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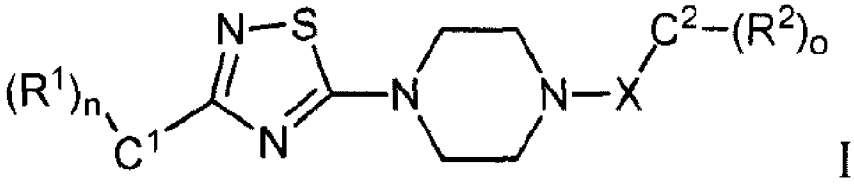
(54) **Titre : DERIVES DE 1 , 2 , 4 -THIADIAZOL- 5 -YLPIPERAZINE UTILES DANS LE TRAITEMENT DE MALADIES NEURODEGENERATIVES**

(54) **Title: 1 , 2 , 4 -THIADIAZOL- 5 -YLPIPERAZINE DERIVATIVES USEFUL IN THE TREATMENT NEURODEGENERATIVE DISEASES**



IA

(57) **Abrégé/Abstract:**
The present invention relates to a compound of formula (IA) The present invention also relates to the use of the compound of formula IA for treating certain neurodegenerative disorders characterized by cytotoxic TAU misfolding and/or aggregation.

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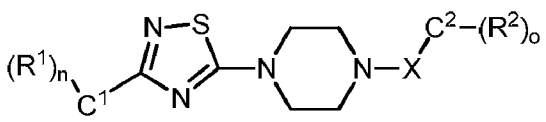
(54) **Title**: 1, 2, 4 -THIADIAZOL- 5 -YLPIPERAZINE DERIVATIVES USEFUL IN THE TREATMENT NEURODEGENERATIVE DISEASES



(IA)

(57) **Abstract**: The present invention relates to a compound of formula (IA) The present invention also relates to the use of the compound of formula IA for treating certain neurodegenerative disorders characterized by cytotoxic TAU misfolding and/or aggregation.

1 , 2 , 4 -THIADIAZOL- 5 -YLPIPERAZINE DERIVATIVES USEFUL IN THE TREATMENT NEURODEGENERATIVE DISEASES

Field of the invention

The present invention relates to arylthiadiazoles and their use for treating certain neurodegenerative disorders characterized by cytotoxic TAU misfolding and/or aggregation.

Background of the invention

TAU is a protein with the ability to bind -and consequently stabilise and define- microtubule structure and function in neurons. The binding of TAU to microtubules is regulated by phosphorylation of TAU; several TAU phosphorylation sites and their corresponding kinases have been identified which control phosphorylation status of TAU and consequently modulate the affinity of TAU-binding to microtubules.

Tauopathies are characterised by insoluble aggregates or polymers of hyperphosphorylated TAU which are formed by self-polymerisation of TAU monomers.

An important aspect of the TAU aggregation is its associated cytotoxicity, which reduces neuronal integrity and functionality and ultimately resulting in disease symptoms. A direct role of TAU in disease onset has been established unequivocally by the elucidation of familial mutations in TAU, which appear to be responsible for a very early and sometimes aggressive form of tauopathy. Such mutations comprise changes in the amino acid sequence of TAU that -directly or indirectly promote neurotoxic aggregation.

Alzheimer's disease is the best known of these, where TAU protein is deposited within neurons in the form of neurofibrillary tangles (NFTs). They were first described by the eponymous Alois Alzheimer in one of his patients suffering from the disorder.

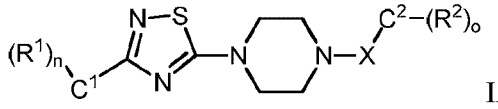
Currently used treatments for tauopathies, including Alzheimer's disease, offer only symptomatic benefit without impacting the underlying neurodegeneration.

WO2007/090617 discloses substituted 1,2,4-thiadiazole derivatives for use in the treatment of an α-synucleopathy such as Parkinson's disease, diffuse Lewy body disease, traumatic brain injury, amyotrophic lateral sclerosis, Niemann-Pick disease, Hallervorden-Spatz syndrome, Down syndrome, neuroaxonal dystrophy, multiple system atrophy and Alzheimer's disease.

Treatments aimed to suppress cytotoxic TAU misfolding and/or aggregation, in order to delay or halt the progression of disease, are presently not available. Thus there is a need for new treatments that target the underlying molecular mechanism of noxious TAU misfolding and/or aggregation in order to reduce neuronal cell death and/or degeneration in patients suffering from tauopathies such as Alzheimer's disease (AD).

Summary of the invention

A first aspect of the present invention relates to compounds of formula IA



IA

wherein

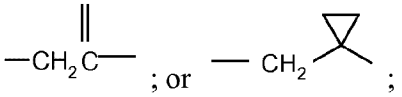
R^1 is hydrogen; lower alkyl; lower alkyl substituted by halogen; halogen; lower alkoxy; lower alkoxy substituted by halogen; or cyano;

R^2 is hydrogen; lower alkyl; lower alkyl substituted by halogen; halogen; lower alkoxy; or is lower alkoxy substituted by halogen;

C^1 is phenyl; benzo[1,3]dioxol; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; thiophen-2-yl; pyrazine-2-yl; pyridazin-4-yl; pyrimidin-5-yl; piperidin-1yl; tetrahydro-2H-pyran-4-yl; or cycloalkyl;

C^2 is phenyl; benzo[1,3]dioxol; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; thiophen-2-yl; pyrazine-2-yl; pyridazin-4-yl; pyrimidin-5-yl; piperidin-1yl; tetrahydro-2H-pyran-4-yl; or cycloalkyl;

X is $-CH_2-$; $-CH_2-CHR-$; $-CH_2-CH_2-CH_2-$; $-CH_2C(O)-$; $-CHR'-CH_2-$;



; or

;

R is hydrogen; hydroxyl; halogen or lower alkyl;

R' is lower alkyl;

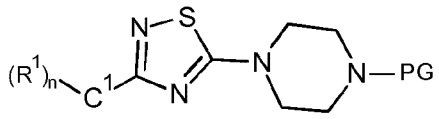
n is 1 or 2; if n is 2, R^1 may be independently selected from each other;

o is 1 or 2; if o is 2, R^2 may be independently selected from each other;

or to a pharmaceutically active salt thereof; to a stereoisomeric form, including an individual diastereoisomer or enantiomer of the compound of formula IA as well as to a racemic or non-racemic mixture thereof.

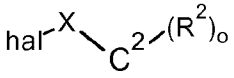
A second aspect of the invention relates to a process for preparation of compounds of formula AI according to a first aspect of the invention, which process comprises

coupling a compound of formula

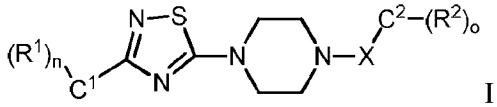


IV

with a compound of formula



to give a compound of formula



I

wherein the definitions are as described in the first aspect of the invention, wherein PG is hydrogen or a protecting group, wherein hal is a halogen or

if desired, converting the compounds obtained into pharmaceutically acceptable acid addition salts.

A third aspect of the invention relates to a medicament containing one or more compounds according to the first aspect of the invention and pharmaceutically acceptable excipients.

A fourth aspect of the invention relates to a medicament according to the third aspect, for use in the treatment of a disease selected from the group consisting of are Alzheimer's disease, Pick's disease, corticobasal degeneration, progressive supranuclear palsy, frontotemporal dementia, and parkinsonism (linked to chromosome 17, FTDP-17).

A fifth aspect of the invention relates to the use of a compound according to the first aspect of the invention for the manufacture of medicaments for the treatment of Alzheimer's

disease, Pick's disease, corticobasal degeneration, progressive supranuclear palsy, frontotemporal dementia and parkinsonism (linked to chromosome 17, FTDP-17).

A sixth aspect of the invention relates to a method for the treatment of Alzheimer's disease, Pick's disease, corticobasal degeneration, progressive supranuclear palsy, frontotemporal dementia and parkinsonism (linked to chromosome 17, FTDP-17), which method comprising administering an effective amount of a compound as defined in the first aspect of the invention.

Detailed description

In an embodiment, the present invention encompasses a compound of formula IA, wherein,

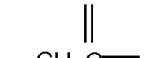
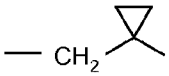
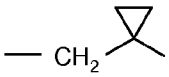
R^1 is hydrogen; lower alkyl; lower alkyl substituted by halogen; halogen; lower alkoxy; lower alkoxy substituted by halogen; or is cyano; preferably R^1 is lower alkyl substituted by halogen; halogen; or lower alkoxy; preferably R^1 is lower alkyl substituted by halogen; or halogen;

R^2 is hydrogen; lower alkyl; lower alkyl substituted by halogen; halogen; lower alkoxy; or is lower alkoxy substituted by halogen; preferably R^2 is hydrogen; lower alkyl; halogen; or is lower alkoxy; preferably R^2 is hydrogen; halogen; or is lower alkoxy;

C_1 is phenyl; benzo[1,3]dioxol; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; thiophen-2-yl; pyrazine-2-yl; pyridazin-4-yl; pyrimidin-5-yl; piperidin-1yl; tetrahydro-2H-pyran-4-yl; or cycloalkyl; preferably C_1 is phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; thiophen-2-yl; pyrazine-2-yl; pyridazin-4-yl; pyrimidin-5-yl; piperidin-1yl; or tetrahydro-2H-pyran-4-yl; preferably C_1 is phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; pyrazine-2-yl; pyridazin-4-yl; pyrimidin-5-yl; or piperidin-1yl; preferably C_1 is phenyl; pyridine-3-yl; pyridine-4-yl; pyrazine-2-yl; pyridazin-4-yl; or piperidin-1yl; preferably C_1 is phenyl; pyridine-3-yl; pyridine-4-yl; or pyridazin-4-yl; preferably C_1 is phenyl; or pyridine-3-yl;

C_2 is phenyl; benzo[1,3]dioxol; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; thiophen-2-yl; pyrazine-2-yl; pyridazin-4-yl; pyrimidin-5-yl; piperidin-1yl; tetrahydro-2H-pyran-4-yl; or cycloalkyl; preferably C_2 is phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; pyrazine-2-yl; pyridazin-4-yl; pyrimidin-5-yl; piperidin-1yl; tetrahydro-2H-pyran-4-yl; or cycloalkyl; preferably C_2 is phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; piperidin-1yl;

tetrahydro-2H-pyran-4-yl; or cycloalkyl; preferably C_2 is phenyl; pyridine-3-yl; pyridine-4-yl; or tetrahydro-2H-pyran-4-yl; preferably C_2 is phenyl; pyridine-3-yl; pyridine-4-yl; or tetrahydro-2H-pyran-4-yl;

X is $-CH_2-$; $-CH_2-CHR-$; $-CH_2-CH_2-CH_2-$; $-CH_2C(O)-$; $-CHR'-CH_2-$;  ; or  ; preferably X is $-CH_2-$; $-CH_2-CHR-$; $-CH_2-CH_2-CH_2-$; $-CHR'-CH_2-$; or  ; preferably X is $-CH_2-$; $-CH_2-CHR-$; $-CH_2-CH_2-CH_2-$; or $-CHR'-CH_2-$; preferably X is $-CH_2-$; $-CH_2-CHR-$; or $-CHR'-CH_2-$;

R is hydrogen; hydroxyl; halogen or lower alkyl; preferably R is hydrogen; halogen or lower alkyl; preferably R is hydrogen or halogen;

n is 1 or 2; if n is 2, R^1 may be independently from each other; preferably n is 1;

o is 1 or 2; if o is 2, R^2 may be independently from each other; preferably o is 1.

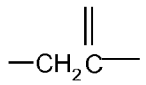
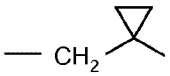
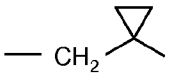
In an embodiment, the invention provides compounds of formula IA wherein

R^1 is hydrogen; C_{1-6}alkyl; C_{1-6}alkyl substituted by halogen; halogen; lower alkoxy; C_{1-6}alkoxy substituted by halogen; or is cyano; preferably R^1 is C_{1-6}alkyl substituted by halogen; halogen; or C_{1-6}alkoxy; preferably R^1 is C_{1-6}alkyl substituted by halogen; or halogen;

R^2 is hydrogen; C_{1-6}alkyl; C_{1-6}alkyl substituted by halogen; halogen; C_{1-6}alkoxy; or is C_{1-6}alkoxy substituted by halogen; preferably R^2 is hydrogen; C_{1-6}alkyl; halogen; or is C_{1-6}alkoxy; preferably R^2 is hydrogen; halogen; or is C_{1-6}alkoxy;

C_1 is phenyl; benzo[1,3]dioxol; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; thiophen-2-yl; pyrazine-2-yl; pyridazin-4-yl; pyrimidin-5-yl; piperidin-1yl; tetrahydro-2H-pyran-4-yl; or cycloalkyl; preferably C_1 is phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; thiophen-2-yl; pyrazine-2-yl; pyridazin-4-yl; pyrimidin-5-yl; piperidin-1yl; or tetrahydro-2H-pyran-4-yl; preferably C_1 is phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; pyrazine-2-yl; pyridazin-4-yl; pyrimidin-5-yl; or piperidin-1yl; preferably C_1 is phenyl; pyridine-3-yl; pyridine-4-yl; pyrazine-2-yl; pyridazin-4-yl; or piperidin-1yl; preferably C_1 is phenyl; pyridine-3-yl; pyridine-4-yl; or pyridazin-4-yl; preferably C_1 is phenyl; or pyridine-3-yl;

C_2 is phenyl; benzo[1,3]dioxol; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; thiophen-2-yl; pyrazine-2-yl; pyridazin-4-yl; pyrimidin-5-yl; piperidin-1yl; tetrahydro-2H-pyran-4-yl; or cycloalkyl; preferably C_2 is phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; pyrazine-2-yl; pyridazin-4-yl; pyrimidin-5-yl; piperidin-1yl; tetrahydro-2H-pyran-4-yl; or cycloalkyl; preferably C_2 is phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; piperidin-1yl; tetrahydro-2H-pyran-4-yl; or cycloalkyl; preferably C_2 is phenyl; pyridine-3-yl; pyridine-4-yl; or tetrahydro-2H-pyran-4-yl; preferably C_2 is phenyl; pyridine-3-yl; pyridine-4-yl; or tetrahydro-2H-pyran-4-yl;

X is $-CH_2-$; $-CH_2-CHR-$; $-CH_2-CH_2-CH_2-$; $-CH_2C(O)-$; $-CHR'-CH_2-$;  ; or  ; preferably X is $-CH_2-$; $-CH_2-CHR-$; $-CH_2-CH_2-CH_2-$; $-CHR'-CH_2-$; or  ; preferably X is $-CH_2-$; $-CH_2-CHR-$; $-CH_2-CH_2-CH_2-$; or $-CHR'-CH_2-$; preferably X is $-CH_2-$; $-CH_2-CHR-$; or $-CHR'-CH_2-$;

R is hydrogen; hydroxyl; halogen or C_{1-6}alkyl; preferably R is hydrogen; halogen or C_{1-6}alkyl; preferably R is hydrogen or halogen;

n is 1 or 2; if n is 2, R^1 may be independently from each other; preferably n is 1;

o is 1 or 2; if o is 2, R^2 may be independently from each other; preferably o is 1.

In another particular embodiment of the present invention, the compounds have a structure according to formula IA, wherein C^1 is selected from: phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; pyrazine-2-yl; pyridazin-4-yl; or pyrimidin-5-yl.

In another particular embodiment of the present invention, the compounds have a structure according to formula IA, wherein C^2 is selected from: phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; pyrazine-2-yl; tetrahydro-2H-pyran-4-yl; or cycloalkyl.

In a particular embodiment of the invention, the compounds have a structure of formula IA, whereby C^1 is pyridine-2-yl; pyridine-3-yl; or pyridine-4-yl; and C^2 is phenyl; yet more in particular C^1 is pyridine-3-yl; or pyridine-4-yl; yet more in particular C^1 is pyridine-3-yl.

In another particular embodiment of the present invention, the compounds have a structure according to formula IA, wherein C^1 is phenyl and C^2 is phenyl.

In another particular embodiment of the present invention, the compounds have a structure according to formula IA, wherein C^1 is phenyl; C^2 is phenyl and n is 1.

In another particular embodiment of the present invention, the compounds have a structure according to formula IA, wherein C^1 is phenyl; C^2 is phenyl and n is 2.

In another particular embodiment of the present invention, the compounds have a structure according to formula IA, wherein C^1 is phenyl; C^2 is phenyl and o is 1.

In another particular embodiment of the present invention, the compounds have a structure according to formula IA, wherein C^1 is phenyl; C^2 is phenyl and o is 2.

In another particular embodiment of the present invention, the compounds have a structure according to formula IA, wherein C^1 is phenyl and C^2 is tetrahydro-2H-pyran-4-yl.

In a particular embodiment of the invention, the compounds have a structure of formula IA, whereby C^1 is pyridine-2-yl; pyridine-3-yl; or pyridine-4-yl; and C^2 is tetrahydro-2H-pyran-4-yl; yet more in particular C^1 is pyridine-3-yl; or pyridine-4-yl; yet more in particular C^1 is pyridine-3-yl.

In a particular embodiment of the invention, the compounds have a structure of formula IA, whereby C^1 is phenyl; and C^2 is pyridine-2-yl; pyridine-3-yl; or pyridine-4-yl; yet more in particular C^2 is pyridine-3-yl; or pyridine-4-yl; yet more in particular C^2 is pyridine-3-yl.

In another particular embodiment of the present invention, the compounds have a structure according to formula IA, wherein C^1 is pyridazin-4-yl and C^2 is phenyl.

In a particular embodiment of the invention, the compounds have a structure of formula IA, whereby C^1 is pyridine-2-yl; pyridine-3-yl; or pyridine-4-yl; and C^2 is pyridine-3-yl; yet more in particular C^1 is pyridine-3-yl; or pyridine-4-yl; yet more in particular C^1 is pyridine-3-yl.

In a particular embodiment of the invention, the compounds have a structure of formula IA, whereby C^1 is pyridine-2-yl; pyridine-3-yl; or pyridine-4-yl; and C^2 is

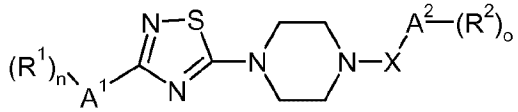
pyridine-4-yl; yet more in particular C^1 is pyridine-3-yl; or pyridine-4-yl; yet more in particular C^1 is pyridine-3-yl.

In a particular embodiment of the invention, the compounds have a structure of formula IA, whereby C^1 is pyridine-3-yl; and C^2 is pyridine-2-yl; pyridine-3-yl; or pyridine-4-yl; yet more in particular C^2 is pyridine-3-yl; or pyridine-4-yl; yet more in particular C^2 is pyridine-3-yl.

In a particular embodiment of the invention, the compounds have a structure of formula IA, whereby C^1 is pyridine-4-yl; and C^2 is pyridine-2-yl; pyridine-3-yl; or pyridine-4-yl; yet more in particular C^2 is pyridine-3-yl; or pyridine-4-yl; yet more in particular C^2 is pyridine-3-yl.

In a particular embodiment, the present invention relates to the following compounds, uses, medicaments and processes:

E1. A compound of formula I



I

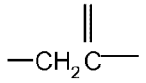
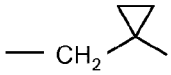
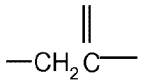
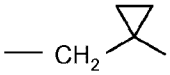
wherein

R^1 is hydrogen; lower alkyl; lower alkyl substituted by halogen; halogen; lower alkoxy; lower alkoxy substituted by halogen; or cyano;

R^2 is hydrogen; lower alkyl; lower alkyl substituted by halogen; halogen; lower alkoxy; or is lower alkoxy substituted by halogen;

A^1 is phenyl; benzo[1,3]dioxol; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; thiophen-2-yl; pyrazine-2-yl; or cycloalkyl;

A^2 is phenyl; benzo[1,3]dioxol; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; thiophen-2-yl; pyrazine-2-yl; or cycloalkyl;

X is a bond; -CH_2-; -CH_2-CHR-; -CH_2-CH_2-CH_2-; -$CH_2C(O)$-; -C(O)NH-; -CHR'-CH_2-;  ;or  ; preferably is -CH_2-; -CH_2-CHR-; -CH_2-CH_2-CH_2-; -$CH_2C(O)$-; -CHR'-CH_2-;  ;or  ;

R is hydrogen; hydroxyl; halogen; or lower alkyl;

R' is lower alkyl;

n is 1 or 2; if n is 2, R^1 may be independently from each other;

o is 1 or 2; if o is 2, R^2 may be independently from each other;

or a pharmaceutically active salt thereof, a stereoisomeric form, including an individual diastereoisomer or enantiomer of the compound of formula (I) as well as a racemic or non-racemic mixture thereof.

E2. A compound of formula I according to E1, wherein A^1 and A^2 are both phenyl.

E3. Compound of formula I according to E2, which compounds are

1-(2,4-Dichloro-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine

1-Phenethyl-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine

1-[2-(3,4-Dichloro-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine

1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine

1-[3-(3-Methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine

1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(3-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(3-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[2-(4-Methoxy-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-fluoro-phenyl)-ethyl]-piperazine

1-[2-(3-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-*m*-tolyl-ethyl)-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine
1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-*p*-tolyl-ethyl)-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-phenyl)-ethyl]-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-fluoro-phenyl)-ethyl]-piperazine
1-[2-(2-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(3,5-Dichloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(3-methoxy-phenyl)-propyl]-piperazine
1-[3-(4-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine
1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(4-trifluoromethoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(4-trifluoromethoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethoxy-phenyl)-ethyl]-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(2-methoxy-phenyl)-propyl]-piperazine
1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(4-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(3,5-Dichloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
1-[3-(4-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine

1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(4-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-ethoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-isopropoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(4-methoxy-phenyl)-propyl]-piperazine

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(4-methoxy-phenyl)-ethanone

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(4-methoxy-phenyl)-ethanol

1-[3-(4-Chloro-2-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-2-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[3-(2-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine

1-[3-(2-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-allyl]-piperazine

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-methoxy-phenyl)-ethanone

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-methoxy-phenyl)-ethanol

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-fluoro-phenyl)-ethanone

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-fluoro-phenyl)-ethanol

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-fluoro-2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-fluoro-2-(3-methoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Fluoro-2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Fluoro-2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[1-(4-Chloro-phenyl)-cyclopropylmethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-difluoromethoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-difluoromethoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-isopropoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-propyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-1-methyl-ethyl]-piperazine

4-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-fluoro-4-methoxy-phenyl)-ethyl]-piperazine

3-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine

1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine

1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine

1-[2-(4-Fluoro-phenyl)-ethyl]-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine

1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine

1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine

1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine

1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine
4-[5-(4-Phenethyl-piperazin-1-yl)-[1,2,4]thiadiazol-3-yl]-benzonitrile
3-[5-(4-Phenethyl-piperazin-1-yl)-[1,2,4]thiadiazol-3-yl]-benzonitrile
4-(5-{4-[2-(4-Fluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
3-(5-{4-[2-(4-Fluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
4-(5-{4-[2-(4-Chloro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
3-(5-{4-[2-(4-Chloro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
4-{5-[4-(2-Methyl-benzyl)-piperazin-1-yl]-[1,2,4]thiadiazol-3-yl}-benzonitrile
3-{5-[4-(2-Methyl-benzyl)-piperazin-1-yl]-[1,2,4]thiadiazol-3-yl}-benzonitrile
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine
1-[2-(3,4-Difluoro-phenyl)-ethyl]-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
3-(5-{4-[2-(3,4-Difluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
4-(5-{4-[2-(3,4-Difluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine
1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine
4-(5-{4-[2-(3-Trifluoromethyl-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine
1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine or

4-(5-{4-[2-(4-Trifluoromethyl-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile.

E4. A compound of formula I according to E1, wherein at least one of A^1 or A^2 is pyridine-2-yl, pyridine-3-yl or pyridine-4-yl.

