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- (54) Benævnelse: **Carbonylerede (aza)cyclohexaner som dopamin D3-receptorligander**
- (56) Fremdragne publikationer:
WO-A-98/50364
WO-A-2005/012266
WO-A-2006/082456
US-A- 5 047 406
THOMAS R. BELLIOU ET AL.: "Novel cyclohexyl amides as potent and selective D3 dopamine receptor ligands" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 7, no. 18, 1997, page 2403-2408, XP002405747
WALTER S. TRAHANOVSKY, PATRICK J. FLASH, AND LAWRENCE M. SMITH: "Oxidation of organic

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compounds with cerium(IV). VIII. Oxidation of bicyclo[2.2.1]-2-heptanols and bicyclo[2.2.2]-2-octanol" J. AM. CHEM. SOC., vol. 91, no. 18, 1968, page 5068 - 5072, XP002459943

WUSTROW D ET AL: "Aminopyrimidines with High Affinity for Both Serotonin and Dopamine Receptors" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 41, no. 5, 6 February 1998 (1998-02-06), pages 760-771, XP002378781 ISSN: 0022-2623

WERMUTH C G: "MOLECULAR VARIATIONS BASED ON ISOSTERIC REPLACEMENTS" PRACTICE OF MEDICINAL CHEMISTRY, XX, XX, 1996, pages 203-237, XP002190259

DESCRIPTION

[0001] The present patent application concerns new ligands of the D₃ receptor, their process of preparation and their therapeutic use.

[0002] These ligands of the human D₃ receptor behave as antagonists, or inverse agonists or partial agonists or full agonists.

BACKGROUND

[0003] The invention relates to novel carbonylated (aza)cyclohexane derivatives that potently bind to the dopamine D₃ receptor as partial, full or inverse agonists and antagonists. This receptor, a D₂-like receptor, is discretely expressed in only but a few brain projections areas of dopamine neurons, within dopamine neurons themselves (auto-receptors) and in discrete peripheral organs, e.g. the kidney (Schwartz et al. Clinical NeuroPharmacol, 1993, 16, 295). It has been suggested, or even demonstrated that such brain localisations imply a role of this receptor subtype in a number of physiological or pathological processes such as cognition, dementia, psychosis, substance abuse and dependence, mood regulation and disorders (e.g. depression or anxiety), motor regulation and disorders (e.g. Parkinson disease, dyskinesias or equilibration disorders).

[0004] In addition, peripheral D₃ receptors, namely in kidney, seem involved in the control of hormone secretion, diabetic disorders or blood pressure (Jose et al., Curr. Opin. Nephrol. Hypertens., 2002, 11, 87; Gross et al Lab. Invest., 2006, 86, 862). These considerations indicate that modulation (via partial, full or inverse agonism or antagonism) of dopamine D₃ receptors represents a potentially novel approach to treating diseases of the central nervous system in neurology and psychiatry as well as diseases of the cardiovascular or hormonal systems.

[0005] The international patent application WO 01/49679 discloses arylpiperazine derivatives that display dopamine antagonist properties on its receptors D₃ and D₄; however, these compounds have a phenyl group on the position 4 of the piperazine substituted by an halogen atom, and, on the other hand, on the position 1 of the piperazine, an alkylene group optionally substituted by a carbonyl group, and then a 5- or 6-membered aza heterocycle fused with a phenyl group, such as indoline or isoquinoline.

[0006] The international patent application PCT/FR05/02964 discloses arylpiperazine derivatives having an alkylene group and an indoline cycle. These compounds are selective ligands of D₃ receptor.

[0007] WO 98/50364 discloses tetrahydroisoquinoline derivatives as modulators of dopamine D₃ receptors, while WO 2005/012266 discloses carbamoyl-cyclohexane derivatives as D₃/D₂ receptor antagonists. Bellioti et al. (Bioorganic & Medicinal Chemistry Letters, vol. 7, n°18, 1997, p. 2403-2408) discloses cyclohexylamides derivatives. US 5,047,406 discloses cyclohexanols, cyclohexylamide and derivatives. US 5 047 406 concerns the use of compounds for treating psychoses such as Schizophrenia. However, US 5 047 406 does not disclose ligands of the D₂ or D₃ receptors.

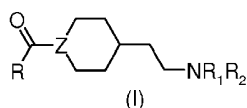
[0008] Unexpectedly, it has now been discovered that the compounds according to the invention, which represent a new family of arylpiperazine derivatives, display a high affinity for the D₃ receptor of dopamine. By contrast to the compounds disclosed in WO 01/49769 and in PCT/FR05/02964, the compounds according to the invention have an aza heterocycle, such as an arylpiperazine, and an alkylene group substituted by an (aza)cyclohexyl group. Further, they are selective ligands of D₃ receptor.

[0009] These compounds are useful as medicaments, notably in neurology and psychiatry, particularly in Parkinson's disease, schizophrenia, dementia, depression, mania, anxiety, dyskinesias, equilibration disorders, Gilles de la Tourette's disease. Further, these compounds are useful for treating drug and tobacco dependency.

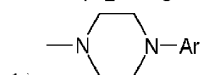
[0010] They are also useful for preventing or treating cardiovascular disorders implying the peripheral dopamine receptors, particularly in kidneys, such as hypertension, cardiac failure, and other disorders such as renal insufficiency or diabetes.

[0011] These compounds are also useful for preventing or treating hormonal disorders implying dopamine receptors in the hypothalamus pituitary complex, such as menopausal disorders or growth disorders.

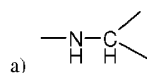
[0012] According to a first object, the present invention concerns new compounds of formula (I):



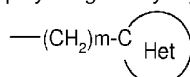
with NR_1R_2 being:



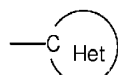
1)
Z being:



R representing cyanoalkyl ; monohalogenocyanoalkyl ; polyhalogenocyanoalkyl ; hydroxyalkyl ; monohalogenoalkyl (with halogeno being Cl, Br or I); polyhalogenoalkyl ; alkoxyalkyl ; monohalogeno-alkoxyalkyl ; polyhalogenoalkoxyalkyl ; alkoxyalkoxyalkyl ; monohalogeno-alkoxyalkoxyalkyl ; polyhalogenoalkoxyalkoxyalkyl ; aryloxyalkyl ; mono- or polyhalogenoaryloxyalkyl ; cycloalkenylalkyl ; dialkylaminoalkyl ; halodialkylaminoalkyl ; polyhalogenodialkylaminoalkyl ;



where



is a non aromatic heterocycle optionally fused with aryl or optionally substituted with one or more acyl, alkyl or halogen ; arylaminoalkyl ; alkylcarbonylalkyl ; acylaminoalkyl ; aminocarbonylalkyl ; alkylsulfanylalkyl ; alkylsulfinylalkyl ; alkylsulfonylalkyl ; m being 2 or 4;

Ar representing an aryl; an heteroaryl or an aryl fused with a cycloalkyl or an heterocycle; Ar being optionally substituted with one or more alkyl; alkenyl; alkynyl; cyano; halogeno; alkoxy; monohalogenoalkoxy; polyhalogenoalkoxy; alkoxyalkyl; dialkylamino; non aromatic heterocyclyl attached by a nitrogen; alkylsulfanyl; alkylsulfinyl; alkylsulfonyl; monohalogenoalkylsulfanyl; monohalogenoalkylsulfinyl; monohalogenoalkylsulfonyl; polyhalogenoalkylsulfanyl; polyhalogenoalkylsulfinyl; polyhalogenoalkylsulfonyl; heteroaryl; aryl; aralkyl; aryloxy; alkoxy-carbonylamino; acyl; acylamino; aminocarbonyl; monoalkylaminocarbonyl; dialkylaminocarbonyl; alkylsulfonylamino; monohalogenoalkyl; polyhalogenoalkyl; hydroxyl; hydroxyalkyl; oxoalkyl;

or their pharmaceutically acceptable salts, hydrates, or hydrated salts, or the polymorphic, crystalline structures of these compounds or their optical isomers, racemates, diastereomers or enantiomers,

wherein :

"Alkyl" means an aliphatic hydrocarbon group which may be straight or branched having 1 to 12 carbon atoms in the chain;

"Alkenyl" means an aliphatic hydrocarbon group containing a carbon-carbon double bond and which may be straight or branched having 2 to 4 carbon atoms in the chain;

"Alkynyl" means an aliphatic hydrocarbon group containing a carbon-carbon triple bond and which may be straight or branched having 2 to 4 carbon atoms in the chain;

"Aryl" means an aromatic monocyclic or multicyclic hydrocarbon ring system of 6 to 10 carbon atoms;

"Cycloalkyl" means a non-aromatic mono- or multicyclic hydrocarbon ring system of 5 to 6 carbon atoms;

"Cycloalkenyl" means a non-aromatic mono- or multicyclic ring system of about 5 to about 10 carbon atoms, and which contains at least one carbon-carbon double bond;

"Heteroaryl" or aromatic heterocycles refers to a 5 to 10 membered aromatic hetero, mono-, bi- or multicyclic ring;

"Heterocycle" or "Heterocyclic" refer to a saturated, partially unsaturated or unsaturated, non aromatic stable 5 to 10 membered mono, bi or multicyclic rings wherein at least one member of the ring is a hetero atom.

[0013] Preferably, R is cyanoalkyl, polyhalogenocyanoalkyl, hydroxyalkyl, polyhalogenoalkyl, alkoxyalkyl, alkoxyalkoxyalkyl, aryloxyalkyl, mono- or polyhalogenoaryloxyalkyl, non aromatic heterocyclyl(CH₂)_m wherein the non aromatic heterocycle is optionally fused with aryl or optionally substituted with one or more acyl, alkyl or halogen, alkylcarbonylalkyl, acylaminoalkyl,

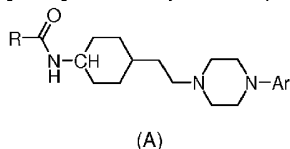
aminocarbonylalkyl, alkylsulfanylalkyl, alkylsulfonylalkyl,
m being 2 or 4.

[0014] Preferably, Ar represents an aryl, more preferably phenyl.

[0015] Preferably, Ar is substituted with one or more alkyl, cyano, halogeno, alkoxy, polyhalogenoalkoxy, alcanediyl, dialkylamino, alkylsulfanyl, aryl, aralkyl, aryloxy, alkoxy-carbonylamino, acyl, alkylsulfonylamino, polyhalogenoalkyl, hydroxy, hydroxyalkyl, oxoalkyl.

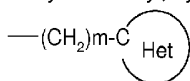
[0016] Preferably, Ar is unsubstituted or substituted with one or more alkyl, polyhalogenoalkyl, halogen or cyano, more preferably with alkyl or polyhalogenoalkyl.

[0017] Preferably, the compounds of the invention are those of formula (A):

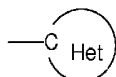


where:

R is chosen from cyanoalkyl; monohalogenoalkyl (with halogeno being Cl, Br or I); polyhalogenoalkyl; alkoxyalkyl; monohalogenoalkoxyalkyl; polyhalogenoalkoxyalkyl; alkoxyalkoxyalkyl; monohalogenoalkoxyalkoxyalkyl; polyhalogenoalkoxyalkoxyalkyl; monohalogenocycanoalkyl; polyhalogenocycanoalkyl; aryloxyalkyl; cycloalkenylalkyl; dialkylaminoalkyl; hydroxyalkyl; polyhalogenodialkylaminoalkyl;



where



is a non aromatic heterocycle optionally fused with aryl or optionally substituted with one or more acyl, alkyl or halogen; arylaminoalkyl; alkylcarbonylalkyl; acylamino-alkyl; aminocarbonylalkyl; alkylsulfanylalkyl; alkylsulfinylalkyl; alkylsulfonylalkyl; mono- or polyhalogenoaryl; mono- or polyhalogenoaryloxyalkyl;

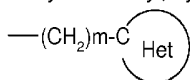
m being 2 or 4,

Ar represents an aryl; an heteroaryl or an aryl fused with a cycloalkyl or an heterocycle; Ar being optionally substituted with one or more alkyl; alkenyl; alkynyl; cyano; halogeno; alkoxy; monohalogenoalkoxy; polyhalogenoalkoxy; alkoxyalkyl; dialkylamino; non aromatic heterocyclyl attached by a nitrogen; alkylsulfanyl; alkylsulfinyl; alkylsulfonyl; monohalogenoalkylsulfanyl; monohalogenoalkylsulfinyl; monohalogenoalkylsulfonyl; polyhalogenoalkylsulfanyl; polyhalogenoalkylsulfinyl; polyhalogenoalkylsulfonyl; heteroaryl; aryl; aralkyl; aryloxy; alkoxy-carbonylamino; acyl; acylamino; aminocarbonyl; monoalkylaminocarbonyl; dialkylaminocarbonyl; alkylsulfonylamino; monohalogenoalkyl; polyhalogenoalkyl; hydroxyl; hydroxyalkyl; oxoalkyl;

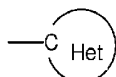
or their pharmaceutically acceptable salts, hydrates, or hydrated salts, or the polymorphic, crystalline structures of these compounds or their optical isomers, racemates, diastereomers or enantiomers.

[0018] Preferably, in formula (A) :

R is chosen from cyanoalkyl; polyhalogenoalkyl; alkoxyalkyl; polyhalogenocycanoalkyl; aryloxyalkyl; cycloalkenylalkyl; dialkylaminoalkyl; hydroxyalkyl; alkylcarbonylalkyl; acylaminoalkyl; aminocarbonylalkyl; alkylsulfinylalkyl; alkylsulfonylalkyl;



where



is a non aromatic heterocycle optionally fused with aryl or optionally substituted with one or more acyl, alkyl or halogen;

Ar represents an aryl optionally fused with a cycloalkyl or an heterocycle and/or Ar being optionally substituted with one or more alkyl; cyano; halogeno; alkoxy; polyhalogenoalkoxy; alkoxyalkyl; dialkylamino; alkylsulfanyl; alkylsulfonyl; polyhalogenoalkylsulfanyl; heteroaryl; aryloxy; alkoxy-carbonylamino; acyl; aminocarbonyl; alkylsulfonylamino; polyhalogenoalkyl; hydroxyl; hydroxyalkyl;

or their pharmaceutically acceptable salts, hydrates, or hydrated salts, or the polymorphic, crystalline structures of these compounds or their optical isomers, racemates, diastereomers or enantiomers.

[0019] Preferred compounds of formula (I) can be chosen from:

- 2-cyano-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(3-acetylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- 2,2,2-Trifluoro-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Methoxy-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Methoxy-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, hydrochloride,
- 2,2-Difluoro-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Hydroxy-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, hydrochloride,
- 3-Methoxy-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide,
- *N*-(4-{2-[4-(2,4-Difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide,
- *N*-(4-{2-[4-(2-Cyano-3-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide,
- *N*-(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide,
- 2-Ethoxy-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, hydrochloride,
- 2-Ethoxy-*N*-(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(2-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide,
- 2-Methoxy-*N*-(4-{2-[4-(phenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Phenoxy-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 3,3,3-Trifluoro-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide,
- 4-Methoxy-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide,
- *N*-(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxypropanamide,
- *N*-(4-{2-[4-(2-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide,
- *N*-(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxypropanamide,
- *N*-(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide,
- 2-Methoxy-2-methyl-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide,
- *N*-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide,
- 2-Cyano-*N*-(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Methylsulfanyl-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-(2-Methoxyethoxy)-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, hydrochloride,
- *N*-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide,
- 3,3,3-Trifluoro-*N*-(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide,
- *N*-(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-phenoxyacetamide,
- 2-Cyano-*N*-(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(2,3-Difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide,
- 2-Dimethylamino-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-isopropoxyacetamide,
- 4-Methoxy-*N*-(4-{2-[4-(phenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide,
- 2-Isopropoxy-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(2-Cyano-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-isopropoxyacetamide,
- *N*-(4-{2-[4-(2-Cyano-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide,
- 2-Cyano-*N*-(4-{2-[4-(2-cyano-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(phenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, hydrochloride,
- 2-Acetylmino-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(3,5-Bistrifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- *N*-(4-{2-[4-(3,5-Bistrifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide,
- 3-Oxo-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide,
- 2-Cyano-*N*-(4-{2-[4-(2,6-di-tert-butylpyrimidin-4-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(2,3-Difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide,
- 2-Cyano-*N*-(4-{2-[4-(2,3-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,

- 2-Cyano-*N*-(4-{2-[4-(2-cyano-3-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(2-Cyano-3-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide,
- 2-Cyano-*N*-(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-1-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Ethoxy-*N*-(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-1-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(3,5-Bistrifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide,
- *N*-(4-{2-[4-(2-Cyano-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide,
- 2-Cyano-*N*-(4-{2-[4-(4-pyridin-4-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(2,6-Di-*tert*-butylpyrimidin-4-yl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide,
- *N*-(4-{2-[4-(2,6-Di-*tert*-butylpyrimidin-4-yl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide,
- 2-Ethoxy-*N*-(4-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Methoxy-*N*-(4-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, hydrochloride,
- 2-Acetylmino-*N*-(4-{2-[4-(4-phenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(2-Chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide,
- 2-Methoxy-*N*-(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-1-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(2-Chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- *N*-(4-{2-[4-(2-Chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide,
- 2-Cyano-*N*-(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Acetylmino-*N*-(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-*tert*-Butoxy-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(3-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- *N*-(4-{2-[4-(3-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide,
- 2-Cyano-*N*-(4-{2-[4-(3-cyano-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(3-Cyano-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide,
- *N*-(4-{2-[4-(3-Cyano-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide,
- *N*-(4-{2-[4-(2,3-Dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide,
- 2-Cyano-*N*-(4-{2-[4-(2,3-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(2,3-Dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide,
- 2-Acetylmino-*N*-(4-{2-[4-(2,3-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(2,3-Difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-isopropoxyacetamide, hydrochloride,
- 2-Cyano-*N*-(4-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(3-dimethylaminophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(3,5-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(2,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(3-Trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamide,
- *N*-(4-{2-[4-(5-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- *N*-(4-{2-[4-(3-Chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- 2-Cyano-*N*-(4-{2-[4-(3-trifluoromethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(3,5-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(3-methoxy-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 4-Cyano-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide,
- 2-Cyano-*N*-(4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(3-isopropoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, hydrochloride,
- 2-Cyano-*N*-(4-{2-[4-(3-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, hydrochloride,
- 2-Cyano-*N*-(4-{2-[4-(2-methoxy-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(4-m-tolyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 3-Diethylamino-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide,
- 3-Cyano-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide, hydrochloride,
- *N*-(4-{2-[4-(3-*tert*-Butylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- 2-Cyano-*N*-(4-{2-[4-(3-ethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(5-Chloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- 4-Cyano-*N*-(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide,
- 2-Cyano-*N*-(4-{2-[4-(6-trifluoromethylbenzo[b]thiophen-3-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,

- 2-Cyano-*N*-(4-{2-[4-(3-hydroxyphenyl)piperazin-1-yl]ethyl}cyclo-hexyl)acetamide hydrochloride,
- *N*-(4-{2-[4-(5-Chloro-2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- *N*-(4-{2-[4-(2-*tert*-Butyl-6-trifluoromethylpyrimidin-4-yl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- 2-Cyano-*N*-(4-{2-[4-(2-methyl-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(5-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide,
- 2-Cyano-*N*-(4-{2-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(3-Chloro-5-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- 2-Cyano-*N*-(4-{2-[4-(3-methylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(4-naphthalen-1-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(3,5-Bistrifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide,
- *N*-(4-{2-[4-(3-Chloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- *N*-(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamide,
- *N*-(4-{2-[4-(4-Phenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamide,
- 3,3,3-Trifluoro-*N*-(4-{2-[4-(4-phenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide,
- *N*-(4-{2-[4-(2-Chloro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- *N*-(4-{2-[4-(5-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamide,
- 4-Oxopentanoic acid (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amide,
- 2-Cyano-*N*-(4-{2-[4-(2-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(2-Chloro-5-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- 2-Cyano-*N*-(4-{2-[4-(2-methylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(2-methoxy-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(5-fluoro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(5-*tert*-Butyl-2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- 2-Cyano-*N*-(4-{2-[4-(5-methoxy-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 5-Oxohexanoic acid (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amide,
- 4-Cyano-*N*-(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide, hydrochloride,
- 4-Cyano-*N*-(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide,
- *N*-(4-{2-[4-(3-Chloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide,
- 4-Cyano-*N*-(4-{2-[4-(3-trifluoromethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide,
- 4-Cyano-*N*-(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide,
- 2-Cyano-*N*-(4-{2-[4-(2-cyano-3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 4-Cyano-*N*-(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-1-yl)piperazin-1-yl]ethyl}cyclohexyl)butanamide,
- 4-Cyano-*N*-(4-{2-[4-(2,3-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide,
- 2-Cyano-*N*-(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-2-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(4-indan-5-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(3,5-Bistrifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-cyanopropanamide,
- 3-Cyano-*N*-(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide,
- *N*-(4-{2-[4-(3-Chloro-2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- *N*-(4-{2-[4-(3-Benzylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- [3-(4-{2-[4-(2-Cyanoacetyl)amino]cyclohexyl}ethyl)piperazin-1-yl]phenyl]carbamic acid ethyl ester,
- 2-Cyano-*N*-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(4-*o*-tolyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(2,5-dimethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 4-Oxopentanoic acid (4-{2-[4-(3,5-bis-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amide,
- 4-Dimethylamino-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide,
- 2-(4-Fluorophenoxy)-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-{2-[4-(2-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, hydrochloride,
- 2-Cyano-*N*-(4-{2-[4-(2,5-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(2-Chloro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide,
- 2-Cyano-*N*-(4-{2-[4-(2,5-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(3-Chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide,
- 4-Cyano-*N*-(4-{2-[4-(2-methyl-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide,
- 4-Oxopentanoic acid (4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amide,
- 2-Cyano-*N*-(4-{2-[4-(3,5-di-*tert*-butylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide,
- *N*-(4-{2-[4-(2-Chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide,
- 4-Cyano-*N*-(4-{2-[4-(*m*-tolyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide,
- 3,3,3-Trifluoro-*N*-(4-{2-[4-(*m*-tolyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide,
- 4-Cyano-*N*-(4-{2-[4-(2-methylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide,

