experiment.

Conflict drinking test (Vogel test) in rats

Anxiety Monitoring System "Vogel test" produced by TSE Systems was used. It was consisted of a polycarbonate cage (dimensions 26.5 x 15 x 42 cm), equipped with a grid floor made from stainless steel bars and a drinking bottle containing tap water. Experimental chambers (two) were connected to PC software by control chassis and a device that generates electric shocks. On the first day of the experiment, the rats were adapted to the test chamber for 10 min. After the adaptation period, the animals were deprived of water for 24 h and were then placed in the test chamber for another 10-min adaptation period during which they had free access to the drinking bottle. Afterwards, they were allowed a 30-min free-drinking session in their home cage. After another 24-h water deprivation period, the rats were placed again in the test chamber. Recording data started immediately after the first lick and every 20 licks rats were punished with an electric shock (0.5 mA, lasting 1 s). The impulses were released via the spout of the drinking bottle. If a rat was drinking when an impulse was released, it received a shock. The number of licks and the number of shocks received throughout a 5-min experimental session was recorded automatically. Compounds 22 and 36 were administered to 10 rats per treatment group, 60 min before the experiment.

Table 30: Results of tests in rats

	Compound MED [mg/kg]	
Test	**22**	**36**
Apomorphine-induced stereotyped behaviour (pharmacological dopamine-related psychosis model)	10	-
MK-801-induced stereotyped behaviour (pharmacological glutamate-related psychosis model)	3	-

	Compound MED [mg/kg]	
Test	**22**	**36**
DOI-induced head twitches (pharmacological serotonin-related psychosis model)	1 *	-
Active-avoidance response (model of positive symptoms of schizophrenia)	3	-
Passive-avoidance (model of memory disturbance)	>30	-
Prepulse inhibition disruption caused by amphetamine administration (model of sensorimotor gating deficits involved in schizophrenia pathomechanism; dopaminergic psychotomimetic)	30	-
Porsolt forced swimm test (test indicative of potential antidepressant activity)	0.3	1 *
Vogel test in rats (test indicative of potential anxiolytic activity)	3	1 *
Elevated plus-maze (test indicative of potential anxiolytic activity)	0.3 *	-

* - lower doses not tested

Results of behavioral tests described in Example 8 confirm potential activity of the compounds of invention in therapy of psychotic symptoms.

Data for the representative compound 22 in Examples 8 and 9 show its wide antipsychotic activity in all applied rodent models. It is noteworthy that the compound was active in models utilizing psychotomimetic substances affecting either dopaminergic (d-amphetamine, apomorphine), serotoninergic (DOI) or glutamatergic transmission (MK-801) as well as in specific conditioning procedure (active avoidance response). Compound 22 was active in procedures indicative of efficacy in either positive symptoms of schizophrenia, such as: d-amphetamine and MK-801 induced hyperlocomotion, stereotyped behavior induced by apomorphine and DOI, active avoidance response, as well as in procedure assessing ability to treat attention deficits and information filtering (dimensions of cognitive deficits), underlying the pathomechanism of schizophrenia - reversal of deficits in prepulse inhibition in rats. Moreover compound 22 was active in well established models for detecting substances with potential antidepressant activity, i.e. tail suspension test in mice and forced swim test (Porsolt) in rats as well as potential anxiolytic activity, i.e. four plates test in mice, elevated plus maze and conflict drinking test (Vogel) in rats. Such a wide pharmacological activity, beyond the purely antipsychotic effects is a particularly desirable feature of modern antipsychotic drug, considering complexity of clinical conditions associated with schizophrenia, including depression and anxiety.

Data for compound 36 show its wide antidepressant and anxiolytic activity in all applied models in mice and rats (tail suspension test in mice and forced swim test (Porsolt) in rats, four plates test in mice and conflict drinking test (Vogel) in rats). This confirms its potential efficacy in treatment of depression and anxiety, as well as its potential use as add on therapy for currently used antipsychotics in treatment of negative symptoms of schizophrenia.