E5. Compounds of formula I according to E4, which compounds are

1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine

1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(6-trifluoromethyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(6-trifluoromethyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[2-(4-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine

1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine

1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine

1-[3-(6-Methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine

1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[2-(4-Fluoro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine

1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine

1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine

4-(5-{4-[2-(6-Methoxy-pyridin-3-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile

3-(5-{4-[2-(6-Methoxy-pyridin-3-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile

4-(5-{4-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile

3-(5-{4-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile

1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine

1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine

1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine

1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(5-chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine

1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine

1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine

1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine
1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine
1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(5-chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine
1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine
1-[2-(3,4-Difluoro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine
1-(2-Methyl-benzyl)-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine or
1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine.

E6. A compound of formula I according to E1, wherein one of A^1 or A^2 is benzo[1,3]dioxol.

E7. A compound of formula I according to E6, which compound is

1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine.

E8. A compound of formula I according to E1, wherein at least one of A^1 or A^2 is thiophen-2-yl.

E9. Compound of formula I according to E8, which compounds are

1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-thiophen-2-yl-[1,2,4]thiadiazol-5-yl)-piperazine or

1-[2-(4-Methoxy-phenyl)-ethyl]-4-(3-thiophen-2-yl-[1,2,4]thiadiazol-5-yl)-piperazine.

E10. A compound of formula I according to E1, wherein at least one of A^1 or A^2 are pyrazine-2-yl.

E11. Compounds of formula I according to E10, which compounds are

2-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-pyrazine or

2-(5-{4-[2-(3-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-pyrazine.

E12. A compound of formula I according to E1, wherein A^2 is cycloalkyl.

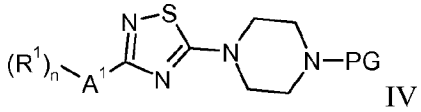
E13. Compounds of formula I according to E12, which compounds are

1-(2-Cyclohexyl-ethyl)-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine or

1-(2-Cyclohexyl-ethyl)-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine.

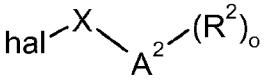
E14. A process for preparation of compounds of formula I according to E1, which process comprises

coupling a compound of formula

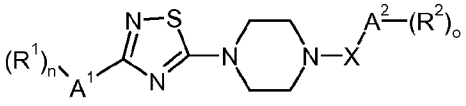


IV

with a compound of formula



to give a compound of formula



I

wherein the definitions are as described in E1, or

if desired, converting the compounds obtained into pharmaceutically acceptable acid addition salts.

E15. A compound according to any one of E1 -E13, when manufactured according to a process of E14.

E16. A compound according to any one of E1 – E13 for use as therapeutically active substance.

E17. A medicament containing one or more compounds as described in any one of E1 to E13 and pharmaceutically acceptable excipients.

E18. A medicament according to E17, wherein the illnesses which may be treated are Alzheimer's disease, Pick's disease, corticobasal degeneration, progressive

supranuclear palsy, frontotemporal dementia and parkinsonism (linked to chromosome 17, FTDP-17).

E19. The use of a compound as according to any one of E1 to E13 for the treatment of Alzheimer's disease, Pick's disease, corticobasal degeneration, progressive supranuclear palsy, frontotemporal dementia and parkinsonism (linked to chromosome 17, FTDP-17).

E20. The use of a compound according to any one of E1 to E13 for the manufacture of medicaments for the treatment of Alzheimer's disease, Pick's disease, corticobasal degeneration, progressive supranuclear palsy, frontotemporal dementia and parkinsonism (linked to chromosome 17, FTDP-17).

E21. A method for the treatment of Alzheimer's disease, Pick's disease, corticobasal degeneration, progressive supranuclear palsy, frontotemporal dementia and parkinsonism (linked to chromosome 17, FTDP-17), which method comprising administering an effective amount of a compound as defined in any one of E1 – E13.

E22. The invention as described herein .

In an embodiment, the compounds of formula IA have a structure of formula I.

For example, the present invention encompasses a compound of formula I or IA, wherein C^1 has the same meaning as defined for A^1 and C^2 has the same meaning as defined for A^2; wherein,

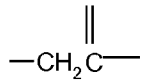
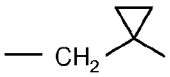
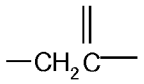
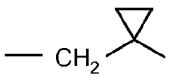
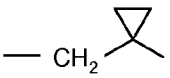
R^1 is hydrogen; lower alkyl; lower alkyl substituted by halogen; halogen; lower alkoxy; lower alkoxy substituted by halogen; or is cyano; preferably R^1 is lower alkyl substituted by halogen; halogen; or lower alkoxy; preferably R^1 is lower alkyl substituted by halogen; or halogen;

R^2 is hydrogen; lower alkyl; lower alkyl substituted by halogen; halogen; lower alkoxy; or is lower alkoxy substituted by halogen; preferably R^2 is hydrogen; lower alkyl; halogen; or is lower alkoxy; preferably R^2 is hydrogen; halogen; or is lower alkoxy;

A^1 is phenyl; benzo[1,3]dioxol; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; thiophen-2-yl; pyrazine-2-yl; or cycloalkyl; preferably A^1 is phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; thiophen-2-yl; pyrazine-2-yl; or cycloalkyl; preferably A^1 is phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; pyrazine-2-yl; or cycloalkyl; preferably A^1 is

phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; or pyrazine-2-yl; preferably A^1 is phenyl; pyridine-3-yl or pyridine-4-yl; preferably A^1 is phenyl; or pyridine-3-yl;

A^2 is phenyl; benzo[1,3]dioxol; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; pyrazine-2-yl; thiophen-2-yl; or cycloalkyl; preferably A^2 is phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; thiophen-2-yl; pyrazine-2-yl; or cycloalkyl; preferably A^2 is phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; or pyrazine-2-yl; preferably A^2 is phenyl; pyridine-3-yl; pyridine-4-yl; or pyrazine-2-yl; preferably A^2 is phenyl; pyridine-3-yl; or pyridine-4-yl;

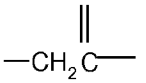
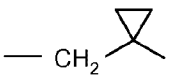
X is a bond; $-CH_2-$; $-CH_2-CHR-$; $-CH_2-CH_2-CH_2-$; $-CH_2C(O)-$; $-C(O)NH-$; $-CHR'-CH_2-$;  ; or  ; preferably X is $-CH_2-$; $-CH_2-CHR-$; $-CH_2-CH_2-CH_2-$; $-CH_2C(O)-$; $-CHR'-CH_2-$;  ; or  ; preferably X is $-CH_2-$; $-CH_2-CHR-$; $-CH_2-CH_2-CH_2-$; $-CHR'-CH_2-$; or  ; preferably X is $-CH_2-$; $-CH_2-CHR-$; $-CHR'-CH_2-$;

R is hydrogen; hydroxyl; halogen; or lower alkyl; preferably R is hydrogen; halogen or lower alkyl; preferably R is hydrogen or halogen;

R' is lower alkyl;

n is 1 or 2; if n is 2, R^1 may be independently from each other; preferably n is 1;

o is 1 or 2; if o is 2, R^2 may be independently from each other;

In a yet more particular embodiment, the compounds of the present invention have a structure according to formula I or IA, whereby X is $-CH_2-$; $-CH_2-CHR-$; $-CH_2-CH_2-CH_2-$; $-CH_2C(O)-$; $-CHR'-CH_2-$;  ; or  .

In a particular embodiment of the present invention, the compounds have a structure according to formula IA or formula I, wherein X is selected from $-CH_2-CHR-$; or $-CHR'-CH_2-$. In yet another particular embodiment, R is selected from hydrogen or lower alkyl. In a yet more particular embodiment, R is hydrogen.

In another particular embodiment of the present invention, the compounds have a structure according to formula IA or formula I, wherein X is selected from $-CH_2-CHR-$; or $-CHR'-CH_2-$. In yet another particular embodiment, R is hydrogen. In another particular embodiment of the present invention, the compounds have a structure according to formula I, wherein A^1 is selected from: phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; pyrazine-2-yl.

In another particular embodiment of the present invention, the compounds have a structure according to formula I, wherein A^2 is selected from: phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; pyrazine-2-yl; or cycloalkyl.

In a particular embodiment of the invention, the compounds have a structure of formula I, whereby A^1 is pyridine-2-yl; pyridine-3-yl; or pyridine-4-yl; and A^2 is phenyl; yet more in particular A^1 is pyridine-3-yl; or pyridine-4-yl; yet more in particular A^1 is pyridine-3-yl.

In another particular embodiment of the present invention, the compounds have a structure according to formula I, wherein A^1 is phenyl; A^2 is phenyl and n is 1.

In another particular embodiment of the present invention, the compounds have a structure according to formula I, wherein A^1 is phenyl; A^2 is phenyl and n is 2.

In another particular embodiment of the present invention, the compounds have a structure according to formula I, wherein A^1 is phenyl; A^2 is phenyl and o is 1.

In another particular embodiment of the present invention, the compounds have a structure according to formula I, wherein A^1 is phenyl; A^2 is phenyl and o is 2.

In a particular embodiment of the invention, the compounds have a structure of formula I, whereby A^1 is phenyl; and A^2 is pyridine-2-yl; pyridine-3-yl; or pyridine-4-yl; yet more in particular A^2 is pyridine-3-yl; or pyridine-4-yl; yet more in particular A^2 is pyridine-3-yl.

In a particular embodiment of the invention, the compounds have a structure of formula I, whereby A^1 is pyridine-2-yl; pyridine-3-yl; or pyridine-4-yl; and A^2 is pyridine-3-yl; yet more in particular A^1 is pyridine-3-yl; or pyridine-4-yl; yet more in particular A^1 is pyridine-3-yl.

In a particular embodiment of the invention, the compounds have a structure of formula I, whereby A^1 is pyridine-2-yl; pyridine-3-yl; or pyridine-4-yl; and A^2 is pyridine-4-yl; yet more in particular A^1 is pyridine-3-yl; or pyridine-4-yl; yet more in particular A^1 is pyridine-3-yl.

In a particular embodiment of the invention, the compounds have a structure of formula I, whereby A^1 is pyridine-3-yl; and A^2 is pyridine-2-yl; pyridine-3-yl; or pyridine-4-yl; yet more in particular A^2 is pyridine-3-yl; or pyridine-4-yl; yet more in particular A^2 is pyridine-3-yl.

In a particular embodiment of the invention, the compounds have a structure of formula I, whereby A^1 is pyridine-4-yl; and A^2 is pyridine-2-yl; pyridine-3-yl; or pyridine-4-yl; yet more in particular A^2 is pyridine-3-yl; or pyridine-4-yl; yet more in particular A^2 is pyridine-3-yl.

The present compounds are useful for treating certain neurodegenerative disorders characterized by cytotoxic TAU misfolding and/or aggregation in order to delay or halt the progression of such diseases. Such diseases are summarized under the term tauopathy. The term "Tauopathy" refers to a disease characterised by dysfunctioning and/or toxicity of the TAU protein, characterised by oligomers, aggregates or polymers of said protein. Such diseases include, but are not limited to, Alzheimer's disease, Pick's disease, corticobasal degeneration, progressive supranuclear palsy, frontotemporal dementia and parkinsonism (linked to chromosome 17, FTDP-17).

Tauopathies are characterised by insoluble aggregates or polymers of hyperphosphorylated TAU which are formed by self-polymerisation of TAU monomers. The precise molecular mechanisms involved in TAU aggregation are not precisely known, but may involve a partial denaturation or misfolding of TAU in conformations which have a high propensity to self-organise into higher order structures. The misfolding and aggregation may be triggered by hyperphosphorylation of TAU, although at present, it cannot be excluded that such aberrant phosphorylation is a consequence rather than the cause of aggregation.

TAU is a protein with the ability to bind -and consequently stabilise and define- microtubule structure and function in neurons. The binding of TAU to microtubules is regulated by phosphorylation of TAU; several TAU phosphorylation sites and their

corresponding kinases have been identified which control phosphorylation status of TAU and consequently modulate the affinity of TAU-binding to microtubules.

An important aspect of the TAU aggregation is its associated cytotoxicity, which reduces neuronal integrity and functionality and ultimately resulting in disease symptoms. A direct role of TAU in disease onset has been established unequivocally by the elucidation of familial mutations in TAU, which appear to be responsible for a very early and sometimes aggressive form of tauopathy. Such mutations comprise changes in the amino acid sequence of TAU that -directly or indirectly promote neurotoxic aggregation.

Alzheimer's disease is the best known of these, where TAU protein is deposited within neurons in the form of neurofibrillary tangles (NFTs). They were first described by the eponymous Alois Alzheimer in one of his patients suffering from the disorder. The term "Alzheimer's disease" as used herein, refers to a chronic progressive nervous disease characterised by neurodegeneration with as most important (early) symptom being memory loss. As the disease advances, symptoms may include confusion, irritability and aggression, mood swings, language breakdown, long-term memory loss, and the general withdrawal of the sufferer as their senses decline.

Tangles are formed by hyperphosphorylation of a microtubule-associated protein known as TAU, causing it to aggregate in an insoluble form. (These aggregations of hyperphosphorylated TAU protein are also referred to as PHF, or "paired helical filaments"). The precise mechanism of tangle formation is not completely understood, and it is still controversial whether tangles are a primary causative factor in the disease or play a more peripheral role. AD is also classified as an amyloidosis because of the presence of senile plaques.

Other conditions in which neurofibrillary tangles are commonly observed include: Progressive supranuclear palsy, dementia pugilistica (chronic traumatic encephalopathy), frontotemporal dementia and parkinsonism linked to chromosome 17, Lytico-Bodig disease (Parkinson-dementia complex of Guam), tangle-predominant dementia with NFTs, similar to AD, but without plaques, ganglioglioma and gangliocytoma, meningioangiomatosis, subacute sclerosing panencephalitis, tuberous sclerosis, Hallervorden-Spatz disease, and lipofuscinosis.

The non-Alzheimer's tauopathies are sometimes grouped together as "Pick's complex". In Pick's disease and corticobasal degeneration TAU proteins are deposited in the form of inclusion bodies within swollen or "ballooned" neurons. Argyrophilic grain disease (AGD), another type of dementia, is marked by the presence of abundant argyrophilic grains and coiled bodies on microscopic examination of brain tissue.

Similar compounds as described in formula IA and I of the present invention have been described in WO2007/090617.

In contradiction to the findings in WO2007/090617, it has been found that if there is no linking group between the phenyl moiety and the thiadiazole group, there was a marked decrease of the clearance (Clint), in particular in the human *in-vitro* microsomes assay. It is very important for a drug to have a moderate or low clearance, as this often leads to a higher oral bioavailability. Reducing the clearance of a compound/drug, could then potentially reduce drastically the daily dose required for efficacy and therefore give also a much better safety profile as well. Therefore a low clearance is an essential feature for therapeutic applicability.

The following examples in the table below highlight these finding, where the use of compounds, wherein no linking group between the phenyl moiety and the thiadiazole group exists, have led to compounds with a lower clearance (Clint) and higher metabolic stability (MAB) in human *in vitro* microsomes.

Microsomal Stability Testing – Assay description

The microsomal stability assay measures the rate of disappearance of a test compound from an incubation containing human or animal liver microsomes and metabolic cofactors (typically NADPH). The assay is primarily used for ranking the relative CYP-mediated metabolism propensities of compounds within a chemical series and as a guide to selecting sufficiently stable compounds for pharmacokinetics and pharmacodynamics experiments. [In addition to CYPs, microsomally located enzymes which also make use of NADPH (such as flavone mono-oxygenases) and those which require no cofactors (such as carboxylesterases) are active.]

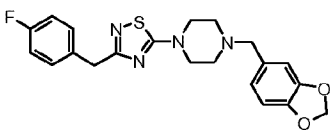
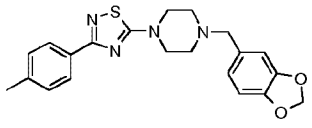
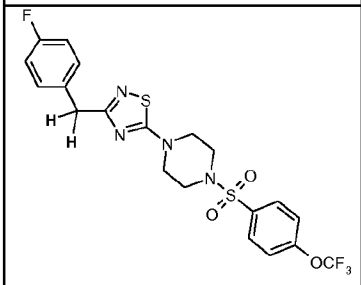
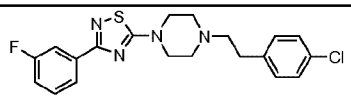
Incubations are performed in 96-well deep-well plates with a final incubation volume of 600 µL. Incubations contain (finally) 1-2µM test compound, 0.5 mg/mL liver microsomes (typically human, rat or mouse) and NADPH regenerating system. 50 µL

aliquots are removed after 1, 3, 6, 9, 15, 25, 35 and 45 minutes and quenched in 150 µL acetonitrile containing internal standard. Samples are then cooled and centrifuged before analysis by LC-MS/MS.

Log peak area ratio (test compound peak area / internal standard peak area) is plotted against incubation time and a linear fit made to the data with emphasis upon the initial rate of compound disappearance. The slope of the fit is then used to calculate the intrinsic clearance:

Cl_{int} (µL/min/mg) = -slope (min^{-1}) * 1000 / [protein concentration (mg/mL)]

Table 1

Compounds disclosed in WO2007/090617	**MAB and Clint data**	**Compounds disclosed in the present application**	**MAB and Clint data**
 According to WO2007/090617	Clint.(Hum/Rat) **39**/482 uL/min/mg protein	 Example 2	Clint.(Hum/Rat) **19**/48 uL/min/mg protein
 According to WO2007/090617	Clint.(Hum/Rat) **46**/103 uL/min/mg protein	 Example 88	Clint.(Hum/Rat) **12**/23 uL/min/mg protein

As it can be seen in the table above, it has been found a marked increase of metabolic stability (increase MAB, decrease of the clearance Clint) in particular in human in vitro microsomes.

Objects of the present invention are new compounds of formula IA and I and their pharmaceutically acceptable salts, their use for the treatment of diseases related to the biological function of dysfunction of TAU protein, which diseases comprise Alzheimer's disease, Pick's disease, corticobasal degeneration, progressive supranuclear palsy,

frontotemporal dementia and parkinsonism (linked to chromosome 17, FTDP-17), their manufacture and medicaments based on a compound in accordance with the invention in the control or prevention of illnesses.

The preferred indication using the compounds of the present invention is Alzheimer's disease.

As used herein, the term "lower alkyl" denotes a saturated straight- or branched-chain group containing from 1 to 7 carbon atoms, preferably from 1 to 6 carbon atoms, for example, methyl, ethyl, propyl, isopropyl, n-butyl, i-butyl, 2-butyl, t-butyl and the like. Preferred alkyl groups are groups with 1 - 4 carbon atoms.

As used herein, the term "lower alkoxy" denotes a group wherein the alkyl residue is as defined above and which is attached via an oxygen atom.

As used herein, the term "lower alkyl substituted by halogen" denotes an alkyl group as defined above, wherein at least one hydrogen atom is replaced by halogen, for example CF_3, CHF_2, CH_2F, CH_2CF_3, $CH_2CH_2CF_3$, $CH_2CF_2CF_3$ and the like.

As used herein, the term "lower alkoxy substituted by halogen" denotes an alkoxyl group as defined above, wherein at least one hydrogen atom is replaced by halogen, for example OCF_3, $OCHF_2$, OCH_2F, OCH_2CF_3, $OCH_2CH_2CF_3$, $OCH_2CF_2CF_3$ and the like.

The term "halogen" denotes chlorine, iodine, fluorine and bromine.

The term "cycloalkyl" is an alkylene ring, containing from 3 to 6 carbon ring atoms. Preferred is cyclopropyl.

The term "pharmaceutically acceptable acid addition salts" embraces salts with inorganic and organic acids, such as hydrochloric acid, nitric acid, sulfuric acid, phosphoric acid, citric acid, formic acid, fumaric acid, maleic acid, acetic acid, succinic acid, tartaric acid, methane-sulfonic acid, p-toluenesulfonic acid and the like.

One embodiment of the invention are compounds of formula IA, wherein C^1 and C^2 are both phenyl, for example the following compounds

1-(2,4-Dichloro-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine

1-Phenethyl-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine

1-[2-(3,4-Dichloro-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine

1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine
1-[3-(3-Methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine
1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(3-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(3-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[2-(4-Methoxy-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-fluoro-phenyl)-ethyl]-piperazine
1-[2-(3-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-*m*-tolyl-ethyl)-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine
1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-*p*-tolyl-ethyl)-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-phenyl)-ethyl]-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-fluoro-phenyl)-ethyl]-piperazine
1-[2-(2-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(3,5-Dichloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(3-methoxy-phenyl)-propyl]-piperazine
1-[3-(4-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine
1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(4-trifluoromethoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(4-trifluoromethoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(2-methoxy-phenyl)-propyl]-piperazine

1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(4-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[3-(3,5-Dichloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine

1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(4-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-ethoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-isopropoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(4-methoxy-phenyl)-propyl]-piperazine

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(4-methoxy-phenyl)-ethanone

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(4-methoxy-phenyl)-ethanol

1-[3-(4-Chloro-2-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-2-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[3-(2-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine

1-[3-(2-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-allyl]-piperazine

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-methoxy-phenyl)-ethanone

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-methoxy-phenyl)-ethanol

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-fluoro-phenyl)-ethanone

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-fluoro-phenyl)-ethanol

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-fluoro-2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-fluoro-2-(3-methoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Fluoro-2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Fluoro-2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[1-(4-Chloro-phenyl)-cyclopropylmethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-difluoromethoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-difluoromethoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-isopropoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-propyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-1-methyl-ethyl]-piperazine

4-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-fluoro-4-methoxy-phenyl)-ethyl]-piperazine

3-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine

1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine

1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine
1-[2-(4-Fluoro-phenyl)-ethyl]-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine
1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine
1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine
1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine
1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine
4-[5-(4-Phenethyl-piperazin-1-yl)-[1,2,4]thiadiazol-3-yl]-benzonitrile
3-[5-(4-Phenethyl-piperazin-1-yl)-[1,2,4]thiadiazol-3-yl]-benzonitrile
4-(5-{4-[2-(4-Fluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
3-(5-{4-[2-(4-Fluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
4-(5-{4-[2-(4-Chloro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
3-(5-{4-[2-(4-Chloro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
4-{5-[4-(2-Methyl-benzyl)-piperazin-1-yl]-[1,2,4]thiadiazol-3-yl}-benzonitrile
3-{5-[4-(2-Methyl-benzyl)-piperazin-1-yl]-[1,2,4]thiadiazol-3-yl}-benzonitrile
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine
1-[2-(3,4-Difluoro-phenyl)-ethyl]-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
3-(5-{4-[2-(3,4-Difluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
4-(5-{4-[2-(3,4-Difluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine

1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine

4-(5-{4-[2-(3-Trifluoromethyl-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine

1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine

4-(5-{4-[2-(4-Trifluoromethyl-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile.

5-(4-(3-phenylpropyl)piperazin-1-yl)-3-(p-tolyl)-1,2,4-thiadiazole

5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-3-(3-fluorophenyl)-1,2,4-thiadiazole or

3-(3,4-difluorophenyl)-5-(4-(3-(trifluoromethyl)phenethyl)piperazin-1-yl)-1,2,4-thiadiazole.

One further embodiment of the invention are compounds of formula IA, wherein at least one of C^1 or C^2 is pyridine-2-yl, pyridine-3-yl or pyridine-4-yl, for example the following compounds

1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine

1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(6-trifluoromethyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(6-trifluoromethyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[2-(4-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine

1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine

1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine

1-[3-(6-Methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine

1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[2-(4-Fluoro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine

1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine

1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine

4-(5-{4-[2-(6-Methoxy-pyridin-3-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile

3-(5-{4-[2-(6-Methoxy-pyridin-3-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile

4-(5-{4-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile

3-(5-{4-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile

1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine

1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine
1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine
1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(5-chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine
1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine
1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine
1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine
1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine
1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(5-chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine
1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine
1-[2-(3,4-Difluoro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine
1-(2-Methyl-benzyl)-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine
1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine.