- 2-Cyano-*N*-(4-[2-(4-quinolin-8-yl)piperazin-1-yl]ethyl)cyclohexyl)acetamide,
- 4-Cyano-*N*-(4-[2-[4-(3-methylsulfonylphenyl)piperazin-1-yl]ethyl]cyclohexyl)butanamide,
- 2-Cyano-*N*-(4-[2-(4-quinolin-5-yl)piperazin-1-yl]ethyl)cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-[2-[4-(3-methanesulfonylaminophenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-[2-[4-(4-fluoro-phenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-[2-(4-p-tolyl)piperazin-1-yl]ethyl)cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-[2-[4-(2-ethoxyphenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide,
- *N*-(4-[2-[4-(2-*tert*-Butyl-6-trifluoromethylpyrimidin-4-yl)piperazin-1-yl]ethyl]cyclohexyl)-3-cyanopropanamide,
- 2-Cyano-*N*-(4-[2-[4-(2-phenoxyphenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide,
- *N*-(4-[2-[4-(3-Chloro-2-cyanophenyl)piperazin-1-yl]ethyl]cyclohexyl)-2-cyanoacetamide,
- 2-Cyano-*N*-(4-[2-[4-(2-ethylphenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide,
- *N*-(4-[2-[4-(5-Chloro-2-methylphenyl)piperazin-1-yl]ethyl]cyclohexyl)-4-cyanobutanamide,
- 4-Cyano-*N*-(4-[2-[4-(3,5-dimethylphenyl)piperazin-1-yl]ethyl]cyclohexyl)butanamide,
- *N*-(4-[2-[4-(3-Ethylphenyl)piperazin-1-yl]ethyl]cyclohexyl)-3,3,3-trifluoropropanamide,
- 3-Cyano-*N*-(4-[2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl]cyclohexyl)propanamide,
- 4-Cyano-*N*-(4-[2-[4-(6-trifluoromethylbenzo[b]thiophen-3-yl)piperazin-1-yl]ethyl]cyclohexyl)butanamide,
- 4-Cyano-*N*-(4-[2-[4-(3,5-difluorophenyl)piperazin-1-yl]ethyl]cyclohexyl)butanamide,
- 2-Cyano-*N*-(4-[2-[4-(2,4-diethylphenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide,
- 3,3,3-Trifluoro-*N*-(4-[2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl]cyclohexyl)propanamide,
- *N*-(4-[2-[4-(5-Chloro-2-methylphenyl)piperazin-1-yl]ethyl]cyclohexyl)-3-cyanopropanamide,
- *N*-(4-[2-[4-(3-Chloro-2-methylphenyl)piperazin-1-yl]ethyl]cyclohexyl)-4-cyanobutanamide,
- *N*-(4-[2-[4-(3-Chloro-5-fluorophenyl)piperazin-1-yl]ethyl]cyclohexyl)-4-cyanobutanamide,
- *N*-(4-[2-[4-(2-Fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl]cyclohexyl)-2-methoxyacetamide,
- 4-Cyano-*N*-(4-[2-[4-(3,5-dichlorophenyl)piperazin-1-yl]ethyl]cyclohexyl)butanamide,
- 4-Cyano-*N*-(4-[2-(4-quinolin-8-yl)piperazin-1-yl]ethyl)cyclohexyl)butanamide,
- 4,4,4-Trifluoro-*N*-(4-[2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl]cyclohexyl)butanamide,
- 3-Cyano-*N*-(4-[2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl]cyclohexyl)propanamide,
- 2-Cyano-*N*-(4-[2-[4-(2,6-dimethylphenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-[2-[4-(3-hydroxymethylphenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide,
- 3-Cyano-*N*-(4-[2-[4-(3-methylsulfonylphenyl)piperazin-1-yl]ethyl]cyclohexyl)propanamide,
- 2-Cyano-*N*-(4-[2-[4-(3-methoxymethylphenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-[2-[4-(3-propylphenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-[2-[4-(3,4-dichlorophenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-[2-[4-(3-(1-hydroxyethyl)phenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide,
- 2-Cyano-*N*-(4-[2-[4-(4-trifluoromethylphenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide,
- *N*-(4-[2-[4-(4-Chlorophenyl)piperazin-1-yl]ethyl]cyclohexyl)-2-cyanoacetamide,
- *N*-(4-[2-[4-(Biphenyl-3-yl)piperazin-1-yl]ethyl]cyclohexyl)-2-cyanoacetamide,
- 2-Cyano-*N*-(4-[2-[4-(4-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide,
- 3-Cyano-*N*-(4-[2-[4-(5-fluoro-2-methylphenyl)piperazin-1-yl]ethyl]cyclohexyl)propanamide,
- 4-Cyano-*N*-(4-[2-[4-(5-fluoro-2-methylphenyl)piperazin-1-yl]ethyl]cyclohexyl)butanamide,
- *N*-(4-[2-[4-(3-Bromophenyl)piperazin-1-yl]ethyl]cyclohexyl)-2-cyanoacetamide,
- 2-Cyano-*N*-(4-[2-[4-(3-(1,1-difluoroethyl)phenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide,
- 2-Cyano-2,2-dimethyl-*N*-(4-[2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide,
- 4-Cyano-*N*-(4-[2-[4-(4-fluorophenyl)piperazin-1-yl]ethyl]cyclohexyl)butanamide,
- 3,3,3-Trifluoro-*N*-(4-[2-[4-(4-fluorophenyl)piperazin-1-yl]ethyl]cyclohexyl)propanamide,
- 2-Cyano-*N*-(4-[2-[4-(4-ethylphenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide,
- 4-Cyano-*N*-(4-[2-[4-(2-ethylphenyl)piperazin-1-yl]ethyl]cyclohexyl)butanamide,
- 4-cyano-*N*-(4-[2-[4-(3-propylphenyl)piperazin-1-yl]ethyl]cyclohexyl)butanamide
- 2-cyano-*N*-(4-[2-[4-(3-fluoro-2-methylphenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide
- 4-cyano-*N*-(4-[2-[4-(3-(1,1-difluoroethyl)phenyl)piperazin-1-yl]ethyl]cyclohexyl)butanamide
- *N*-(4-[2-(4-benzo[1,3]dioxol-5-yl)piperazin-1-yl]ethyl]cyclohexyl)-2-cyanoacetamide
- 2-cyano-*N*-(4-[2-[4-(2,3-dihydrobenzo[1,4]dioxin-6-yl)piperazin-1-yl]ethyl]cyclohexyl)acetamide
- 3,3,3-trifluoro-*N*-(4-[2-(4-quinolin-5-yl)piperazin-1-yl]ethyl]cyclohexyl)propanamide
- 4-cyano-*N*-(4-[2-(4-quinolin-5-yl)piperazin-1-yl]ethyl]cyclohexyl)butanamide
- 2-cyano-*N*-(4-[2-[4-(4-fluoro-3-methylphenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide
- 2-cyano-*N*-(4-[2-[4-(3,4-difluorophenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide
- 2-methanesulfinyl-*N*-(4-[2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide

- 2-cyano-*N*-(4-{2-[4-(3-isopropylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 2-cyano-*N*-(4-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 2-methanesulfonyl-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 2-cyano-*N*-(4-{2-[4-(3-fluoro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 2-cyano-*N*-(4-{2-[4-(3,4-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 2-cyano-*N*-(4-{2-[4-(3,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 2-cyano-*N*-(4-{2-[4-(3-trifluoromethylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 2-cyano-*N*-(4-{2-[4-(3-methanesulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 2-cyano-*N*-(4-{2-[4-(3-difluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(3-fluoro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4-cyano-*N*-(4-{2-[4-(3,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4-cyano-*N*-(4-{2-[4-(4-fluoro-3-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(4-chloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide
- *N*-(4-{2-[4-(4-chloro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide
- 4-cyano-*N*-(4-{2-[4-(3-trifluoromethylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4-cyano-*N*-(4-{2-[4-(3-difluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(benzo[1,3]dioxol-5-yl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- 4-cyano-*N*-(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4-cyano-*N*-(4-{2-[4-(4-fluoro-3-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide, hydrochloride
- 4-cyano-*N*-(4-{2-[4-(3,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(3-chloro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide
- 2-cyano-*N*-(4-{2-[4-(4-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(2,5-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 2-cyclopent-2-enyl-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(3,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(3-acetylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- 2-cyano-*N*-(4-{2-[4-(2-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(2-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(3-chloro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- 4-cyano-*N*-(4-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-(4-fluorophenoxy)acetamide
- *N*-(4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide
- 2-cyclopent-3-enyl-*N*-(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- *N*-(4-{2-[4-(2-chloro-4-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide
- *N*-(4-{2-[4-(2-chloro-4-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- 4-cyano-*N*-(4-{2-[4-(5-methoxy-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4-cyano-*N*-(4-{2-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(3-chloro-2-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- 4-cyano-*N*-(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-phenoxyacetamide
- *N*-(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamide
- *N*-(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamide
- 4-cyano-*N*-(4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 3-cyano-*N*-(4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide
- *N*-(4-{2-[4-(2-chloro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- 4-cyano-*N*-(4-{2-[4-(2-methoxy-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 3,3,3-trifluoro-*N*-(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide
- 3-diethylamino-*N*-(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide
- 3-cyano-*N*-(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide
- 4-cyano-*N*-(4-{2-[4-(2,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(5-chloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- *N*-(4-{2-[4-(5-chloro-2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- 4-cyano-*N*-(4-{2-[4-(3-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 3-cyano-*N*-(4-{2-[4-(3-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide
- *N*-(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- 2-cyclopent-2-enyl-*N*-(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(3-methoxy-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(2-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide

- 2-cyano-*N*-(4-{2-[4-(2,4-dichloro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(2,4-dichloro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methanesulfonylacetamide
- *N*-(4-{2-[4-(2,3-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methanesulfonylacetamide
- *N*-(4-{2-[4-(3-chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methanesulfonylacetamide
- 4-cyano-*N*-(4-{2-[4-(4-*o*-tolyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4-cyano-*N*-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4-cyano-*N*-(4-{2-[4-(4-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4-cyano-*N*-(4-{2-[4-(3-cyano-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4-cyano-*N*-(4-{2-[4-(2-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide, hydrochloride
- *N*-(4-{2-[4-(3-chloro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide
- *N*-(4-{2-[4-(3-chloro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- 4-cyano-*N*-(4-{2-[4-(2-ethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4-cyano-*N*-(4-{2-[4-(2-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4-cyano-*N*-(4-{2-[4-(2,5-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 2,2-difluoro-*N*-(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(2,3-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(2,3-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide
- 4-cyano-*N*-(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(3-chloro-2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- 2-cyano-*N*-(4-{2-[4-(2,3,4-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(2,3,4-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 3,3,3-trifluoro-*N*-(4-{2-[4-(3-methanesulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide
- 2-cyano-*N*-(4-{2-[4-(4-indan-4-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(4-indan-4-yl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamide
- 4-cyano-2,2-difluoro-*N*-(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 2,2,2-trifluoro-*N*-(4-{2-[4-(3-methanesulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- *N*-(4-{2-[4-(biphenyl-3-yl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- 2-ethoxy-*N*-(4-{2-[4-(3,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(*p*-tolyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4,4,4-trifluoro-*N*-(4-{2-[4-(3-methanesulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- *N*-(4-{2-[4-(4-chloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- 2-cyano-*N*-(4-{2-[4-(2,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(2,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 2-ethoxy-*N*-(4-{2-[4-(*p*-tolyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 3,3,3-trifluoro-*N*-(4-{2-[4-(3-(1-hydroxyethyl)phenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide
- 2-ethoxy-*N*-(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- *N*-(4-{2-[4-(4-chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- *N*-(4-{2-[4-(4-chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide
- 4-cyano-*N*-(4-{2-[4-(2-methoxy-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 2-cyano-*N*-(4-{2-[4-(2-fluoro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(2-fluoro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(3,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide
- *N*-(4-{2-[4-(3-chloro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide
- *N*-(4-{2-[4-(3-chloro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide
- 3,3,3-trifluoro-*N*-(4-{2-[4-(*p*-tolyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide
- *N*-(4-{2-[4-(3,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- *N*-(4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide
- *N*-(4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- 4-cyano-*N*-(4-{2-[4-(3,4-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(3,4-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- *N*-(4-{2-[4-(3,4-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide
- *N*-(4-{2-[4-(3,4-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide
- 4-cyano-*N*-(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-2-yl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide

- *N*-(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- 2-ethoxy-*N*-(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- *N*-(4-{2-[4-(4-chloro-phenyl)piperazin-1-yl]ethyl}-cyclohexyl)-2-ethoxyacetamide
- *N*-(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-propoxyacetamide
- 2-cyano-*N*-(4-{2-[4-(3,4-dichloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(3,4-dichloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(2,5-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide
- 4-cyano-*N*-(4-{2-[4-(2-cyano-3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4-cyano-*N*-(4-{2-[4-(3-oxazol-2-ylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(3-chloro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide
- *N*-(4-{2-[4-(3-chloro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- 2-cyano-*N*-(4-{2-[4-(3-oxazol-2-ylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(3-ethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4-cyano-*N*-(4-{2-[4-(3-fluoro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 2-ethoxy-*N*-(4-{2-[4-(3-fluoro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(3-(1-hydroxypropyl)phenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 2-methoxy-*N*-(4-{2-[4-(3,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(4-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(2,5-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide
- *N*-(4-{2-[4-(3-chloro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- *N*-(4-{2-[4-(3-chloro-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide
- *N*-(4-{2-[4-(3-chloro-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- 2-ethoxy-*N*-(4-{2-[4-(4-o-tolylpiperazin-1-ylethyl}cyclohexyl)acetamide
- *N*-(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- 2-ethoxy-*N*-(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 2-cyano-*N*-(4-{2-[4-(3-(1-hydroxypropyl)phenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-methoxy-*N*-(4-{2-[4-(3,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 2-ethoxy-*N*-(4-{2-[4-(4-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 2-cyano-*N*-(4-{2-[4-(4-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 2-cyano-*N*-(4-{2-[4-(3,5-difluoro-4-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 2-cyano-*N*-(4-{2-[4-(3-(1-hydroxy-2-methylpropyl)phenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- *N*-(4-{2-[4-(3-chloro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide
- *N*-(4-{2-[4-(3-chloro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- *N*-(4-{2-[4-(2-chloro-4-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide
- *N*-(4-{2-[4-(2-chloro-4-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- 4-cyano-*N*-(4-{2-[4-(4-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 2-cyano-*N*-(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- *N*-(4-{2-[4-(3-chloro-4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide
- *N*-(4-{2-[4-(3-chloro-4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- *N*-(4-{2-[4-(2-chloro-5-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide
- *N*-(4-{2-[4-(2-chloro-5-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- *N*-(4-{2-[4-(3-chloro-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamide
- 2-cyano-*N*-(4-{2-[4-(4-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- *N*-(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- 3-cyano-*N*-(4-{2-[4-(4-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide
- 3-cyano-*N*-(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide
- 2-cyano-*N*-(4-{2-[4-(2-fluoro-4-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(2-fluoro-4-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-butanamide
- 4-methoxy-*N*-(4-{2-[4-(2,3,4-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4,4,4-trifluorobutanamide
- *N*-(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-methoxypropanamide
- 2-cyano-*N*-(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)-3,6-dihydro-2*H*-pyridin-1-yl]ethyl}cyclohexyl)acetamide
- *N*-(4-{2-[4-(3-cyano-4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- 4-cyano-*N*-(4-{2-[4-(3-cyano-4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 2-cyano-*N*-(4-{2-[4-(3-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(3-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 3-cyano-*N*-(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide
- *N*-(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-propoxyacetamide, hydrochloride

- 3,3,3-trifluoro-*N*-(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide
- *N*-(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-malonamide
- 2-cyano-*N*-(4-{2-[4-(5-ethyl-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(5-ethyl-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4-methoxy-*N*-(4-{2-[4-(*m*-tolyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(3,4-dichloro-2-fluoro-phenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- 2-cyano-*N*-(4-{2-[4-(3-cyano-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(3-cyano-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(3-fluoro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- *N*-(4-{2-[4-(3,5-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- *N*-(4-{2-[4-(3-cyano-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- *N*-(4-{2-[4-(4-chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- *N*-(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide
- *N*-(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methanesulfonylacetamide
- *N*-(4-{2-[4-(2-fluoro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- 2-cyano-*N*-(4-{2-[4-(2,3,4,5-tetrafluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 2-cyano-*N*-(4-{2-[4-(2,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- *N*-(4-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- 3-cyano-*N*-(4-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide
- 2-cyano-*N*-(4-{2-[4-(2,4,5-trichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- *N*-(4-{2-[4-(3,4-dichloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide
- 3-cyano-*N*-(4-{2-[4-(3,4-dichloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide
- 2-cyano-*N*-(4-{2-[4-(3-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(3-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 2-cyano-*N*-(4-{2-[4-(2,3,4-trichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 5-cyano-pentanoic acid (4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amide
- *N*-(4-{2-[4-(3-chloro-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-cyanopropanamide
- 2-methoxy-*N*-(4-{2-[4-(2-methyl-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-methoxy-*N*-(4-{2-[4-(2-methyl-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4,4,4-trifluoro-*N*-(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(3,5-bistrifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)malonamide
- *N*-(4-{2-[4-(3-chloro-5-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- *N*-(4-{2-[4-(3,5-bistrifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- *N*-(4-{2-[4-(3-chloro-5-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide
- *N*-(4-{2-[4-(3-chloro-5-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-cyanopropanamide
- 5-cyano-pentanoic acid (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide
- 2-cyano-*N*-(4-{2-[4-(pentafluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- *N*-(4-{2-[4-(4-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- *N*-(4-{2-[4-(4-chloro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- *N*-(4-{2-[4-(4-chloro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- *N*-(4-{2-[4-(3-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- *N*-(4-{2-[4-(4-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide
- *N*-(4-{2-[4-(2,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- 4-cyano-*N*-(4-{2-[4-(2,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4-cyano-*N*-(4-{2-[4-(2,4,5-trichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 4-cyano-*N*-(4-{2-[4-(2,3,4-trichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 3-(4-{2-[4-(4-methoxybutanoylamino)cyclohexyl]ethyl}piperazin-1-yl)benzamide
- *N*-(4-{2-[4-(3-acetylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide
- 2-cyano-*N*-(4-{2-[4-(3-propanoylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-cyano-*N*-(4-{2-[4-(3-propanoylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 2-cyano-*N*-(4-{2-[4-(3-isobutanoylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, dihydrochloride
- 4-Methoxy-*N*-(4-{2-[4-(2,3,4,5-tetrafluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butyramide
- 4-Cyano-*N*-(4-{2-[4-(2,3,4,5-tetrafluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butyramide
- 2-Cyano-*N*-(4-{2-[4-(2-methyl-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-Cyano-*N*-(4-{2-[4-(2-methyl-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butyramide

or their pharmaceutically acceptable salts, hydrates, or hydrated salts, or the polymorphic, crystalline structures of these compounds or their optical isomers, racemates, diastereomers or enantiomers.

[0020] More particularly :

- 1
- 4-Methoxy-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide
- *N*-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide
- *N*-(4-{2-[4-(3,5-Bistrifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide
- *N*-(4-{2-[4-(3-Cyano-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide
- *N*-(4-{2-[4-(3-Cyano-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide
- 2-Cyano-*N*-(4-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 2-Cyano-*N*-(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-Cyano-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 2-Cyano-*N*-(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- *N*-(4-{2-[4-(3-Chloro-5-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide
- 4-Cyano-*N*-(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(5-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-cyanopropanamide
- 2-Cyano-*N*-(4-{2-[4-(4-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 2-Cyano-*N*-(4-{2-[4-(4-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 4-Cyano-*N*-(4-{2-[4-(3-(1,1-difluoroethyl)phenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 2-Cyano-*N*-(4-{2-[4-(3-methanesulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- 2-Cyano-*N*-(4-{2-[4-(3-difluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- *N*-(4-{2-[4-(3-Acetylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- 4-Cyano-*N*-(4-{2-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- 3,3,3-Trifluoro-*N*-(4-{2-[4-(3-methanesulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide
- *N*-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- 4-Cyano-*N*-(4-{2-[4-(3-(1-hydroxypropyl)phenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide
- *N*-(4-{2-[4-(3-Chloro-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide
- 2-Cyano-*N*-(4-{2-[4-(3-(1-hydroxypropyl)phenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide
- *N*-(4-{2-[4-(3-Chloro-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamide
- *N*-(4-{2-[4-(2-Fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide
- *N*-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4,4,4-trifluorobutanamide
- *N*-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-methoxypropanamide

or their pharmaceutically acceptable salts, free forms, hydrates, or hydrated salts, or the polymorphic, crystalline structures of these compounds or their optical isomers, racemates, diastereomers or enantiomers.

[0021] Still more preferably:

N-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide

N-(4-{2-[4-(3,5-Bistrifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide

2-Cyano-*N*-(4-{2-[4-(3-methanesulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide

2-Cyano-*N*-(4-{2-[4-(3-(1-hydroxypropyl)phenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide

N-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4,4,4-trifluorobutanamide

N-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-methoxypropanamide

or their pharmaceutically acceptable salts, free forms, hydrates, or hydrated salts, or the polymorphic, crystalline structures of these compounds or their optical isomers, racemates, diastereomers or enantiomers.

[0022] As used hereabove or hereafter:

"Acyl" means an H-CO- or alkyl-CO- group wherein the alkyl group is as herein described. Preferred acyls contain a lower alkyl. Exemplary acyl groups include formyl, acetyl, propanoyl, 2-methylpropanoyl, butanoyl and palmitoyl.

"Acylamino" is an acyl-NH- group wherein acyl is as defined herein.

"Acylaminoalkyl" means an acyl-NH-alkyl wherein acyl and alkyl are as defined herein.

"Alcanediyl" means a $-(CH_2)_q-$ wherein q is an integer from 3 to 6, preferably from 3 to 5.

[0023] According to the disclosure, "Alkenyl" may mean an aliphatic hydrocarbon group containing a carbon-carbon double bond and which may be straight or branched having 2 to 15 carbon atoms in the chain. Alkenyl groups may have 2 to 12 carbon atoms in the chain.