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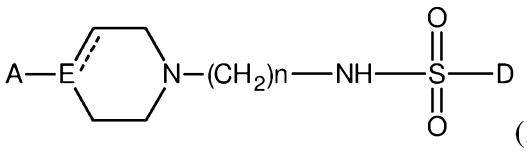
CLAIMS

1. Compounds of the general formula (I)



(I)

and pharmaceutically acceptable salts thereof,

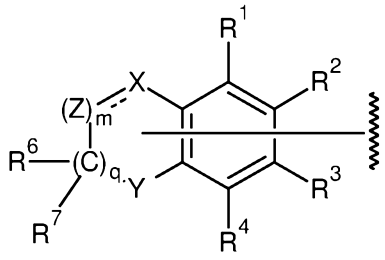
wherein

E represents C;

 represents double bond;

n represents an integer from 2 to 6, inclusive;

A represents a 9- or 10-membered bicyclic group, consisting of benzene ring fused with 5- or 6-membered heterocyclic ring, which group is linked to E through one of its carbon atoms and has the following formula (A):



(A)

wherein

X represents CR^5, $C(R^5)_2$, NH or O;

Z represents CR^5, $C(R^5)_2$, N;

R^5 represents hydrogen atom, halogen atom or C_1-C_4-alkyl;

Y represents NH, O or S;

each of R^1, R^2, R^3 and R^4 independently represents hydrogen atom or halogen atom;

each of R^6 and R^7 independently represents hydrogen atom, halogen atom, C_1-C_4-alkyl;

or R^6 and R^7 together form carbonyl group =O;

wherein one of R^1, R^2, R^3, R^4, R^5, R^6 or R^7 is replaced by a bond to E;

 represents single bond or double bond;

m is 0 or 1;

q is 0 or 1;

wherein at least one of q and m is 1;

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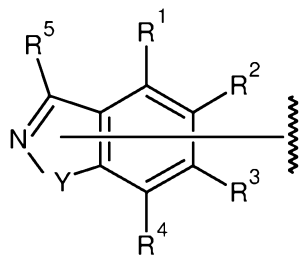
D represents a group selected from:

- unsubstituted phenyl or phenyl substituted with one or more substituents independently selected from the group consisting of branched C_1-C_4-alkyl; straight C_1-C_4-alkyl in ortho or meta position with respect to sulphonamide group; C_1-C_3-alkyloxy; halogeno-C_1-C_3-alkyl; halogeno-C_1-C_3-alkyloxy; halogen atom; -CN; -OH; and phenyl;
- unsubstituted naphthyl or naphthyl substituted with one or more substituents independently selected from the group consisting of C_1-C_4-alkyl; C_1-C_3-alkyloxy; halogeno-C_1-C_3-alkyl; halogen atom; -CN; -OH; and phenyl;
- 5-membered aromatic heterocyclic group having 1 to 3 heteroatoms independently selected from the group consisting of N, O, S, the group being unsubstituted or substituted with one or more substituents independently selected from the group consisting of C_1-C_4-alkyl; C_1-C_3-alkyloxy; halogeno-C_1-C_3-alkyl; halogen atom; -CN; -OH; and phenyl;
- bicyclic group consisting of benzene or pyridine ring fused with 5-membered aromatic or non-aromatic heterocyclic ring having 1 to 3 heteroatoms independently selected from the group consisting of N, O, S, which group is unsubstituted or substituted with one or more substituents independently selected from the group consisting of C_1-C_4-alkyl; C_1-C_3-alkyloxy; halogeno-C_1-C_3-alkyl; halogen atom; =O; -CN; -OH; and phenyl;
- bicyclic group consisting of benzene or pyridine ring fused with 6-membered non-aromatic heterocyclic ring having from 1 to 3 heteroatoms independently selected from the group consisting of N, O, S, which group is unsubstituted or substituted with one or more substituents independently selected from the group consisting of C_1-C_4-alkyl; C_1-C_3-alkyloxy; halogeno-C_1-C_3-alkyl; halogen atom; =O; -CN; -OH; and phenyl.

2. The compounds according to claim 1, wherein A is represented by the general formula (A1):



(A1)

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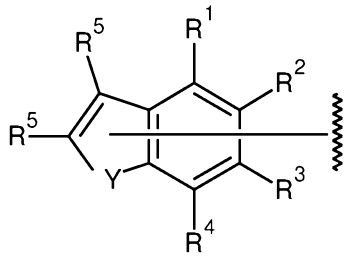
wherein Y, R^1, R^2, R^3, R^4 and R^5 are as defined in claim 1.

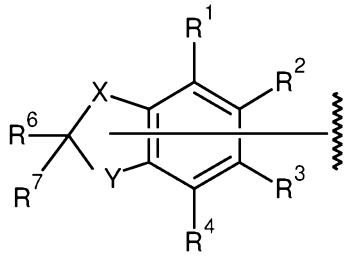
3. The compounds according to claim 1, wherein A is represented by the general formula (A2):



(A2)

wherein Y, R^1, R^2, R^3, R^4 and R^5 are as defined in claim 1.