3-(4-chloropyridin-2-yl)-5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-1,2,4-thiadiazole
3-(4-chloropyridin-2-yl)-5-(4-(3-(trifluoromethyl)phenethyl)piperazin-1-yl)-1,2,4-thiadiazole
3-(5-chloropyridin-3-yl)-5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-1,2,4-thiadiazole
3-(2-chloropyridin-4-yl)-5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole
5-(4-(4-chlorophenethyl)piperazin-1-yl)-3-(2-chloropyridin-4-yl)-1,2,4-thiadiazole
3-(2-chloropyridin-4-yl)-5-(4-phenethylpiperazin-1-yl)-1,2,4-thiadiazole
3-(2-methylpyridin-4-yl)-5-(4-phenethylpiperazin-1-yl)-1,2,4-thiadiazole or
5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-3-(2-methylpyridin-4-yl)-1,2,4-thiadiazole.

One further embodiment of the invention are compounds of formula IA, wherein C^2 is cycloalkyl, for example the following compounds

1-(2-Cyclohexyl-ethyl)-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
1-(2-Cyclohexyl-ethyl)-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
3-(4-chlorophenyl)-5-(4-(2-cyclohexylethyl)piperazin-1-yl)-1,2,4-thiadiazole or
3-(3-chlorophenyl)-5-(4-(2-cyclohexylethyl)piperazin-1-yl)-1,2,4-thiadiazole.

One further embodiment of the invention are compounds of formula IA, wherein C^2 is piperidin-1yl, for example the following compound

3-(5-chloropyridin-3-yl)-5-(4-(2-(piperidin-1-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole.

One further embodiment of the invention are compounds of formula IA, wherein C^2 is tetrahydro-2H-pyran-4-yl, for example the following compounds

3-(3,4-difluorophenyl)-5-(4-(2-(tetrahydro-2H-pyran-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole
3-(3-chlorophenyl)-5-(4-(2-(tetrahydro-2H-pyran-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole
3-(5-chloropyridin-3-yl)-5-(4-(2-(tetrahydro-2H-pyran-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole or
3-(4-chlorophenyl)-5-(4-(2-(tetrahydro-2H-pyran-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole.

One further embodiment of the invention are compounds of formula IA, wherein C^1 is pyridazin-4-yl, for example the following compounds

3-(6-methylpyridazin-4-yl)-5-(4-phenethylpiperazin-1-yl)-1,2,4-thiadiazole
5-(4-(4-fluorophenethyl)piperazin-1-yl)-3-(6-methylpyridazin-4-yl)-1,2,4-thiadiazole
5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-3-(6-methylpyridazin-4-yl)-1,2,4-thiadiazole
5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-3-(6-methylpyridazin-4-yl)-1,2,4-thiadiazole or

5-(4-(4-methoxyphenethyl)piperazin-1-yl)-3-(6-methylpyridazin-4-yl)-1,2,4-thiadiazole.

One further embodiment of the invention are compounds of formula IA, wherein C^1 is pyrimidin-5-yl, for example the following compounds

3-(2-methylpyrimidin-5-yl)-5-(4-phenethylpiperazin-1-yl)-1,2,4-thiadiazole
5-(4-(4-methoxyphenethyl)piperazin-1-yl)-3-(2-methylpyrimidin-5-yl)-1,2,4-thiadiazole
5-(4-(4-chlorophenethyl)piperazin-1-yl)-3-(2-methylpyrimidin-5-yl)-1,2,4-thiadiazole
5-(4-(4-fluorophenethyl)piperazin-1-yl)-3-(2-methylpyrimidin-5-yl)-1,2,4-thiadiazole
5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-3-(2-methylpyrimidin-5-yl)-1,2,4-thiadiazole or

5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-3-(2-methylpyrimidin-5-yl)-1,2,4-thiadiazole.

One embodiment of the invention are compounds of formula I, wherein A^1 and A^2 are both phenyl, for example the following compounds

1-(2,4-Dichloro-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine; 1-Phenethyl-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine; 1-[2-(3,4-Dichloro-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine; 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine; 1-[3-(3-Methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine; 1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(3-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine; 1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(3-methoxy-

phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[2-(4-Methoxy-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-fluoro-phenyl)-ethyl]-piperazine; 1-[2-(3-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-*m*-tolyl-ethyl)-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine; 1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-*p*-tolyl-ethyl)-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-phenyl)-ethyl]-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-fluoro-phenyl)-ethyl]-piperazine; 1-[2-(2-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[3-(3,5-Dichloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(3-methoxy-phenyl)-propyl]-piperazine; 1-[3-(4-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine; 1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(4-trifluoromethoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(4-trifluoromethoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethoxy-phenyl)-ethyl]-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(2-methoxy-phenyl)-propyl]-piperazine; 1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(4-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine ;1-[3-(3,5-Dichloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine; 1-[3-(4-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(4-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-ethoxy-phenyl)-ethyl]-piperazine1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-isopropoxy-phenyl)-ethyl]-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(4-methoxy-phenyl)-propyl]-piperazine; 2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(4-methoxy-phenyl)-ethanone; 2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(4-methoxy-phenyl)-ethanol; 1-[3-(4-Chloro-2-

fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine; 1-[3-(4-Chloro-2-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine; 1-[3-(2-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine1-[3-(2-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-allyl]-piperazine2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-methoxy-phenyl)-ethanone; 2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-methoxy-phenyl)-ethanol; 2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-fluoro-phenyl)-ethanone; 2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-fluoro-phenyl)-ethanol; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-fluoro-2-(4-methoxy-phenyl)-ethyl]-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-fluoro-2-(3-methoxy-phenyl)-ethyl]-piperazine; 1-[3-(4-Fluoro-2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine; 1-[3-(4-Fluoro-2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine; 1-[1-(4-Chloro-phenyl)-cyclopropylmethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-difluoromethoxy-phenyl)-ethyl]-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-difluoromethoxy-phenyl)-ethyl]-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-isopropoxy-phenyl)-ethyl]-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-propyl]-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-1-methyl-ethyl]-piperazine; 4-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-fluoro-4-methoxy-phenyl)-ethyl]-piperazine; 3-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile; 1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine; 1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine; 1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine; 1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine; 1-[2-(4-Fluoro-phenyl)-ethyl]-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine;

1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine; 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine; 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine; 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine; 1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine; 4-[5-(4-Phenethyl-piperazin-1-yl)-[1,2,4]thiadiazol-3-yl]-benzonitrile; 3-[5-(4-Phenethyl-piperazin-1-yl)-[1,2,4]thiadiazol-3-yl]-benzonitrile; 4-(5-{4-[2-(4-Fluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile; 3-(5-{4-[2-(4-Fluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile; 4-(5-{4-[2-(4-Chloro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile; 3-(5-{4-[2-(4-Chloro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile; 4-{5-[4-(2-Methyl-benzyl)-piperazin-1-yl]-[1,2,4]thiadiazol-3-yl}-benzonitrile; 3-{5-[4-(2-Methyl-benzyl)-piperazin-1-yl]-[1,2,4]thiadiazol-3-yl}-benzonitrile; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine; 1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine; 1-[2-(3,4-Difluoro-phenyl)-ethyl]-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine; 3-(5-{4-[2-(3,4-Difluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile; 4-(5-{4-[2-(3,4-Difluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine; 1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine;1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine; 4-(5-{4-[2-(3-Trifluoromethyl-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine; 1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine; 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine; or 4-(5-{4-[2-(4-Trifluoromethyl-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile.

One further embodiment of the invention are compounds of formula I, wherein at least one of A^1 or A^2 is pyridine-2-yl, pyridine-3-yl or pyridine-4-yl, for example the following compounds: 1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine; 1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(6-trifluoromethyl-pyridin-3-yl)-

[1,2,4]thiadiazol-5-yl]-piperazine; 1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(6-trifluoromethyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[2-(4-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine; 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine; 1[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine; 1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine; 1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine; 1-[3-(6-Methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine; 1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[2-(4-Fluoro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine; 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine; 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine; 4-(5-{4-[2-(6-Methoxy-pyridin-3-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile; 3-(5-{4-[2-(6-Methoxy-pyridin-3-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile; 4-(5-{4-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile; 3-(5-{4-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile ; 1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine ; 1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine; 1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine; 1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(5-chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine ; 1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine; 1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine; 1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-

benzyl)-piperazine; 1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine; 1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine; 1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine; 1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(5-chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine; 1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine; 1-[2-(3,4-Difluoro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine; 1-(2-Methyl-benzyl)-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine; 1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine; or 1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine.

One further embodiment of the invention are compounds of formula I, wherein one of A^1 or A^2 is benzo[1,3]dioxol, for example the following compound: 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine.

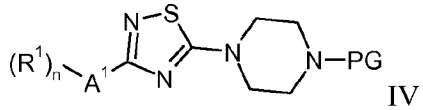
One further embodiment of the invention are compounds of formula I, wherein at least one of A^1 or A^2 is thiophen-2-yl, for example the following compounds: 1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-thiophen-2-yl-[1,2,4]thiadiazol-5-yl)-piperazine or 1-[2-(4-Methoxy-phenyl)-ethyl]-4-(3-thiophen-2-yl-[1,2,4]thiadiazol-5-yl)-piperazine.

One further embodiment of the invention are compounds of formula I, wherein at least one of A^1 or A^2 are pyrazine-2-yl, for example the following compounds: 2-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-pyrazine; or 2-(5-{4-[2-(3-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-pyrazine.

One further embodiment of the invention are compounds of formula I, wherein A^2 is cycloalkyl, for example the following compounds: 1-(2-Cyclohexyl-ethyl)-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine; or 1-(2-Cyclohexyl-ethyl)-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine.

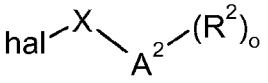
The present compounds of formula IA or I, and their pharmaceutically acceptable salts can be prepared by methods known in the art, for example, by processes described below, which process comprises

coupling a compound of formula

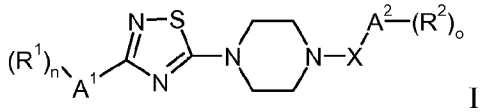


IV

with a compound of formula



to give a compound of formula



I

wherein PG is hydrogen or a protecting group such as tert-butyloxycarbonyl (BOC), 9-fluorenylmethyloxycarbonyl (FMOC) and the like, and hal is halogen such as chloro, bromo, fluoro, or iodo, wherein the definitions are as described above, or if desired, converting the compounds obtained into pharmaceutically acceptable acid addition salts. In an embodiment, A^1 has the same meaning as defined for C^1, and A^2 has the same meaning as defined for C^2.

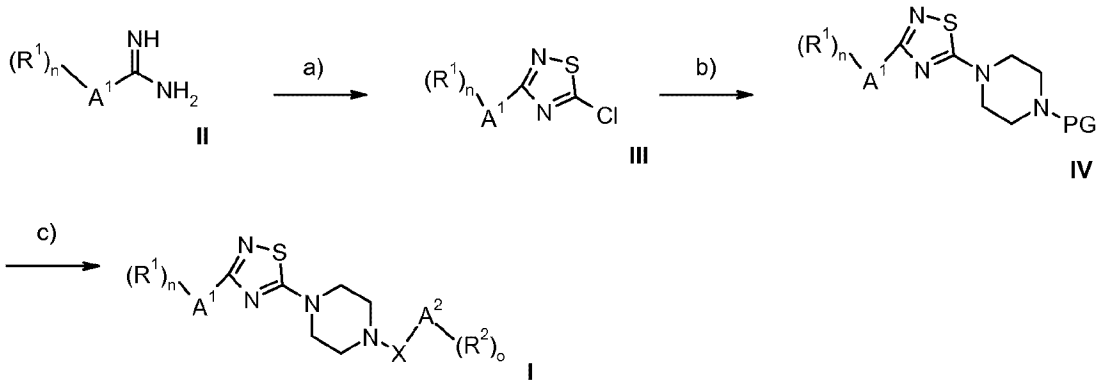
General experimental part:

The preparation of compounds of formula IA or I of the present invention may be carried out in sequential or convergent synthetic routes. Syntheses of the compounds of the invention are shown in the following schemes. The skills required for carrying out the reactions and purifications of the resulting products are known to those skilled in the art. The substituents and indices used in the following description of the processes have the significance given herein before unless indicated to the contrary.

In more detail, the compounds of formula IA or I can be manufactured by the methods given below, by the methods given in the examples or by analogous methods. Appropriate reaction conditions for the individual reaction steps are known to a person skilled in the art. Also, for reaction conditions described in literature affecting the described reactions see for example: *Comprehensive Organic Transformations: A Guide to Functional Group Preparations, 2nd Edition, Richard C. Larock. John Wiley & Sons, New York, NY. 1999*). We find it convenient to carry out the reactions in the presence or absence

of a solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or the reagents involved and that it can dissolve the reagents, at least to some extent. The described reactions can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. It is convenient to carry out the described reactions in a temperature range between -78 °C to reflux. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents. However, a period of from 0.5 h to several days will usually suffice to yield the described intermediates and compounds. The reaction sequence is not limited to the one displayed in the schemes, however, depending on the starting materials and their respective reactivity the sequence of reaction steps can be freely altered. Starting materials are either commercially available or can be prepared by methods analogous to the methods given below, by methods described in references cited in the description or in the examples, or by methods known in the art.

Scheme 1:



In an embodiment, A^1 has the same meaning as defined for C^1, and A^2 has the same meaning as defined for C^2.

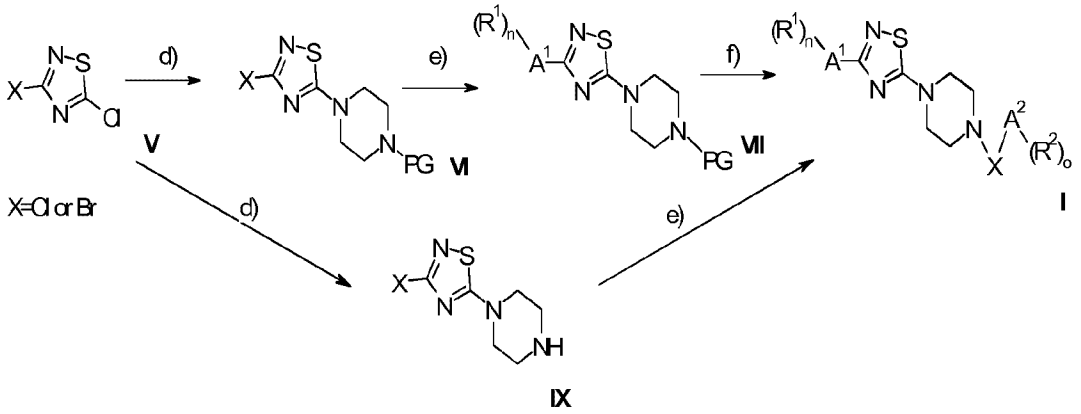
a) Amidines **II** are either commercially available or can be synthesized according to methods known in the art. These amidine derivatives **II** are conveniently reacted with perchloromethyl mercaptan with a base (NEt_3, DIPEA and the like) to afford chloro-thiadiazole derivatives **III**.

b) Chloro-thiadiazole derivatives **III** are conveniently reacted with either substituted piperazine derivatives to directly access final thiadiazole derivatives **I** or alternatively **III** is

reacted with a protected piperazine (PG = Boc, and the like) to afford thiadiazole derivatives **IV**.

c) Deprotection of **IV** is done under suitable conditions, in case of PG=Boc under acidic conditions, to yield the free piperazine derivatives which are conveniently reacted with suitable electrophiles to access final thiadiazole derivatives **I**

Scheme 2:



d) 3-Bromo-5-chloro-1,2,4-thiadiazole and 3,5-dichloro-1,2,4-thiadiazole **V** are commercially available and can conveniently be reacted with protected (PG=Boc and the like) or substituted piperazines to yield thiadiazole derivatives **VI** or **IX**.

e) Thiadiazole derivatives **VI** or **IX** are conveniently reacted under Palladium catalysis with suitable boronic acids or esters to yield in case of **IX** the final derivatives **I** or in case of **VI** the protected thiadiazole derivatives **VII**.

f) Deprotection of **VII** is done under suitable conditions, in case of PG=Boc under acidic conditions, to yield the free piperazine derivatives which are conveniently reacted with suitable electrophiles to access final thiadiazole derivatives **I**.

Experimental part

Abbreviations:

DCM = dichloromethane;

DAST = dimethylaminosulfur trifluoride;

DIPEA = N,N-diisopropylethylamine;

DME = dimethoxyethane;

EtOH = ethanol;

EtOAc = ethyl acetate;

HPLC = high pressure liquid chromatography;

MeCN = Acetonitrile;

MeOH = methanol;

RT = room temperature;

THF = Tetrahydrofuran

Exemplary compounds of the present invention are listed in table II.

Table 2.

Example	Chemical name
2	1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine
3	1-(2,4-Dichloro-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine
4	1-Phenethyl-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine
5	1-[2-(3,4-Dichloro-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine
6	1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine
12	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine
13	1-[3-(3-Methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine
14	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine
15	1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(3-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
16	1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine
17	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
18	1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(3-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
19	1-[2-(4-Methoxy-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine
20	1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine

Example	Chemical name
21	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-fluoro-phenyl)-ethyl]-piperazine
22	1-[2-(3-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
23	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-*m*-tolyl-ethyl)-piperazine
24	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine
25	1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
26	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-*p*-tolyl-ethyl)-piperazine
27	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-phenyl)-ethyl]-piperazine
28	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-fluoro-phenyl)-ethyl]-piperazine
29	1-[2-(2-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
30	1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(6-trifluoromethyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
31	1-[3-(3,5-Dichloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine
32	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(3-methoxy-phenyl)-propyl]-piperazine
33	1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-thiophen-2-yl-[1,2,4]thiadiazol-5-yl)-piperazine
34	1-[3-(4-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine
35	1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
36	1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(4-trifluoromethoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
37	1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(4-trifluoromethoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
38	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethoxy-phenyl)-ethyl]-piperazine
39	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(2-methoxy-phenyl)-propyl]-piperazine
40	1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(4-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
41	1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
42	1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(6-trifluoromethyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

Example	Chemical name
43	1-[2-(4-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine
44	1-[2-(4-Methoxy-phenyl)-ethyl]-4-(3-thiophen-2-yl-[1,2,4]thiadiazol-5-yl)-piperazine
45	1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
46	1-[3-(3,5-Dichloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
47	1-[3-(4-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
48	1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine
49	1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(4-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
50	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-ethoxy-phenyl)-ethyl]-piperazine
51	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-isopropoxy-phenyl)-ethyl]-piperazine
52	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(4-methoxy-phenyl)-propyl]-piperazine
53	2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(4-methoxy-phenyl)-ethanone
54	2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(4-methoxy-phenyl)-ethanol
55	1-[3-(4-Chloro-2-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine
56	1-[3-(4-Chloro-2-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
57	1-[3-(2-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine
58	1-[3-(2-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
59	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-allyl]-piperazine
60	2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-methoxy-phenyl)-ethanone
61	2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-methoxy-phenyl)-ethanol
62	2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-fluoro-phenyl)-ethanone
63	2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-fluoro-phenyl)-ethanol
64	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-fluoro-2-(4-methoxy-phenyl)-ethyl]-piperazine

Example	Chemical name
65	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-fluoro-2-(3-methoxy-phenyl)-ethyl]-piperazine
66	1-[3-(4-Fluoro-2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine
67	1-[3-(4-Fluoro-2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
68	1-[1-(4-Chloro-phenyl)-cyclopropylmethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
69	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-difluoromethoxy-phenyl)-ethyl]-piperazine
70	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-difluoromethoxy-phenyl)-ethyl]-piperazine
71	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-isopropoxy-phenyl)-ethyl]-piperazine
72	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-propyl]-piperazine
73	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-1-methyl-ethyl]-piperazine
75	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine
76	2-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-pyrazine
77	2-(5-{4-[2-(3-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-pyrazine
78	4-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
79	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine
80	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-fluoro-4-methoxy-phenyl)-ethyl]-piperazine
81	3-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
82	1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine
83	1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine
84	1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
85	1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine
86	1-[2-(4-Fluoro-phenyl)-ethyl]-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
87	1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

Example	Chemical name
88	1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
89	1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine
90	1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine
91	1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
92	1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine
93	1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine
94	1-[3-(6-Methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine
95	1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
96	1-[2-(4-Fluoro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
97	1-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
98	1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
99	1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine
100	1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine
101	1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine
102	1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
103	1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine
104	1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
105	1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine
106	1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine
107	1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine
108	4-[5-(4-Phenethyl-piperazin-1-yl)-[1,2,4]thiadiazol-3-yl]-benzonitrile
109	3-[5-(4-Phenethyl-piperazin-1-yl)-[1,2,4]thiadiazol-3-yl]-benzonitrile

Example	Chemical name
110	4-(5-{4-[2-(4-Fluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
111	3-(5-{4-[2-(4-Fluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
112	4-(5-{4-[2-(4-Chloro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
113	3-(5-{4-[2-(4-Chloro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
114	4-(5-{4-[2-(6-Methoxy-pyridin-3-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
115	3-(5-{4-[2-(6-Methoxy-pyridin-3-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
116	4-(5-{4-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
117	3-(5-{4-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
118	4-{5-[4-(2-Methyl-benzyl)-piperazin-1-yl]-[1,2,4]thiadiazol-3-yl}-benzonitrile
119	3-{5-[4-(2-Methyl-benzyl)-piperazin-1-yl]-[1,2,4]thiadiazol-3-yl}-benzonitrile
120	1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine
121	1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine
122	1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine
123	1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
124	1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(5-chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
125	1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
126	1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine
127	1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine
128	1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine
129	1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine
130	1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine
131	1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine

Example	Chemical name
132	1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(5-chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
133	1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine
134	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine
135	1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine
136	1-[2-(3,4-Difluoro-phenyl)-ethyl]-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
137	3-(5-{4-[2-(3,4-Difluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
138	4-(5-{4-[2-(3,4-Difluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
139	1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine
140	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine
141	1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine
142	1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine
143	4-(5-{4-[2-(3-Trifluoromethyl-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
144	1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine
145	1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine
146	1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine
147	4-(5-{4-[2-(4-Trifluoromethyl-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile
148	1-[2-(3,4-Difluoro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
149	1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine
150	1-(2-Methyl-benzyl)-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine
151	1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine
152	1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine
153	1-(2-Cyclohexyl-ethyl)-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