[0024] According to the invention, "Alkenyl" means an aliphatic hydrocarbon group containing a carbon-carbon double bond and which may be straight or branched having about 2 to 4 carbon atoms in the chain. Exemplary alkenyl groups may include ethenyl, propenyl, *n*-butenyl, *i*-butenyl, 3-methylbut-2-enyl, *n*-pentenyl, heptenyl, octenyl, nonenyl, decenyl.

[0025] "Alkoxy" means an alkyl-O- group wherein the alkyl group is as herein described. Exemplary alkoxy groups include methoxy, ethoxy, *n*-propoxy, *i*-propoxy, *n*-butoxy and heptoxy.

[0026] "Alkoxyalkyl" means an alkyl-O-alkyl- group wherein the alkyl groups are independent as herein described. Exemplary alkoxy groups include methoxyethyl, ethoxymethyl, *n*-butoxymethyl and cyclopentylmethoxyethyl.

[0027] "Alkoxyalkoxyalkyl" means an alkyl-O-alkyl-O-alkyl- group wherein the alkyl groups independently are as defined above.

[0028] "Alkoxyalkylamino" means an alkyl-O-alkyl-NH- wherein alkyl is as defined herein.

[0029] "Alkoxy(alkyl)amino" means an alkyl-O-N(alkyl)- wherein alkyl is as defined herein.

[0030] "Alkoxycarbonylamino" means an alkyl-O-CO-NH- wherein alkyl is as defined herein.

[0031] According to the disclosure, "Alkyl" may mean an aliphatic hydrocarbon group which may be straight or branched having 1 to 20 carbon atoms in the chain.

[0032] According to the invention, alkyl groups have 1 to 12 carbon atoms in the chain. Branched means that one or more lower alkyl groups such as methyl, ethyl or propyl are attached to a linear alkyl chain. Exemplary alkyl groups include methyl, ethyl, *n*-propyl, *i*-propyl, *n*-butyl, *t*-butyl, *n*-pentyl, 3-pentyl, octyl, nonyl, decyl.

[0033] Alkyl groups may be substituted with a cyano group ("Cyanoalkyl"), a hydroxyl group ("Hydroxyalkyl"), a halogeno group ("Monohalogenoalkyl") or more ("Polyhalogenoalkyl").

[0034] "Alkylamino" means an alkyl-NH- group wherein the alkyl group is as herein described.

[0035] "Alkylcarbonylalkyl" means an alkyl-CO-alkyl- wherein alkyl are independently as defined herein.

[0036] "Alkylsulfanyl" means an alkyl-S- group wherein the alkyl group is as herein described.

[0037] "Alkylsulfanylalkyl" means an alkyl-S-alkyl- group wherein the alkyl groups are independently as herein described.

[0038] "Alkylsulfinyl" means an alkyl-SO- group wherein the alkyl group is as defined herein. Preferred groups are those wherein the alkyl group is lower alkyl.

[0039] "Alkylsulfinylalkyl" means an alkyl-SO-alkyl- group wherein the alkyl groups are independently as defined above. Preferred groups are those wherein the alkyl group is lower alkyl.

[0040] "Alkylsulfonyl" means an alkyl-SO₂- group wherein the alkyl group is as defined herein. Preferred groups are those wherein the alkyl group is lower alkyl.

[0041] "Alkylsulfonylalkyl" means an alkyl-SO₂-alkyl- group wherein the alkyl groups are independently as defined herein. Preferred groups are those wherein the alkyl group is lower alkyl.

[0042] "Alkylsulfonylamino" means an alkyl-SO₂-NH- wherein alkyl is as defined herein.

[0043] According to the disclosure, "Alkynyl" may mean an aliphatic hydrocarbon group containing a carbon-carbon triple bond and which may be straight or branched having 2 to 15 carbon atoms in the chain. Alkynyl groups may have 2 to 12 carbon atoms in the chain.

[0044] According to the invention, alkynyl means an aliphatic hydrocarbon group containing a carbon-carbon triple bond and which may be straight or branched having 2 to 4 carbon atoms in the chain. Exemplary alkynyl groups may include ethynyl, propynyl, *n*-butynyl, 2-butynyl, 3-methylbutynyl, *n*-pentynyl, heptynyl, octynyl and decynyl.

[0045] "Aminocarbonylalkyl" means an NH₂-CO-alkyl- wherein alkyl is as defined herein.

[0046] "Aralkyl" means an aryl-alkyl- group wherein the aryl and alkyl are as herein described. Preferred aralkyls contain a lower alkyl moiety. Exemplary aralkyl groups include benzyl, 2-phenethyl and naphthylmethyl.

[0047] According to the disclosure, "Aryl" may mean an aromatic monocyclic or multicyclic hydrocarbon ring system of 6 to 14 carbon atoms.

[0048] According to the invention, "aryl" means an aromatic monocyclic or multicyclic hydrocarbon ring system of 6 to 10 carbon atoms. Exemplary aryl groups include phenyl or naphthyl.

[0049] "Arylaminoalkyl" means an aryl-NH-alkyl- wherein aryl and alkyl are as defined herein.

[0050] "Arylalkoxy" means an aryl-alkyl-O- group wherein the aryl or alkyl groups are as herein described.

[0051] "Aryloxy" means an aryl-O- group wherein the aryl group is as defined herein. Exemplary groups include phenoxy and 2-naphthyloxy.

[0052] "Aryloxyalkyl" means an aryl-O-alkyl- group wherein the aryl or alkyl groups are as herein described. An exemplary aryloxyalkyl groups is phenoxypropyl.

[0053] According to the disclosure, "Cycloalkenyl" may mean a non-aromatic mono- or multicyclic ring system of about 3 to about 10 carbon atoms or about 5 to about 10 carbon atoms, and which contains at least one carbon-carbon double bond.

[0054] According to the invention, "Cycloalkenyl" means a non-aromatic mono- or multicyclic ring system of about 5 to about 6 carbon atoms, and which contains at least one carbon-carbon double bond.

[0055] Exemplary monocyclic cycloalkenyl may include cyclopentenyl, cyclohexenyl, cycloheptenyl. An exemplary multicyclic cycloalkenyl is norbornenyl.

[0056] "Cycloalkyl" means a non-aromatic mono- or multicyclic hydrocarbon ring system of 3 to 10 carbon atoms, preferably of 5 to 10 carbon atoms. Preferred ring sizes of rings of the ring system include 5 to 6 ring atoms. Exemplary monocyclic cycloalkyl include cyclopentyl, cyclohexyl, cycloheptyl, and the like. Exemplary multicyclic cycloalkyl include 1-decalin, norbornyl, adamant-(1- or 2-)yl.

[0057] "Dialkylamino" means an (alkyl)₂N- group wherein the alkyl groups are independently as herein described.

[0058] "Dialkylaminoalkyl" means an (alkyl)₂N-alkyl- group wherein the alkyl groups are independently as herein described.

[0059] "Halogeno" refers to fluorine, chlorine, bromine or iodine atom; preferably fluorine and chlorine atom.

[0060] According to the disclosure, the term "Heteroaryl" or aromatic heterocycles may refer to a 5 to 14 membered aromatic hetero, mono-, bi- or multicyclic ring.

[0061] According to the invention, the term "Heteroaryl" or aromatic heterocycles refers to a 5 to 10 membered aromatic hetero, mono-, bi- or multicyclic ring. Examples may include pyrrolyl, pyridyl, pyrazolyl, thienyl, pyrimidinyl, pyrazinyl, tetrazolyl, indolyl, quinolinyl, purinyl, imidazolyl, thiazolyl, benzothiazolyl, furanyl, benzofuranyl, 1,2,4-thiadiazolyl, isothiazolyl, triazolyl, isoquinolyl, benzothienyl, isobenzofuryl, carbazolyl, benzimidazolyl, isoxazolyl, pyridyl-N-oxide, as well as the fused systems resulting from the

condensation with a phenyl group.

[0062] According to the disclosure, the terms "Heterocycle" or "Heterocyclic" may refer to a saturated, partially unsaturated or unsaturated, non aromatic stable 3 to 14, membered mono, bi or multicyclic rings wherein at least one member of the ring is a hetero atom.

[0063] According to the invention, the terms "Heterocycle" or "Heterocyclic" may refer to a saturated, partially unsaturated or unsaturated, non aromatic stable 5 to 10 membered mono, bi or multicyclic rings wherein at least one member of the ring is a hetero atom. Typically, heteroatoms include, but are not limited to, oxygen, nitrogen, sulfur, selenium, and phosphorus atoms. Preferable heteroatoms are oxygen, nitrogen and sulfur.

[0064] Suitable heterocycles are also disclosed in The Handbook of Chemistry and Physics, 76th Edition, CRC Press, Inc., 1995-1996, pages 2-25 to 2-26, the disclosure of which is hereby incorporated by reference.

[0065] Preferred non aromatic heterocyclic include, but are not limited to pyrrolidinyl, pyrazolidinyl, imidazolidinyl, oxiranyl, tetrahydrofuranyl, dioxolanyl, dioxanyl, piperidyl, piperazinyl, morpholinyl, pyranal, imidazolinal, pyrrolinal, pyrazolinal, thiazolidinal, tetrahydrothiopyranal, dithianal, thiomorpholinyl, dihydropyranal, tetrahydropyranal, dihydropyranal, tetrahydro-pyridyl, dihydropyridyl, tetrahydropyrimidinyl, dihydrothiopyranal, azepanyl, as well as the fused systems resulting from the condensation with a phenyl group.

[0066] "Oxoalkyl" means an alkyl where a CH₂ is replaced by a CO wherein alkyl is as defined herein.

[0067] "Polymethylenedioxy" means a -O-(CH₂)_p-O- wherein p is an integer from 1 to 4.

[0068] "Fused arylheterocyclyl" means a fused aryl and heterocyclyl as defined herein. Preferred fused arylheterocyclyls are those wherein the aryl thereof is phenyl and the heterocyclyl consists of about 5 to about 6 ring atoms. A fused arylheterocyclyl as a variable may be bonded through any atom of the ring system thereof capable of such. The designation of the aza, oxa or thia as a prefix before heterocyclyl portion of the fused arylheterocyclyl define that at least a nitrogen, oxygen or sulphur atom is present respectively as a ring atom. The nitrogen atom of a fused arylheterocyclyl may be a basic nitrogen atom. The nitrogen or sulphur atom of the heterocyclyl portion of the fused arylheterocyclyl may also be optionally oxidized to the corresponding N-oxide, S-oxide or S,S-dioxide. Exemplary preferred fused arylheterocyclyl ring systems include indolinal, 1,2,3,4-tetrahydroisoquinoline, 1,2,3,4-tetrahydroquinoline, 1H-2,3-dihydroisoindol-2-yl, 2,3-dihydrobenz[f]isoindol-2-yl, 1,2,3,4-tetrahydrobenz[g]isoquinolin-2-yl.

[0069] "Fused arylcycloalkyl" means a fused aryl and cycloalkyl as defined herein. Preferred fused arylcycloalkyls are those wherein the aryl thereof is phenyl and the cycloalkyl consists of about 5 to about 6 ring atoms. A fused arylcycloalkyl as a variable may be bonded through any atom of the ring system thereof capable of such. Exemplary fused arylcycloalkyl includes 1,2,3,4-tetrahydronaphthyl.

[0070] As used herein, "pharmaceutically acceptable salts" refer to derivatives of the disclosed compounds wherein the parent compound is modified by making acid or base salts thereof. The pharmaceutically acceptable salts include the conventional non-toxic salts or the quaternary ammonium salts of the parent compound formed, for example, from non-toxic inorganic or organic acids. For example, such conventional non-toxic salts include those derived from inorganic acids such as hydrochloric, hydrobromic, sulfuric, sulfamic, phosphoric, nitric and the like; and the salts prepared from organic acids such as acetic, propanoic, succinic, tartaric, citric, methanesulfonic, benzenesulfonic, glucuronic, glutamic, benzoic, salicylic, toluenesulfonic, oxalic, fumaric, maleic, and the like. Further addition salts include ammonium salts such as tromethamine, meglumine, epolamine, etc., metal salts such as sodium, potassium, calcium, zinc or magnesium. Hydrochloride and oxalate salts are preferred.

[0071] The pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound which contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent, or in a mixture of the two. Generally, non-aqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile are preferred. Lists of suitable salts are found in Remington's Pharmaceutical Sciences, 17th ed., Mack Publishing Company, Easton, PA, 1985, p. 1418, the disclosure of which is hereby incorporated by reference.

[0072] The compounds of the general formula (I) having geometrical and stereoisomers are also a part of the invention.

[0073] According to a further object, the present invention is also concerned with the process of preparation of the compounds of formula (I).

[0074] The compounds and process of the present invention may be prepared in a number of ways well known to those skilled in the art. The compounds can be synthesized, for example, by application or adaptation of the methods described below, or variations thereon as appreciated by the skilled artisan. The appropriate modifications and substitutions will be readily apparent and well known or readily obtainable from the scientific literature to those skilled in the art.

[0075] In particular, such methods can be found in R.C. Larock, *Comprehensive Organic Transformations*, VCH publishers, 1989.

[0076] It will be appreciated that the compounds of the present invention may contain one or more asymmetrically substituted carbon atoms, and may be isolated in optically active or racemic forms. Thus, all chiral, diastereomeric, racemic forms and all geometric isomeric forms of a structure are intended, unless the specific stereochemistry or isomeric form is specifically indicated. It is well known in the art how to prepare and isolate such optically active forms. For example, mixtures of stereomers may be separated by standard techniques including, but not limited to, resolution of racemic forms, normal, reverse-phase, and chiral chromatography, preferential salt formation, recrystallization, and the like, or by chiral synthesis either from chiral starting materials or by deliberate synthesis of target chiral centers.

[0077] Compounds of the present invention may be prepared by a variety of synthetic routes. The reagents and starting materials are commercially available, or readily synthesized by well-known techniques by one of ordinary skill in the arts. All substituents, unless otherwise indicated, are as previously defined.

[0078] In the reactions described hereinafter, it may be necessary to protect reactive functional groups, for example hydroxy, amino, imino, thio or carboxy groups, where these are desired in the final product, to avoid their unwanted participation in the reactions. Conventional protecting groups may be used in accordance with standard practice, for examples see T.W. Greene and P. G. M. Wuts in *Protective Groups in Organic Chemistry*, John Wiley and Sons, 1991; J. F. W. McOmie in *Protective Groups in Organic Chemistry*, Plenum Press, 1973.

[0079] Some reactions may be carried out in the presence of a base. There is no particular restriction on the nature of the base to be used in this reaction, and any base conventionally used in reactions of this type may equally be used here, provided that it has no adverse effect on other parts of the molecule. Examples of suitable bases include: sodium hydroxide, potassium carbonate, triethylamine, alkali metal hydrides, such as sodium hydride and potassium hydride; alkyllithium compounds, such as methylolithium and butyllithium; and alkali metal alkoxides, such as sodium methoxide and sodium ethoxide.

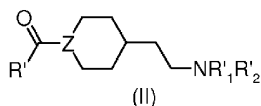
[0080] Usually, reactions are carried out in a suitable solvent. A variety of solvents may be used, provided that it has no adverse effect on the reaction or on the reagents involved. Examples of suitable solvents include: hydrocarbons, which may be aromatic, aliphatic or cycloaliphatic hydrocarbons, such as hexane, cyclohexane, methylcyclohexane, toluene and xylene; amides, such as *N,N*-dimethylformamide; alcohols such as ethanol and methanol and ethers, such as diethyl ether, methyl *tert*-butyl ether, methyl cyclopentyl ether and tetrahydrofuran.

[0081] The reactions can take place over a wide range of temperatures. In general, we find it convenient to carry out the reaction at a temperature of from 0°C to 150°C (more preferably from about room temperature to 100°C). 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, provided that the reaction is effected under the preferred conditions outlined above, a period of from 3 hours to 20 hours will usually suffice.

[0082] The compound thus prepared may be recovered from the reaction mixture by conventional means. For example, the compounds may be recovered by distilling off the solvent from the reaction mixture or, if necessary, after distilling off the solvent from the reaction mixture, pouring the residue into water followed by extraction with a water-immiscible organic solvent and distilling off the solvent from the extract. Additionally, the product can, if desired, be further purified by various well-known techniques, such as recrystallization, reprecipitation or the various chromatography techniques, notably column chromatography or preparative thin layer chromatography.

[0083] The process of preparation of a compound of formula (I) of the invention is another object of the present invention.

[0084] According to the disclosure, compounds of the formula (I) can be obtained from corresponding compounds of formula (II)



wherein R', R'₁ and R'₂ represent respectively R, R₁ and R₂ or a precursor group of respectively R, R₁ and R₂.

[0085] According to the disclosure, compounds of formula (I) can be obtained by a method comprising the steps of:

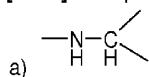
1. a) converting the compound of formula (II) into a compound of formula (I); and optionally
2. b) isolating the obtained compound of formula (I).

[0086] According to the present invention, "precursor group" of a functional group refers to any group which can, by one or more reactions, lead to the desired function, by means of one or more suitable reagents. Those reactions include the deprotections of functional groups, as well as usual addition, substitution, reduction, oxidation or functionalization reaction.

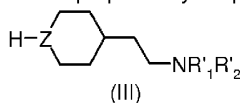
[0087] Preferably, a compound of formula (I) in which Ar in NR₁R₂ is substituted with an acyl group can be prepared from a corresponding compound of formula (II) in which Ar in NR₁R₂ is substituted with a hydroxylated chain. This reaction can be performed by Swern or Swern Moffatt oxidation as well as action of metallic oxide such as chromium or manganese oxides.

[0088] Preferably, a compound of formula (I) in which R is alkyl can be prepared from a corresponding compound of formula in which R is alkoxy by hydrolyzing this ester into the corresponding acid (R=OH), converting the acid into Weinreb's amide (R=N(Me)OMe) and finally reacting with a Grignard's reagent.

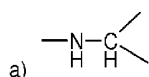
[0089] Compounds of the invention of the formula (I) in which Z is



can be prepared by coupling compounds of formula (III) with acid or acid derivatives R'COX or R'COCOX



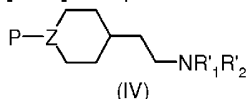
in which R' and NR₁R₂ represent respectively R, NR₁R₂ as defined above, and Z is:



[0090] More precisely, when the reaction can be a peptidic coupling with R'COOH or R'COCOOH and is performed using reagents such as a carbodiimide, carbonyldiimidazole or a chloroformate in the presence of catalysts such as DMAP, HOBt in an inert solvent such as dichloromethane, *N,N*-dimethylformamide, tetrahydrofuran or ethyl acetate at a temperature comprised between 0°C and 40°C.

[0091] Compound R'COX or R'COCOX can also be an activated form of a carboxylate such as an acid chloride (X=Cl), an imidazolide (X=imidazol-1-yl), an hydroxysuccinimidoyl (X=OSu), a paranitrophenyl ester (X= 4-nitrophenoxy), a mixed anhydride or a symmetric anhydride. The reaction is performed in an inert solvent such as dichloromethane, *N,N*-dimethylformamide, tetrahydrofuran or ethyl acetate at a temperature comprised between 0°C and 40°C, optionally in the presence of a catalyst such as DMAP or HOBt and a base such as triethylamine or a carbonate.

[0092] Compounds of formula (III) can be obtained by deprotection of compounds of formula (IV)

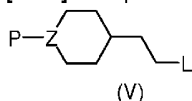


where P represents a nitrogen protecting group such as benzyloxycarbonyl or *tert*-butoxycarbonyl.

[0093] When P is benzyloxycarbonyl, deprotection can be performed using dihydrogen, cyclohexene or a formate in the presence of a catalyst such as palladium on charcoal in an alcohol such as methanol or ethanol at a temperature comprised between room temperature and 80 °C, or with aluminum trichloride in the presence of anisole.

[0094] When P is *tert*-butoxycarbonyl, deprotection can be performed using trimethylsilyliodide, or a Bronsted acid such as trifluoroacetic acid or hydrochloric acid, or a Lewis acid such as tin tetrachloride in a suitable solvent at a temperature comprised between 0 and 40°C.

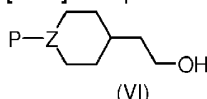
[0095] Compounds of formula (IV) can be prepared by nucleophilic substitution of compounds of formula (V)



where L represents a leaving group such as an halogen or a sulfonate (mesylate or arylsulfonate).

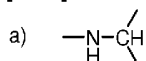
[0096] This substitution can be performed by mixing compound (V) and the amine $\text{HNR}'_1\text{R}'_2$ in a suitable solvent such as acetonitrile, acetone, *N,N*-dimethylformamide, dichloromethane or an alcohol, in the presence of a base such as a carbonate, a bicarbonate or a tertiary amine, at a temperature comprised between room temperature and the refluxing temperature.

[0097] Compounds of formula (V) can be prepared from the corresponding alcohol of formula (VI)

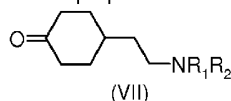


[0098] This reaction can be performed using thionyl chloride with or without imidazole, or a phosphine and tetrahalomethane or hexahaloethane, or a sulfonyl chloride or anhydride in a suitable solvent at a temperature comprised between 0° and 40°C.

[0099] Alternatively, compounds of formula (I) in which Z represents

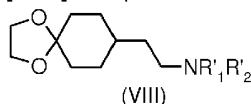


can be prepared from compounds of formula (VII) by reductive amination



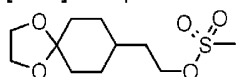
[0100] This reaction can be performed with an ammonium such as ammonium acetate or chloride in the presence of a reducing agent such as sodium triacetoxyborohydride, sodium borohydride or sodium cyanoborohydride in an alcohol such as methanol or ethanol and optionally water at a temperature comprised between -20°C and reflux.

[0101] Compounds of formula (VII) can be prepared by deprotecting spiroketal of formula (VIII)



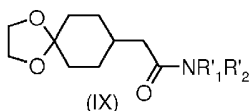
[0102] This deprotection can be performed with an acid such as hydrochloric acid, sulfuric acid or a sulfonic acid in an alcohol such as methanol or ethanol and water at a temperature comprised between room temperature and reflux.

[0103] Compounds of formula (VIII) can be prepared from the corresponding mesylate



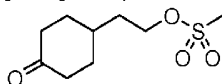
[0104] This substitution can be performed by mixing the mesylate and the amine $\text{HNR}'_1\text{R}'_2$ in a suitable solvent such as acetonitrile, acetone, *N,N*-dimethylformamide, dichloromethane or an alcohol, in the presence of a base such as a carbonate, a bicarbonate or a tertiary amine, at a temperature comprised between room temperature and the refluxing temperature.