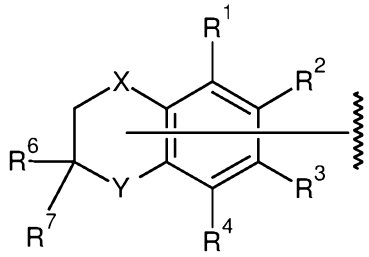
4. The compounds according to claim 1, wherein A is represented by the general formula (A3):



(A3)

wherein X, Y, R^1, R^2, R^3, R^4, R^6 and R^7 are as defined in claim 1.

5. The compounds according to claim 1, wherein A is represented by the general formula (A4):



(A4)

wherein X, Y, R^1, R^2, R^3, R^4, R^6 and R^7 are as defined in claim 1.

6. The compounds according to any one of claims 1-5, wherein D represents unsubstituted phenyl or phenyl substituted with one or more substituents independently selected from the group consisting of branched C_1-C_4-alkyl; straight C_1-C_4-alkyl in ortho or meta position with respect to sulphonamide group; C_1-C_3-alkyloxy; halogeno-C_1-C_3-alkyl; halogeno-C_1-C_3-alkyloxy; halogen atom; -CN; -OH; and phenyl.

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7. The compounds according to any one of claims 1-5, wherein D represents unsubstituted naphthyl or naphthyl substituted with one or more substituents independently selected from the group consisting of C_1-C_4-alkyl; C_1-C_3-alkyloxy; halogeno-C_1-C_3-alkyl; halogen atom; -CN; -OH; and phenyl.

8. The compounds according to any one of claims 1-5, wherein D represents 5-membered aromatic heterocyclic group having 1 to 3 heteroatoms independently selected from the group consisting of N, O, and S, and wherein D is unsubstituted or substituted with one or more substituents independently selected from the group consisting of C_1-C_4-alkyl; C_1-C_3-alkyloxy; halogeno-C_1-C_3-alkyl; halogen atom; -CN; -OH; and phenyl.

9. The compounds according to any one of claims 1-5, wherein D represents benzene ring fused with 5-membered aromatic heterocyclic ring having 1 to 3 heteroatoms independently selected from the group consisting of N, O, S, and wherein D is unsubstituted or substituted with one or more substituents independently selected from the group consisting of C_1-C_4-alkyl; C_1-C_3-alkyloxy; halogeno-C_1-C_3-alkyl; halogen atom, -CN; -OH; and phenyl.

10. The compounds according to any one of claims 1-5, wherein D represents bicyclic group consisting of benzene ring fused with 5-membered non-aromatic heterocyclic ring having from 1 to 3 heteroatoms independently selected from the group consisting of N, O, S, and wherein D is unsubstituted or substituted with one or more substituents independently selected from the group consisting of C_1-C_4-alkyl; C_1-C_3-alkyloxy; halogeno-C_1-C_3-alkyl; halogen atom; =O; -CN; -OH; and phenyl.

11. The compounds according to any one of claims 1-10, wherein n is 2.

12. The compounds according to any one of claims 1-10, wherein n is 3.

13. The compounds according to any one of claims 1-10, wherein n is 4.

14. The compounds according to any one of claims 1-13, wherein A is linked to E through carbon atom of benzene ring.

15. The compounds according to any one of claims 1-13, wherein A is linked to E through carbon atom of heterocyclic ring.

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16. The compound according to claim 1 selected from the group consisting of the following compounds:

N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}naphthalene-1-sulphonamide,

N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}naphthalene-2-sulphonamide,

4-fluoro-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide,

3-fluoro-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide,

4-chloro-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide

3-chloro-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide,

3-methyl-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide,

3-hydroxy-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide,

4-methoxy-N-{4-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]butyl}benzene-sulphonamide

N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}naphthalene-1-sulphonamide,

N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}naphthalene-2-sulphonamide,

4-fluoro-N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}benzene-sulphonamide,

3-fluoro-N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}benzene-sulphonamide,

4-chloro-N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}-benzenesulphonamide,

3-chloro-N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}benzene-sulphonamide,

3-hydroxy-N-{3-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]propyl}benzene-sulphonamide,

N-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}naphthalene-1-sulphonamide,

N-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}naphthalene-2-sulphonamide,

N-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}-4-fluorobenzene-sulphonamide,

3-fluoro-N-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}benzene-sulphonamide,