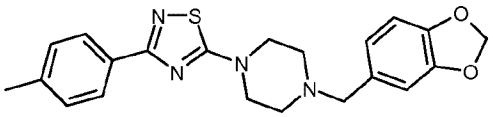
Example	Chemical name
154	1-(2-Cyclohexyl-ethyl)-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine
155	5-(4-(3-phenylpropyl)piperazin-1-yl)-3-(p-tolyl)-1,2,4-thiadiazole
156	5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-3-(3-fluorophenyl)-1,2,4-thiadiazole
157	3-(4-chloropyridin-2-yl)-5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-1,2,4-thiadiazole
158	3-(3,4-difluorophenyl)-5-(4-(3-(trifluoromethyl)phenethyl)piperazin-1-yl)-1,2,4-thiadiazole
159	3-(4-chloropyridin-2-yl)-5-(4-(3-(trifluoromethyl)phenethyl)piperazin-1-yl)-1,2,4-thiadiazole
160	3-(5-chloropyridin-3-yl)-5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-1,2,4-thiadiazole
161	3-(4-chlorophenyl)-5-(4-(2-cyclohexylethyl)piperazin-1-yl)-1,2,4-thiadiazole
162	3-(3-chlorophenyl)-5-(4-(2-cyclohexylethyl)piperazin-1-yl)-1,2,4-thiadiazole
163	3-(5-chloropyridin-3-yl)-5-(4-(2-(piperidin-1-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole
164	3-(3,4-difluorophenyl)-5-(4-(2-(tetrahydro-2H-pyran-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole
165	3-(3-chlorophenyl)-5-(4-(2-(tetrahydro-2H-pyran-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole
166	3-(5-chloropyridin-3-yl)-5-(4-(2-(tetrahydro-2H-pyran-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole
167	3-(4-chlorophenyl)-5-(4-(2-(tetrahydro-2H-pyran-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole
168	3-(2-chloropyridin-4-yl)-5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole
169	5-(4-(4-chlorophenethyl)piperazin-1-yl)-3-(2-chloropyridin-4-yl)-1,2,4-thiadiazole
170	3-(2-chloropyridin-4-yl)-5-(4-phenethylpiperazin-1-yl)-1,2,4-thiadiazole
171	3-(2-methylpyridin-4-yl)-5-(4-phenethylpiperazin-1-yl)-1,2,4-thiadiazole
172	5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-3-(2-methylpyridin-4-yl)-1,2,4-thiadiazole
173	3-(6-methylpyridazin-4-yl)-5-(4-phenethylpiperazin-1-yl)-1,2,4-thiadiazole
174	5-(4-(4-fluorophenethyl)piperazin-1-yl)-3-(6-methylpyridazin-4-yl)-1,2,4-thiadiazole
175	5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-3-(6-methylpyridazin-4-yl)-1,2,4-thiadiazole

Example	Chemical name
176	5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-3-(6-methylpyridazin-4-yl)-1,2,4-thiadiazole
177	5-(4-(4-methoxyphenethyl)piperazin-1-yl)-3-(6-methylpyridazin-4-yl)-1,2,4-thiadiazole
178	3-(2-methylpyrimidin-5-yl)-5-(4-phenethylpiperazin-1-yl)-1,2,4-thiadiazole
179	5-(4-(4-methoxyphenethyl)piperazin-1-yl)-3-(2-methylpyrimidin-5-yl)-1,2,4-thiadiazole
180	5-(4-(4-chlorophenethyl)piperazin-1-yl)-3-(2-methylpyrimidin-5-yl)-1,2,4-thiadiazole
181	5-(4-(4-fluorophenethyl)piperazin-1-yl)-3-(2-methylpyrimidin-5-yl)-1,2,4-thiadiazole
182	5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-3-(2-methylpyrimidin-5-yl)-1,2,4-thiadiazole
183	5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-3-(2-methylpyrimidin-5-yl)-1,2,4-thiadiazole

Experimental part

Example 2

1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine



a) 5-Chloro-3-p-tolyl-1,2,4-thiadiazole

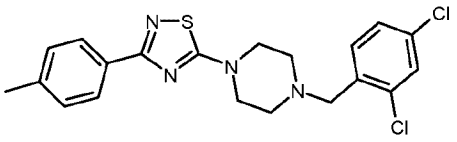
A mixture of 4-methylbenzimidamide hydrochloride (1.55 g, 9.08 mmol) and Et_3N (4.6 g, 6.33 ml, 45.4 mmol) in DCM (30 mL) was cooled with a NaCl/ice-bath to -10°C. Perchloromethyl mercaptan (1.86 g, 1.09 ml, 9.99 mmol) in DCM (10 mL) was added during 40 min. The resulting yellow suspension was stirred for 20 min at 0 °C and 2 h at RT. Water (40 mL) and aq. 2 N NaOH (10 mL) was added. The organic layer was separated and extracted with brine (50 mL). The aqueous layers were extracted with DCM (2 x 40 mL). The combined organic layers were dried over Na_2SO_4, filtered off and concentrated in vacuo. The residue was purified by silica chromatography (Flash 50 g Si-cartridge using AcOEt: Heptane 1:19 to 1:9.) to yield 5-chloro-3-p-tolyl-1,2,4-thiadiazole (1.63 g, 7.74 mmol, 85 % yield) as light yellow solid.

b) 1-(benzo[d][1,3]dioxol-5-ylmethyl)piperazine

In a 5 mL microwave vial, 5-chloro-3-p-tolyl-1,2,4-thiadiazole (75.0 µmol), 1-(benzo[d][1,3]dioxol-5-ylmethyl)piperazine (300 µmol) and DIPEA (750 µmol) in 0.6 mL N-Methyl-2-pyrrolidinone was heated in the microwave at 165 °C for 12 min. The resulting reaction mixture solution was purified by preparative HPLC on reversed phase eluting with a gradient formed from MeCN, water and NEt_3 to yield after evaporation of the product containing fractions of the title compound as light brown solid. MS(m/e): 395.2 (MH^+).

Example 3

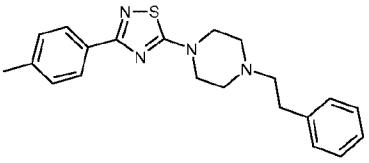
1-(2,4-Dichloro-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-p-tolyl-1,2,4-thiadiazole and 1-(2,4-dichlorobenzyl)piperazine as light brown solid. MS(m/e): 419.2 (MH^+).

Example 4

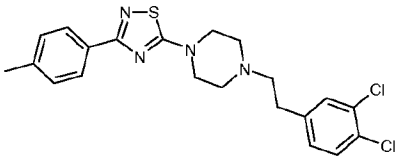
1-Phenethyl-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-p-tolyl-1,2,4-thiadiazole and 1-phenethylpiperazine as light brown solid. MS(m/e): 365.3 (MH^+).

Example 5

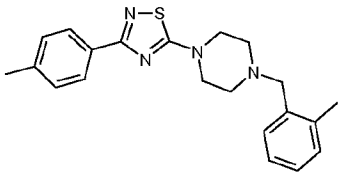
1-[2-(3,4-Dichloro-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-p-tolyl-1,2,4-thiadiazole and 1-(3,4-dichlorophenethyl)piperazine as brown solid. MS(m/e): 433.3 (MH^+).

Example 6

1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine



a) 1-(3-p-Tolyl-[1,2,4]thiadiazol-5-yl)-piperazine

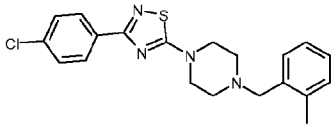
A mixture of 5-chloro-3-p-tolyl-1,2,4-thiadiazole (900 mg, 4.27 mmol) and piperazine (1.84 g, 21.4 mmol) in 25 mL EtOH were heated to reflux and stirred for 1 h at this temperature. The resulting yellow solution was cooled to room temperature and concentrated in vacuo. The residue was purified by flash column chromatography on silica eluting with a gradient formed from DCM, MeOH and NEt_3 to yield after evaporation of the product containing fractions 1.1 g (99 %) of the title compound as light yellow solid. MS(m/e): 261.3 (MH^+).

b) 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine

A mixture of 5-(piperazin-1-yl)-3-p-tolyl-1,2,4-thiadiazole (17.3 mg, 66.4 µmol), 1-(chloromethyl)-2-methylbenzene (14.0 mg, 99.7 µmol) and DIPEA (42.9 mg, 58.0 µl) in 0.8 mL N-Methyl-2-pyrrolidinone was heated in the microwave oven 165 °C for 12.5 min. The resulting reaction mixture solution was purified by preparative HPLC on reversed phase eluting with a gradient formed from MeCN, water and NEt_3 to yield after evaporation of the product containing fractions 17.5 mg (72 %) of the title compound as yellow viscous oil. MS(m/e): 365.3 (MH^+).

Example 12

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine



a) 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

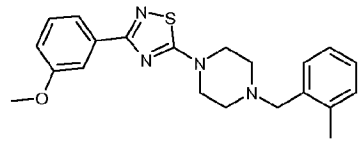
In analogy to the procedure described for the synthesis of 1-(3-p-Tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6, step a) the title compound was prepared from 5-chloro-3-(4-chlorophenyl)-1,2,4-thiadiazole and piperazine as light yellow solid. MS(m/e): 281.2 (MH^+).

b) 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine

In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(chloromethyl)-2-methylbenzene as off-white foam. MS(m/e): 385.2 (MH^+).

Example 13

1-[3-(3-Methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine



a) 1-[3-(3-Methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

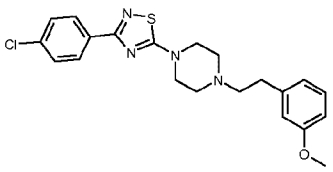
In analogy to the procedure described for the synthesis of 1-(3-p-Tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6, step a) the title compound was prepared from 5-chloro-3-(3-methoxyphenyl)-1,2,4-thiadiazole and piperazine as yellow solid. MS(m/e): 277.2 (MH^+).

b) 1-[3-(3-Methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine

In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3-Methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(chloromethyl)-2-methylbenzene as light yellow viscous oil. MS(m/e): 381.4 (MH^+).

Example 14

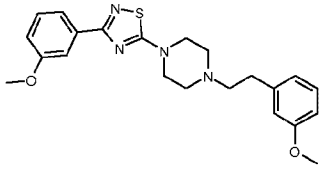
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-3-methoxybenzene as light yellow foam. MS(m/e): 415.2 (MH^+).

Example 15

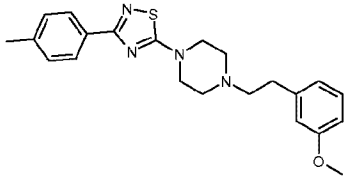
1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(3-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3-Methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-3-methoxybenzene as light brown viscous oil. MS(m/e): 411.3 (MH^+).

Example 16

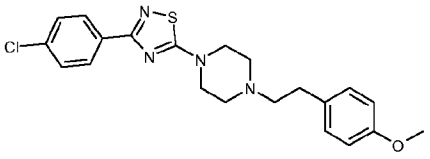
1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 5-(piperazin-1-yl)-3-(p-tolyl)-1,2,4-thiadiazole and 1-(2-bromoethyl)-3-methoxybenzene as light yellow foam. MS(m/e): 395.2 (MH^+).

Example 17

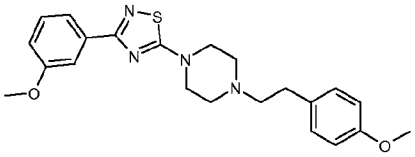
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-4-methoxybenzene as light yellow foam. MS(m/e): 415.2 (MH^+).

Example 18

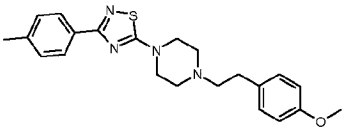
1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(3-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3-Methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-4-methoxybenzene as light yellow foam. MS(m/e): 411.3 (MH^+).

Example 19

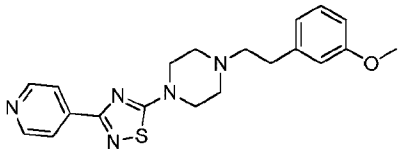
1-[2-(4-Methoxy-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 5-(piperazin-1-yl)-3-(p-tolyl)-1,2,4-thiadiazole and 1-(2-bromoethyl)-4-methoxybenzene as off-white foam. MS(m/e): 395.2 (MH^+).

Example 20

1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine



a) 4-(5-Chloro-[1,2,4]thiadiazol-3-yl)-pyridine

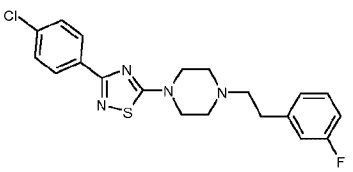
A mixture of isonicotinimidamide hydrochloride (1.0 g, 6.35 mmol) and NEt_3 (3.21 g, 4.42 mL, 31.7 mmol) in 50 mL DCM was cooled to -5 and -10 °C. Perchloromethyl mercaptan (1.3 g, 763 µl, 6.98 mmol) in 10 mL DCM was added drop wise over 1 h. The mixture was warmed to 0 °C over 30 min and stirred for 2 h. Water (50 mL) and 2M NaOH (10 mL) was added. The suspension was filtrated. The organic layer was extracted with DCM and washed with brine (50 mL) and the aqueous layer was extracted with DCM (50 mL). The organic layers were combined, dried over Na_2SO_4 and filtered off. The crude product was concentrated under vacuum and the residue dissolved in DCM, taken up on Isolute® and purified by column chromatography on silica eluting with a gradient formed from heptane and EtOAc to yield after evaporation of the product containing fraction 0.43 g (34 %) of the title compound as a brown solid. MS(m/e): 198.1 (MH^+).

b) 1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine

A mixture of 5-chloro-3-(pyridin-4-yl)-1,2,4-thiadiazole (42 mg, 213 µmol), 1-(3-methoxyphenethyl)piperazine dihydrochloride (62.3 mg, 213 µmol)and DIPEA (137 mg, 186 µl, 1.06 mmol) in 10 mL EtOH was stirred for 2.5 h at RT the mixture was filtered, washed with EtOH and dried *in vacuo* at 50 °C for 2 hours to yield 12.6 mg (15 %) of the title compounds as orange solid. MS(m/e): 382.2 (MH^+).

Example 21

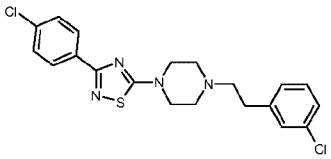
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-fluoro-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-3-fluorobenzene as off-white solid. MS(m/e): 403.3 (MH^+).

Example 22

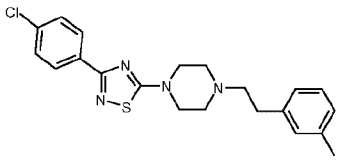
1-[2-(3-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-3-chlorobenzene as light yellow solid. MS(m/e): 419.2 (MH^+).

Example 23

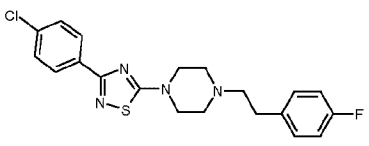
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-*m*-tolyl-ethyl)-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-3-methylbenzene as light yellow solid. MS(m/e): 399.2 (MH^+).

Example 24

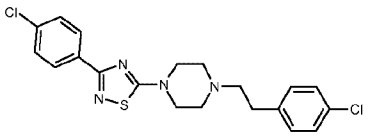
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-4-fluorobenzene as light yellow solid. MS(m/e): 403.3 (MH^+).

Example 25

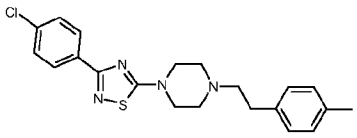
1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-4-chlorobenzene as light yellow solid. MS(m/e): 419.1 (MH^+).

Example 26

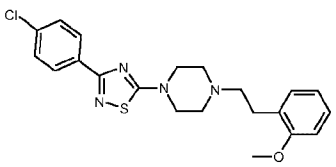
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-*p*-tolyl-ethyl)-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-4-methylbenzene as light yellow solid. MS(m/e): 399.1 (MH^+).

Example 27

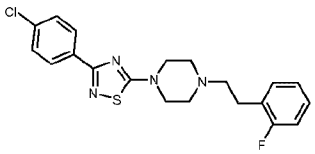
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-2-methoxybenzene as light yellow solid. MS(m/e): 415.2 (MH^+).

Example 28

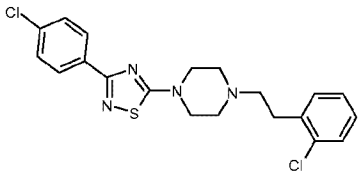
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-fluoro-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-2-fluorobenzene as light yellow solid. MS(m/e): 403.2 (MH^+).

Example 29

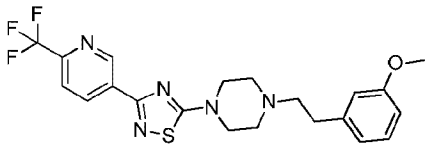
1-[2-(2-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-2-chlorobenzene as light yellow solid. MS(m/e): 419.1 (MH^+).

Example 30

1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(6-trifluoromethyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine



a) 5-(5-Chloro[1,2,4]thiadiazol-3-yl)-2-trifluoromethyl-pyridine

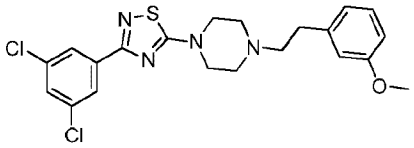
In analogy to the procedure described for the synthesis of 4-(5-Chloro-[1,2,4]thiadiazol-3-yl)-pyridine (example 20, step a) the title compound was prepared from 6-(trifluoromethyl) nicotinimidamide hydrochloride and perchloromethyl mecaptan as light brown solid. MS(m/e): 266.0 (MH^+).

b) 1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(6-trifluoromethyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

In analogy to the procedure described for the synthesis of 1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 20, step b) the title compound was prepared from 5-(5-Chloro-[1,2,4]thiadiazol-3-yl)-2-trifluoromethyl-pyridine and 1-(3-methoxyphenethyl)piperazine dihydrochloride as white solid. MS(m/e): 350.3 (MH^+).

Example 31

1-[3-(3,5-Dichloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine



a) 5-Chloro-3-(3,5-dichloro-phenyl)-[1,2,4]thiadiazole

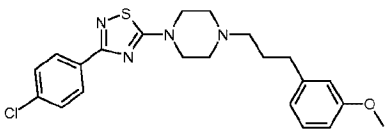
In analogy to the procedure described fort he synthesis of 4-(5-Chloro-[1,2,4]thiadiazol-3-yl)-pyridine (example 20, step a) the title compound was prepared from 3,5-dichlorobenzimidamide hydrochloride and perchloromethyl mecaptan as off-white solid. MS(m/e): 265.9 (MH^+).

b) 1-[3-(3,5-Dichloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine

In analogy to the procedure described for the synthesis of 1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 20, step b) the title compound was prepared from 5-Chloro-3-(3,5-dichloro-phenyl)-[1,2,4]thiadiazole and 1-(3-methoxyphenethyl)piperazine dihydrochloride as off-white solid. MS(m/e): 449.1 (MH^+).

Example 32

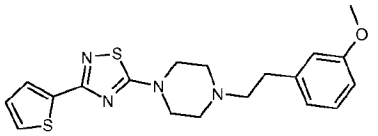
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(3-methoxy-phenyl)-propyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(3-bromopropyl)-3-methoxybenzene as light yellow solid. MS(m/e): 429.2 (MH^+).

Example 33

1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-thiophen-2-yl-[1,2,4]thiadiazol-5-yl)-piperazine



a) 5-Chloro-3-thiophen-2-yl-[1,2,4]thiadiazole

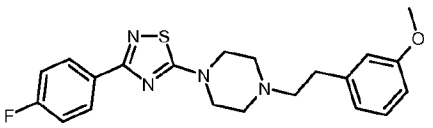
In analogy to the procedure described for the synthesis of 4-(5-Chloro-[1,2,4]thiadiazol-3-yl)-pyridine (example 20, step a) the title compound was prepared from thiophene-2-carboximidamide hydrochloride and perchloromethyl mecaptan as yellow oil. MS(m/e): 202 (MH^+).

b) 1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-thiophen-2-yl-[1,2,4]thiadiazol-5-yl)-piperazine

In analogy to the procedure described for the synthesis of 1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 20, step b) the title compound was prepared from 5-Chloro-3-thiophen-2-yl-[1,2,4]thiadiazole and 1-(3-methoxyphenethyl)piperazine dihydrochloride as yellow oil. MS(m/e): 387.2 (MH^+).

Example 34

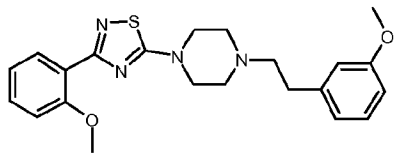
1-[3-(4-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 20) the title compound was prepared from 5-chloro-3-(4-fluorophenyl)-1,2,4-thiadiazole and 1-(3-methoxyphenethyl)piperazine dihydrochloride as off-white solid. MS(m/e): 399.2 (MH^+).

Example 35

1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine



a) 5-Chloro-3-(2-methoxy-phenyl)-[1,2,4]thiadiazole

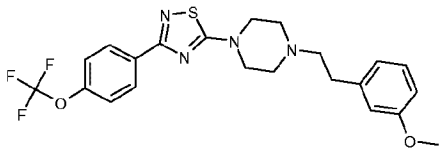
In analogy to the procedure described fort he synthesis of 4-(5-Chloro-[1,2,4]thiadiazol-3-yl)-pyridine (example 20, step a) the title compound was prepared from 2-methoxybenzimidamide hydrochloride and perchloromethyl mecaptan as yellow oil. MS(m/e): 227.1 (MH^+).

b) 1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

In analogy to the procedure described for the synthesis of 1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 20, step b) the title compound was prepared from 5-Chloro-3-(2-methoxy-phenyl)-[1,2,4]thiadiazole and 1-(3-methoxyphenethyl)piperazine dihydrochloride as yellow oil. MS(m/e): 411.3 (MH^+).

Example 36

1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(4-trifluoromethoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine



a) 5-Chloro-3-(4-trifluoromethoxy-phenyl)-[1,2,4]thiadiazole

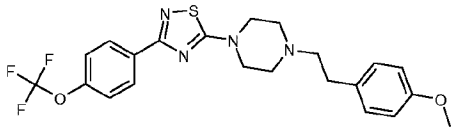
In analogy to the procedure described for the synthesis of 4-(5-Chloro-[1,2,4]thiadiazol-3-yl)-pyridine (example 20, step a) the title compound was prepared from 4-(trifluoromethoxy) benzimidamide hydrochloride and perchloromethyl mecaptan as light brown solid. MS(m/e): 280.0 (MH^+).

b) 1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(4-trifluoromethoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

In analogy to the procedure described for the synthesis of 1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 20, step b) the title compound was prepared from 5-Chloro-3-(4-trifluoromethoxy-phenyl)-[1,2,4]thiadiazole and 1-(3-methoxyphenethyl)piperazine dihydrochloride as light yellow solid. MS(m/e): 465.3 (MH^+).

Example 37

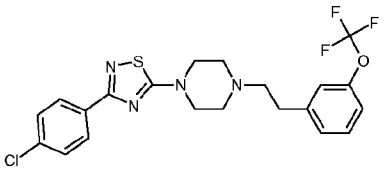
1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(4-trifluoromethoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 20) the title compound was prepared from 5-Chloro-3-(4-trifluoromethoxy-phenyl)-[1,2,4]thiadiazole and 1-(4-methoxyphenethyl)piperazine dihydrochloride as off-white solid. MS(m/e): 465.3 (MH^+).

Example 38

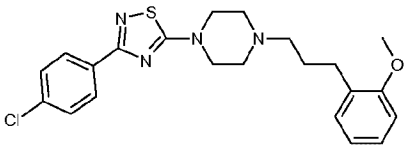
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-3-(trifluoromethoxy)benzene as off-white solid. MS(m/e): 469.2 (MH^+).

Example 39

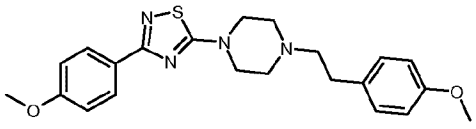
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(2-methoxy-phenyl)-propyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(3-bromopropyl)-2-methoxybenzene as off-white solid. MS(m/e): 429.2 (MH^+).

Example 40

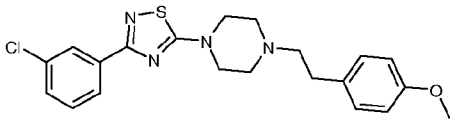
1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(4-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-(4-methoxyphenyl)-1,2,4-thiadiazole and 1-(4-methoxyphenethyl) piperazine dihydrochloride as off-white solid. MS(m/e): 411.2 (MH^+).