[0105] Compounds of formula (VIII) can also be prepared by reduction of amides of formula (IX)



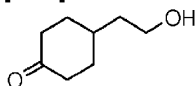
[0106] This reduction can be performed with lithium aluminum hydride in an ether such as diethyl ether, methyl *tert*-butyl ether, methyl cyclopentyl ether or tetrahydrofuran at a temperature comprised between 0°C and reflux.

[0107] Compounds of formula (VIII) can also be prepared from the corresponding further mesylate of formula:



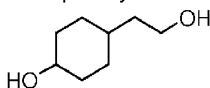
[0108] This substitution can be performed by mixing the mesylate and the amine $\text{HNR}'_1\text{R}'_2$ in a suitable solvent such as acetonitrile, acetone, *N,N*-dimethylformamide, dichloromethane or an alcohol, in the presence of a base such as a carbonate, a bicarbonate or a tertiary amine, at a temperature comprised between room temperature and the refluxing temperature.

[0109] This further mesylate can be prepared from the corresponding 4-(2-hydroxyethyl)cyclohexanone



[0110] This reaction can be performed by reacting 4-(2-hydroxyethyl)cyclohexanone with methanesulfonyl chloride, methanesulfonyl fluoride or methanesulfonic anhydride in the presence of an organic or inorganic base such as pyridine, triethylamine, 1,4-diazabicyclo[2,2,2]octane, 1,5-diazabicyclo[4,3,0]non-5-ene, 1,8-diazabicyclo[5,4,0]undec-7-ene, a carbonate or a bicarbonate in an inert solvent such as dichloromethane, dichloroethane, an aromatic solvent, an ether or a mixture thereof, at a temperature comprised between -20°C and the refluxing temperature.

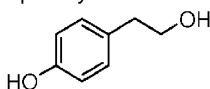
[0111] 4-(2-hydroxyethyl)cyclohexanone is a known intermediate in various industrial fields such as pharmaceutical synthesis and liquid crystals elaboration, it can be prepared from 4-(2-hydroxyethyl)cyclohexanol by selective oxydation



[0112] This oxydation can be performed with an oxydant able to convert a secondary alcohol into a ketone in the presence of a primary alcohol. Such oxydant can be a hypochlorite salt such as sodium or calcium hypochlorite in a suitable solvent such as a carboxylic acid, water, or a mixture thereof.

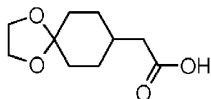
[0113] Alternatively, non selective oxydant can be used with prior protection of the primary alcohol before the oxydation step.

[0114] 4-(2-hydroxyethyl)cyclohexanol is a known intermediate in various industrial fields such as pharmaceutical synthesis and liquid crystals elaboration, it can be prepared by reduction of 4-(2-hydroxyethyl)phenol



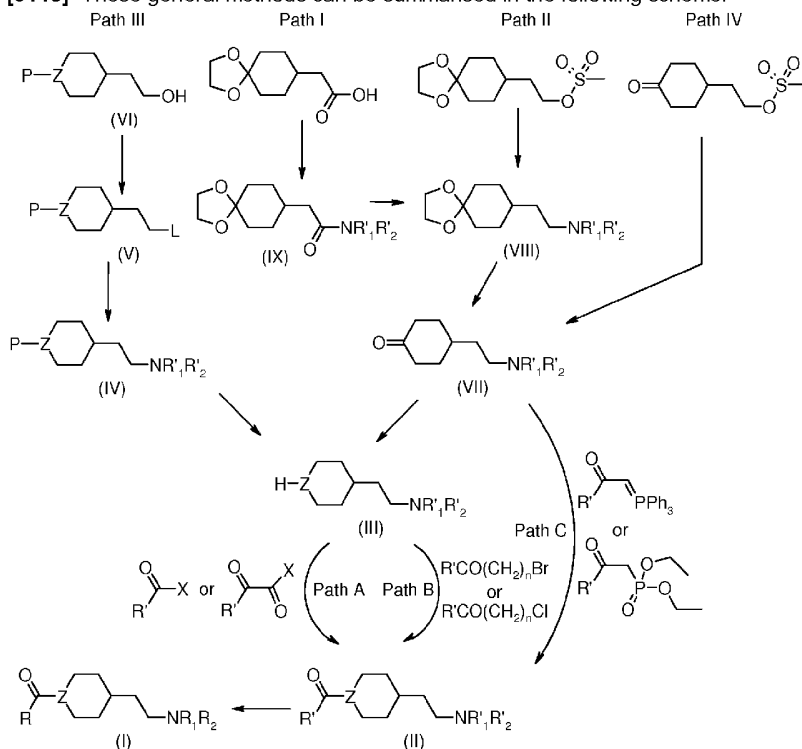
[0115] This reduction can be performed with hydrogen or a hydrogen donor (such as cyclohexene, formic acid, formic acid triethylamine eutectic mixture) in the presence of a metal catalyst (such as palladium, platinum, nickel or ruthenium supported on charcoal, silica or alumina) eventually in the presence of an additive (such as borax, sodium acetate, potassium acetate, lithium acetate, sodium hydroxyde, lithium hydroxyde, potassium carbonate, sodium carbonate, potassium hydrogenocarbonate or sodium hydrogenocarbonate in a suitable solvent such as an alcohol (methanol, ethanol, isopropanol), water, a carboxylic acid (acetic acid, propanoic acid), an ether (diethyl ether, methyl *tert*-butyl ether, tetrahydrofurane, dioxane, cyclopentyl methyl ether), an aromatic solvent (toluene, xylene) or a mixture thereof

[0116] Amides of formula (IX) can be prepared by condensing amine $\text{HNR}'_1\text{R}'_2$ with (1,4-dioxaspiro[4.5]dec-8-yl)acetic acid.



[0117] This reaction can be performed using reagents such as a carbodiimide, carbonyldiimidazole or a chloroformate in the presence of catalysts such as DMAP, HOBt in an inert solvent such as dichloromethane, *N,N*-dimethylformamide, tetrahydrofuran or ethyl acetate at a temperature comprised between 0°C and 40°C.

[0118] These general methods can be summarised in the following scheme:



[0119] According to a further object, the present invention is also concerned with pharmaceutical compositions comprising a compound of formula (I) together with a pharmaceutically acceptable excipient or carrier.

[0120] According to another object, the present invention also relates to the use of compounds of general formula (I) for the preparation of pharmaceutical compositions intended to prevent and/or treat a neuropsychiatric illness or any illness involving the dopamine D_3 receptor. Said neuropsychiatric illnesses are preferably selected from Parkinson's disease, schizophrenia, dementia, psychosis or psychotic states, depression, mania, anxiety, dyskinesias, equilibration disorders, Gilles de la Tourette's disease.

[0121] According to the invention, said prevention and/or treatment of Parkinson's disease is preferably an adjunct therapy for Parkinson's disease.

[0122] Other illnesses include substance dependency, sexual disorders, motor disorders, cardiovascular disorders, hormonal disorders, renal insufficiency or diabetes.

[0123] According to the invention, substance dependency is taken to mean any state associated with withdrawal, abstinence and/or detoxification of an individual dependent on any agent, in particular therapeutically active agents, such as opioids, and/or drugs such as cocaine, heroin, or alternatively alcohol and/or nicotine.

[0124] According to the invention, sexual disorders are in particular taken to mean impotence, in particular male impotence.

[0125] According to the invention, motor disorders are in particular taken to mean essential or iatrogenic dyskinesia, and/or essential or iatrogenic tremor.

[0126] According to the invention, cardiovascular disorders comprise hypertension, cardiac failure.

[0127] According to the invention, hormonal disorders comprise menopausal disorders or growth disorders.

[0128] According to another object, the present invention also relates to the above-mentioned therapeutic treatment methods comprising the administration of a compound according to the invention together with a pharmaceutically acceptable carrier or excipient to a patient in the need thereof.

[0129] According to a further object, the present invention also relates to combinations comprising a compound of the invention and one or more further active ingredient(s).

[0130] In particular, for treating neuropsychiatric disorders, compounds of the invention may be advantageously administered with one or more other neuropsychiatric agent(s) such as anxiolytic, antipsychotic, antidepressant, precognitive or antidementia agents.

[0131] Also, for treating cardiovascular or metabolic disorders, compounds of the invention may be advantageously administered with one or more antihypertensive, cardiotonic or antidiabetic agent(s).

[0132] The identification of those subjects who are in need of treatment of herein-described diseases and conditions is well within the ability and knowledge of one skilled in the art. A clinician skilled in the art can readily identify, by the use of clinical tests, physical examination, genetic tests and medical/family history, those subjects who are in need of such treatment.

[0133] A therapeutically effective amount can be readily determined by the attending diagnostician, as one skilled in the art, by the use of conventional techniques and by observing results obtained under analogous circumstances. In determining the therapeutically effective amount, a number of factors are considered by the attending diagnostician, including, but not limited to: the species of subject; its size, age, and general health; the specific disease involved; the degree of involvement or the severity of the disease; the response of the individual subject; the particular compound administered; the mode of administration; the bioavailability characteristic of the preparation administered; the dose regimen selected; the use of concomitant medication; and other relevant circumstances.

[0134] The amount of a compound of formula (I), which is required to achieve the desired biological effect, will vary depending upon a number of factors, including the dosage of the drug to be administered, the chemical characteristics (e.g. hydrophobicity) of the compounds employed, the potency of the compounds, the type of disease, the diseased state of the patient and the route of administration.

[0135] "Pharmaceutically" or "pharmaceutically acceptable" refer to molecular entities and compositions that do not produce an adverse, allergic or other untoward reaction when administered to an animal, or a human, as appropriate.

[0136] As used herein, "pharmaceutically acceptable carrier" includes any diluents, adjuvants, excipients, or vehicles, such as preserving agents, fillers, disintegrating agents, wetting agents, emulsifying agents, suspending agents, solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents and the like. The use of such media and agents for pharmaceutical active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, its use in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions.

[0137] In the context of the invention, the term "treating" or "treatment", as used herein, means reversing, alleviating, inhibiting the progress of, or preventing the disorder or condition to which such term applies, or one or more symptoms of such disorder or condition.

[0138] "Therapeutically effective amount" means an amount of a compound/ medicament according to the present invention effective in producing the desired therapeutic effect.

[0139] According to the invention, the term "patient", or "patient in need thereof", is intended for a human or non-human mammal affected or likely to be affected with a neuropsychological disorder. Preferably, the patient is a human.

[0140] In general terms, the compounds of this invention may be provided in an aqueous physiological buffer solution containing 0.1 to 10% w/v compound for parenteral administration. Typical dose ranges are from 1 µg/kg to 0.1 g/kg of body weight per day; a preferred dose range is from 0.01 mg/kg to 10 mg/kg of body weight per day. A preferred daily dose for adult humans includes 5, 50, 100 and 200 mg, and an equivalent dose in a human child. The preferred dosage of drug to be administered is likely to depend on such variables as the type and extent of progression of the disease or disorder, the overall health status of the particular patient, the relative biological efficacy of the compound selected, and formulation of the compound excipient, and its route of administration.

[0141] The compounds of the present invention are capable of being administered in unit dose forms, wherein the term "unit dose" means a single dose which is capable of being administered to a patient, and which can be readily handled and packaged, remaining as a physically and chemically stable unit dose comprising either the active compound itself, or as a pharmaceutically acceptable composition, as described hereinafter. As such, typical daily dose ranges are from 0.01 to 10 mg/kg of body weight. By way of general guidance, unit doses for humans range from 0.1 mg to 1000 mg per day. Preferably the unit dose range is from 1 to 500 mg administered one to four times a day, and even more preferably from 10 mg to 300 mg, two times a day. Compounds provided herein can be formulated into pharmaceutical compositions by admixture with one or more pharmaceutically acceptable excipients. Such compositions may be prepared for use in oral administration, particularly in the form of tablets or capsules; or parenteral administration, particularly in the form of liquid solutions, suspensions or emulsions; or intranasally, particularly in the form of powders, nasal drops, or aerosols; or dermally, for example, topically or via trans-dermal patches.

[0142] The compositions may conveniently be administered in unit dosage form and may be prepared by any of the methods well known in the pharmaceutical art, for example, as described in Remington: The Science and Practice of Pharmacy, 20th ed.; Gennaro, A. R., Ed.; Lippincott Williams & Wilkins: Philadelphia, PA, 2000. Pharmaceutically compatible binding agents and/or adjuvant materials can be included as part of the composition. Oral compositions will generally include an inert diluent carrier or an edible carrier.

[0143] The tablets, pills, powders, capsules, troches and the like can contain one or more of any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, or gum tragacanth; a diluent such as starch or lactose; a disintegrant such as starch and cellulose derivatives; a lubricant such as magnesium stearate; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, or methyl salicylate. Capsules can be in the form of a hard capsule or soft capsule, which are generally made from gelatin blends optionally blended with plasticizers, as well as a starch capsule. In addition, dosage unit forms can contain various other materials that modify the physical form of the dosage unit, for example, coatings of sugar, shellac, or enteric agents. Other oral dosage forms syrup or elixir may contain sweetening agents, preservatives, dyes, colorings, and flavorings. In addition, the active compounds may be incorporated into fast dissolve, modified-release or sustained-release preparations and formulations, and wherein such sustained-release formulations are preferably bi-modal.

[0144] Preferred formulations include pharmaceutical compositions in which a compound of the present invention is formulated for oral or parenteral administration, or more preferably those in which a compound of the present invention is formulated as a tablet. Preferred tablets contain lactose, cornstarch, magnesium silicate, croscarmellose sodium, povidone, magnesium stearate, or talc in any combination. It is also an aspect of the present disclosure that a compound of the present invention may be incorporated into a food product or a liquid.

[0145] Liquid preparations for administration include sterile aqueous or non-aqueous solutions, suspensions, and emulsions. The liquid compositions may also include binders, buffers, preservatives, chelating agents, sweetening, flavoring and coloring agents, and the like. Non-aqueous solvents include alcohols, propylene glycol, polyethylene glycol, vegetable oils such as olive oil, and organic esters such as ethyl oleate. Aqueous carriers include mixtures of alcohols and water, buffered media, and saline. In particular, biocompatible, biodegradable lactide polymer, lactide/glycolide copolymer, or polyoxyethylene-polyoxypropylene copolymers may be useful excipients to control the release of the active compounds. Intravenous vehicles can include fluid and nutrient replenishers, electrolyte replenishers, such as those based on Ringer's dextrose, and the like. Other potentially useful parenteral delivery systems for these active compounds include ethylene-vinyl acetate copolymer particles, osmotic pumps, implantable infusion systems, and liposomes.

[0146] Alternative modes of administration include formulations for inhalation, which include such means as dry powder, aerosol, or drops. They may be aqueous solutions containing, for example, polyoxyethylene-9-lauryl ether, glycocholate and deoxycholate, or oily solutions for administration in the form of nasal drops, or as a gel to be applied intranasally. Formulations for buccal administration include, for example, lozenges or pastilles and may also include a flavored base, such as sucrose or acacia, and other excipients such as glycocholate. Formulations suitable for rectal administration are preferably presented as unit-dose

suppositories, with a solid based carrier, such as cocoa butter, and may include a salicylate. Formulations for topical application to the skin preferably take the form of an ointment, cream, lotion, paste, gel, spray, aerosol, or oil. Carriers which can be used include petroleum jelly, lanolin, polyethylene glycols, alcohols, or their combinations. Formulations suitable for transdermal administration can be presented as discrete patches and can be lipophilic emulsions or buffered, aqueous solutions, dissolved and/or dispersed in a polymer or an adhesive.

[0147] The following examples and comparative examples illustrate the invention, but do not limit it. The starting products used are products which are known or prepared using known methods.

[0148] Unless otherwise stated, percentages are weight percentages.

EXAMPLES

[0149] Melting points are determined on Büchi capillary melting point apparatus.

[0150] Proton NMR spectra are recorded on a Bruker 250 MHz NMR instrument. Deuteriochloroform is used as solvent unless otherwise stated. The chemical shifts δ are expressed in ppm. The following abbreviations are used to denote signal patterns: s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet, ms = massif. The coupling constants are expressed in Hz. The spectra recorded are consistent with the proposed structures.

[0151] TLC are performed on 0.25 mm silica gel F254 plates.

[0152] Arylpiperazines are commercially available or can be prepared according to methods described in French patent applications FR 04 11303 and FR 04 12763. The 2,4-di-*tert*-butyl-6-piperazin-1-ylpyrimidine and 2-*tert*-butyl-6-trifluoromethyl-4-piperazin-1-ylpyrimidine can be prepared according to US 2004/0259882 A1, 1-(6-trifluoromethylbenzo[b]thiophen-3-yl)piperazine (WO 02/066469) ; *N*-(3-piperazin-1-ylphenyl)methanesulfonamide (Pharmazie, 57, (8), 515-518, (2002)).

[0153] The 4-aryl-3,6-dihydro-2*H*-pyridine and 4-arylpiperidine are commercially available or can be prepared according to methods described in French application FR 04 12763.

[0154] The 1,2,3,4-tetrahydroisoquinoline-7-carbonitrile can be prepared according to Synth. Commun., 25, (20), 3255-3261, (2001).

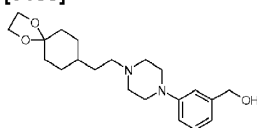
[0155] 3-Oxazol-2-ylaniline can be prepared according to J. Org. Chem. 42, (19), 3208-3209, (1977).

[0156] The carboxylic acid derivatives are commercially available or prepared. The 3-cyanopropanoic acid can be prepared from β -propanolactone according to J. Am. Chem. Soc., 74, 1323, (1952) ; 4-cyanobutanoic acid (J. Org. Chem., 61, (19), 6486-6487, (1996) ; 2-methoxy-2-methylpropanoic (Tetrahedron, 53, (42), 14286, (1997)) ; 2-isopropoxyacetic acid (Tetrahedron, 59, 7915-7920, (2003) ; 2-*tert*-butoxyacetic acid (Bioorg. Med. Chem. 11, 4287-4293, (2003) ; cyanodimethylacetic acid (J. Org. Chem., 46, (24), 4907-4911, (1981) ; methanesulfonylacetic acid, (Arch. Pharm. Med. Chem. 333, 293-298, (2000)) ; 5,6-dihydro-4*H*-pyran-3-carboxylic acid and 4,5-dihydrofuran-3-carboxylic acid (Synthesis, 12, 1016-1017, (1986)) ; 5-cyanopentanoic acid, (Tetrahedron, 48, 43, 9531-9536, (1992)) ; (2-cyanoethoxy)acetic acid, US 4,105,687.

[0157] Some acids have been prepared by usual saponification of the corresponding ethyl ester with aqueous sodium hydroxide solution : *trans*-2-cyanocyclopropanecarboxylic acid from *trans*-2-cyanocyclopropanecarboxylic acid ethyl ester (Synthesis, 301-303, (1982)) ; 5-cyano-2,2-difluoropentanoic acid from 5-cyano-2,2-difluoro-pentanoic acid ethyl ester (J. Fluorine Chem. 121, 105-107, (2003)).

Preparation A: 1-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]-4-(3-hydroxymethylphenyl)-piperazine

[0158]

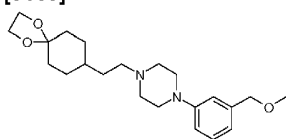


[0159] To a cooled solution of 2.5 g (6.25 mmol) of 1-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]-4-(3-ethoxycarbonylphenyl)piperazine (prepared by path II), is added, under argon, 0.36 g (9.36 mmol) of lithium aluminum hydride. The suspension is stirred overnight at room temperature. Hydrolysis is performed at 0°C by slow addition of 0.35 mL of water, 0.35 mL of 15% aqueous sodium hydroxide solution and 1.0 mL of water. The slurry is stirred for 15 minutes at room temperature then magnesium sulfate is added. The mixture is filtered and the salts are washed with ethyl acetate. The filtrate is concentrated under reduced pressure to give 2.0 g (89%) of 1-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]-4-(3-hydroxymethylphenyl)piperazine as a solid.

¹H NMR: 7.25 (t, 1H, J = 7.5) ; 6.95 (s, 1H) ; 6.9 to 6.8 (ms, 2H) ; 4.65 (s, 2H) ; 3.95 (s, 4H) ; 3.2 (m, 4H) ; 2.6 (m, 4H) ; 2.4 (m, 2H) ; 2.0 (broad s, 1H) ; 1.85 to 1.65 (ms, 4H) ; 1.65 to 1.4 (ms, 3H) ; 1.4 to 1.2 (ms, 4H)

Preparation B: 1-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]-4-(3-methoxymethylphenyl)-piperazine

[0160]

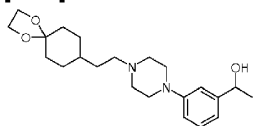


[0161] To a solution of 1.2 g (3.42 mmol) of 1-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]-4-(3-hydroxymethylphenyl)piperazine (preparation A) in 15 mL of dimethyl sulfoxide are added, at room temperature, 1.0 g (17.2 mmol) of potassium fluoride, 0.52 g (3.66 mmol) of iodomethane and 0.68 g (10.3 mmol) of potassium hydroxide. The mixture is stirred overnight at room temperature, partitioned between with ethyl acetate and water. The aqueous phase is separated and the organic phase is washed with water, dried over magnesium sulfate, filtered and concentrated. The oily residue is purified by chromatography over silica gel (eluant hexane/ethyl acetate 1/1) to give 0.3 g of 1-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]-4-(3-methoxymethylphenyl)piperazine as an oil.

¹H NMR: 7.25 (t, 1H, J = 7.5) ; 6.9 (s, 1H) ; 6.9 to 6.75 (ms, 2H) ; 4.4 (s, 2H) ; 3.95 (s, 4H) ; 3.35 (s, 3H) ; 3.2 (m, 4H) ; 2.6 (m, 4H) ; 2.45 (m, 2H) ; 1.85 to 1.65 (ms, 4H) ; 1.65 to 1.4 (ms, 3H) ; 1.4 to 1.2 (ms, 4H)

Preparation C: 1-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]-4-(3-(1-hydroxyethyl)phenyl)-piperazine

[0162]

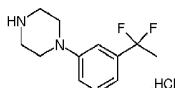
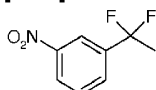


[0163] To a cooled solution of 1.6 g (4.3 mmol) of 1-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]-4-(3-acetylphenyl) piperazine (prepared by path II) in 15 mL of methanol is added, by portion, 0.18 g (4.7 mmol) of sodium borohydride. The mixture is stirred for 3 hours at room temperature. Methanol is evaporated under reduced pressure and the residue is taken off with water and extracted twice with ethyl acetate. The organic phases are combined, washed with water, then brine, dried over magnesium sulfate, filtered and concentrated to give 1.61 g (100%) of 1-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]-4-(3-(1-hydroxyethyl)phenyl)piperazine as an oil.