4-chloro-N-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}benzene-sulphonamide,

3-chloro-N-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}benzene-sulphonamide,

3-methyl-N-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}benzene-sulphonamide,

3-hydroxy-N-{2-[4-(5-chloro-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]ethyl}benzene-sulphonamide,

4-chloro-N-{4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydropyridin-1(2H)-yl]-butyl}-benzenesulphonamide,

N-[4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-3-chloro-benzenesulphonamide,

N-[3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-3-chloro-benzenesulphonamide,

N-[4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-3-fluoro-benzenesulphonamide,

N-[3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-3-fluoro-benzenesulphonamide,

N-[4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-4-tert-butyl-benzenesulphonamide,

N-[4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-naphthalene-1-sulphonamide,

N-[4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-naphthalene-2-sulphonamide,

N-[4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-4-fluoro-benzenesulphonamide

N-[4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-3-hydroxy-benzenesulphonamide,

N-[4-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-3-methyl-benzenesulphonamide,

N-[4-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]naphthalene-2-sulphonamide,

3-fluoro-N-[4-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]benzene-sulphonamide,

N-[4-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-3-hydroxybenzene-sulphonamide,

N-[4-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]butyl]-3-methylbenzene-sulphonamide,

3-fluoro-N-[3-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]benzene-sulphonamide,

N-[3-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-3-hydroxybenzene-sulphonamide,

N-[2-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]naphthalene-2-sulphonamide,

3-fluoro-N-[2-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]benzene-sulphonamide,

N-[2-[4-(5-fluoro-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-3-methylbenzene-sulphonamide,

N-[3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-naphthalene-1-sulphonamide,

N-[3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-naphthalene-2-sulphonamide,

N-[3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-4-fluoro-benzenesulphonamide,

4-chloro-N-[3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-benzenesulphonamide,

N-[3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-3-hydroxy-benzenesulphonamide,

N-[3-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]propyl]-3-methyl-benzenesulphonamide,

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N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-naphthalene-1-sulphonamide,
N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-naphthalene-2-sulphonamide,
N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-4-fluoro-benzenesulphonamide,
N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-3-fluoro-benzenesulphonamide,
4-chloro-N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-benzenesulphonamide,
3-chloro-N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-benzenesulphonamide,
N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-3-hydroxy-benzenesulphonamide,
N-[2-[4-(5-chloro-2-methyl-1H-indol-3-yl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-3-methyl-benzenesulphonamide,
and pharmaceutically acceptable salts thereof.

17. A pharmaceutical composition comprising a compound of formula (I) as defined in any one of claims 1-16 as an active ingredient in combination with pharmaceutically acceptable carrier(s) and/or excipient(s).

18. Use of a compound of formula (I) as defined in any one of claims 1-16 or a pharmaceutical composition as defined in claim 17 in the treatment and/or prevention of disorders of the central nervous system related to dopaminergic and/or serotoninergic and/or noradrenergic transmission.

19. The use according to claim 18, wherein the disorder of the central nervous system is selected from schizophrenia; schizoaffective disorders; schizophreniform disorders; delusional syndromes and other psychotic conditions related and not related to taking psychoactive substances; affective disorder; bipolar disorder; mania; depression; anxiety disorders of various aetiology; stress reactions; consciousness disorders; coma; delirium of alcoholic or other aetiology; aggression; psychomotor agitation and other conduct disorders; sleep disorders of various aetiology; withdrawal syndromes of various aetiology; addiction; pain syndromes of various aetiology; intoxication with psychoactive substances; cerebral circulatory disorders of

various aetiology; psychosomatic disorders of various aetiology; conversion disorders; dissociative disorders; urination disorders; autism and other developmental disorders, including nocturia, stuttering, tics; cognitive disorders of various types, including Alzheimer's disease; and, psychopathological symptoms and neurological disorders in the course of other diseases of the central and peripheral nervous systems.

20. A method of treatment and/or prevention of disorders of the central nervous system related to serotoninergic and dopaminergic transmission in mammals, comprising administration of a pharmaceutically effective amount of a compound of formula (I) as defined in any one of claims 1 to 16 or a pharmaceutical composition as defined in claim 17.

21. Use of a compound of formula (I) as defined in any one of claims 1 to 16, or a pharmaceutical composition as defined in claim 17, for the manufacture of a medicament for the treatment and/or prevention of disorders of the central nervous system related to dopaminergic and/or serotoninergic and/or noradrenergic transmission.

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