Example 41

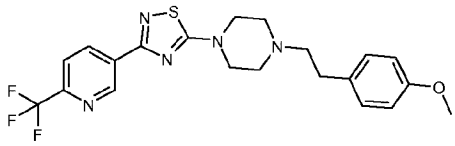
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-(3-chlorophenyl)-1,2,4-thiadiazole and 1-(4-methoxyphenethyl) piperazine dihydrochloride as off-white solid. MS(m/e): 415.3 (MH^+).

Example 42

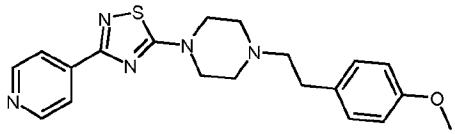
1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(6-trifluoromethyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-(5-Chloro-[1,2,4]thiadiazol-3-yl)-2-trifluoromethyl-pyridine and 1-(4-methoxyphenethyl) piperazine dihydrochloride as off-white solid. MS(m/e): 450.2 (MH^+).

Example 43

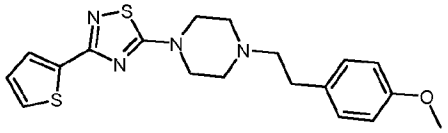
1-[2-(4-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 4-(5-Chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-(4-methoxyphenethyl) piperazine dihydrochloride as off-white solid. MS(m/e): 382.3 (MH^+).

Example 44

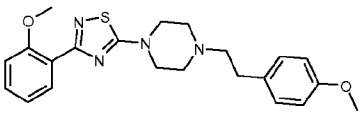
1-[2-(4-Methoxy-phenyl)-ethyl]-4-(3-thiophen-2-yl-[1,2,4]thiadiazol-5-yl)-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-Chloro-3-thiophen-2-yl-[1,2,4]thiadiazole and 1-(4-methoxyphenethyl) piperazine dihydrochloride as off-white solid. MS(m/e): 387.2 (MH^+).

Example 45

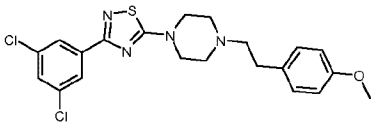
1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-Chloro-3-(2-methoxy-phenyl)-[1,2,4]thiadiazole and 1-(4-methoxyphenethyl) piperazine dihydrochloride as yellow oil. MS(m/e): 411.2 (MH^+).

Example 46

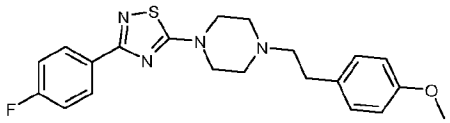
1-[3-(3,5-Dichloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-Chloro-3-(3,5-dichloro-phenyl)-[1,2,4]thiadiazole and 1-(4-methoxyphenethyl) piperazine dihydrochloride as off-white solid. MS(m/e): 449.2 (MH^+).

Example 47

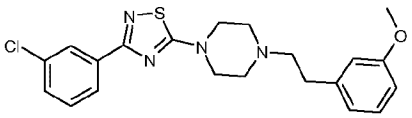
1-[3-(4-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-(4-fluorophenyl)-1,2,4-thiadiazole and 1-(4-methoxyphenethyl) piperazine dihydrochloride as off-white solid. MS(m/e): 399.2 (MH^+).

Example 48

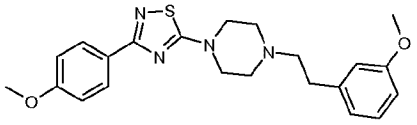
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-(3-chlorophenyl)-1,2,4-thiadiazole and 1-(3-methoxyphenethyl) piperazine dihydrochloride as off-white solid. MS(m/e): 415.3 (MH^+).

Example 49

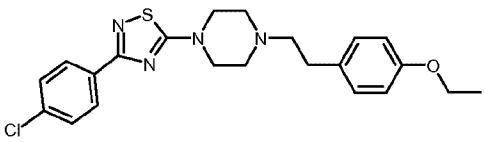
1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(4-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-(4-methoxyphenyl)-1,2,4-thiadiazole and 1-(3-methoxyphenethyl) piperazine dihydrochloride as white solid. MS(m/e): 411.3 (MH^+).

Example 50

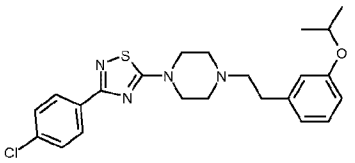
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-ethoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-4-ethoxybenzene as off-white solid. MS(m/e): 429.3 (MH^+).

Example 51

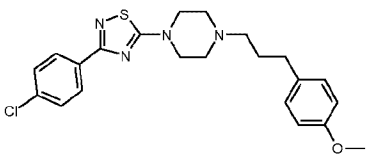
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-isopropoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-3-isopropoxybenzene as light yellow solid. MS(m/e): 443.2 (MH^+).

Example 52

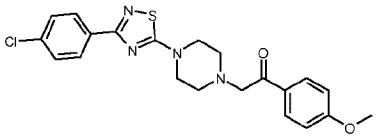
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(4-methoxy-phenyl)-propyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(3-bromopropyl)-4-methoxybenzene as off-white solid. MS(m/e): 429.3 (MH^+).

Example 53

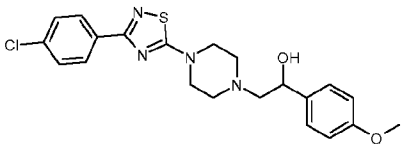
2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(4-methoxy-phenyl)-ethanone



A mixture of 3-(4-chlorophenyl)-5-(piperazin-1-yl)-1,2,4-thiadiazole (539 mg, 1.92 mmol), 2-bromo-4'-methoxyacetophenone (440 mg, 1.92 mmol) and DIPEA (744 mg, 1.01 ml, 5.76 mmol) in 10 mL EtOH was stirred for 2 h at RT. Another portion 2-bromo-4'-methoxyacetophenone (220 mg, 960 µmol) was added and stirring continued for 2 h. The reaction was filtered off and washed with MeOH (4x5 mL) and Et_2O (2x5 mL).The filter cake was dried in vacuo at 50°C to yield 526 mg (64 %) of the title compound as white solid. MS(m/e): 429.2 (MH^+).

Example 54

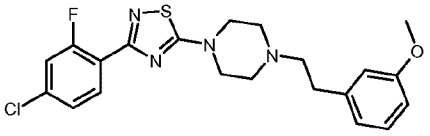
2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(4-methoxy-phenyl)-ethanol



A mixture of 2-(4-(3-(4-chlorophenyl)-1,2,4-thiadiazol-5-yl)piperazin-1-yl)-1-(4-methoxyphenyl)ethanone (75 mg, 175 µmol) and NaBH4 (10 mg, 264 µmol) in THF (5 mL) and MeOH (1 mL) was stirred at RT. Water (5 mL) and 10% aq.Na_2CO_3 (5 mL) was added and stirred for 10 min. The mixture was extracted with EtOAc; the organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered off and concentrated in vacuo. The residue was purified by column chromatography on silica eluting with EtOAc to yield after evaporation of the product containing fraction 70 mg (93 %) of the title compound as white solid. MS(m/e): 431.2 (MH^+).

Example 55

1-[3-(4-Chloro-2-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine



a) 5-Chloro-3-(4-chloro-2-fluoro-phenyl)-[1,2,4]thiadiazole

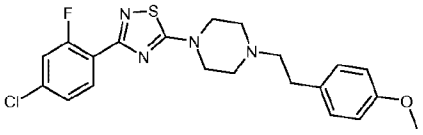
In analogy to the procedure described for the synthesis of 4-(5-Chloro-[1,2,4]thiadiazol-3-yl)-pyridine (example 20, step a) the title compound was prepared from 4-chloro-2-fluorobenzimidamide hydrochloride and perchloromethyl mecaptan as yellow solid. MS(m/e): 248.0 (MH^+).

b) 1-[3-(4-Chloro-2-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine

In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-Chloro-3-(4-chloro-2-fluoro-phenyl)-[1,2,4]thiadiazole and 1-(3-methoxyphenethyl) piperazine dihydrochloride as yellow oil. MS(m/e): 433.2 (MH^+).

Example 56

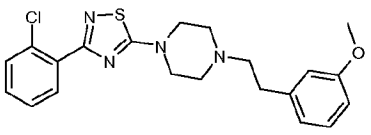
1-[3-(4-Chloro-2-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-Chloro-3-(4-chloro-2-fluoro-phenyl)-[1,2,4]thiadiazole and 1-(4-methoxyphenethyl) piperazine dihydrochloride as light yellow oil. MS(m/e): 433.2 (MH^+).

Example 57

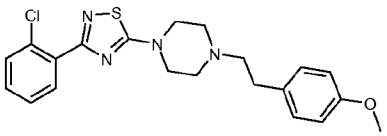
1-[3-(2-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-Chloro-3-(2-chloro-phenyl)-[1,2,4]thiadiazole and 1-(3-methoxyphenethyl) piperazine dihydrochloride as yellow oil. MS(m/e): 415.3 (MH^+).

Example 58

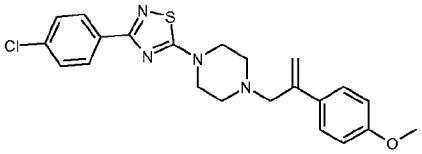
1-[3-(2-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-Chloro-3-(2-chloro-phenyl)-[1,2,4]thiadiazole and 1-(4-methoxyphenethyl) piperazine dihydrochloride as light yellow solid. MS(m/e): 415.3 (MH^+).

Example 59

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-allyl]-piperazine

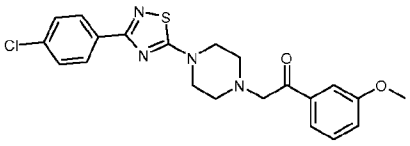


A mixture of methyltriphenylphosphonium bromide/ sodium amide (57.7 mg, 146 μmol) was combined with THF (5 mL) to give a yellow suspension and stirred for 1 h at RT. 2-(4-(3-(4-chlorophenyl)-1,2,4-thiadiazol-5-yl)piperazin-1-yl)-1-(4-methoxyphenyl)ethanone (50 mg, 117 μmol) dissolved in THF (3 mL) was added drop-wise via syringe over 5 min. The resulting orange suspension was stirred over night at RT. Water (10 mL) and EtOAc (10 mL) was added and stirred for 10 min. The aqueous layer was separated and extracted with EtOAc (1x10 mL). The organic layers were washed with brine (1x10 mL), dried over Na_2SO_4, filtered off and concentrated in vacuo. The residue was purified by column chromatography on silica eluting with a gradient formed from heptane and EtOAc to yield,

after evaporation of the product containing fraction, 33 mg (66 %) of the title compound as off-white solid. MS(m/e): 427.2 (MH^+).

Example 60

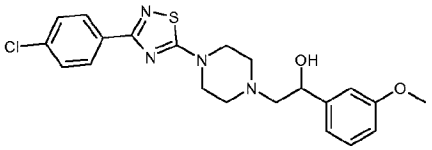
2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-methoxy-phenyl)-ethanone



In analogy to the procedure described for the synthesis of 2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(4-methoxy-phenyl)-ethanone (example 53) the title compound was prepared from 3-(4-chlorophenyl)-5-(piperazin-1-yl)-1,2,4-thiadiazole and 2-bromo-3'-methoxyacetophenone as off-white solid. MS(m/e): 429.2 (MH^+).

Example 61

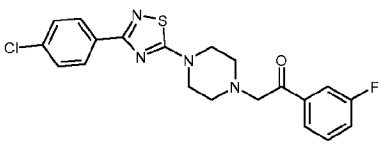
2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-methoxy-phenyl)-ethanol



In analogy to the procedure described for the synthesis of 2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(4-methoxy-phenyl)-ethanol (Example 54) the title compounds was prepared from 2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-methoxy-phenyl)-ethanone through reduction as white solid. MS(m/e): 431.3 (MH^+).

Example 62

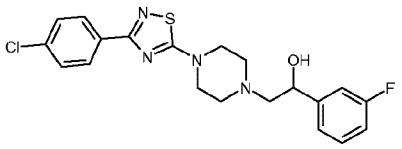
2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-fluoro-phenyl)-ethanone



In analogy to the procedure described for the synthesis of 2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(4-methoxy-phenyl)-ethanone (example 53) the title compound was prepared from 3-(4-chlorophenyl)-5-(piperazin-1-yl)-1,2,4-thiadiazole and 2-bromo-3'-fluoroacetophenone as white solid. MS(m/e): 417.1 (MH^+).

Example 63

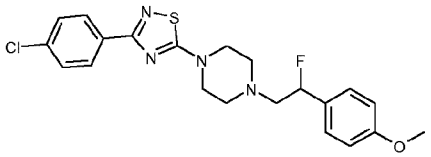
2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-fluoro-phenyl)-ethanol



In analogy to the procedure described for the synthesis of 2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(4-methoxy-phenyl)-ethanol (Example 54) the title compound was prepared from 2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-fluoro-phenyl)-ethanone through reduction as white solid. MS(m/e): 431.3 (MH^+).

Example 64

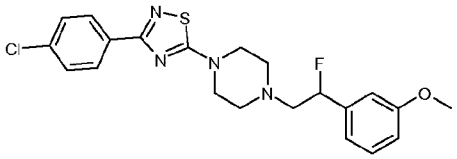
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-fluoro-2-(4-methoxy-phenyl)-ethyl]-piperazine



A mixture of 2-(4-(3-(4-chlorophenyl)-1,2,4-thiadiazol-5-yl)piperazin-1-yl)-1-(4-methoxyphenyl)ethanol (30 mg, 69.6 µmol) and DAST (22.4 mg, 18.4 µl, 139 µmol) in 2 mL DCM at 0 – 5 °C was warmed to RT and stirred for 2 h. 10% aq. Na_2CO_3-solution was added and stirred for 10 min. The organic layer was separated and concentrated in vacuo. The residue was purified by column chromatography on silica eluting with a gradient formed from heptane and EtOAc to yield, after evaporation of the product containing fraction, 24 mg (80 %) of the title compound as light yellow solid. MS(m/e): 433.3 (MH^+).

Example 65

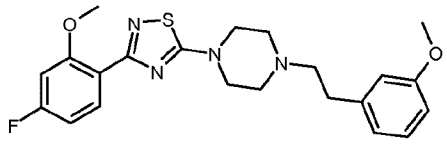
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-fluoro-2-(3-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-fluoro-2-(4-methoxy-phenyl)-ethyl]-piperazine (Example 64) the title compound was prepared from 2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-methoxy-phenyl)-ethanol and DAST as light yellow solid. MS(m/e): 433.3 (MH^+).

Example 66

1-[3-(4-Fluoro-2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine



a) 5-Chloro-3-(4-fluoro-2-methoxy-phenyl)-[1,2,4]thiadiazole

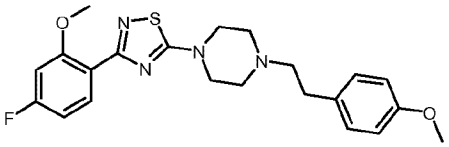
In analogy to the procedure described for the synthesis of 4-(5-Chloro-[1,2,4]thiadiazol-3-yl)-pyridine (example 20, step a) the title compound was prepared from 4-fluoro-2-methoxybenzimidamide hydrochloride and perchloromethyl mecaptan as yellow oil. MS(m/e): 245.0 (MH^+).

b) 1-[3-(4-Fluoro-2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine

In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-Chloro-3-(4-fluoro-2-methoxy-phenyl)-[1,2,4]thiadiazole and 1-(3-methoxyphenethyl) piperazine dihydrochloride as yellow oil. MS(m/e): 429.4 (MH^+).

Example 67

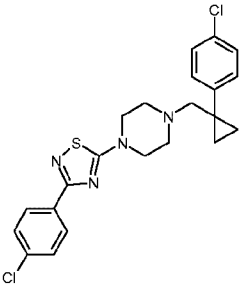
1-[3-(4-Fluoro-2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-Chloro-3-(4-fluoro-2-methoxy-phenyl)-[1,2,4]thiadiazole and 1-(4-methoxyphenethyl) piperazine dihydrochloride as yellow oil. MS(m/e): 429.3 (MH^+).

Example 68

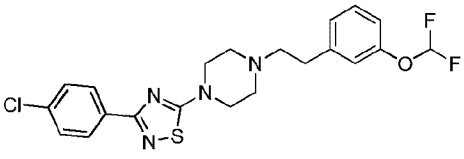
1-[1-(4-Chloro-phenyl)-cyclopropylmethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(1-(bromomethyl)cyclopropyl)-4-chlorobenzene as white solid. MS(m/e): 455.1 (MH^+).

Example 69

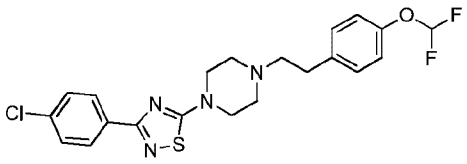
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-difluoromethoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-3-(difluoromethoxy)benzene as yellow solid. MS(m/e): 451.1 (MH^+).

Example 70

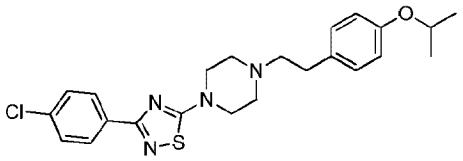
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-difluoromethoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-4-(difluoromethoxy)benzene as off-white solid. MS(m/e): 451.0 (MH^+).

Example 71

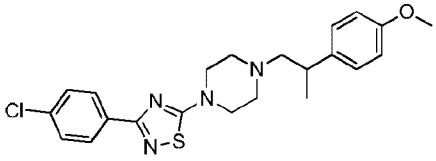
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-isopropoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-4-isopropoxybenzene as off-white solid. MS(m/e): 433.3 (MH^+).

Example 72

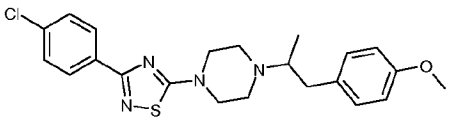
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-propyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(1-bromopropan-2-yl)-4-methoxybenzene as off-white solid. MS(m/e): 429.2 (MH^+).

Example 73

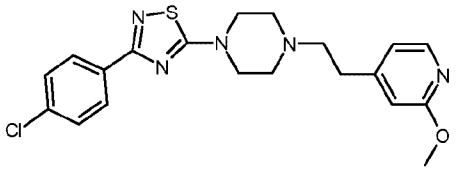
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-1-methyl-ethyl]-piperazine



A mixture of 3-(4-chlorophenyl)-5-(piperazin-1-yl)-1,2,4-thiadiazole (100 mg, 356 µmol),4-methoxyphenylacetophenone (64.3 mg, 392 µmol) and titanium IV propoxide (152 mg, 158 µl, 534 µmol) in 2 mL THF was stirred for 3 h at RT. $NaBH_4$ (40.4 mg, 1.07 mmol) was added in three portions. MeOH (0.2 mL) was added and stirred over the weekend at RT. Water (5 mL), EtOAc(10 mL) and aq. 2N NaOH (3 mL) was added, stirred for 10 min and filtered over a dicalit-plug. The aqueous layer was separated and extracted once with EtOAc (20 mL). The organic layers were washed with brine (1x20 mL), dried over Na_2SO_4, filtered off and concentrated in vacuo. The residue was purified by column chromatography on silica eluting with a gradient formed from heptane and EtOAc and again with preparative HPLC to yield, after evaporation of the product containing fraction, 39 mg (25 %) of the title compound as off-white solid. MS(m/e): 429.2 (MH^+).

Example 75

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine



a) 4-(2-Bromo-ethyl)-2-methoxy-pyridine

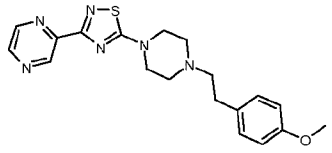
A mixture of 2-(2-methoxypyridin-4-yl)ethanol (commercially available) (700 mg, 4.57 mmol,), CBr_4 (2.27 g, 6.85 mmol) and triphenylphosphine (1.8 g, 6.85 mmol) in 75 mL toluene was stirred at RT for 64 h. The mixture was filtered over a silica-plug and washed with toluene. The filtrate concentrated under vacuum to yield the crude product. The residue was purified by column chromatography on silica eluting with a gradient formed from heptane and EtOAc to yield, after evaporation of the product containing fraction, 624 mg (63 %) of the title compound as colourless liquid. MS(m/e): 216.2 (MH^+).

b) 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine

In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 4-(2-Bromo-ethyl)-2-methoxy-pyridine as off-white solid. MS(m/e): 416.2 (MH^+).

Example 76

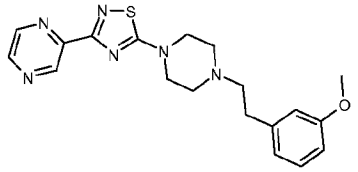
2-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-pyrazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-(pyrazin-2-yl)-1,2,4-thiadiazole and 1-(4-methoxyphenethyl) piperazine dihydrochloride as off-white solid. MS(m/e): 383.2 (MH^+).

Example 77

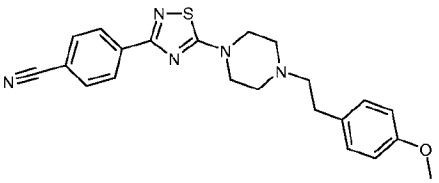
2-(5-{4-[2-(3-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-pyrazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-(pyrazin-2-yl)-1,2,4-thiadiazole and 1-(3-methoxyphenethyl) piperazine dihydrochloride as purple viscous oil. MS(m/e): 383.2 (MH^+).

Example 78

4-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile



a) 1-(3-Chloro-[1,2,4]thiadiazol-5-yl)-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

A mixture of 1-(4-methoxyphenethyl)piperazine dihydrochloride (1.04 g, 3.55 mmol), 3,5-dichloro-1,2,4-thiadiazole (500 mg, 3.23 mmol) and DIPEA (1.33 g, 1.8 ml, 10.3 mmol) in 23 mL EtOH was stirred for 1 h at RT. The reaction solution was concentrated in vacuo and the crude product was purified by column chromatography on silica eluting with a gradient formed from heptane and EtOAc to yield, after evaporation of the product containing fraction, 1.06 g (97 %) of the title compound as white solid. MS(m/e): 339.2 (MH^+).

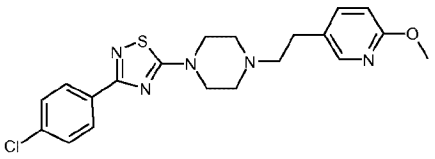
b) 4-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile

A 5 ml micro wave vial was charged with 3-chloro-5-(4-(4-methoxyphenethyl)piperazin-1-yl)-1,2,4-thiadiazole (50 mg, 148 µmol) in 3 mL DME. 4-Cyanophenylboronic acid (26.0 mg, 177 µmol), Na_2CO_3 (18.8 mg, 177 µmol), tetrakis(triphenylphosphine) palladium (0) (3.41 mg, 2.95 µmol) and water (1.5 mL) was added. The vial was capped and the mixture was heated in oil bath at 110°C over night. 2 mL EtOAc were added and the aqueous part was separated. The organic layer was dried over Na_2SO_4, filtered off and concentrated in

vacuo. The crude product was dissolved in MeCN (3 mL)/ DIPEA (100 µL) and purified by preparative HPLC on reversed phase eluting with a gradient formed from MeCN, water and NEt_3 to yield, after evaporation of the product containing fractions, 13.6 mg (23 %) of the title compound as white solid. MS(m/e): 406.3 (MH^+).

Example 79

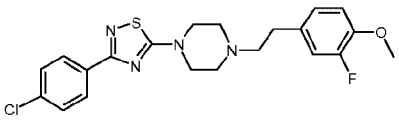
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 5-(2-bromoethyl)-2-methoxypyridine as white solid. MS(m/e): 416.3 (MH^+).

Example 80

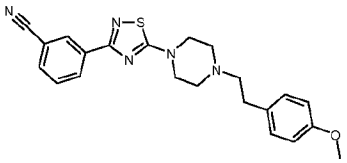
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-fluoro-4-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 4-(2-bromoethyl)-2-fluoro-1-methoxybenzene as white solid. MS(m/e): 433.2 (MH^+).