¹H NMR: 7.25 (t, 1H, J = 7.5) ; 7.0 (s, 1H) ; 6.9 to 6.75 (ms, 2H) ; 4.85 (q, 1H, J = 7.5) ; 3.95 (s, 4H) ; 3.2 (m, 4H) ; 2.6 (m, 4H) ; 2.4 (m, 2H) ; 2.0 (broad s, 1H) ; 1.8 to 1.65 (ms, 4H) ; 1.6 to 1.4 (ms, 7H) ; 1.4 to 1.2 (ms, 3H)

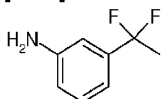
Preparation D: 1-[3-(1,1-difluoroethyl)phenyl]piperazine, hydrochloride

[0164]

**Step 1: 1-(1,1-difluoroethyl)-3-nitrobenzene****[0165]**

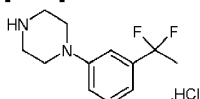
[0166] A mixture of 2.0 g (12 mmol) of 1-(3-nitrophenyl)ethanone and 7.4 g (16.7 mmol) of 50% bis(2-methoxyethyl)aminosulfurtrifluoride solution in toluene is warmed to 80°C overnight. The mixture is slowly poured into cooled water and extracted twice with ethyl acetate. The organic phases are combined, washed with an aqueous saturated sodium hydrogen carbonate solution, then with brine, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue (2.5 g) is purified over 160 g of silica gel (eluant heptane/ethyl acetate 85/15) to give 1.6 g (71%) of 1-(1,1-difluoroethyl)-3-nitrobenzene as an oil.

¹H NMR: 8.4 (s, 1 H) ; 8.3 (d, 1 H, J = 7.5) ; 7.9 (d, 1 H, J = 7.5) ; 7.65 (t, 1 H, J = 7.5) ; 2.0 (t, 3H, J=17.5)

Step 2: 3-(1,1 -difluoroethyl)aniline**[0167]**

[0168] A mixture of 3.0 g (16 mmol) of 1-(1,1-difluoroethyl)-3-nitrobenzene, 18.0 g (80 mmol) of tin chloride dihydrate and 50 mL of ethanol is refluxed for one hour. The mixture is slowly poured on cooled water. The pH is adjusted to 7 by addition of an aqueous 10N solution of sodium hydroxide, then adjusted to 9 by addition of an aqueous saturated solution of sodium hydrogen carbonate. The product is extracted 4 times with ethyl acetate. The organic phases are combined, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The oily residue (2.2 g) is purified over 100 g of silica gel (eluant heptane/ethyl acetate 2/1) to give 1.7 g (68%) of 3-(1,1 -difluoroethyl)aniline as an oil.

¹H NMR: 7.2 (t, 1 H, J = 7.5) ; 6.9 (d, 1 H, J = 7.5) ; 6.8 (s, 1 H) ; 6.9 (d, 1 H, J = 7.5) ; 3.8 (broad s, 2H) ; 1.9 (t, 3H, J = 17.5)

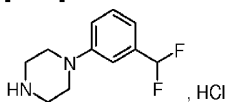
Step 3: 1-[3-(1,1-difluoroethyl)phenyl]piperazine, hydrochloride**[0169]**

[0170] A mixture of 2.5 g (15.9 mmol) of 3-(1,1 -difluoroethyl)aniline and 2.8 g (15.9 mmol) of bis(2-chloroethyl)amine in 20 mL of chlorobenzene is refluxed overnight. After cooling to room temperature, diethyl ether is added and precipitation occurs. The solid is filtered, washed with diethyl ether and dried under reduced pressure to give 3.8 g (90%) of 1-[3-(1,1-difluoroethyl)phenyl]piperazine, hydrochloride as a white solid.

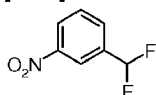
¹H NMR (DMSO D₆): 9.2 (broad s, 2H) ; 7.3 (t, 1 H, J = 7.5) ; 7.15 to 6.95 (ms, 2H) ; 7.0 (d, 1H, J = 7.5) ; 3.4 (m, 4H) ; 3.2 (m, 4H) ; 1.9 (t, 3H, J = 14.5)

Preparation E: 1-(3-difluoromethylphenyl)piperazine, hydrochloride

[0171]

**Step 1: 1-difluoromethyl-3-nitrobenzene**

[0172]

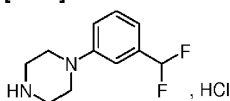


[0173] To a solution of 2.6 g (17 mmol) of 3-nitrobenzaldehyde in 5 mL of dichloromethane is added 11.4 mL of 50% bis(2-methoxyethyl)aminosulfurtrifluoride solution in toluene. The mixture is stirred overnight at room temperature, washed twice with a saturated aqueous sodium hydrogen carbonate solution then with brine, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue is purified over 150 g of silica gel (eluant heptane/ethyl acetate 85/15) to give 2.3 g (78%) of 1-difluoromethyl-3-nitrobenzene as an oil.

$^1\text{H NMR}$: 8.4 (s, 1 H) ; 8.35 (d, 1 H, $J = 7.5$) ; 7.9 (d, 1 H, $J = 7.5$) ; 7.7 (t, 1 H, $J = 7.5$) ; 7.0 (t, 1 H, $J = 55$)

Step 2: 1-(3-difluoromethylphenyl)piperazine, hydrochloride

[0174]

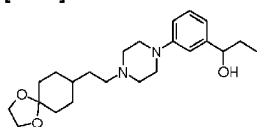


[0175] The 1-(3-difluoromethylphenyl)piperazine, hydrochloride is obtained from 1-difluoromethyl-3-nitrobenzene using the procedure described in preparation D, steps 2 and 3.

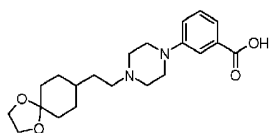
$^1\text{H NMR}$ (DMSO D_6): 9.25 (broad s, 2H) ; 7.35 (m, 1 H) ; 7.2 (m, 2H) ; 7.0 (d, 1 H, $J = 7.5$) ; 6.9 (t, 1 H, $J = 55$) ; 3.4 (m, 4H) ; 3.2 (m, 4H)

Preparation F: 1-(3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}phenyl)propan-1-ol

[0176]

**Step 1: 3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}benzoic acid**

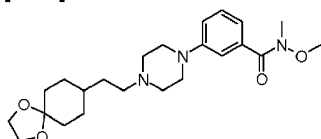
[0177]



[0178] To a solution of 3.75 g (9.3 mmol) of 3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}benzoic acid ethyl ester in 20 mL of ethanol are added 10.2 mL of an aqueous 1 N sodium hydroxide solution. Stirring is maintained overnight. The mixture is cooled and 2.55 mL (10.2 mmol) of 4N hydrochloric acid solution are added. After evaporation under reduced pressure, the solid is taken off with ethyl acetate, filtered and dried at 50°C under vacuum to give 3.7 g of crude 3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}benzoic acid.

Step 2: 3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}-*N*-methoxy-*N*-methylbenzamide

[0179]

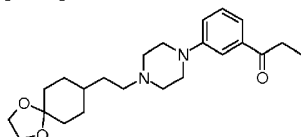


[0180] The 3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}-*N*-methoxy-*N*-methyl-benzamide is obtained from 3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}benzoic acid using the procedure described in example 4, step c giving the title compound in 85% yield.

¹H NMR: 7.25 (m, 1 H) ; 7.2 (m, 1 H) ; 7.15 (m, 1 H) ; 7.0 (m, 1 H) ; 3.95 (s, 4H) ; 3.6 (s, 3H) ; 3.35 (s, 3H) ; 3.3 (m, 4H) ; 2.65 (m, 4H) ; 2.45 (m, 2H) ; 1.75 (m, 4H) ; 1.65 to 1.4 (ms, 4H) ; 1.4 to 1.2 (ms, 3H)

Step 3: 1-{3-[4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl]phenyl}propan-1-one

[0181]

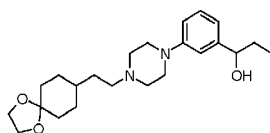


[0182] To a solution of 1.6 g (3.8 mmol) of 3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}-*N*-methoxy-*N*-methylbenzamide in 25 mL of dry tetrahydrofuran cooled to 0°C are added 8 mL of 1 M ethylmagnesium bromide solution in tetrahydrofuran. The mixture is stirred for 90 minutes then poured in 100 mL of an aqueous saturated sodium hydrogen carbonate solution. The product is extracted twice with ethyl acetate. The organic phases are combined, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue (1.4 g) is purified over 50 g of silica gel (eluant heptane/ethyl acetate 1/1) to give 1.06 g (72%) of 1-{3-[4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl]phenyl}propan-1-one as an oil.

¹H NMR: 7.55 (s, 1 H) ; 7.45 (m, 1 H) ; 7.35 (t, 1 H, J = 7.5) ; 7.15 (m, 1 H) ; 3.95 (s, 4H) ; 3.3 (m, 4H) ; 3.0 (q, 2H, J = 7.5) ; 2.65 (m, 4H) ; 2.5 (m, 2H) ; 1.8 (m, 4H) ; 1.7 to 1.35 (ms, 4H) ; 1.35 to 1.25 (ms, 3H) ; 1.2 (t, 3H, J = 7.5)

Step 4: 1-{3-[4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl]phenyl}propan-1-ol

[0183]

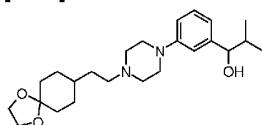


[0184] The 1-(3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}phenyl)propan-1-ol is prepared from 1-(3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}phenyl)-propan-1-one using the procedure described in preparation C.

¹H NMR: 7.25 (t, 1 H, J = 7.5) ; 6.95 (s, 1 H) ; 6.9 to 6.75 (ms, 2H) ; 4.55 (m, 1 H) ; 3.95 (s, 4H) ; 3.25 (m, 4H) ; 2.65 (m, 4H) ; 2.5 (m, 2H) ; 2.0 (m, 1 H) ; 1.9 to 1.75 (ms, 6H) ; 1.65 to 1.4 (ms, 5H) ; 1.4 to 1.2 (ms, 5H)

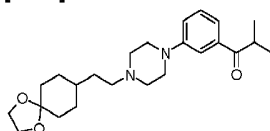
Preparation G: 1-(3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}phenyl)-2-methylpropan-1-ol

[0185]



Step 1: 1-(3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}phenyl)-2-methylpropan-1-one

[0186]

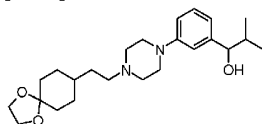


[0187] The 1-(3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}phenyl)-2-methylpropan-1-one is prepared by addition of isopropylmagnesium bromide onto 3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}-N-methoxy-N-methylbenzamide using the procedure described in preparation F, step 3, to give the title compound in 27% yield.

¹H NMR: 7.5 (s, 1 H) ; 7.4 to 7.25 (ms, 2H) ; 7.1 (d, 1 H, J = 7.5) ; 3.95 (s, 4H) ; 3.55 (m, 1 H) ; 3.35 (m, 4H) ; 2.7 (m, 4H) ; 2.55 (m, 2H) ; 1.75 (m, 4H) ; 1.65 to 1.45 (ms, 5H) ; 1.45 to 1.2 (ms, 8H)

Step 2: 1-(3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}phenyl)-2-methylpropan-1-ol

[0188]

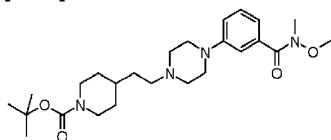


[0189] The 1-(3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}phenyl)-2-methylpropan-1-ol is prepared from 1-(3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}phenyl)-2-methylpropan-1-one using the procedure described in preparation C.

¹H NMR: 7.25 (t, 1 H, J = 7.5) ; 6.9 (s, 1 H) ; 6.9 to 6.75 (m, 2H) ; 4.3 (m, 1H) ; 3.95 (s, 4H) ; 3.35 (m, 4H) ; 2.8 (m, 4H) ; 2.65 (m, 2H) ; 1.95 (m, 1 H) ; 1.85 (m, 1 H) ; 1.8 to 1.2 (ms, 11 H) ; 1.0 (d, 3H, J = 7.5) ; 0.8 (d, 3H, J = 7.5)

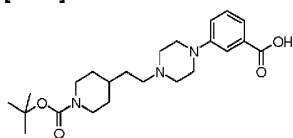
Preparation H: 4-(2-{4-[3-(methoxymethylcarbamoyl)phenyl]piperazin-1-yl}ethyl)-piperidine-1-carboxylic acid *tert*-butyl ester

[0190]



Step 1 : 4-[2-[4-(3-carboxyphenyl)piperazin-1-yl]ethyl]piperidine-1-carboxylic acid *tert*-butyl ester

[0191]

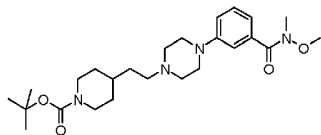


[0192] To a solution of 2.8 g (12.8 mmol) of 4-[2-[4-(3-ethoxycarbonylphenyl)piperazin-1-yl]ethyl]piperidine-1-carboxylic acid *tert*-butyl ester are added 12.8 mL of 1 N aqueous sodium hydroxide solution. The mixture is stirred overnight at room temperature then concentrated under reduced pressure. The residue is acidified with 12.8 mL of 1N aqueous hydrochloric acid solution. The product is extracted with ethyl acetate, washed with water, dried over magnesium sulfate, filtered and concentrated under reduced pressure to give 2.5 g (47%) of 4-[2-[4-(3-carboxyphenyl)piperazin-1-yl]ethyl]piperidine-1-carboxylic acid *tert*-butyl ester.

^1H NMR: 8.5 (broad s, 1H) ; 7.7 to 7.5 (ms, 2H) ; 7.3 (t, 1H, $J = 7.5$) ; 7.1 (d, 1H, $J = 7.5$) ; 4.1 (m, 2H) ; 3.45 (m, 4H) ; 3.1 (m, 4H) ; 2.85 (m, 2H) ; 2.7 (m, 2H) ; 1.7 (m, 2H) ; 1.65 to 1.35 (ms, 12H) ; 1.3 to 1.0 (ms, 2H)

Step 2: 4-[2-(4-{3-[methoxy(methyl)carbamoyl]phenyl})piperazin-1-yl)ethyl]piperidine-1-carboxylic acid *tert*-butyl ester

[0193]



[0194] The 4-[2-(4-{3-[methoxy(methyl)carbamoyl]phenyl})piperazin-1-yl)ethyl]piperidine-1-carboxylic acid *tert*-butyl ester is prepared from 4-[2-[4-(3-carboxyphenyl)piperazin-1-yl]ethyl]piperidine-1-carboxylic acid *tert*-butyl ester using the procedure described in preparation F, step 2.

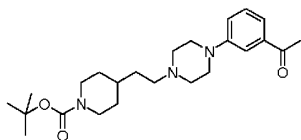
^1H NMR: 7.25 (t, 1H, $J = 7.5$) ; 7.2 (s, 1H) ; 7.1 (d, 1H, $J = 7.5$) ; 7.0 (d, 1H, $J = 7.5$) ; 4.1 (m, 2H) ; 3.6 (s, 3H) ; 3.3 (s, 3H) ; 3.2 (m, 4H) ; 2.8 to 2.5 (m, 6H) ; 2.4 (m, 2H) ; 1.7 (m, 2H) ; 1.65 to 1.2 (ms, 12H) ; 1.3 to 1.0 (ms, 2H)

Preparations I, J and K:

[0195] Starting from 4-[2-(4-{3-[methoxy(methyl)carbamoyl]phenyl})piperazin-1-yl)ethyl]-piperidine-1-carboxylic acid *tert*-butyl ester and using the procedure described in preparation F, step 3, the following compounds are obtained:

Preparation I: 4-[2-[4-(3-acetylphenyl)piperazin-1-yl]ethyl]piperidine-1-carboxylic acid *tert*-butyl ester

[0196]



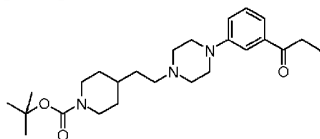
[0197] A solution of methylmagnesium chloride is used.

Yield : 88%

^1H NMR: 7.5 (s, 1H) ; 7.4 (d, 1H, J = 7.5) ; 7.35 (t, 1H, J = 7.5) ; 7.15 (d, 1H, J = 7.5) ; 4.1 (m, 2H) ; 3.3 (m, 4H) ; 1.7 (m, 2H) ; 1.65 to 1.55 (ms, 7H) ; 2.45 (m, 2H) ; 1.7 (m, 2H) ; 1.6 to 1.35 (ms, 12H) ; 1.25 to 1.0 (ms, 2H)

Preparation J: 4-{2-[4-(3-propanoylphenyl)piperazin-1-yl]ethyl}piperidine-1-carboxylic acid *tert*-butyl ester

[0198]



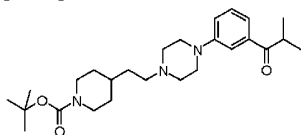
[0199] A solution of ethylmagnesium bromide is used.

Yield : 80%

^1H NMR: 7.55 (s, 1H) ; 7.4 (d, 1H, J = 7.5) ; 7.3 (t, 1H, J = 7.5) ; 7.1 (d, 1H, J = 7.5) ; 4.1 (m, 2H) ; 3.3 (m, 4H) ; 3.0 (q, 2H, J = 7.5) ; 3.7 (m, 2H) ; 2.6 (m, 4H) ; 2.45 (m, 2H) ; 1.65 (m, 2H) ; 1.6 to 1.35 (ms, 12H) ; 1.3 to 1.0 (ms, 5H)

Preparation K: 4-{2-[4-(3-isobutanoylphenyl)piperazin-1-yl]ethyl}piperidine-1-carboxylic acid *tert*-butyl ester

[0200]



[0201] A solution of isopropylmagnesium bromide is used.

Yield : 60%

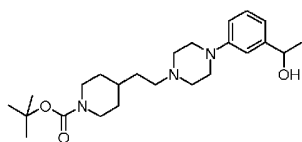
^1H NMR: 7.5 (s, 1H) ; 7.5 to 7.25 (ms, 2H) ; 7.1 (d, 1H, J = 7.5) ; 4.1 (m, 2H) ; 3.55 (m, 1H) ; 3.3 (m, 4H) ; 2.7 (m, 2H) ; 2.6 (m, 4H) ; 2.45 (m, 2H) ; 1.7 (m, 2H) ; 1.6 to 1.35 (ms, 12H) ; 1.3 to 1.0 (ms, 8H)

Preparations L, M and N:

[0202] Starting from preparations I, J and K and using the reduction procedure described in preparation C, the following compounds are obtained:

Preparation L: 4-{2-[4-[3-(1-hydroxyethyl)phenyl]piperazin-1-yl]ethyl}piperidine-1-carboxylic acid *tert*-butyl ester

[0203]

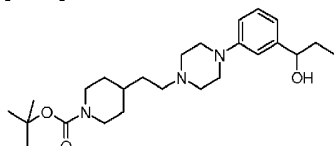


Yield : quantitative

$^1\text{H NMR}$: 7.3 (t, 1H, $J = 7.5$) ; 6.95 (s, 1H) ; 6.9 to 6.8 (ms, 2H) ; 4.85 (q, 1H, $J = 6.5$) ; 4.1 (m, 2H) ; 3.25 (m, 4H) ; 2.7 (m, 2H) ; 2.6 (m, 4H) ; 2.55 (m, 2H) ; 1.85 (broad s, 1H) ; 1.7 (m, 2H) ; 1.55 to 1.4 (ms, 15H) ; 1.25 to 1.0 (ms, 2H)

Preparation M: 4-(2-{4-[3-(1-hydroxypropyl)phenyl]piperazin-1-yl}ethyl)piperidine-1-carboxylic acid *tert*-butyl ester

[0204]

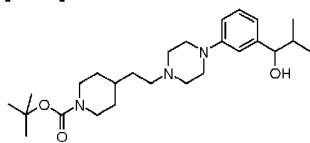


Yield : quantitative

$^1\text{H NMR}$: 7.25 (t, 1H, $J = 7.5$) ; 6.9 (s, 1H) ; 6.9 to 6.75 (ms, 2H) ; 4.55 (t, 1H, $J = 7.5$) ; 4.1 (m, 2H) ; 3.2 (m, 4H) ; 1.7 (m, 2H) ; 2.6 (m, 2H) ; 2.45 (m, 4H) ; 1.95 to 1.6 (ms, 5H) ; 1.6 to 1.4 (ms, 12H) ; 1.3 to 1.05 (ms, 2H) ; 0.9 (t, 3H, $J = 7.5$)

Preparation N: 4-(2-{4-[3-(1-hydroxy-2-methylpropyl)phenyl]piperazin-1-yl}ethyl)piperidine-1-carboxylic acid *tert*-butyl ester

[0205]

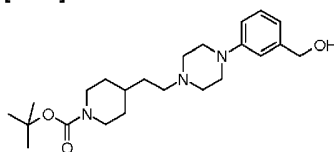


Yield : 78%

$^1\text{H NMR}$: 7.25 (t, 1H, $J = 7.5$) ; 6.9 (s, 1H) ; 6.85 (d, 1H, $J = 7.5$) ; 6.8 (d, 1H, $J = 7.5$) ; 4.3 (d, 1H) ; 4.2 (m, 2H) ; 3.25 (m, 4H) ; 1.7 (m, 2H) ; 2.6 (m, 4H) ; 2.45 (m, 2H) ; 1.95 (m, 1H) ; 1.85 (broad s, 1H) ; 1.7 (m, 2H) ; 1.65 to 1.35 (ms, 12H) ; 1.3 to 1.05 (ms, 2H) ; 1.0 (d, 3H, $J = 7.5$) ; 0.8 (d, 3H, $J = 7.5$)

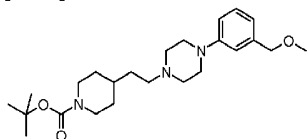
Preparation O: 4-(2-{4-[3-(1-hydroxymethylphenyl)phenyl]piperazin-1-yl}ethyl)piperidine-1-carboxylic acid *tert*-butyl ester

[0206]



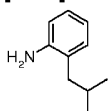
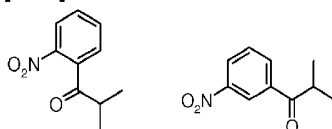
[0207] A solution of 1.5 g (3.59 mmol) of 4-{2-[4-(3-carboxyphenyl)piperazin-1-yl]ethyl}piperidine-1-carboxylic acid *tert*-butyl ester in 20 mL of dry tetrahydrofuran is cooled to -10°C under argon. An addition of 11 mL of a 1 M solution of boranetetrahydrofuran complex in tetrahydrofuran is performed at -10°C . Stirring is maintained overnight at room temperature. The mixture is cooled to 0°C and 12 mL of 1 N aqueous sodium hydroxide solution are added. The product is extracted with ethyl acetate, washed with water, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue is stirred with diisopropyl ether, filtered and dried under reduced pressure to give 1.0 g (69%) of 4-{2-[4-(3-hydroxymethylphenyl)piperazin-1-yl]ethyl}piperidine-1-carboxylic acid *tert*-butyl ester.