Example 81

3-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile



a) 1-(3-Bromo-[1,2,4]thiadiazol-5-yl)-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

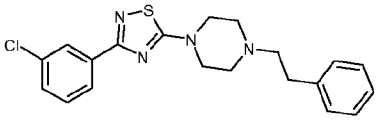
In analogy to the procedure described for the synthesis of 1-(3-Chloro-[1,2,4]thiadiazol-5-yl)-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine (example 78, step a) the title compound was prepared from 3-bromo-5-chloro-1,2,4-thiadiazole and 1-(4-methoxyphenethyl)piperazine dihydrochloride as off-white solid. MS(m/e): 383.2 (MH^+).

b) 3-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile

In analogy to the procedure described for the synthesis of 4-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile (example 78, step b) the title compound was prepared from 1-(3-Bromo-[1,2,4]thiadiazol-5-yl)-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine and 3-cyanophenylboronic acid under palladium catalysis as light yellow solid. MS(m/e): 406.3 (MH^+).

Example 82

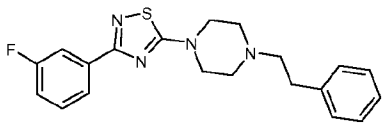
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-(3-chlorophenyl)-1,2,4-thiadiazole and 1-phenethylpiperazine dihydrochloride as off-white solid. MS(m/e): 385.1 (MH^+).

Example 83

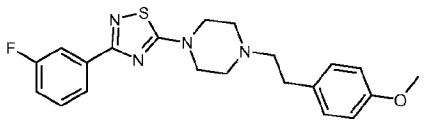
1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-(3-fluorphenyl)-1,2,4-thiadiazole and 1-phenethylpiperazine dihydrochloride as off-white solid. MS(m/e): 369.1 (MH^+).

Example 84

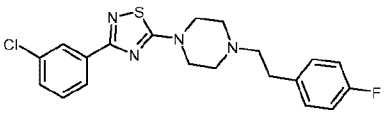
1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-(3-fluorphenyl)-1,2,4-thiadiazole and 1-(4-methoxyphenethyl)piperazine dihydrochloride as off-white solid. MS(m/e): 399.2 (MH^+).

Example 85

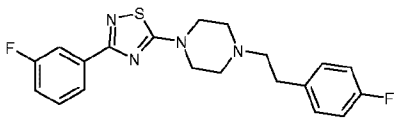
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-(3-chlorophenyl)-1,2,4-thiadiazole and 1-(4-fluorophenethyl)piperazine dihydrochloride as off-white solid. MS(m/e): 40.3.3 (MH^+).

Example 86

1-[2-(4-Fluoro-phenyl)-ethyl]-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

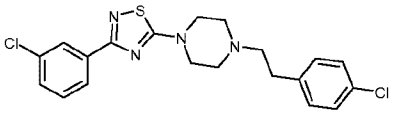


In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was

prepared from 5-chloro-3-(3-fluorphenyl)-1,2,4-thiadiazole and 1-(4-fluorophenethyl)piperazine dihydrochloride as off-white solid. MS(m/e): 387.2 (MH^+).

Example 87

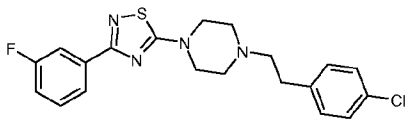
1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-(3-chlorophenyl)-1,2,4-thiadiazole and 1-(4-chlorophenethyl)piperazine dihydrochloride as off-white solid. MS(m/e): 419.1 (MH^+).

Example 88

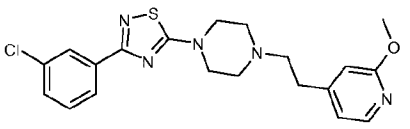
1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-(3-fluorphenyl)-1,2,4-thiadiazole and 1-(4-chlorophenethyl)piperazine dihydrochloride as off-white solid. MS(m/e): 403.3 (MH^+).

Example 89

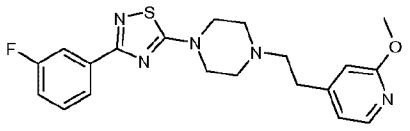
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-(3-chlorophenyl)-1,2,4-thiadiazole and 1-(2-(2-methoxypyridin-4-yl)ethyl)piperazine trihydrochloride as off-white solid. MS(m/e): 416.2 (MH^+).

Example 90

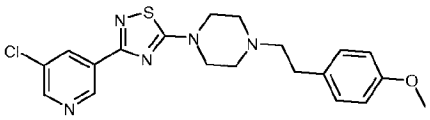
1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-chloro-3-(3-fluorphenyl)-1,2,4-thiadiazole and 1-(2-(2-methoxypyridin-4-yl)ethyl)piperazine trihydrochloride as off-white solid. MS(m/e): 400.1 (MH^+).

Example 91

1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine



a) 3-Chloro-5-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine

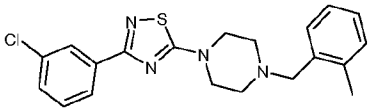
In analogy to the procedure described for the synthesis of 4-(5-Chloro-[1,2,4]thiadiazol-3-yl)-pyridine (example 20, step a) the title compound was prepared from 5-chloronicotinimidamide hydrochloride and perchloromethyl mecaptan as light yellow solid. MS(m/e): 232.0 (MH^+).

b) 1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine

In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 3-Chloro-5-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-(4-methoxyphenethyl)piperazine dihydrochloride (heating not mandatory) as white solid. MS(m/e): 416.3 (MH^+).

Example 92

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine



a) 4-(3-Bromo-[1,2,4]thiadiazol-5-yl)-piperazine-1-carboxylic acid tert-butyl ester

In analogy to the procedure described for the synthesis of 1-(3-Bromo-[1,2,4]thiadiazol-5-yl)-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine (example 81, step a) the title compound was prepared from 3-bromo-5-chloro-1,2,4-thiadiazole and tert-butyl piperazine-1-carboxylate as white solid. MS(m/e): 351.2 (MH^+).

b) 1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride

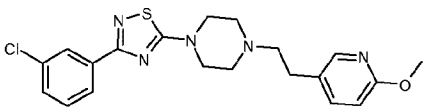
A mixture of tert-butyl 4-(3-bromo-1,2,4-thiadiazol-5-yl)piperazine-1-carboxylate (1 g, 2.86 mmol), 3-chlorophenylboronic acid (537 mg, 3.44 mmol), Na_2CO_3 (364 mg, 3.44 mmol) and tetrakis(triphenylphosphine) palladium (0) (66.2 mg, 57.3 µmol) in 36 mL DME/ 12 mL water was heated to 100 °C over night. The mixture was extracted with EtOAc (80 mL)/ water (80 mL). The organic layer was dried over Na_2SO_4, filtered off and concentrated in vacuo to give amber oil which was dissolved in 25 mL dioxane, 7.16 mL 4N HCl/dioxane was added and stirred over night at RO. Et_2O was added and the mixture was filtered and washed with Et_2O. The filter cake was dried in vacuo at 50°C to yield 926 mg (90 %) of the intermediate compound as light yellow solid. MS(m/e): 281.0 (MH^+).

c) 1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine

In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 2-methylbenzyl chloride as colorless viscous oil. MS(m/e): 385.1 (MH^+).

Example 93

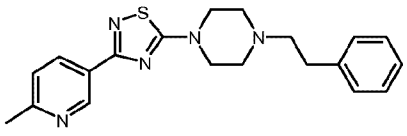
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 5-(2-bromoethyl)-2-methoxypyridine as off-white solid. MS(m/e): 416.2 (MH^+).

Example 94

1-[3-(6-Methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine



a) 5-(5-Chloro-[1,2,4]thiadiazol-3-yl)-2-methyl-pyridine

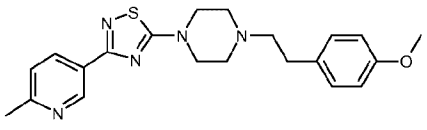
In analogy to the procedure described fort he synthesis of 4-(5-Chloro-[1,2,4]thiadiazol-3-yl)-pyridine (example 20, step a) the title compound was prepared from 6-methylnicotinimidamide hydrochloride and perchloromethyl mecaptan as light brown solid. MS(m/e): 212.0 (MH^+).

b) 1-[3-(6-Methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine

In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-(5-Chloro-[1,2,4]thiadiazol-3-yl)-2-methyl-pyridine and 1-phenethylpiperazine dihydrochloride as off-white solid. MS(m/e): 366.2 (MH^+).

Example 95

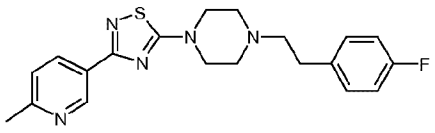
1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-(5-Chloro-[1,2,4]thiadiazol-3-yl)-2-methyl-pyridine and 1-(4-methoxyphenethyl)piperazine dihydrochloride as off-white solid. MS(m/e): 396.2 (MH^+).

Example 96

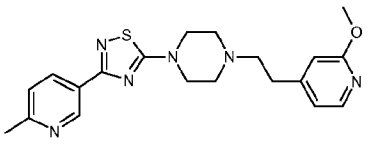
1-[2-(4-Fluoro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-(5-Chloro-[1,2,4]thiadiazol-3-yl)-2-methyl-pyridine and 1-(4-fluorophenethyl)piperazine dihydrochloride as off-white solid. MS(m/e): 384.2 (MH^+).

Example 97

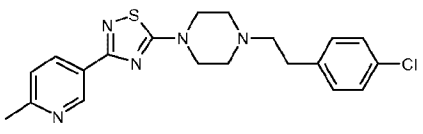
1-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-(5-Chloro-[1,2,4]thiadiazol-3-yl)-2-methyl-pyridine and 1-(2-(2-methoxypyridin-4-yl)ethyl)piperazine trihydrochloride as off-white solid. MS(m/e): 397.2 (MH^+).

Example 98

1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

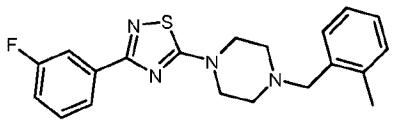


In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was

prepared from 5-(5-Chloro-[1,2,4]thiadiazol-3-yl)-2-methyl-pyridine and 1-(4-chlorophenethyl)piperazine dihydrochloride as off-white solid. MS(m/e): 400.1 (MH^+).

Example 99

1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine



a) 1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride

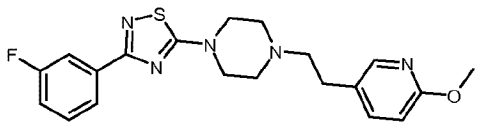
In analogy to the procedure described for the synthesis of 1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 20) the title compound was prepared from 5-chloro-3-(3-fluorophenyl)-1,2,4-thiadiazole and 1-BOC-piperazine with subsequent removal of the protecting group under acidic conditions as white solid. MS(m/e): 265.2 (MH^+).

b) 1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine

In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 2-methylbenzyl chloride as colorless viscous oil. MS(m/e): 369.1 (MH^+).

Example 100

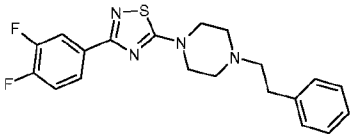
1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 5-(2-bromoethyl)-2-methoxypyridine as light brown solid. MS(m/e): 400.1 (MH^+).

Example 101

1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine



a) 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride

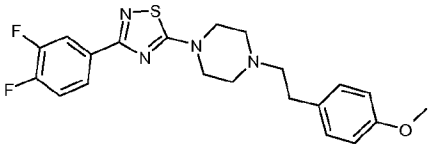
In analogy to the procedure described for the synthesis of tert-butyl 4-(3-bromo-1,2,4-thiadiazol-5-yl)piperazine-1-carboxylate (example 92, step a) the title compound was prepared from 1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 3,4-difluorophenylboronic acid with subsequent removal of the protecting group under acidic conditions as light yellow solid. MS(m/e): 283.1 (MH^+).

b) 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine

In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and (2-bromoethyl)benzene as off-white solid. MS(m/e): 387.2 (MH^+).

Example 102

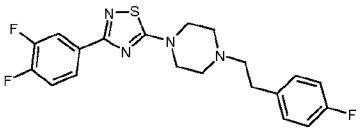
1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 1-(2-bromoethyl)-4-methoxybenzene as off-white solid. MS(m/e): 417.3 (MH^+).

Example 103

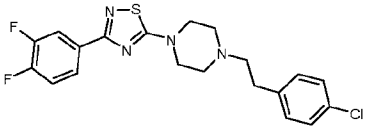
1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 1-(2-bromoethyl)-4-fluorobenzene as off-white solid. MS(m/e): 405.3 (MH^+).

Example 104

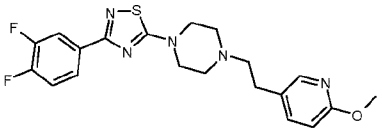
1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 1-(2-bromoethyl)-4-chlorobenzene as off-white solid. MS(m/e): 421.2 (MH^+).

Example 105

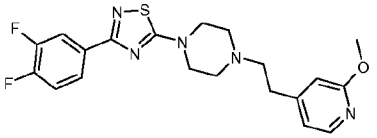
1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 5-(2-bromoethyl)-2-methoxypyridine as off-white solid. MS(m/e): 418.3 (MH^+).

Example 106

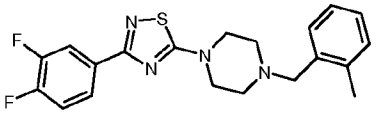
1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 4-(2-bromoethyl)-2-methoxypyridine as off-white solid. MS(m/e): 418.2 (MH^+).

Example 107

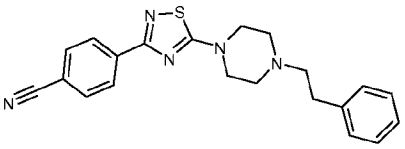
1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 1-(chloromethyl)-2-methylbenzene as off-white solid. MS(m/e): 387.2 (MH^+).

Example 108

4-[5-(4-Phenethyl-piperazin-1-yl)-[1,2,4]thiadiazol-3-yl]-benzonitrile



a) 4-(5-Piperazin-1-yl-[1,2,4]thiadiazol-3-yl)-benzonitrile

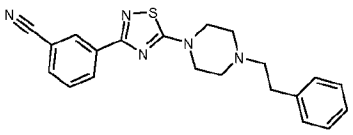
In analogy to the procedure described for the synthesis of tert-butyl 4-(3-bromo-1,2,4-thiadiazol-5-yl)piperazine-1-carboxylate (example 92, step a) the title compound was prepared from 1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 4-cyanophenylboronic acid with subsequent removal of the protecting group under acidic conditions as light yellow solid. MS(m/e): 272.1 (MH^+).

b) 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine

In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[4-cyano-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and (2-bromoethyl)benzene as off-white solid. MS(m/e): 376.3 (MH^+).

Example 109

3-[5-(4-Phenethyl-piperazin-1-yl)-[1,2,4]thiadiazol-3-yl]-benzonitrile



a) 3-(5-Piperazin-1-yl-[1,2,4]thiadiazol-3-yl)-benzonitrile

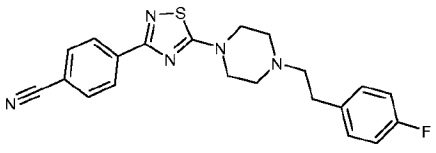
In analogy to the procedure described for the synthesis of tert-butyl 4-(3-bromo-1,2,4-thiadiazol-5-yl)piperazine-1-carboxylate (example 92, step a) the title compound was prepared from 1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 3-cyanophenylboronic acid with subsequent removal of the protecting group under acidic conditions as light yellow solid. MS(m/e): 272.1 (MH^+).

b) 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine

In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[(3-cyano-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and (2-bromoethyl)benzene as light brown solid. MS(m/e): 376.3 (MH^+).

Example 110

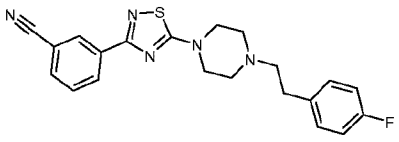
4-(5-{4-[2-(4-Fluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[4-cyano-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 1-(2-bromoethyl)-4-fluorobenzene as off-white solid. MS(m/e): 394.1 (MH^+).

Example 111

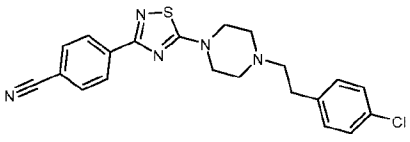
3-(5-{4-[2-(4-Fluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-cyano-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 1-(2-bromoethyl)-4-fluorobenzene as light brown solid. MS(m/e): 394.1 (MH^+).

Example 112

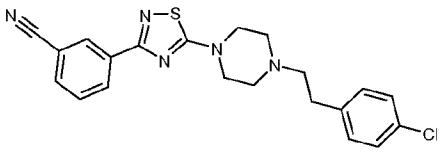
4-(5-{4-[2-(4-Chloro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[4-cyano-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 1-(2-bromoethyl)-4-chlorobenzene as off-white solid. MS(m/e): 410.2 (MH^+).

Example 113

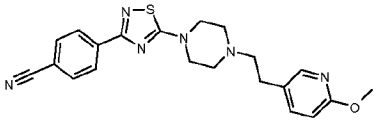
3-(5-{4-[2-(4-Chloro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-cyano-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 1-(2-bromoethyl)-4-chlorobenzene as light brown solid. MS(m/e): 410.2 (MH^+).

Example 114

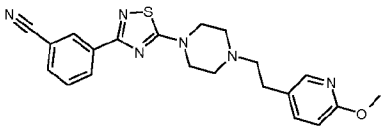
4-(5-{4-[2-(6-Methoxy-pyridin-3-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[4-cyano-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 5-(2-bromoethyl)-2-methoxypyridine as off-white solid. MS(m/e): 407.3 (MH^+).

Example 115

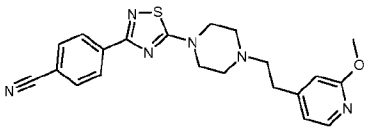
3-(5-{4-[2-(6-Methoxy-pyridin-3-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-cyano-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 5-(2-bromoethyl)-2-methoxypyridine as light brown solid. MS(m/e): 407.4 (MH^+).

Example 116

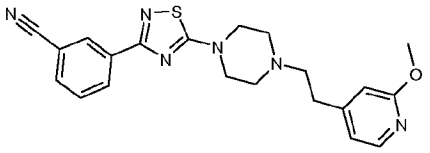
4-(5-{4-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[4-cyano-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 4-(2-bromoethyl)-2-methoxypyridine as off-white solid. MS(m/e): 407.3 (MH^+).

Example 117

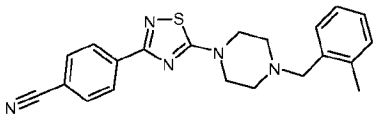
3-(5-{4-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-cyano-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 4-(2-bromoethyl)-2-methoxypyridine as light brown solid. MS(m/e): 407.4 (MH^+).

Example 118

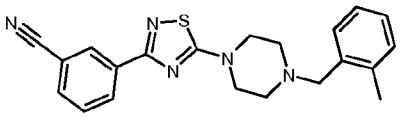
4-{5-[4-(2-Methyl-benzyl)-piperazin-1-yl]-[1,2,4]thiadiazol-3-yl}-benzonitrile



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[4-cyano-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 1-(chloromethyl)-2-methylbenzene as off-white solid. MS(m/e): 376.3 (MH^+).

Example 119

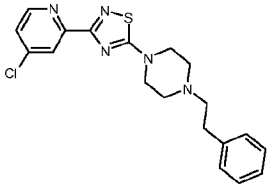
3-{5-[4-(2-Methyl-benzyl)-piperazin-1-yl]-[1,2,4]thiadiazol-3-yl}-benzonitrile



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-cyano-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 1-(chloromethyl)-2-methylbenzene as light brown solid. MS(m/e): 376.3 (MH^+).

Example 120

1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine



a) 4-Chloro-2-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine

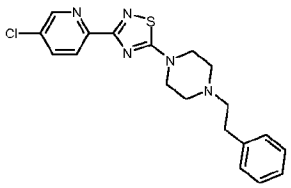
In analogy to the procedure described fort the synthesis of 4-(5-Chloro-[1,2,4]thiadiazol-3-yl)-pyridine (example 20, step a) the title compound was prepared from 4-chloropicolinimidamide hydrochloride and perchloromethyl mecaptan as brown solid. MS(m/e): 232.0 (MH^+).

b) 1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine

In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 4-Chloro-2-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-phenethylpiperazine dihydrochloride. MS(m/e): 386.2 (MH^+).

Example 121

1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine



a) 5-Chloro-2-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine

In analogy to the procedure described for the synthesis of 4-(5-Chloro-[1,2,4]thiadiazol-3-yl)-pyridine (example 20, step a) the title compound was prepared from 5-chloropicolinimidamide hydrochloride and perchloromethyl mecaptan as brown solid. MS(m/e): 232.0 (MH^+).

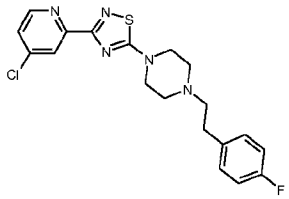
b) 1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine

In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was

prepared from 5-Chloro-2-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-phenethylpiperazine dihydrochloride. MS(m/e): 386.2 (MH^+).

Example 122

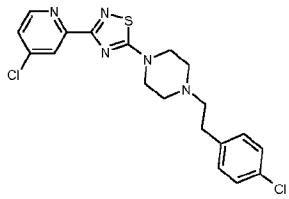
1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 4-Chloro-2-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-(4-fluorophenethyl)piperazine dihydrochloride. MS(m/e): 404.3 (MH^+).

Example 123

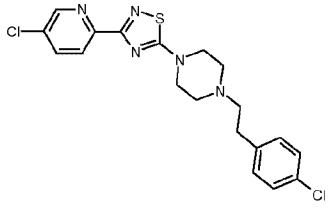
1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 4-Chloro-2-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-(4-chlorophenethyl)piperazine dihydrochloride. MS(m/e): 420.1 (MH^+).

Example 124

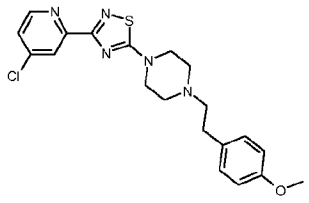
1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(5-chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-Chloro-2-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-(4-chlorophenethyl)piperazine dihydrochloride. MS(m/e): 420.1 (MH^+).

Example 125

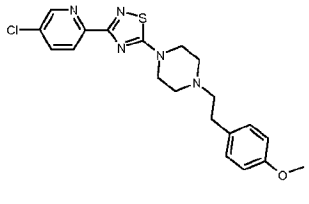
1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 4-Chloro-2-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-(4-methoxyphenethyl)piperazine dihydrochloride. MS(m/e): 416.3 (MH^+).

Example 126

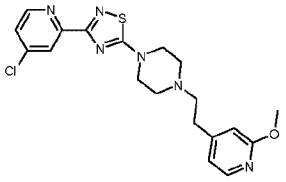
1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 5-Chloro-2-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-(4-methoxyphenethyl)piperazine dihydrochloride. MS(m/e): 416.3 (MH^+).

Example 127

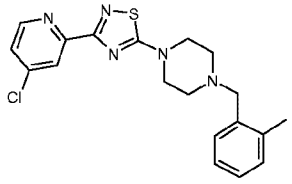
1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 4-Chloro-2-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-(2-(2-methoxypyridin-4-yl)ethyl)piperazine trihydrochloride. MS(m/e): 417.3 (MH^+).

Example 128

1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine



a) 1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

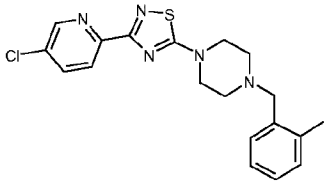
In analogy to the procedure described for the synthesis of 1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 20) the title compound was prepared from 4-Chloro-2-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-BOC-piperazine with subsequent removal of the protecting group under acidic conditions as white solid. MS(m/e): 265.2 (MH^+).

b) 1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine

In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(chloromethyl)-2-methylbenzene. MS(m/e): 386.2 (MH^+).

Example 129

1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine



a) 1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

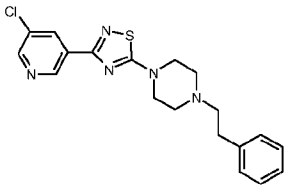
In analogy to the procedure described for the synthesis of 1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 20) the title compound was prepared from 5-Chloro-2-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-BOC-piperazine with subsequent removal of the protecting group under acidic conditions as light brown solid. MS(m/e): 282.2 (MH^+).

b) 1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine

In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(chloromethyl)-2-methylbenzene. MS(m/e): 386.2 (MH^+).

Example 130

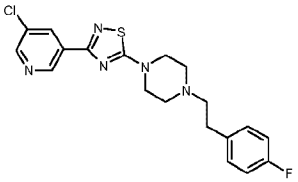
1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 3-Chloro-5-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-phenethylpiperazine dihydrochloride as white solid. MS(m/e): 386.2 (MH^+).

Example 131

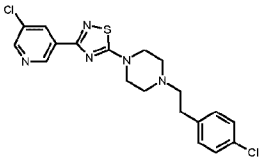
1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 3-Chloro-5-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-(4-fluorophenethyl)piperazine dihydrochloride as white solid. MS(m/e): 404.3 (MH^+).

Example 132

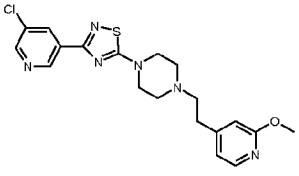
1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(5-chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 3-Chloro-5-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-(4-chlorophenethyl)piperazine dihydrochloride as white solid. MS(m/e): 420.1 (MH^+).

Example 133

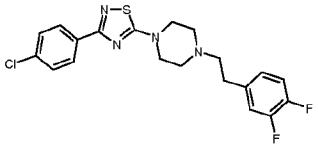
1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 3-Chloro-5-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-(2-(2-methoxypyridin-4-yl)ethyl)piperazine trihydrochloride as viscous colorless oil. MS(m/e): 417.2 (MH^+).

Example 134

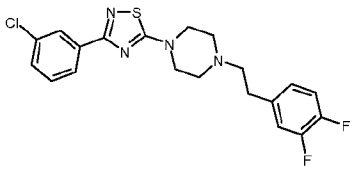
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 4-(2-bromoethyl)-1,2-difluorobenzene. MS(m/e): 421.1 (MH^+).

Example 135

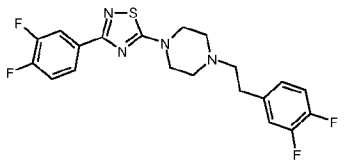
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 4-(2-bromoethyl)-1,2-difluorobenzene. MS(m/e): 421.1 (MH^+).

Example 136

1-[2-(3,4-Difluoro-phenyl)-ethyl]-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine

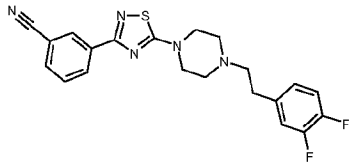


In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from

3-(3,4-difluorophenyl)-5-(piperazin-1-yl)-1,2,4-thiadiazole dihydrochloride and 4-(2-bromoethyl)-1,2-difluorobenzene. MS(m/e): 423.2 (MH^+).

Example 137

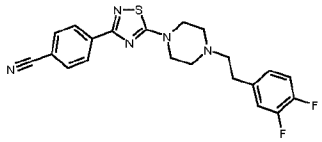
3-(5-{4-[2-(3,4-Difluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 3-(5-(piperazin-1-yl)-1,2,4-thiadiazol-3-yl)benzonitrile and 4-(2-bromoethyl)-1,2-difluorobenzene. MS(m/e): 412.2 (MH^+).

Example 138

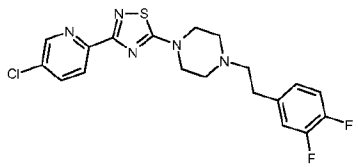
4-(5-{4-[2-(3,4-Difluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 4-(5-(piperazin-1-yl)-1,2,4-thiadiazol-3-yl)benzonitrile and 4-(2-bromoethyl)-1,2-difluorobenzene. MS(m/e): 412.2 (MH^+).

Example 139

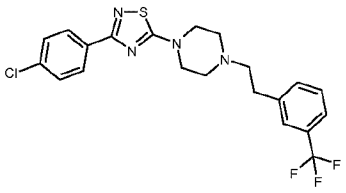
1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 3-(5-chloropyridin-2-yl)-5-(piperazin-1-yl)-1,2,4-thiadiazole and 4-(2-bromoethyl)-1,2-difluorobenzene. MS(m/e): 422.1 (MH^+).

Example 140

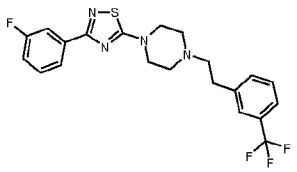
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-3-(trifluoromethyl)benzene. MS(m/e): 453.1 (MH^+).

Example 141

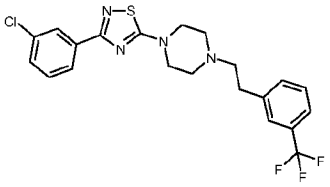
1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 1-(2-bromoethyl)-3-(trifluoromethyl)benzene. MS(m/e): 437.2 (MH^+).

Example 142

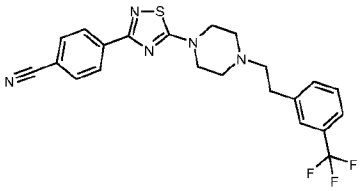
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-3-(trifluoromethyl)benzene. MS(m/e): 453.1 (MH^+).

Example 143

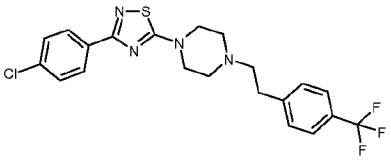
4-(5-{4-[2-(3-Trifluoromethyl-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 3-(5-(piperazin-1-yl)-1,2,4-thiadiazol-3-yl)benzonitrile and 1-(2-bromoethyl)-3-(trifluoromethyl)benzene. MS(m/e): 444.3 (MH^+).

Example 144

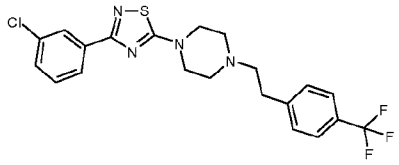
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-4-(trifluoromethyl)benzene. MS(m/e): 453.1 (MH^+).

Example 145

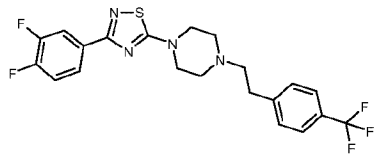
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine and 1-(2-bromoethyl)-4-(trifluoromethyl)benzene. MS(m/e): 453.1 (MH^+).

Example 146

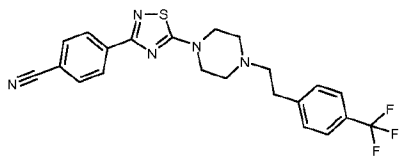
1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 3-(3,4-difluorophenyl)-5-(piperazin-1-yl)-1,2,4-thiadiazole dihydrochloride and 1-(2-bromoethyl)-4-(trifluoromethyl)benzene. MS(m/e): 455.2 (MH^+).

Example 147

4-(5-{4-[2-(4-Trifluoromethyl-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile

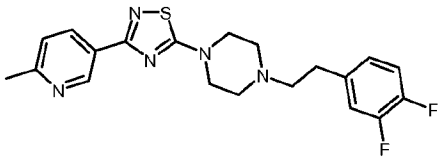


In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from

3-(5-(piperazin-1-yl)-1,2,4-thiadiazol-3-yl)benzonitrile and 1-(2-bromoethyl)-4-(trifluoromethyl)benzene. MS(m/e): 444.3 (MH^+).

Example 148

1-[2-(3,4-Difluoro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine



a) 1-[3-(6-Methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

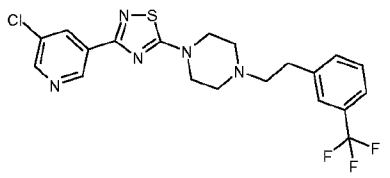
In analogy to the procedure described for the synthesis of 1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 20) the title compound was prepared from 5-(5-Chloro-[1,2,4]thiadiazol-3-yl)-2-methyl-pyridine and 1-BOC-piperazine with subsequent removal of the protecting group under acidic conditions as off-white solid. MS(m/e): 262.1 (MH^+).

b) 1-[2-(3,4-Difluoro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 3-(6-methylpyridin-3-yl)-5-(piperazin-1-yl)-1,2,4-thiadiazole and 4-(2-bromoethyl)-1,2-difluorobenzene. MS(m/e): 402.3 (MH^+).

Example 149

1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine



a) 1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine

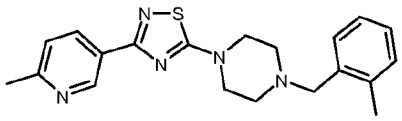
In analogy to the procedure described for the synthesis of 1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 20) the title compound was prepared from 3-Chloro-5-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-BOC-piperazine with subsequent removal of the protecting group under acidic conditions as white solid. MS(m/e): 282.2 (MH^+).

b) 1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine

In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 3-(6-methylpyridin-3-yl)-5-(piperazin-1-yl)-1,2,4-thiadiazole and 1-(2-bromoethyl)-3-(trifluoromethyl)benzene. MS(m/e): 454.1 (MH^+).

Example 150

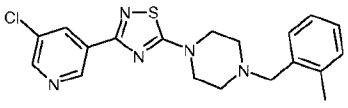
1-(2-Methyl-benzyl)-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 3-(6-methylpyridin-3-yl)-5-(piperazin-1-yl)-1,2,4-thiadiazole and 1-(chloromethyl)-2-methylbenzene. MS(m/e): 366.2 (MH^+).

Example 151

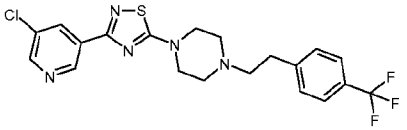
1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 3-(6-methylpyridin-3-yl)-5-(piperazin-1-yl)-1,2,4-thiadiazole and 1-(chloromethyl)-2-methylbenzene. MS(m/e): 386.2 (MH^+).

Example 152

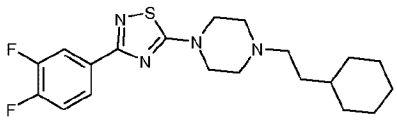
1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 3-(6-methylpyridin-3-yl)-5-(piperazin-1-yl)-1,2,4-thiadiazole and 1-(2-bromoethyl)-4-(trifluoromethyl)benzene. MS(m/e): 454.1 (MH^+).

Examples 153

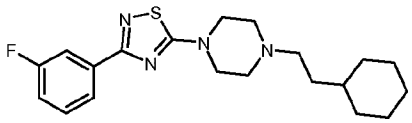
1-(2-Cyclohexyl-ethyl)-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 3-(3,4-difluorophenyl)-5-(piperazin-1-yl)-1,2,4-thiadiazole dihydrochloride and (2-bromoethyl)cyclohexane. MS(m/e): 393.2 (MH^+).

Example 154

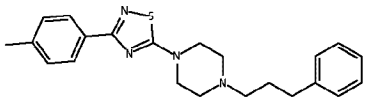
1-(2-Cyclohexyl-ethyl)-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and (2-bromoethyl)cyclohexane. MS(m/e): 375.3 (MH^+).

Example 155

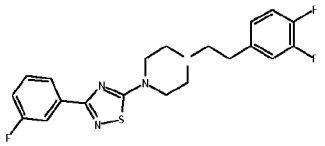
5-(4-(3-phenylpropyl)piperazin-1-yl)-3-(p-tolyl)-1,2,4-thiadiazole



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-(3-p-Tolyl-[1,2,4]thiadiazol-5-yl)-piperazine and (3-bromopropyl)benzene.

Example 156

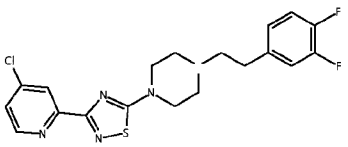
5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-3-(3-fluorophenyl)-1,2,4-thiadiazole



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 3-(3-fluorophenyl)-5-(piperazin-1-yl)-1,2,4-thiadiazole and 4-(2-bromoethyl)-1,2-difluorobenzene.

Example 157

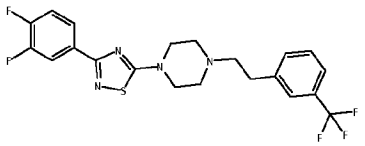
3-(4-chloropyridin-2-yl)-5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-1,2,4-thiadiazole



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 4-Chloro-2-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 4-(2-bromoethyl)-1,2-difluorobenzene.

Example 158

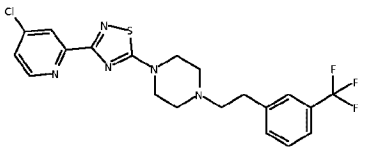
3-(3,4-difluorophenyl)-5-(4-(3-(trifluoromethyl)phenethyl)piperazin-1-yl)-1,2,4-thiadiazole



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine dihydrochloride and 1-(2-bromoethyl)-3-(trifluoromethyl)benzene.

Example 159

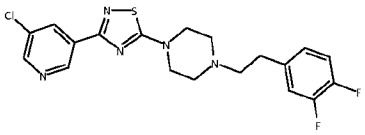
3-(4-chloropyridin-2-yl)-5-(4-(3-(trifluoromethyl)phenethyl)piperazin-1-yl)-1,2,4-thiadiazole



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 4-Chloro-2-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 1-(2-bromoethyl)-3-(trifluoromethyl)benzene.

Example 160

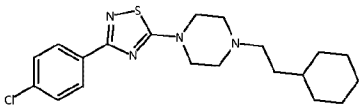
3-(5-chloropyridin-3-yl)-5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-1,2,4-thiadiazole



In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was prepared from 3-Chloro-5-(5-chloro-[1,2,4]thiadiazol-3-yl)-pyridine and 4-(2-bromoethyl)-1,2-difluorobenzene.

Example 161

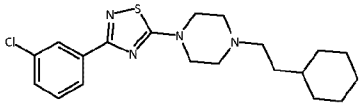
3-(4-chlorophenyl)-5-(4-(2-cyclohexylethyl)piperazin-1-yl)-1,2,4-thiadiazole



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 5-chloro-3-(4-chlorophenyl)-1,2,4-thiadiazole and (2-bromoethyl)cyclohexane.

Example 162

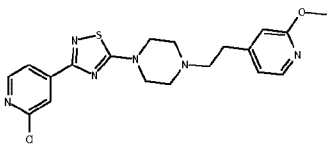
3-(3-chlorophenyl)-5-(4-(2-cyclohexylethyl)piperazin-1-yl)-1,2,4-thiadiazole



In analogy to the procedure described for the synthesis of 1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (example 6) the title compound was prepared from 5-chloro-3-(3-chlorophenyl)-1,2,4-thiadiazole and (2-bromoethyl)cyclohexane.

Example 168

3-(2-chloropyridin-4-yl)-5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole



a) 5-chloro-3-(2-chloropyridin-4-yl)-1,2,4-thiadiazole

In analogy to the procedure described for the synthesis of 4-(5-Chloro-[1,2,4]thiadiazol-3-yl)-pyridine (Example 20, step a) the title compound was prepared from 2-chloroisonicotinimidamide.

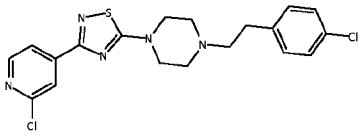
b) 3-(2-chloropyridin-4-yl)-5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole

In analogy to the procedure described for the synthesis of 1-Benzo[1,3]dioxol-5-ylmethyl-4-(3-p-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine (Example 2) the title compound was

prepared from 5-chloro-3-(2-chloropyridin-4-yl)-1,2,4-thiadiazole and 1-(2-(2-methoxypyridin-4-yl)ethyl)piperazine trihydrochloride.

Example 169

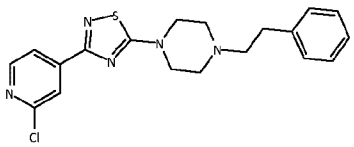
5-(4-(4-chlorophenethyl)piperazin-1-yl)-3-(2-chloropyridin-4-yl)-1,2,4-thiadiazole



In analogy to the procedure described for the synthesis of 3-(2-chloropyridin-4-yl)-5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole (Example 168), the tile compound was prepared from 5-chloro-3-(2-chloropyridin-4-yl)-1,2,4-thiadiazole and 1-(2-bromoethyl)-4-chlorobenzene.

Example 170

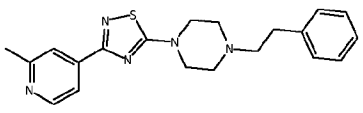
3-(2-chloropyridin-4-yl)-5-(4-phenethylpiperazin-1-yl)-1,2,4-thiadiazole



In analogy to the procedure described for the synthesis of 3-(2-chloropyridin-4-yl)-5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole (Example 168), the tile compound was prepared from 5-chloro-3-(2-chloropyridin-4-yl)-1,2,4-thiadiazole and (2-bromoethyl)benzene.

Example 171

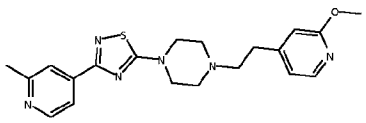
3-(2-methylpyridin-4-yl)-5-(4-phenethylpiperazin-1-yl)-1,2,4-thiadiazole



In analogy to the procedure described for the synthesis of 3-(2-chloropyridin-4-yl)-5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole (Example 168), the tile compound was prepared from 5-chloro-3-(2-chloropyridin-4-yl)-1,2,4-thiadiazole and (2-bromoethyl)benzene.

Example 172

5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-3-(2-methylpyridin-4-yl)-1,2,4-thiadiazole



In analogy to the procedure described for the synthesis of 3-(2-chloropyridin-4-yl)-5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole (Example 168), the tile compound was prepared from 5-chloro-3-(2-chloropyridin-4-yl)-1,2,4-thiadiazole and 1-(2-(2-methoxypyridin-4-yl)ethyl)piperazine trihydrochloride.

The compounds of formula IA or I and their pharmaceutically usable addition salts possess valuable pharmacological properties. Specifically, it has been found that the compounds of the present invention are useful for treating certain neurological disorders characterized by dysfunction of TAU protein, which diseases comprise Alzheimer's disease, Pick's disease, corticobasal degeneration, progressive supranuclear palsy, frontotemporal dementia and parkinsonism (linked to chromosome 17, FTDP-17). The compounds were investigated in accordance with the test given hereinafter.

Construction of a TAU gene over-expressing cell line

A TAU expression plasmid was constructed by sub-cloning the cDNA encoding for human TAU-P301L protein, wherein proline at position 301 is substituted by a leucine residue, into mammalian expression vector pcDNA3.1 resulting in the plasmid pcDNA3.1-TAUP301L. Plasmids pcDNA3.1 and pcDNA3.1-TAU P301L were transfected into human neuroblastoma cells (BE-M17; ATCC No. CRL-2267^{TM}) using lipofectamine reagent and subsequently, independent clonal cell lines with the plasmids stably integrated into the genome were selected by antibiotic resistance selection (Geneticin (G418)), resulting in cell lines M17.pcDNA3 and M17_3TAUP301L. Expression of the TAUP301L gene in the M17_3TAUP301L cells was confirmed by Western blot analysis.

Use of TAU expressing cells as a model of neuronal degeneration

The expression of TAU P301L in M17_3TAU(P301L) cells was found to confer increased toxicity relative to control cells expressing no TAU after 7 days of cell

differentiation using retinoic acid (RA). Differentiation of the cells with RA leads to phosphorylation and subsequent aggregation of TAU, inducing a tauopathy in these cells. Cytotoxicity of cells was measured by quantification of lactate dehydrogenase (LDH) levels. In dead cells LDH is leaked out of the cells into the medium due to a loss of plasma-membrane integrity.

Briefly, 3 days preceding the experiment pre-cultures of M17.pcDNA3 and M17_3TAU(P301L) cells were prepared, starting from a stock culture, at a density of 50.000-100.000 cells/cm2 in detection medium (Optimem Reduced Serum without phenol red (Gibco, Cat. 31985-047) supplemented with 1% fetal calf serum (FCS), 1 mM sodium pyruvate, 1 x non-essential amino acids (NEAA), 500 µg/ml G418 and 0,5 x antibiotic/antimycotic (ABAM)).At the day of the experiment these precultures were diluted to ~0,1.106 cells/ml in detection medium without FCS and 60 µL of this suspension is dispensed per well into a 96-well microtiter plate. After 3 hours of incubation at 37°C/5% CO2 an equal volume of detection medium containing 2.5 µM RA was added and subsequently incubated for 7 days at 37°C/5% CO_2. After 7 days, LDH activity was determined using the Promega Cytotox 96 Non-Radioactive cytotoxicity assay (Cat. G1780), according the manufacturer's instructions. Cytotoxicity is measured as the ratio of LDH increase in the supernatant divided by the LDH increase in the total cell suspension (sum of the LDH measured in cells and supernatant). Figure 1 shows toxicity after 7 days of differentiation with retinoic acid in M17_3TAU(P301L) cells compared to M17.pcDNA3 cells. Toxicity is clearly higher in the M17_3TAU(P301L) cells demonstrating that it is specifically provoked by the presence of the mutant TAU P301 protein.

Use of the neuroblastoma tauopathy model to screen compounds

The M17_3TAU(P301L) cell line makes it possible to assess the ability of novel compounds to inhibit TAU-induced cytotoxicity. Active inhibitors of Tauopathy in these cells were found to inhibit cytotoxicity or LDH increase in the medium of M17_3TAU(P301L) cells treated as described in Example above. Compounds were tested for their ability to hamper TAU-induced toxicity at different concentrations, ranging from low non-effective concentrations to high potent concentrations. Afterwards, the dose-dependent inhibition curve was used to calculate their EC_{50} (Table 1).

Although the pharmacological properties of the compounds disclosed in this invention vary with structural change, active compounds most particularly possess EC_{50} in a cell-based assay in a range from about 0.0001 to 1.0 μM.

The tested compounds show a EC_{50} value (μM) as shown in the table below.