$^1\text{H NMR}$: 7.25 (m, 1H) ; 6.95 (s, 1H) ; 6.9 to 6.75 (ms, 2H) ; 4.7 (s, 2H) ; 4.1 (m, 2H) ; 3.6 (m, 2H) ; 3.4 to 3.1 (ms, 4H) ; 3.0 to 2.8 (ms, 4H) ; 2.7 (m, 2H) ; 1.85 (m, 2H) ; 1.75 to 1.55 (ms, 3H) ; 1.55 to 1.3 (ms, 10H) ; 1.2 (m, 2H)

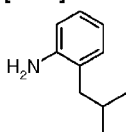
Preparation P: 4-{2-[4-(3-methoxymethylphenyl)piperazin-1-yl]ethyl}piperidine-1-carboxylic acid *tert*-butyl ester**[0208]**

[0209] A solution of 0.4 g (1 mmol) of 4-{2-[4-(3-hydroxymethylphenyl)piperazin-1-yl]ethyl}piperidine-1-carboxylic acid *tert*-butyl ester in 10 mL of dry dimethyl sulfoxide is cooled at a temperature close to 5°C and 40 mg (1 mmol) of sodium hydride (60% suspension) is added. The mixture is stirred for 30 minutes at room temperature then 140 mg (1 mmol) of iodomethane are added and stirring is maintained overnight at room temperature. The mixture is concentrated under reduced pressure. The residue is dissolved in ethyl acetate, washed with water, dried over magnesium sulfate, filtered and concentrated under reduced pressure to give 0.3 g (73%) of crude 4-{2-[4-(3-methoxymethylphenyl)piperazin-1-yl]ethyl}piperidine-1-carboxylic acid *tert*-butyl ester which is used without purification in the next step.

TLC (eluant dichloromethane/methanol/ammonia solution 90/10/1): Rf: 0.6

Preparation Q: 2-isobutylaniline**[0210]****Step 1: 2-methyl-1-(2-nitrophenyl)propan-1-one and 2-methyl-1-(3-nitrophenyl)propan-1-one****[0211]**

[0212] To a cooled solution of 14.8 g (100 mmol) of 2-methyl-1-phenylpropan-1-one in 2 mL of glacial acetic acid are added over a period of one hour, 90 g of fuming nitric acid. The mixture is stirred at 5°C for 90 minutes then poured on crushed ice. The product is extracted 3 times with diethyl ether. The organic phases are combined, washed with an aqueous saturated sodium hydrogen carbonate solution, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The oily residue (20 g) is purified over 350 g of silica gel (eluant heptane/ethyl acetate 4/1) to give a first crop of 7.1 g containing mainly 2-methyl-1-(2-nitrophenyl)propan-1-one and a second crop of 10.2 g containing mainly 2-methyl-1-(3-nitrophenyl)propan-1-one. These two fractions were used without further purification in the next step.

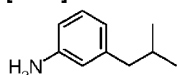
Step 2: 2-isobutylaniline**[0213]**

[0214] To a cooled solution of 5.7 g (29.5 mmol) of 2-methyl-1-(2-nitrophenyl)propan-1-one in 35 mL of ethanol and 7 mL of concentrated hydrochloric acid is added under inert atmosphere, 0.7 g of 10% palladium on activated carbon. The mixture is hydrogenated at 50°C under 4 bar for 2 hours. The suspension is filtered over celite and the filtrate is concentrated under reduced pressure. The residue is dissolved in water, alcalinized to pH 9 with a concentrated solution of sodium hydroxide and extracted 3 times with ethyl acetate. The organic phases are combined, washed with water then with brine, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The oily yellow residue (5 g) is purified over 150 g of silica gel (eluant heptane/ethyl acetate 2/1) to give 1.2 g (27%) of 2-isobutylaniline as an oil.

$^1\text{H NMR}$: 7.1 to 6.95 (ms, 2H) ; 6.8 to 6.65 (ms, 2H) ; 3.6 (broad s, 2H) ; 2.4 (d, 2H, $J = 7.5$) ; 1.95 (m, 1 H, $J = 7.5$) ; 1.0 (d, 6H, $J = 7.5$)

Preparation R: 3-isobutylaniline

[0215]

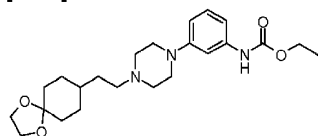


[0216] The 3-isobutylaniline is prepared by catalytic hydrogenation of 2-methyl-1-(3-nitrophenyl)propan-1-one using the procedure described for preparation O to give the title compound in 46% yield.

$^1\text{H NMR}$: 7.05 (t, 1 H, $J = 7.5$) ; 6.65 to 6.55 (m, 2H) ; 6.5 (s, 1 H) ; 3.6 (broad s, 2H) ; 2.4 (d, 2H, $J = 7.5$) ; 1.85 (m, 1 H, $J = 7.5$) ; 0.9 (d, 6H, $J = 7.5$)

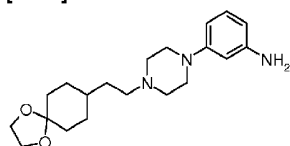
Preparation S: (3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}phenyl)carbamic acid ethyl ester

[0217]



Step 1 : 3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}aniline

[0218]

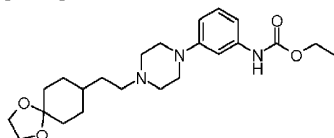


[0219] To a cooled solution of 2.6 g (7.1 mmol) of 1-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]-4-(3-nitrophenyl)piperazine in 50 mL of methanol are added under inert atmosphere, 0.5 g of 10% palladium on activated carbon. The mixture is hydrogenated at 40°C under 4 bar for 17 hours. The suspension is filtered over celite and the filtrate is concentrated under reduced pressure to give 2.3 g (97%) of 3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}aniline.

$^1\text{H NMR}$: 7.1 (t, 1H, $J = 7.5$) ; 6.35 (d, 1H, $J = 7.5$) ; 6.3 (s, 1H) ; 6.2 (d, 1H, $J = 7.5$) ; 3.95 (s, 4H) ; 3.2 (m, 4H) ; 3.6 (broad s, 2H) ; 2.6 (m, 4H) ; 2.4 (m, 2H) ; 1.75 (m, 2H) ; 1.65 to 1.4 (ms, 4H) ; 1.4 to 1.2 (ms, 3H)

Step 2 : (3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}phenyl)carbamic acid ethyl ester

[0220]

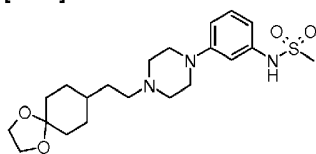


[0221] To a cooled solution of 1 g (3 mmol) of 3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}aniline in 30 mL of dichloromethane and 0.3 g (3 mmol) of triethylamine, is slowly added 0.32 g (3 mmol) of ethyl chloroformate. The mixture is stirred overnight at room temperature then concentrated under reduced pressure. The product is dissolved in ethyl acetate, washed twice with water, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The oily residue is purified over 10 g of silica gel (eluant dichloromethane/methanol 95/5) to give 0.35 g (29%) of (3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}phenyl)carbamate ethyl ester.

¹H NMR: 7.25 to 7.1 (ms, 2H) ; 6.7 (d, 1 H, J = 7.5) ; 6.6 (d, 1 H, J = 7.5) ; 6.5 (s, 1 H) ; 4.2 (q, 2H, J = 7.5) ; 3.95 (s, 4H) ; 3.2 (m, 4H) ; 2.6 (m, 4H) ; 2.45 (m, 2H) ; 1.85 to 1.4 (ms, 8H) ; 1.4 to 1.15 (ms, 6H)

Preparation T: *N*-(3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}phenyl)methanesulfonamide

[0222]

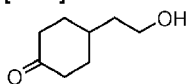


[0223] The *N*-(3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}phenyl)methane-sulfonamide is prepared from 3-{4-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]piperazin-1-yl}aniline and methanesulfonyl chloride using the procedure described for preparation S, step 2 giving the title compound in 89% yield.

¹H NMR: 7.2 (t, 1 H, J = 7.5) ; 8.3 (broad s, 1H) ; 7.05 (s, 1H) ; 6.95 (d, 1 H, J = 7.5) ; 6.65 (d, 1 H, J = 7.5) ; 3.95 (s, 4H) ; 3.6 (m, 4H) ; 3.15 (m, 4H) ; 3.0 (s, 3H) ; 1.9 to 1.65 (ms, 6H) ; 1.6 to 1.2 (ms, 7H)

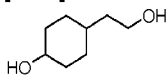
Preparation U: 4-(2-hydroxyethyl)cyclohexanone

[0224]



Step 1: 4-(2-hydroxyethyl)cyclohexanol

[0225]



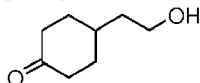
[0226] In a 1L reactor are successively introduced : 50 g (362 mmol) of 4-(2-hydroxyethyl)phenol, 5 g (13,6 mmol) of sodium tetraborate decahydrate, 500 mL of isopropanol, 5 g of palladium (10% on charcoal washed with isopropanol). The vessel is closed, purged three times with nitrogen and three times with hydrogen. The mixture is stirred for 22 hours under 10 bar pressure of hydrogen at 80°C, cooled back to room temperature, filtered over a celite pad and rinsed with isopropanol. Filtrate is concentrated under reduced pressure, toluene (100 mL) is added and evaporated under reduced pressure. This last procedure being repetited to remove trace amount of isopropanol and gives 52 g (99% yield) of 4-(2-hydroxyethyl)cyclohexanol as a clear

viscous oil.

TLC (ethyl acetate/heptane 75/25): $R_f = 0.2$

Step 2: 4-(2-hydroxyethyl)cyclohexanone

[0227]

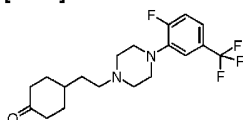


[0228] To a solution of 10 g (69 mmol) of 4-(2-hydroxyethyl)cyclohexanol in 50 mL of acetic acid maintained at a temperature between 18 and 21 °C are added over 35 min 35.9 mL (79 mmol) of an aqueous sodium hypochlorite solution. The mixture is further stirred for 45 min, TLC analysis indicating disappearance of starting material. Isopropanol (0.8 mL) is added, followed 10 min later by water (75 mL) and dichloromethane (100 mL). The two phases are separated by decantation and the aqueous phase is extracted with dichloromethane (50 mL). Combined organic phases are washed with an aqueous 3N sodium hydroxide solution (70 mL). This alkaline aqueous phase is extracted back with dichloromethane (30 mL). Combined organic phases are dried over magnesium sulfate and concentrated under reduced pressure to give 9.42 g (95%) of the title compound.

TLC (ethyl acetate/heptane 75/25): $R_f = 0.29$

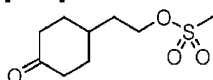
Preparation V: 4-(2-fluoro-5-trifluoromethylphenyl)-1-[2-(4-oxocyclohexyl)ethyl]-piperazine

[0229]



Step 1: 4-(2-hydroxyethyl)cyclohexanone mesylate

[0230]

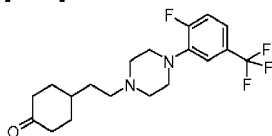


[0231] To a solution of 15.25 g (107.24 mmol) 4-(2-hydroxyethyl)cyclohexanone in 115 mL of dichloromethane cooled at a temperature close to 0°C, is added 18 mL (129.5 mmol) of triethylamine, then 9.25 mL (119.50 mmol) of mesyl chloride. The mixture is stirred for two hours at room temperature. Water (120 mL) is added. The organic phase is separated by decantation, washed with a saturated aqueous solution of sodium hydrogenocarbonate (100 mL), dried over magnesium sulfate and concentrated under reduced pressure to give 28 g of 4-(2-hydroxyethyl)cyclohexanone mesylate used without further purification in the next step.

$^1\text{H NMR}$: 4.30 (t, 2H, $J = 7.5$); 3.05 (s, 3H); 2.40 (m, 4H); 2.20 to 2.05 (m, 2H); 2.00 (m, 1 H); 1.8 (q, 2H, $J = 6.5$); 1.60 to 1.85 (m, 2H)

Step 2: 4-(2-fluoro-5-trifluoromethylphenyl)-1-[2-(4-oxocyclohexyl)ethyl]piperazine

[0232]



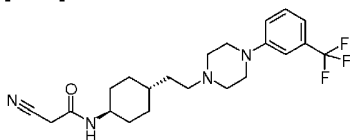
Path IV

[0233] A mixture of 11.6 g (52.66 mmol) of 4-(2-hydroxyethyl)cyclohexanone mesylate, of 13,72 g (55,27 mmol) of 1-(2-fluoro-5-trifluoromethylphenyl)piperazine and 8.37 g (60.65 mmol) of potassium carbonate in 220 mL of acetonitrile is refluxed overnight, then cooled back to room temperature. Water (80 mL) is added. Organics are extracted with ethyl acetate (100 mL). The organic phase is washed with water (20 mL), dried over magnesium sulfate and concentrated under reduced pressure to give a crude product. Purification by column chromatography over 320 g of silica gel (eluant dichloromethane/methanol 98/2 to 96/4) yields 15.86 g of 4-(2-fluoro-5-trifluoromethylphenyl)-1-[2-(4-oxocyclohexyl)ethyl]piperazine melting at 75-76°C.

¹H NMR: 7.30 to 7.00 (m, 3H) ; 3.20 (m, 4H) ; 2.65 (m, 4H) ; 2.50 (t, 2H, J = 7.5) ; 2.40 (m, 4H) ; 2.10 (m, 2H) ; 1.80 (m, 1 H) ; 1.70 to 1.35 (m, 4H)

Example 1: 2-cyano-N-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide (trans isomer)

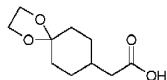
[0234]



Path I

Step a: (1,4-dioxaspiro[4.5]dec-8-yl)acetic acid

[0235]



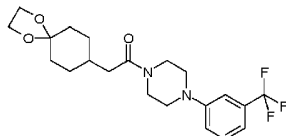
[0236] To a solution of 4 g (17.5 mmol) of (1,4-dioxaspiro[4.5]dec-yl)acetic acid ethyl ester (Tetrahedron, 51, 37, 10259-10280, (1995)) in 35 mL of ethanol are added 22 mL (22 mmol) of an aqueous N sodium hydroxide solution. The mixture is stirred overnight at room temperature.

[0237] After concentration, the residue is taken off in cooled water, neutralized with 22 mL of an aqueous N hydrochloric acid solution and extracted 4 times with diethyl ether. The organic phases are combined, dried over magnesium sulfate, filtered and concentrated under reduced pressure to give 3.0 g (85%) of (1,4-dioxaspiro[4.5]dec-8-yl)acetic acid as an oil that crystallizes upon standing.

¹H NMR: 3.95 (s, 4H) ; 2.3 (d, 2H, J = 7.5) ; 2.0 to 1.7 (ms, 5H) ; 1.6 (m, 2H) ; 1.5 to 1.2 (ms, 2H)

Step b: 2-(1,4-dioxaspiro[4.5]dec-8-yl)-1-[4-(3-trifluoromethylphenyl)-piperazin-1-yl]ethanone

[0238]



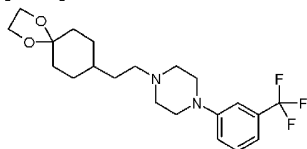
[0239] To a solution of 1.5 g (7.5 mmol) of (1,4-dioxaspiro[4.5]dec-8-yl)acetic acid in 50 mL of dichloromethane stabilized on amylene are successively added at room temperature, 1.0 g (7.5 mmol) of 1-hydroxybenzotriazole and 1.43 g (7.5 mmol) of 3-ethyl-1-(3-dimethylaminopropyl)carbodiimide hydrochloride. The mixture is stirred for 10 minutes then 2.0 g (7.5 mmol) of 1-(3-trifluoromethylphenyl)piperazine hydrochloride and 2.3 mL (16.5 mmol) of triethylamine are added. The mixture is stirred overnight at room temperature.

[0240] After concentration under reduced pressure, the residue is dissolved in ethyl acetate and washed with water. The organic phase is dried over magnesium sulfate, filtered and concentrated under reduced pressure. The solid (3.6 g) is purified by chromatography over 150 g of silica gel (eluant dichloromethane/methanol 97.5/2.5) to give 2.5 g (81%) of 2-(1,4-dioxaspiro[4.5]dec-8-yl)-1-[4-(3-trifluoromethylphenyl)-piperazin-1-yl]ethanone as an oil.

¹H NMR : 7.4 (t, 1H, J = 7.5) ; 7.2 to 7.0 (ms, 3H) ; 3.95 (s, 4H) ; 3.8 (m, 2H) ; 2.7 (m, 2H) ; 3.2 (m, 4H) ; 2.4 (d, 2H, J = 7.5) ; 1.95 (m, 1H) ; 1.9 to 1.7 (ms, 4H) ; 1.7 to 1.5 (ms, 2H) ; 1.45 to 1.2 (ms, 2H)

Step c: 1-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]-4-(3-trifluoromethylphenyl)piperazine

[0241]



[0242] In a three necked round bottom flask, 30 mL of diethyl ether are cooled to -10°C. The system is purged with argon and 0.48 g (12.75 mmol) of lithium aluminum hydride is added. The suspension is stirred and a solution of 3.5 g (8.5 mmol) of 2-(1,4-dioxaspiro[4.5]dec-8-yl)-1-[4-(3-trifluoromethylphenyl)-piperazin-1-yl]ethanone in 20 mL of diethyl ether is added so that the internal temperature does not exceed 10°C. The mixture is refluxed for 4 hours then stirred overnight at room temperature.

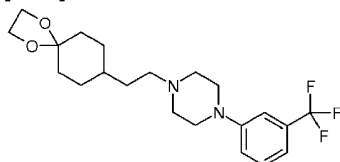
[0243] Hydrolysis is performed at 0°C by slow addition of 0.5 mL of water, 0.5 mL of 15% aqueous sodium hydroxide solution and 1.5 mL of water. The slurry is stirred for 15 minutes at room temperature then magnesium sulfate is added. The mixture is filtered and the salts are washed with a large amount of diethyl ether. The filtrate is concentrated under reduced pressure to give 2.5 g (74%) of 1-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]-4-(3-trifluoromethylphenyl)piperazine as an oil.

¹H NMR: 7.35 (t, 1H, J = 7.5) ; 7.15 (ms, 3H) ; 3.95 (s, 4H) ; 3.25 (m, 4H) ; 2.6 (m, 4H) ; 2.45 (m, 2H) ; 1.85 to 1.65 (ms, 4H) ; 1.65 to 1.45 (ms, 4H) ; 1.45 to 1.2 (ms, 3H)

Path II

Step a: 1-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]-4-(3-trifluoromethylphenyl)piperazine

[0244]



[0245] A mixture of 10 g (37.8 mmol) of 2-(1,4-dioxaspiro[4.5]dec-8-yl)ethylmethanesulfonate (Tetradon, 51, 37, 10259-10280, (1995)), 10.05 g (37.8 mmol) of 1-(3-trifluoromethylphenyl)piperazine hydrochloride, 10.97 g (79.38 mmol) of potassium carbonate and 100 mL of acetonitrile is refluxed overnight.

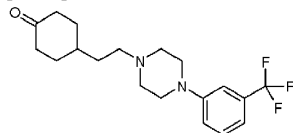
[0246] After concentration of the solvent, the residue is taken off with 100 mL of ethyl acetate and washed with water (twice 50

mL). Organic phase is dried over magnesium sulfate, filtered and concentrated under reduced pressure. The oil thus obtained is purified by chromatography over 250 g of silica gel (eluant heptane/ethyl acetate 50/50) to give 14.4 g (95%) of 1-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]-4-(3-trifluoromethyl-phenyl)piperazine as a colorless oil.

^1H NMR: 7.35 (t, 1 H, $J = 7.5$) ; 7.15 (ms, 3H) ; 3.95 (s, 4H) ; 3.25 (m, 4H) ; 2.6 (m, 4H) ; 2.45 (m, 2H) ; 1.85 to 1.65 (ms, 4H) ; 1.65 to 1.45 (ms, 4H) ; 1.45 to 1.2 (ms, 3H)

Step b: 4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexanone

[0247]



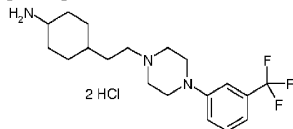
[0248] A solution of 14.4 g (36.1 mmol) of 1-[2-(1,4-dioxaspiro[4.5]dec-8-yl)ethyl]-4-(3-trifluoromethylphenyl)piperazine, 70 mL of methanol, 59 mL of water and 11 mL of a 2N aqueous hydrochloric acid solution is stirred overnight at room temperature.

[0249] An aqueous saturated solution of sodium hydrogen carbonate is added until pH 10. Ethanol is evaporated under reduced pressure and the oily residue is dissolved in 100 mL of ethyl acetate. The organic phase is washed with water (4 times 30 mL), dried over magnesium sulfate, filtered and concentrated to give 11.62 g (91%) of 4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclo-hexanone as a colorless oil.

^1H NMR: 7.35 (t, 1H, $J = 7.5$) ; 7.2 to 7.0 (ms, 3H) ; 3.3 (m, 4H) ; 2.6 (m, 4H) ; 2.5 (t, 2H, $J = 7.5$) ; 2.4 (m, 4H) ; 2.1 (m, 2H) ; 1.8 (m, 1 H) ; 1.7 to 1.35 (ms, 4H)

Step c: 4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclo-hexylamine, dihydrochloride

[0250]



[0251] A mixture of 5.75 g (16.2 mmol) of 4-{2-[4-(3-trifluoro-methylphenyl)piperazin-1-yl]ethyl}cyclohexanone, 12.51 g (162.3 mmol) of ammonium acetate, 200 mL of methanol and 4.07 g (64.8 mmol) sodium cyanoborohydride is refluxed for 3 hours.

[0252] Methanol is concentrated under reduced pressure and the residue is taken off in 20 mL of water. A concentrated aqueous hydrochloric solution is added under cooling until the end of gaseous evolution. The mixture is basified with 35% sodium hydroxide and extracted with dichloromethane (3 times 50 mL). The organic phases are combined, dried over magnesium sulfate, filtered and concentrated under reduced pressure to give an oil that consists in about a 65%/35% mixture (^1H NMR determination) of trans and cis 4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexylamine.

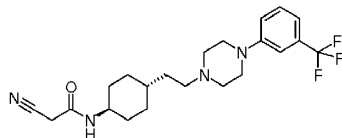
[0253] The isomers are partially separated by dissolution in a hydrochloric acid ethyl acetate solution. After evaporation of the solvent, the solid is mixed with 10 mL of acetonitrile and warmed to 50°C. The suspension is filtered, the solid is washed with acetonitrile (5 mL) and with diethyl ether (15 mL). The hygroscopic solid is dried at 50°C under reduced pressure to give 4.3 g (62%) of about 80%/20% (^1H NMR determination) of trans and cis 4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexylamine, dihydrochloride as a white solid.

Melting point 300-305°C (decomposition)

The ^1H NMR spectra is performed on the free base.

^1H NMR: 7.35 (t, 1 H, $J = 7$) ; 7.15 to 7.0 (ms, 3H) ; 3.25 (m, 4H) ; 3.0 (m, 0,2H equatorial) ; 2.7 to 2.35 (ms, 4,8H) ; 2.0 to 1.35 (ms, 11H) ; 1.35 to 0,9 (ms, 4H)

Path A

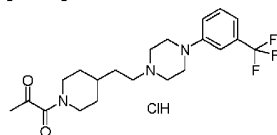
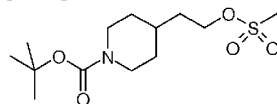
2-cyano-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-acetamide**[0254]**

[0255] To a solution of 43 mg (0.5 mmol) of cyanoacetic acid in 5 mL of dichloromethane stabilized on amylene are successively added 68 mg (0.5 mmol) of 1-hydroxy-benzotriazole, 96 mg (0.5 mmol) of 3-ethyl-1-(3-dimethylaminopropyl)-carbodiimide hydrochloride and 0.21 mL (1.5 mmol) of triethylamine. The mixture is stirred for 15 minutes then 214 mg (0.5 mmol) of the 80% / 20% trans/cis 4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexylamine dihydrochloride is added. The mixture is stirred overnight at room temperature.

[0256] Volatiles are evaporated under reduced pressure, residue is dissolved in ethyl acetate and washed with an aqueous saturated sodium hydrogen carbonate solution, then with water. The organic phase is dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residual solid is recrystallized in a mixture of diisopropyl ether/ethanol 9/1. After filtration, the solid is washed with diisopropyl ether and dried under reduced pressure to give 62 mg (29%) of trans 2-cyano-*N*-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide as a cream colored solid.

Melting point: 185°C

¹H NMR: 7.35 (t, 1 H, J = 7.5) ; 7.15 to 7.0 (ms, 3H) ; 5.85 (d, 1 H, J = 7.5) ; 3.75 (m, 1H) ; 3.35 (s, 2H) ; 3.25 (m, 4H) ; 2.6 (m, 4H) ; 2.45 (m, 2H) ; 2.05 (m, 2H) ; 1.85 (m, 2H) ; 1.45 (m, 2H) ; 1.4 to 1.0 (ms, 5H)

Example 2: 1-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}-piperidin-1-yl)propane-1,2-dione, hydrochloride**[0257]****Path III****Step a: 4-(2-methanesulfonyloxyethyl)piperidine-1-carboxylic acid *tert*-butyl ester****[0258]**

[0259] To a cooled solution of 3 g (13 mmol) of 4-(2-hydroxyethyl)piperidine-1-carboxylic acid *tert*-butyl ester (commercially available) in 20 mL of dichloromethane and 1.45 g (14.5 mmol) of triethylamine is added a solution of 1.5 g (13 mmol) of methanesulfonyl chloride in 4 mL of dichloromethane. The mixture is stirred for 2 hours at room temperature.

[0260] After washing with water, the organic phase is dried over magnesium sulfate, filtered and concentrated to give 4 g (100%)

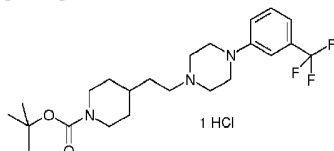
of 4-(2-methanesulfonyloxyethyl)piperidine-1-carboxylic acid *tert*-butyl ester as a white solid.

TLC: 0.53 (heptane/ethyl acetate 1/1)

^1H NMR: 4.3 (t, 2H, $J = 7.5$) ; 4.1 (m, 2H) ; 3.0 (s, 3H) ; 2.7 (m, 2H) ; 1.8 to 1.6 (ms, 5H) ; 1.45 (s, 9H) ; 1.25 to 1.0 (ms, 2H)

Step b: 4-{2[4-(3-trifluoromethylphenyl)piperazin-1-yl]-ethyl}piperidine-1-carboxylic acid *tert*-butyl ester, hydrochloride

[0261]



[0262] A mixture of 1 g (3.25 mmol) of 4-(2-methanesulfonyloxyethyl)-piperidine-1-carboxylic acid *tert*-butyl ester, 0.87 g (3.25 mmol) of 1-(3-trifluoromethylphenyl)piperazine hydrochloride, 0.95 g (6.9 mmol) of potassium carbonate and 20 mL of acetonitrile is refluxed overnight.

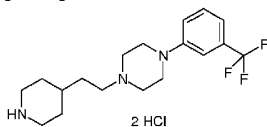
[0263] After concentration of solvent, the residue is taken off with ethyl acetate and water. Organic phase is separated, washed with a 0.5N aqueous solution of hydrochloric acid, dried over magnesium sulfate, filtered and partially concentrated. The solid is filtered, washed with diethyl ether and dried under reduced pressure to give 1.1 g (71%) of 4-{2[4-(3-trifluoromethylphenyl)piperazin-1-yl]-ethyl}piperidine-1-carboxylic acid *tert*-butyl ester, hydrochloride as a white solid.

Melting point 188°C

^1H NMR : 13.1 (broad s, 1H) ; 7.4 (t, 1H, $J = 7.5$) ; 7.25 (d, 1H, $J = 7.5$) ; 7.2 to 7.0 (ms, 2H) ; 4.1 (m, 2H) ; 3.9 to 3.5 (ms, 6H) ; 3.15 to 2.8 (ms, 4H) ; 2.7 (m, 2H) ; 1.95 (m, 2H) ; 1.8 to 1.5 (ms, 3H) ; 1.45 (s, 9H) ; 1.3 (m, 2H)

Step c: 1-(2-piperidin-4-ylethyl)-4-(3-trifluoromethylphenyl)piperazine, dihydrochloride

[0264]



[0265] To a solution of 0.5 g (1.0 mmol) of 4-{2[4-(3-trifluoro-methylphenyl)piperazin-1-yl]ethyl}piperidine-1-carboxylic acid *tert*-butyl ester, hydrochloride in 5 mL of ethyl acetate and 2.5 mL of methanol are added 2.5 mL of a saturated hydrogen chloride solution in diethyl ether. The mixture is stirred for 2 hours at room temperature (precipitation occurs rapidly).

[0266] The solid is filtered, washed with diethyl ether and dried under reduced pressure to give 0.41 g (100%) of 1-(2-piperidin-4-ylethyl)-4-(3-trifluoro-methylphenyl)piperazine, dihydrochloride as a white solid.

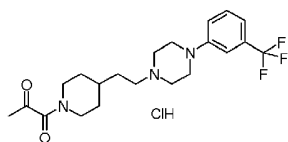
Melting point: 260°C

^1H NMR (DMSO D_6): 11.2 (broad s, 1 H) ; 8.95 (broad s, 1 H) ; 8.8 (broad s, 1H) ; 7.45 (t, 1 H, $J = 7.5$) ; 7.35 (d, 1 H, $J = 7.5$) ; 7.3 (s, 1 H) ; 7.1 (d, 1 H, $J = 7.5$) ; 3.95 (m, 2H) ; 3.6 (m, 2H) ; 3.4 to 2.95 (ms, 8H) ; 2.8 (m, 2H) ; 1.9 to 1.5 (ms, 5H) ; 1.5 to 1.2 (ms, 2H)

Path A

1-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propane-1,2-dione, hydrochloride

[0267]



[0268] 1-(2-Piperidin-4-ylethyl)-4-(3-trifluoromethylphenyl)piperazine, dihydrochloride 150 mg (0.36 mmol) and 38 mg (0.43 mmol) of pyruvic acid are coupled according to the process described in example 1, path A.

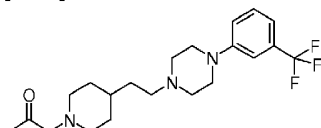
[0269] After work-up, the residue is purified over 5 g of silica gel (eluant dichloromethane/methanol 99/1). The oily product is dissolved in 1 mL of ethyl acetate and acidified by a saturated hydrogen chloride solution in diethyl ether. The solid is filtered, washed with diethyl ether and dried under reduced pressure to give 55 mg (35%) of 1-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propane-1,2-dione, hydrochloride as a white solid.

Melting point: 200°C

¹H NMR (DMSO D₆): 10.8 (broad s, 1 H) ; 7.45 (t, 1 H, J = 7.5) ; 7.3 (d, 1 H, J = 7.5) ; 7.25 (s, 1 H) ; 7.15 (d, 1 H, J = 7.5) ; 4.2 (m, 1 H) ; 3.95 (m, 2H) ; 3.55 (m, 2H) ; 3.3 to 2.95 (ms, 8H) ; 2.75 (m, 1 H) ; 2.3 (s, 3H) ; 1.85 to 1.55 (ms, 5H) ; 1.25 to 0.95 (ms, 2H)

Example 3: 1-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}-piperidin-1-yl)propan-2-one

[0270]



Path B

[0271] A mixture of 0.35 g (0.84 mmol) of 1-(2-piperidin-4-ylethyl)-4-(3-trifluoromethylphenyl)piperazine, dihydrochloride, 0.41 g (2.97 mmol) of potassium carbonate, 10 mL of acetonitrile and 0.1 g (1.08 mmol) of chloroacetone is stirred at room temperature overnight.

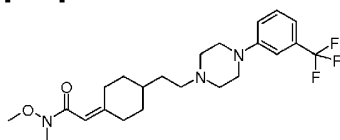
[0272] After concentration of solvent, the residue is partitioned into ethyl acetate and water. Aqueous phase is separated. Organic phase is washed 3 times with water, dried over magnesium sulfate, filtered and concentrated under reduced pressure to give 0.24 g (72%) of 1-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one as a white solid.

Melting point: 82°C

¹H NMR: 7.35 (t, 1H, J = 7.5) ; 7.2 to 7.0 (ms, 3H) ; 3.25 (m, 4H) ; 3.15 (s, 2H) ; 2.85 (m, 2H) ; 2.6 (m, 4H) ; 2.4 (t, 2H, J = 7.5) ; 2.15 (s, 3H) ; 2.05 (m, 2H) ; 1.8 (m, 2H) ; 1.6 to 1.2 (ms, 5H)

Example 4: N-methoxy-N-methyl-2-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexylidene)acetamide

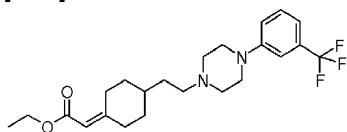
[0273]



Path C

Step a: (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexylidene)acetic acid ethyl ester

[0274]

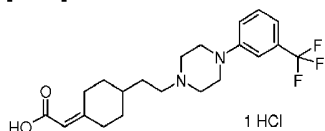


[0275] A mixture of 2.77 g (7.8 mmol) of 4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexanone (example 1, path II, step b) and 3.13 g (9.0 mmol) of (triphenyl- λ^5 -phosphanylidene)acetic acid ethyl ester in 40 mL of toluene is refluxed overnight. After concentration of toluene, the residue is taken off in diethyl ether and the solid is filtered. The filtrate is concentrated and purified over 150 g of silica gel (eluant dichloromethane/heptane 98/2) to give 1.48 g (45%) of (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexylidene)acetic acid ethyl ester as an oil.

$^1\text{H NMR}$: 7.35 (t, 1H) ; 7.2 to 7.0 (m, 3H) ; 5.6 (s, 1H) ; 4.15 (q, 2H, $J = 7.5$) ; 3.75 (m, 1H) ; 3.25 (m, 4H) ; 2.6 (m, 4H) ; 2.45 (t, 2H, $J = 7.5$) ; 2.4 to 1.85 (ms, 5H) ; 1.85 to 1.4 (ms, 4H) ; 1.3 (t, 3H, $J = 7.5$) ; 1.25 to 1.05 (m, 2H)

Step b: (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclo-hexylidene)acetic acid, hydrochloride

[0276]

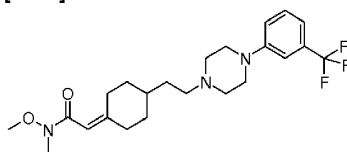


[0277] To a solution of 0.88 g (2.1 mmol) of (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexylidene)acetic acid ethyl ester in 8 mL of methanol are added 2.2 mL of an aqueous N sodium hydroxide solution. Stirring is maintained overnight at room temperature. Methanol is evaporated under reduced pressure and the residue is diluted in 20 mL of water and washed with diethyl ether. The aqueous phase is cooled, acidified to pH 1 with an aqueous 1 N solution of hydrochloric acid. The solid is filtrated, washed with water and dried under reduced pressure to give 0.36 g (44%) of (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexylidene)acetic acid, hydro-chloride as a white solid.

$^1\text{H NMR}$ (DMSO D_6): 11.95 (broad s, 1H) ; 10.7 (broad s, 1H) ; 7.45 (t, 1H, $J = 7.5$) ; 7.3 (d, 1H, $J = 7.5$) ; 7.25 (s, 1H) ; 7.15 (d, 1H, $J = 7.5$) ; 5.5 (s, 1H) ; 3.9 (m, 2H) ; 3.7 to 3.4 (ms, 3H) ; 3.3 to 2.9 (ms, 7H) ; 2.45 to 1.45 (ms, 7H) ; 1.05 (m, 2H)

Step c: *N*-methoxy-*N*-methyl-2-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexylidene)acetamide

[0278]



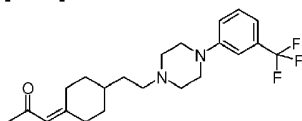
[0279] To a solution of 200 mg (0.46 mmol) of (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexylidene)acetic acid, hydrochloride in 5 mL of dichloromethane stabilized on amylene are successively added 63 mg (0.46 mmol) of 1-hydroxy-benzotriazole, 88 mg (0.46 mmol) of 3-ethyl-1-(3-dimethylaminopropyl)carbodiimide hydrochloride and 140 mg (1.4 mmol) of triethylamine. The mixture is stirred for 15 minutes then 45 mg (0.46 mmol) of *N,O*-dimethylhydroxylamine hydrochloride are added. The mixture is stirred overnight at room temperature, then evaporated under reduced pressure. The residue is dissolved in ethyl acetate and washed twice with water. The organic phase is dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue is purified over 10 g of silica gel (eluant dichloromethane/methanol 98/2) to give 143 mg (71%) of *N*-methoxy-*N*-methyl-2-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexylidene)acetamide as an oil.

$^1\text{H NMR}$: 7.35 (t, 1H, $J = 7.5$) ; 7.15 to 7.0 (ms, 3H) ; 6.05 (s, 1H) ; 3.7 (s, 3H) ; 3.6 (m, 1H) ; 3.25 (m, 4H) ; 3.2 (s, 4H) ; 2.6 (m, 4H)

; 2.45 (t, 2H, J = 7.5) ; 2.4 to 2.1 (ms, 2H) ; 2.1 to 1.85 (ms, 3H) ; 1.6 to 1.4 (m, 2H) ; 1.4 to 1.05 (ms, 2H)

Example 5: 1-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}-cyclohexylidene)propan-2-one

[0280]

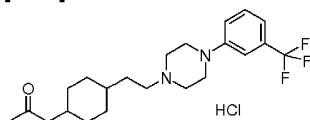


[0281] To a solution of 114 mg (0.25 mmol) of *N*-methoxy-*N*-methyl-2-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}-cyclohexylidene)acetamide in 5 mL of dry tetrahydrofuran cooled to 0°C is added 0.2 mL (0.50 mmol) of a 22% methylmagnesium chloride solution in tetrahydrofuran. The mixture is warmed up to 5°C and stirred for 90 minutes. Hydrolysis is performed by slow addition of 3 mL of water. The product is extracted 3 times with ethyl acetate. The organic phases are combined, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The obtained residue is purified over 5 g of silica gel (eluant dichloromethane/methanol 95/5) to give 43 mg (44%) of 1-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexylidene)propan-2-one as an oil.

¹H NMR: 7.35 (t, 1 H, J = 7.5) ; 7.2 to 7.0 (ms, 3H) ; 6.0 (s, 1 H) ; 3.7 (m, 1 H) ; 3.25 (m, 4H) ; 2.6 (m, 4H) ; 2.45 (m, 4H) ; 2.25 (m, 2H) ; 2.2 (s, 3H) ; 1.95 (m, 3H) ; 1.7 to 1.4 (ms, 1 H) ; 1.35 to 1.0 (ms, 2H)

Example 6: 1-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-propan-2-one, hydrochloride

[0282]



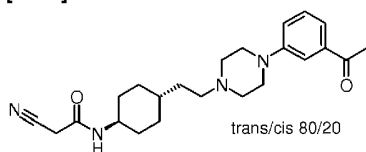
[0283] A solution of 33 mg (0.08 mmol) of 1-(4-{2-[4-(3-trifluoro-methylphenyl)piperazin-1-yl]ethyl}cyclohexylidene)propan-2-one is cooled and purged with argon. After addition of 5 mg of 10% palladium on activated carbon, the mixture is hydrogenated at room temperature and atmospheric pressure overnight. The suspension is filtrated over a bed of celite and the filtrate is concentrated under reduced pressure. The residue is dissolved in acetonitrile, acidified by a saturated hydrochloric acid ethyl acetate solution, filtered and dried under reduced pressure to give 29 mg (85%) of 1-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propan-2-one, hydrochloride as a white solid.

Melting point: 160°C

¹H NMR: 7.35 (t, 1 H, J = 7.5) ; 7.2 to 7.0 (ms, 3H) ; 3.5 (broad s, 1 H) ; 3.25 (m, 4H) ; 2.6 (m, 4H) ; 2.5 to 2.3 (ms, 4H) ; 2.2 (s, 3H) ; 1.9 to 1.65 (ms, 4H) ; 1.65 to 1.15 (ms, 6H) ; 1.0 (m, 2H)

Example 7: *N*-(4-{2-[4-(3-acetylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide trans/cis 80/20

[0284]



[0285] A solution of 44 mg (0.35 mmol) of oxalyl chloride in 1 mL of dichloromethane is purged with argon and cooled to a temperature close to -70°C. A solution of 66 mg (0.8 mmol) of dimethyl sulfoxide in 1 mL of dichloromethane is added. Stirring is maintained at a temperature close to -70°C for 15 minutes and a solution of 120 mg (0.3 mmol) of 2-cyano-*N*-(4-{2-[4-(3-(1-hydroxyethyl)phenyl)piperazin-1-yl]ethyl}-cyclohexyl)acetamide trans/cis 80/20 in 4 mL of dichloromethane is added. After an

additional stirring for 15 minutes at a temperature close to -70°C, 110 mg (1.08 mmol) of triethylamine are added. The mixture is allowed to warm to room temperature then stirred overnight at room temperature. The mixture is poured into water and extracted twice with ethyl acetate. The organic phases are combined, washed with water, then brine, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The oily residue is purified over 5 g silica gel (eluant dichloromethane/methanol 98/2 then 95/5). To give 25 mg (21%) of *N*-(4-{2-[4-(3-acetylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide trans/cis 80/20 as a white solid.

Melting point 160°C

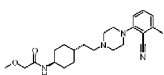
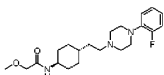
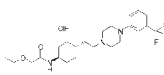
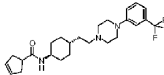
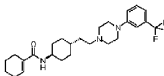
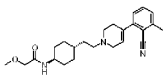
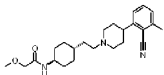
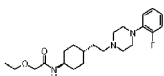
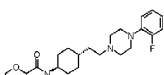
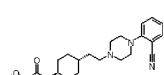
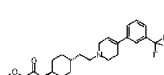
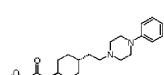
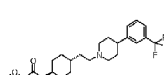
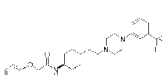
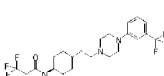
¹H NMR: 7.5 (s, 1 H) ; 7.45 (d, 1 H, J = 7.5) ; 7.35 (t, 1 H, J = 7.5) ; 7.1 (d, 1 H ; J = 7.5) ; 6.15 (broad d, 0.2 H) ; 5.9 (broad d, 0.8H) ; 4.05 (m, 0.2H) ; 3.8 (m, 0.8H) ; 3.4 (s, 0.4H) ; 3.35 (s, 1.6H) ; 3.2 (m, 4H) ; 2.65 (m, 4H) ; 2.6 (s, 3H) ; 2.45 (m, 2H) ; 2.05 (m, 2H) ; 1.85 (m, 2H) ; 1.8 to 1.4 (ms, 4H) ; 1.4 to 1.0 (ms, 3H)

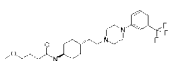
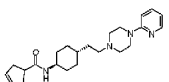
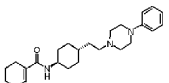
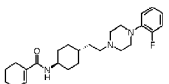
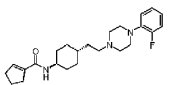
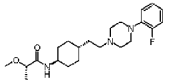
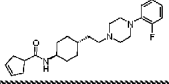
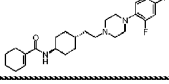
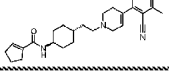
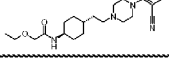
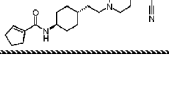
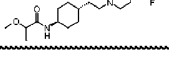
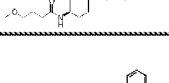
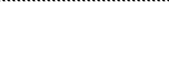
[0286] The following table summarises some further examples and comparative examples and the way they can be obtained.