Example	EC_{50} (μM)	Example	EC_{50} (μM)
2	0.5870	96	0.0281
3	0.9874	97	0.0513
4	0.1152	98	0.0806
5	0.3963	99	0.2714
6	0.2776	100	0.0043
12	0.2685	101	0.0032
13	0.2148	102	0.0009
14	0.0048	103	0.0034
15	0.0214	104	0.0112
16	0.0653	105	0.0021
17	0.0008	106	0.0030
18	0.3672	107	0.0722
19	0.0020	108	0.0079
20	0.1740	109	0.0030
21	0.0095	110	0.0178
22	0.0042	111	0.0031
23	0.0019	112	0.0567
24	0.0007	113	0.0171
25	0.0077	114	0.0079
26	0.0049	115	0.0023
27	0.0167	116	0.0141
28	0.0452	117	0.0058
29	0.0013	118	0.1808
30	0.1469	119	0.0250
31	0.0211	120	0.0161
32	0.3682	121	0.0346

Example	EC_{50} (µM)	Example	EC_{50} (µM)
33	0.1578	122	0.0425
34	0.0014	123	0.0946
35	0.0035	124	0.4584
36	0.1189	125	0.0030
37	0.0029	126	0.0070
38	0.2112	127	0.1092
39	0.0435	128	0.1100
40	0.0141	129	0.0923
41	0.0007	130	0.0009
42	0.0003	131	0.0013
43	0.0033	132	0.0033
44	0.0023	133	0.0014
45	0.0007	134	0.0378
46	0.0312	135	0.0045
47	0.0004	136	0.0062
48	0.0006	137	0.0062
49	0.0496	138	0.0182
50	0.1688	139	0.0472
51	0.1519	140	0.0726
52	0.3270	141	0.1983
53	0.0126	142	0.0037
54	0.0161	143	0.1427
55	0.0042	144	0.6022
56	0.0055	145	0.4615
57	0.0145	146	0.0601
58	0.0022	147	0.1761
59	0.0750	148	0.0675
60	0.0412	149	0.0030
61	0.0444	150	0.1853
62	0.0687	151	0.0082

Example	EC_{50} (µM)	Example	EC_{50} (µM)
63	0.0074	152	0.2150
64	0.0098	153	0.0059
65	0.0599	154	0.0170
66	0.0015	155	0.9765
67	0.0010	156	0.0119
68	0.8992	157	0.0290
69	0.0437	158	0.9984
70	0.1945	159	0.1192
71	0.4291	160	0.0004
72	0.0943	161	0.0396
73	0.0009	162	0.0033
75	0.0134	163	0.0130
76	0.0408	164	0.0034
77	0.2611	165	0.0011
78	0.0021	166	0.0007
79	0.0028	167	0.0059
80	0.0027	168	0.0015
81	0.0006	169	0.0104
82	0.0040	170	0.0007
83	0.0095	171	0.0024
84	0.0007	172	0.0144
85	0.0031	173	0.0029
86	0.0089	174	0.0126
87	0.0131	175	0.0134
88	0.1206	176	0.0195
89	0.0016	177	0.0010
90	0.0068	178	0.0132
91	0.0009	179	0.0034
92	0.0433	180	0.1294
93	0.0009	181	0.0316

Example	EC_{50} (μM)	Example	EC_{50} (μM)
94	0.0095	182	0.1917
95	0.0031	183	0.1518

The compounds of formula IA or I and the pharmaceutically acceptable salts of the compounds of formula IA or I can be used as medicaments, e.g. in the form of pharmaceutical preparations. The pharmaceutical preparations can be administered orally, e.g. in the form of tablets, coated tablets, dragées, hard and soft gelatine capsules, solutions, emulsions or suspensions. The administration can, however, also be effected rectally, e.g. in the form of suppositories, or parenterally, e.g. in the form of injection solutions.

The compounds of formula IA or I can be processed with pharmaceutically inert, inorganic or organic carriers for the production of pharmaceutical preparations. Lactose, corn starch or derivatives thereof; talc, stearic acids or its salts and the like can be used, for example, as such carriers for tablets, coated tablets, dragées and hard gelatine capsules. Suitable carriers for soft gelatine capsules are, for example, vegetable oils, waxes, fats, semi-solid and liquid polyols and the like. Depending on the nature of the active substance no carriers are however usually required in the case of soft gelatine capsules. Suitable carriers for the production of solutions and syrups are, for example, water, polyols, glycerol, vegetable oil and the like. Suitable carriers for suppositories are, for example, natural or hardened oils, waxes, fats, semi-liquid or liquid polyols and the like.

The pharmaceutical preparations can, moreover, contain preservatives, solubilizers, stabilizers, wetting agents, emulsifiers, sweeteners, colorants, flavorants, salts for varying the osmotic pressure, buffers, masking agents or antioxidants. They can also contain still other therapeutically valuable substances.

Medicaments containing a compound of formula IA or I or a pharmaceutically acceptable salt thereof and a therapeutically inert carrier are also an object of the present invention, as is a process for their production, which comprises bringing one or more compounds of formula IA or I and/or pharmaceutically acceptable acid addition salts and, if desired, one or more other therapeutically valuable substances into a galenical administration form together with one or more therapeutically inert carriers.

The most preferred indications in accordance with the present invention are those, which include disorders of the central nervous system, for example the treatment or

prevention of Alzheimer's disease, Pick's disease, corticobasal degeneration, progressive supranuclear palsy, frontotemporal dementia and parkinsonism (linked to chromosome 17, FTDP-17).

The dosage can vary within wide limits and will, of course, have to be adjusted to the individual requirements in each particular case. In the case of oral administration the dosage for adults can vary from about 0.01 mg to about 1000 mg per day of a compound of general formula I or of the corresponding amount of a pharmaceutically acceptable salt thereof. The daily dosage may be administered as single dose or in divided doses and, in addition, the upper limit can also be exceeded when this is found to be indicated.

Tablet Formulation (Wet Granulation)

Item	Ingredients	mg/tablet			
		5 mg	25 mg	100 mg	500 mg
1.	Compound of formula I	5	25	100	500
2.	Lactose Anhydrous DTG	125	105	30	150
3.	Sta-Rx 1500	6	6	6	30
4.	Microcrystalline Cellulose	30	30	30	150
5.	Magnesium Stearate	1	1	1	1
	Total	167	167	167	831

Manufacturing Procedure

1. Mix items 1, 2, 3 and 4 and granulate with purified water.
2. Dry the granules at 50°C.
3. Pass the granules through suitable milling equipment.
4. Add item 5 and mix for three minutes; compress on a suitable press.

Capsule Formulation

Item	Ingredients	mg/capsule			
		5 mg	25 mg	100 mg	500 mg
1.	Compound of formula I	5	25	100	500
2.	Hydrous Lactose	159	123	148	---
3.	Corn Starch	25	35	40	70

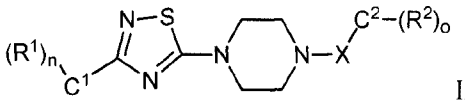
4.	Talc	10	15	10	25
5.	Magnesium Stearate	1	2	2	5
	Total	200	200	300	600

Manufacturing Procedure

1. Mix items 1, 2 and 3 in a suitable mixer for 30 minutes.
2. Add items 4 and 5 and mix for 3 minutes.
3. Fill into a suitable capsule.

Claims:

1. A compound of formula IA



IA

wherein

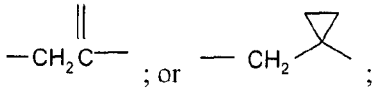
R^1 is hydrogen; lower alkyl; lower alkyl substituted by halogen; halogen; lower alkoxy; lower alkoxy substituted by halogen; or cyano;

R^2 is hydrogen; lower alkyl; lower alkyl substituted by halogen; halogen; lower alkoxy; or is lower alkoxy substituted by halogen;

C^1 is phenyl; benzo[1,3]dioxol; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; thiophen-2-yl; pyrazine-2-yl; pyridazin-4-yl; or pyrimidin-5-yl;

C^2 is phenyl; benzo[1,3]dioxol; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; thiophen-2-yl; pyrazine-2-yl; pyridazin-4-yl; pyrimidin-5-yl; piperidin-1yl; tetrahydro-2H-pyran-4-yl; or cycloalkyl;

X is $-CH_2-$; $-CH_2-CHR-$; $-CH_2-CH_2-CH_2-$; $-CH_2C(O)-$; $-CHR'-CH_2-$;



; or

;

R is hydrogen; hydroxyl; halogen or lower alkyl;

R' is lower alkyl;

n is 1 or 2; if n is 2, R^1 may be independently selected from each other;

o is 1 or 2; if o is 2, R^2 may be independently selected from each other;

or a pharmaceutically active salt thereof; to a stereoisomeric form, an individual diastereoisomer or enantiomer of the compound of formula IA and a racemic or non-racemic mixture thereof,

wherein,

the term "lower alkyl" denotes a saturated straight- or branched-chain group containing from 1 to 7 carbon atoms;

the term "lower alkoxy" denotes a group wherein the alkyl residue is as defined above and which is attached via an oxygen atom;

the term "lower alkyl substituted by halogen" denotes an alkyl group as defined above, wherein at least one hydrogen atom is replaced by halogen;

the term "lower alkoxy substituted by halogen" denotes an alkoxyl group as defined above, wherein at least one hydrogen atom is replaced by halogen.

2. The compound of formula IA according to claim 1, wherein C^1 is: phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; pyrazine-2-yl; pyridazin-4-yl; or pyrimidin-5-yl.

3. The compound of formula IA, according to claim 1 or 2, wherein C^2 is: phenyl; pyridine-2-yl; pyridine-3-yl; pyridine-4-yl; pyrazine-2-yl; tetrahydro-2H-pyran-4-yl; or cycloalkyl.

4. The compound of formula IA according to any one of claims 1-3, wherein C^1 and C^2 are both phenyl.

5. The compound of formula IA according to claim 4, wherein the compound is:

1-(2,4-Dichloro-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine,
1-Phenethyl-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine,
1-[2-(3,4-Dichloro-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine,
1-(2-Methyl-benzyl)-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine,
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine,
1-[3-(3-Methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine,
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine,
1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(3-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,
1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine,
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine,
1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(3-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,
1-[2-(4-Methoxy-phenyl)-ethyl]-4-(3-*p*-tolyl-[1,2,4]thiadiazol-5-yl)-piperazine,
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-fluoro-phenyl)-ethyl]-piperazine,
1-[2-(3-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-*m*-tolyl-ethyl)-piperazine,
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine,
1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-*p*-tolyl-ethyl)-piperazine,
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-phenyl)-ethyl]-piperazine,
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-fluoro-phenyl)-ethyl]-piperazine,
1-[2-(2-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,
1-[3-(3,5-Dichloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine,
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(3-methoxy-phenyl)-propyl]-piperazine,
1-[3-(4-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine,
1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,
1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(4-trifluoromethoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,
1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(4-trifluoromethoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethoxy-phenyl)-ethyl]-piperazine,
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(2-methoxy-phenyl)-propyl]-piperazine,
1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(4-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine,
1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,
1-[3-(3,5-Dichloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine,
1-[3-(4-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine,
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine,
1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(4-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-ethoxy-phenyl)-ethyl]-piperazine,
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-isopropoxy-phenyl)-ethyl]-piperazine,

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[3-(4-methoxy-phenyl)-propyl]-piperazine,

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(4-methoxy-phenyl)-ethanone,

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(4-methoxy-phenyl)-ethanol,

1-[3-(4-Chloro-2-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine,

1-[3-(4-Chloro-2-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine,

1-[3-(2-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine,

1-[3-(2-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine,

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-allyl]-piperazine,

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-methoxy-phenyl)-ethanone,

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-methoxy-phenyl)-ethanol,

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-fluoro-phenyl)-ethanone,

2-{4-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazin-1-yl}-1-(3-fluoro-phenyl)-ethanol,

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-fluoro-2-(4-methoxy-phenyl)-ethyl]-piperazine,

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-fluoro-2-(3-methoxy-phenyl)-ethyl]-piperazine,

1-[3-(4-Fluoro-2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-methoxy-phenyl)-ethyl]-piperazine

1-[3-(4-Fluoro-2-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine,

1-[1-(4-Chloro-phenyl)-cyclopropylmethyl]-4-[3-(4-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-difluoromethoxy-phenyl)-ethyl]-piperazine,

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-difluoromethoxy-phenyl)-ethyl]-piperazine,

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-isopropoxy-phenyl)-ethyl]-piperazine,

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-propyl]-piperazine,

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-1-methyl-ethyl]-piperazine,

4-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile,

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-fluoro-4-methoxy-phenyl)-ethyl]-piperazine,

3-(5-{4-[2-(4-Methoxy-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile,

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine,

1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine,

1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine,

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine,

1-[2-(4-Fluoro-phenyl)-ethyl]-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3-chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine,

1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine,

1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine,

1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine,

1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine,

1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine,

4-[5-(4-Phenethyl-piperazin-1-yl)-[1,2,4]thiadiazol-3-yl]-benzonitrile,

3-[5-(4-Phenethyl-piperazin-1-yl)-[1,2,4]thiadiazol-3-yl]-benzonitrile,

4-(5-{4-[2-(4-Fluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile,

3-(5-{4-[2-(4-Fluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile,
4-(5-{4-[2-(4-Chloro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile,
3-(5-{4-[2-(4-Chloro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile,
4-{5-[4-(2-Methyl-benzyl)-piperazin-1-yl]-[1,2,4]thiadiazol-3-yl}-benzonitrile,
3-{5-[4-(2-Methyl-benzyl)-piperazin-1-yl]-[1,2,4]thiadiazol-3-yl}-benzonitrile,
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine,
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine,
1-[2-(3,4-Difluoro-phenyl)-ethyl]-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,
3-(5-{4-[2-(3,4-Difluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile,
4-(5-{4-[2-(3,4-Difluoro-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile,
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine,
1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine,
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine,
4-(5-{4-[2-(3-Trifluoromethyl-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile,
1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine,
1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine,
1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine,
4-(5-{4-[2-(4-Trifluoromethyl-phenyl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile,
5-(4-(3-phenylpropyl)piperazin-1-yl)-3-(p-tolyl)-1,2,4-thiadiazole,
5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-3-(3-fluorophenyl)-1,2,4-thiadiazole, or

3-(3,4-difluorophenyl)-5-(4-(3-(trifluoromethyl)phenethyl)piperazin-1-yl)-1,2,4-thiadiazole.

6. The compound of formula IA according to any one of claims 1-3, wherein at least one of C^1 or C^2 is pyridine-2-yl, pyridine-3-yl or pyridine-4-yl.

7. The compound of formula IA according to claim 6, wherein the compound is:

1-[2-(3-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine,

1-[2-(3-Methoxy-phenyl)-ethyl]-4-[3-(6-trifluoromethyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(6-trifluoromethyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-[2-(4-Methoxy-phenyl)-ethyl]-4-(3-pyridin-4-yl-[1,2,4]thiadiazol-5-yl)-piperazine,

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine,

1-[3-(4-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine,

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine,

1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine,

1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine,

1-[3-(3-Chloro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine,

1-[3-(6-Methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine,

1-[2-(4-Methoxy-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-[2-(4-Fluoro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-[3-(3-Fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine,

1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(6-methoxy-pyridin-3-yl)-ethyl]-piperazine,

1-[3-(3,4-Difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine,

4-(5-{4-[2-(6-Methoxy-pyridin-3-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile,

3-(5-{4-[2-(6-Methoxy-pyridin-3-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile,

4-(5-{4-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile,

3-(5-{4-[2-(2-Methoxy-pyridin-4-yl)-ethyl]-piperazin-1-yl}-[1,2,4]thiadiazol-3-yl)-benzonitrile,

1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine,

1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine,

1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine,

1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(4-chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(5-chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine,

1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-methoxy-phenyl)-ethyl]-piperazine,

1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine,

1-[3-(4-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine,

1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine,

1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-phenethyl-piperazine,

1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-fluoro-phenyl)-ethyl]-piperazine,

1-[2-(4-Chloro-phenyl)-ethyl]-4-[3-(5-chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(2-methoxy-pyridin-4-yl)-ethyl]-piperazine,

1-[3-(5-Chloro-pyridin-2-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3,4-difluoro-phenyl)-ethyl]-piperazine,

1-[2-(3,4-Difluoro-phenyl)-ethyl]-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperazine,

1-(2-Methyl-benzyl)-4-[3-(6-methyl-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-(2-methyl-benzyl)-piperazine,

1-[3-(5-Chloro-pyridin-3-yl)-[1,2,4]thiadiazol-5-yl]-4-[2-(4-trifluoromethyl-phenyl)-ethyl]-piperazine,

3-(4-chloropyridin-2-yl)-5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-1,2,4-thiadiazole,

3-(4-chloropyridin-2-yl)-5-(4-(3-(trifluoromethyl)phenethyl)piperazin-1-yl)-1,2,4-thiadiazole,

3-(5-chloropyridin-3-yl)-5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-1,2,4-thiadiazole,

3-(2-chloropyridin-4-yl)-5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole,

5-(4-(4-chlorophenethyl)piperazin-1-yl)-3-(2-chloropyridin-4-yl)-1,2,4-thiadiazole,

3-(2-chloropyridin-4-yl)-5-(4-phenethylpiperazin-1-yl)-1,2,4-thiadiazole,

3-(2-methylpyridin-4-yl)-5-(4-phenethylpiperazin-1-yl)-1,2,4-thiadiazole, or

5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-3-(2-methylpyridin-4-yl)-1,2,4-thiadiazole.

8. The compound of formula IA according to any one of claims 1-3, wherein C^2 is cycloalkyl.

9. The compound of formula IA according to claim 8, wherein the compound is:

1-(2-Cyclohexyl-ethyl)-4-[3-(3,4-difluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,

1-(2-Cyclohexyl-ethyl)-4-[3-(3-fluoro-phenyl)-[1,2,4]thiadiazol-5-yl]-piperazine,

3-(4-chlorophenyl)-5-(4-(2-cyclohexylethyl)piperazin-1-yl)-1,2,4-thiadiazole, or

3-(3-chlorophenyl)-5-(4-(2-cyclohexylethyl)piperazin-1-yl)-1,2,4-thiadiazole.

10. The compound of formula IA according to any one of claims 1-2, wherein C^2 is piperidin-1yl.

11. The compound of formula IA according to claim 10, which compound is 3-(5-chloropyridin-3-yl)-5-(4-(2-(piperidin-1-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole.

12. The compound of formula IA according to any one of claims 1-3, wherein C^2 is tetrahydro-2H-pyran-4-yl.

13. The compound of formula IA according to claim 12, wherein the compound is:

3-(3,4-difluorophenyl)-5-(4-(2-(tetrahydro-2H-pyran-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole,

3-(3-chlorophenyl)-5-(4-(2-(tetrahydro-2H-pyran-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole,

3-(5-chloropyridin-3-yl)-5-(4-(2-(tetrahydro-2H-pyran-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole, or

3-(4-chlorophenyl)-5-(4-(2-(tetrahydro-2H-pyran-4-yl)ethyl)piperazin-1-yl)-1,2,4-thiadiazole.

14. The compound of formula IA according to any one of claims 1-3, wherein C^1 is pyridazin-4-yl.

15. The compound of formula IA according to claim 14, wherein the compound is:

3-(6-methylpyridazin-4-yl)-5-(4-phenethylpiperazin-1-yl)-1,2,4-thiadiazole,

5-(4-(4-fluorophenethyl)piperazin-1-yl)-3-(6-methylpyridazin-4-yl)-1,2,4-thiadiazole,

5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-3-(6-methylpyridazin-4-yl)-1,2,4-thiadiazole,

5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-3-(6-methylpyridazin-4-yl)-1,2,4-thiadiazole, or

5-(4-(4-methoxyphenethyl)piperazin-1-yl)-3-(6-methylpyridazin-4-yl)-1,2,4-thiadiazole.

16. The compound of formula IA according to any one of claims 1-3, wherein C^1 is pyrimidin-5-yl.

17. The compound of formula IA according to claim 16, wherein the compound is:

3-(2-methylpyrimidin-5-yl)-5-(4-phenethylpiperazin-1-yl)-1,2,4-thiadiazole,

5-(4-(4-methoxyphenethyl)piperazin-1-yl)-3-(2-methylpyrimidin-5-yl)-1,2,4-thiadiazole,

5-(4-(4-chlorophenethyl)piperazin-1-yl)-3-(2-methylpyrimidin-5-yl)-1,2,4-thiadiazole,

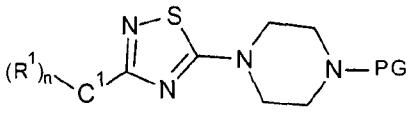
5-(4-(4-fluorophenethyl)piperazin-1-yl)-3-(2-methylpyrimidin-5-yl)-1,2,4-thiadiazole,

5-(4-(3,4-difluorophenethyl)piperazin-1-yl)-3-(2-methylpyrimidin-5-yl)-1,2,4-thiadiazole, or

5-(4-(2-(2-methoxypyridin-4-yl)ethyl)piperazin-1-yl)-3-(2-methylpyrimidin-5-yl)-1,2,4-thiadiazole.

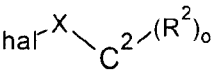
18. A process for preparation of compounds of formula IA as defined in any one of claims 1-17, which process comprises:

coupling a compound of formula

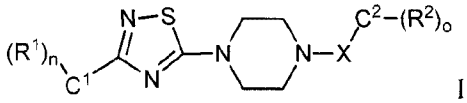


IVa

with a compound of formula



to give a compound of formula



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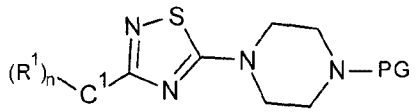
wherein the definitions are as defined in claim 1, wherein PG is hydrogen or a protecting group, and hal is a halogen.

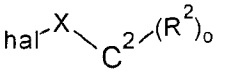
19. A process of for preparation of compounds of formula IA as defined in any one of claims 1-17, which process comprises:

coupling a compound of formula

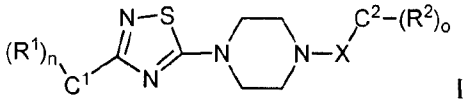


IVa

with a compound of formula



to give a compound of formula



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wherein the definitions are as defined in claim 1, wherein PG is hydrogen or a protecting group, and hal is a halogen, and converting the compound obtained into a pharmaceutically acceptable acid addition salt.

20. A compound as defined in any one of claims 1 to 17, when manufactured as defined in the process of claim 18.

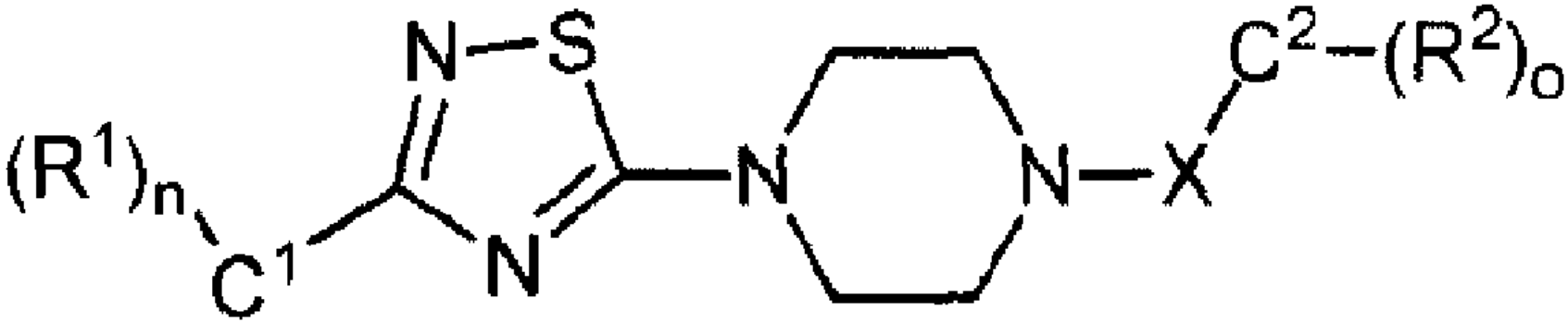
21. A compound as defined in any one of claims 1 to 17, or 20 for use as a therapeutically active substance.

22. A medicament containing one or more compound as claimed in any one of claims 1 to 17, 20 or 21 and a pharmaceutically acceptable excipient.

23. A compound as defined in any one of claims 1 to 17, 20 or 21 or a medicament as defined in claim 22, for use in the treatment of a disease that is: Alzheimer's disease, Pick's disease, corticobasal degeneration, progressive supranuclear palsy, or frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17).

24. Use of the compound of any one of claims 1 to 17, 20 or 21, for the treatment of Alzheimer's disease, Pick's disease, corticobasal degeneration, progressive supranuclear palsy, or frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17).

25. Use of the compound of any one of claims 1 to 17, 20 or 21, for the manufacture of a medicament for the treatment of Alzheimer's disease, Pick's disease, corticobasal degeneration, progressive supranuclear palsy, or frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17).



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