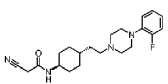
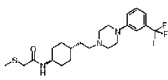
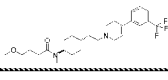
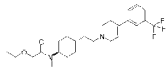
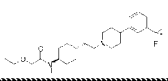
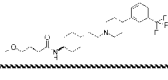
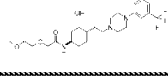
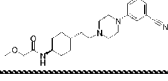
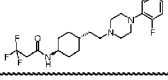
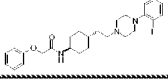
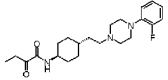
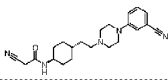
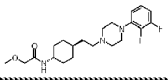
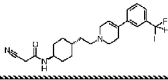
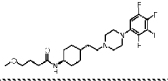
Ex	Structure	Name	M.P. (°C)	Synthetic Path
8		4-{2-[4-(3-Trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidine-1-carboxylic acid tert-butyl ester, hydrochloride	188	IIIB
9		1-(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	250	IIIB
10		(4-{2-[4-(3-Trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)acetic acid <i>tert</i> -butyl ester, dihydrochloride	245	IIIB
11		1-Phenyl-2-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)ethanone, dihydrochloride	260	IIIB
12		1-(4-{2-[4-(3-Trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butane-1,2-dione, hydrochloride	148	IIIA
13		3,3-Dimethyl-1-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-one		IIIB
14		<i>N</i> -[2-Oxo-2-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)ethyl]acetamide	133	IIIA
15		3-Oxo-3-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propanenitrile, hydrochloride	184	IIIA
16		2-Methoxy-1-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)ethanone, hydrochloride	150	IIIA
17		2-Ethoxy-1-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)ethanone, hydrochloride	145	IIIA
18		5-Oxo-5-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)pentanenitrile, hydrochloride	95	IIIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
19		3-(4-{2-[1-(2-Oxo-propyl)piperidin-4-yl]ethyl}piperazin-1-yl)-5-trifluoromethylbenzonitrile, dihydrochloride	280	IIIB
20		1-(4-{2-[4-(2-Methoxy-phenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	260	IIIB
21		1-(4-{2-[4-(2,3-Dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	87	IIIB
22		2-Methyl-6-(4-{2-[1-(2-oxopropyl)piperidin-4-yl]ethyl}piperazin-1-yl)benzonitrile, dihydrochloride	215	IIIB
23		2-(4-{2-[4-(3-Trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)acetamide, dihydrochloride	120	IIIB
24		1-(4-{2-[4-(2-Chlorophenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	265	IIIB
25		3-(4-{2-[1-(2-Oxopropyl)piperidin-4-yl]ethyl}piperazin-1-yl)benzonitrile, dihydrochloride	250	IIIB
26		(4-{2-[4-(3-Trifluoromethyl-phenyl)piperazin-1-yl]ethyl}piperidin-1-yl)acetic acid ethyl ester, dihydrochloride	240	IIIB
27		1-(4-{2-[4-(3,5-Difluorophenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	260	IIIB
28		1-(4-{2-[4-(2,3-Dimethylphenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	290	IIIB
29		1-(4-{2-[4-(3-Chlorophenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	114	IIIB
30		1-(4-{2-[4-(o-Tolyl)piperazin-1-yl]-thyl}piperidin-1-yl)propan-2-one, dihydrochloride	289	IIIB
31		1-(4-{2-[4-(2-Chloro-5-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	283	IIIB
32		1-(4-{2-[4-(5-Fluoro-2-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	281	IIIB
33		1-(3,4-Difluorophenyl)-2-(4-{2-[4-(3-trifluoromethylphenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)ethanone	220	IIIB

Ex	Structure	Name	M.P. (°C)	Synthetic Path
34		1-(4-{2-[4-(3,5-Bistrifluoromethyl-phenyl)piperazin-1-yl]ethyl}-piperidin-1-yl)propan-2-one	260	IIIB
35		1-(4-{2-[4-(2,3-Difluorophenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	270	IIIB
36		1-(4-{2-[4-(Naphthalen-1-yl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	338	IIIB
37		(4-{2-[4-(3-Trifluoromethyl-phenyl)piperazin-1-yl]ethyl}cyclohexyl)carbamic acid benzyl ester		IIA
38		2,2,2-Trifluoro-N-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	134	IIA
39		(4-{2-[4-(3-Trifluoromethyl-phenyl)piperazin-1-yl]ethyl}cyclohexyl)carbamic acid methyl ester	135	IIA
40		Tetrahydrofuran-2-carboxylic acid (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amide	135	IIA
41		2-Methoxy-N-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	123	IIA
42		2-Methoxy-N-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide , hydrochloride	217	IIA
43		1-(4-{2-[4-(2-Isopropylphenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	260	IIIB
44		2,2-Difluoro-N-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	128	IIA
45		Cyclopent-1-enecarboxylic acid (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amide	175	IIA
46		2-Hydroxy-N-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide , hydrochloride		IIA
47		3-Methoxy-N-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	125	IIA
48		N-(4-{2-[4-(2,4-Difluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	154	IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
49		<i>N</i> -(4-{2-[4-(2-Cyano-3-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	136	IIA
50		<i>N</i> -(4-{2-[4-(2-Fluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	143-144	IIA
51		2-Ethoxy- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, hydrochloride	184	IIA
52		Cyclopent-3-enecarboxylic acid (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-amide	183	IIA
53		Cyclohex-1-enecarboxylic acid (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-amide	175	IIA
54		<i>N</i> -(4-{2-[4-(2-Cyano-3-methylphenyl)-3,6-dihydro-2H-pyridin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	158	IIA
55		<i>N</i> -(4-{2-[4-(2-Cyano-3-methylphenyl)piperidin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	141	IIA
56		2-Ethoxy- <i>N</i> -(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	117-118	IIA
57		Tetrahydrofuran-2-carboxylic acid (4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)amide	119-120	IIA
58		<i>N</i> -(4-{2-[4-(2-Cyanophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	113	IIA
59		2-Methoxy- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)-3,6-dihydro-2H-pyridin-1-yl]ethyl}cyclohexyl)acetamide trans/cis 95/5		IIA
60		2-Methoxy- <i>N</i> -(4-{2-[4-(phenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	136	IIA
61		2-Methoxy- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperidin-1-yl]ethyl}cyclohexyl)acetamide trans/cis 95/5	82	IIA
62		2-Phenoxy- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide		IIA
63		3,3,3-Trifluoro- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	156	IIA

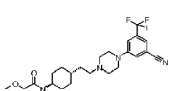
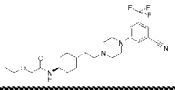
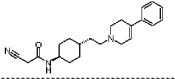
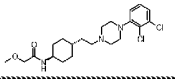
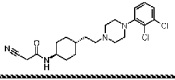
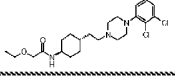
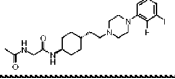
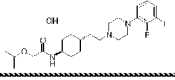
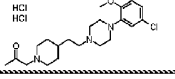
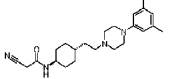
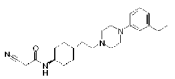
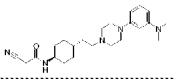
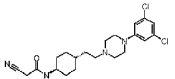
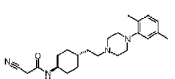
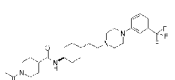
Ex	Structure	Name	M.P. (°C)	Synthetic Path
64		4-Methoxy- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	149	IIA
65		Cyclopent-3-enecarboxylic acid {4-[2-(4-pyridin-2-yl)piperazin-1-yl]ethyl}cyclohexyl}amide	208	IIA
66		Cyclohex-1-enecarboxylic acid {4-[2-(4-phenylpiperazin-1-yl)ethyl]cyclohexyl}amide trans/cis 90/10	193	IIA
67		Cyclohex-1-enecarboxylic acid (4-{2-[4-(2-fluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-amide	209	IIA
68		Cyclopent-1-enecarboxylic acid (4-{2-[4-(2-fluorophenyl)-piperazin-1-yl]ethyl}-cyclohexyl)amide	210- 211	IIA
69		<i>N</i> -(4-{2-[4-(2-Fluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-2-methoxypropanamide	159	IIA
70		Cyclopent-3-enecarboxylic acid (4-{2-[4-(2-fluorophenyl)-piperazin-1-yl]ethyl}-cyclohexyl)amide trans/cis 95/5	204	IIA
71		Cyclohex-1-enecarboxylic acid (4-{2-[4-(2,4-difluorophenyl)-piperazin-1-yl]ethyl}-cyclohexyl)amide	203	IIA
72		Cyclopent-1-enecarboxylic acid (4-{2-[4-(2-cyano-3-methylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-amide	183	IIA
73		<i>N</i> -(4-{2-[4-(2-Cyanophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	96	IIA
74		Cyclopent-1-enecarboxylic acid (4-{2-[4-(2-cyanophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-amide	167	IIA
75		<i>N</i> -(4-{2-[4-(2-Fluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-2-methoxypropanamide	162	IIA
76		<i>N</i> -(4-{2-[4-(2-Fluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	175	IIA
77		2-Methoxy-2-methyl- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)-piperazin-1-yl]ethyl}cyclohexyl)-propanamide	105	IIA
78		<i>N</i> -(4-{2-[4-(3-Cyanophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide trans/cis 75/25	90	IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
79		2-Cyano- <i>N</i> -(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	179-180	IIA
80		2-Methylsulfanyl- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	128	IIA
81		4-Methoxy- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)butanamide	145	IIA
82		2-Ethoxy- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)acetamide trans/cis 95/5	75	IIA
83		2-Ethoxy- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperidin-1-yl]ethyl}cyclohexyl)acetamide	84	IIA
84		4-Methoxy- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperidin-1-yl]ethyl}cyclohexyl)butanamide	134	IIA
85		2-(2-Methoxyethoxy)- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-acetamide, hydrochloride trans/cis 75/25		IIA
86		<i>N</i> -(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	138	IIA
87		3,3,3-Trifluoro- <i>N</i> -(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	207	IIA
88		<i>N</i> -(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-phenoxyacetamide	172	IIA
89		<i>N</i> -(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-oxobutanamide	156	IIA
90		2-Cyano- <i>N</i> -(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide trans/cis 75/25	188	IIA
91		<i>N</i> -(4-{2-[4-(2,3-Difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	155	IIA
92		2-Cyano- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)acetamide	149	IIA
93		4-Methoxy- <i>N</i> -(4-{2-[4-(2,3,4,5-tetrafluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butyramide	201	IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
94		2-Oxo- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide , hydrochloride trans/cis 70/30		IIA
95		2-Oxo- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide , hydrochloride trans/cis 70/30		IIA
96		2-Dimethylamino- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide		IIA
97		<i>N</i> -(4-{2-[4-(2-Fluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-2-isopropoxyacetamide	96	IIA
98		4-Cyano- <i>N</i> -(4-{2-[4-(2,3,4,5-tetrafluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butyramide	180	IIA
99		4-Methoxy- <i>N</i> -{4-[2-(4-phenylpiperazin-1-yl)ethyl]cyclohexyl}butanamide	172	IIA
100		2-Isopropoxy- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide trans/cis 80/20		IIA
101		<i>N</i> -(4-{2-[4-(2-Cyano-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-isopropoxyacetamide	144	IIA
102		<i>N</i> -(4-{2-[4-(2-Cyano-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	173	IIA
103		2-Cyano- <i>N</i> -(4-{2-[4-(2-cyano-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	222	IIA
104		2-Cyano- <i>N</i> -(4-{2-[4-(2-phenyl-piperazin-1-yl)ethyl]cyclohexyl}-acetamide, hydrochloride	243	IIA
105		2-Acetylamino- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	187	IIA
106		2-Chloro-6-fluoro-3-(4-{2-[1-(2-oxopropyl)piperidin-4-yl]ethyl}piperazin-1-yl)benzonitrile	291	IIIB
107		<i>N</i> -(4-{2-[4-(3,5-Bistrifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	196	IIA
108		<i>N</i> -(4-{2-[4-(3,5-Bistrifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	135	IIA

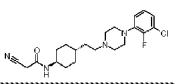
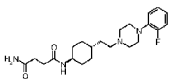
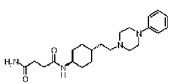
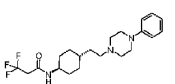
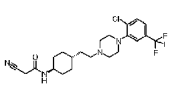
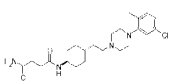
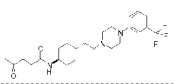
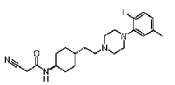
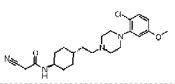
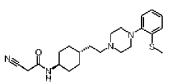
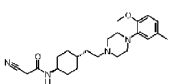
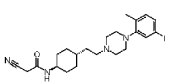
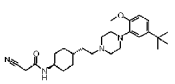
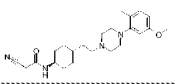
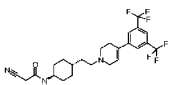
Ex	Structure	Name	M.P. (°C)	Synthetic Path
109		3-Oxo- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide trans/cis 70/30		IIA
110		<i>N</i> -(4-{2-[6-Cyano-3,4-dihydro-1 <i>H</i> -isoquinolin-2-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide	215	IIA
111		2-Cyano- <i>N</i> -(4-{2-[4-(2,6-di- <i>tert</i> -butylpyrimidin-4-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide trans/cis 65/35	145	IIA
112		<i>N</i> -(4-{2-[4-(2,3-Difluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	140	IIA
113		2-Cyano- <i>N</i> -(4-{2-[4-(2,3-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	190	IIA
114		2-Cyano- <i>N</i> -(4-{2-[4-(2-cyano-3-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	221	IIA
115		<i>N</i> -(4-{2-[4-(2-Cyano-3-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide	207	IIA
116		2-Cyano- <i>N</i> -(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-1-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	175	IIA
117		2-Ethoxy- <i>N</i> -(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-1-yl)piperazin-1-yl]ethyl}-cyclohexyl)acetamide	91	IIA
118		<i>N</i> -(4-{2-[4-(3,5-Bistrifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	164	IIA
119		<i>N</i> -(4-{2-[4-(2-Cyano-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	172	IIA
120		2-Cyano- <i>N</i> -(4-{2-[4-pyridin-4-ylpiperazin-1-yl]ethyl}cyclohexyl)acetamide trans/cis 65/35		IIA
121		<i>N</i> -(4-{2-[4-(2,6-Di- <i>tert</i> -butylpyrimidin-4-yl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	104	IIA
122		<i>N</i> -(4-{2-[4-(2,6-Di- <i>tert</i> -butylpyrimidin-4-yl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	130	IIA
123		2-Ethoxy- <i>N</i> -(4-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	210-214	IIA

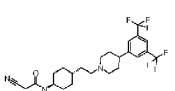
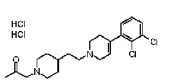
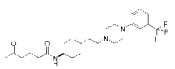
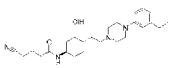
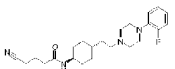
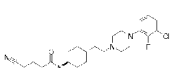
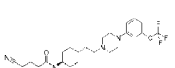
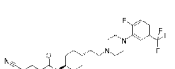
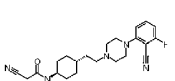
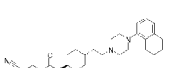
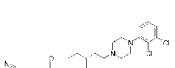
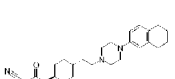
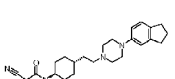
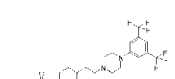
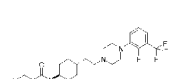
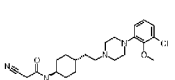
Ex	Structure	Name	M.P. (°C)	Synthetic Path
124		2-Cyano- <i>N</i> -(4-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	187	IIA
125		2-Methoxy- <i>N</i> -(4-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	125-126	IIA
126		2-Cyano- <i>N</i> -(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, hydrochloride	153	IIA
127		2-Cyano- <i>N</i> -(4-{2-[4-(2-fluorophenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-acetamide trans/cis 90/10	156	IIA
128		2-Acetylamino- <i>N</i> -(4-{2-[4-phenylpiperazin-1-yl]ethyl}cyclohexyl)acetamide	227	IIA
129		<i>N</i> -(4-{2-[4-(2-Chlorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	100	IIA
130		2-Methoxy- <i>N</i> -(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-1-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	120	IIA
131		<i>N</i> -(4-{2-[4-(2-Chlorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	194	IIA
132		<i>N</i> -(4-{2-[4-(2-Chlorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	108	IIA
133		2-Cyano- <i>N</i> -(4-{2-[4-(3-fluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)acetamide	202	IIA
134		2-Acetylamino- <i>N</i> -(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	217	IIA
135		2- <i>tert</i> -Butoxy- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide trans/cis 95/5	81	IIA
136		<i>N</i> -(4-{2-[4-(3-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	179-182	IIA
137		<i>N</i> -(4-{2-[4-(3-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	143	IIA
138		2-Cyano- <i>N</i> -(4-{2-[4-(3-cyano-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	186	IIA

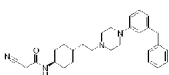
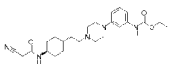
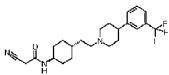
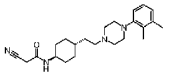
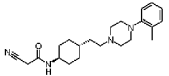
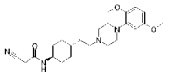
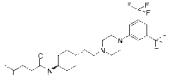
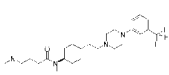
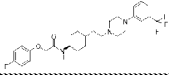
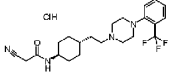
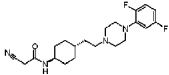
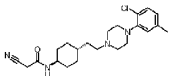
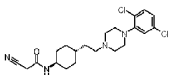
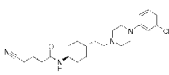
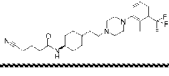
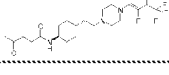
Ex	Structure	Name	M.P. (°C)	Synthetic Path
139		<i>N</i> -(4-{2-[4-(3-Cyano-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	140	IIA
140		<i>N</i> -(4-{2-[4-(3-Cyano-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	133	IIA
141		2-Cyano- <i>N</i> -(4-{2-[4-phenyl-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)acetamide	203	IIA
142		<i>N</i> -(4-{2-[4-(2,3-Dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	148	IIA
143		2-Cyano- <i>N</i> -(4-{2-[4-(2,3-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	188	IIA
144		<i>N</i> -(4-{2-[4-(2,3-Dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	143	IIA
145		2-Acetylamino- <i>N</i> -(4-{2-[4-(2,3-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	218	IIA
146		<i>N</i> -(4-{2-[4-(2,3-Difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-isopropoxyacetamide, hydrochloride	215	IIA
147		1-(4-{2-[4-(5-Chloro-2-methoxyphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	275	IIIB
148		2-Cyano- <i>N</i> -(4-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	192	IIA
149		2-Cyano- <i>N</i> -(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	142	IIA
150		2-Cyano- <i>N</i> -(4-{2-[4-(3-dimethylaminophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	177	IIA
151		2-Cyano- <i>N</i> -(4-{2-[4-(3,5-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	200	IIA
152		2-Cyano- <i>N</i> -(4-{2-[4-(2,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	184	IIA
153		1-Acetylpiperidine-4-carboxylic acid (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amide	173	IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
154		N-(4-{2-[4-(3-Trifluoromethyl-phenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamide trans/cis 65/35		IIA
155		N-(4-{2-[4-(5-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	171-172	IIA
156		N-(4-{2-[4-(3-Chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	186-187	IIA
157		2-Cyano-N-(4-{2-[4-(3-trifluoromethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	173-174	IIA
158		2-Cyano-N-(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	194	IIA
159		2-Cyano-N-(4-{2-[4-(3,5-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide trans/cis 95/5	196	IIA
160		2-Cyano-N-(4-{2-[4-(3-methoxy-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	183-184	IIA
161		4-Cyano-N-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	149	IIA
162		2-Cyano-N-(4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	188	IIA
163		2-Cyano-N-(4-{2-[4-(3-isopropoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, hydrochloride	191	IIA
164		2-Cyano-N-(4-{2-[4-(3-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, hydrochloride	219	IIA
165		2-Cyano-N-(4-{2-[4-(2-methoxy-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	183	IIA
166		2-Cyano-N-(4-{2-[4-(4-m-tolyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	175	IIA
167		3-Diethylamino-N-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide trans/cis 85/15	77	IIA
168		3-Cyano-N-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide, hydrochloride	230	IIA
169		N-(4-{2-[4-(3-tert-Butylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	150	IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
170		2-Cyano- <i>N</i> -(4-{2-[4-(3-ethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	157-159	IIA
171		<i>N</i> -(4-{2-[4-(5-Chloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	200	IIA
172		4-Cyano- <i>N</i> -(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	158-162	IIA
173		2-Cyano- <i>N</i> -(4-{2-[4-(6-trifluoromethylbenzo[b]thiophen-3-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	216	IA
174		2-Cyano- <i>N</i> -(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	197	IIA
175		2-Cyano- <i>N</i> -(4-{2-[4-(3-hydroxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, hydrochloride		IIA
176		<i>N</i> -(4-{2-[4-(5-Chloro-2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	180	IIA
177		<i>N</i> -(4-{2-[4-(2- <i>tert</i> -Butyl-6-trifluoromethylpyrimidin-4-yl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide trans/cis 85/15	188	IIA
178		2-Cyano- <i>N</i> -(4-{2-[4-(2-methyl-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	181	IIA
179		<i>N</i> -(4-{2-[4-(5-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide	177-178	IIA
180		2-Cyano- <i>N</i> -(4-{2-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	181-183	IIA
181		<i>N</i> -(4-{2-[4-(3-Chloro-5-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	181-183	IIA
182		2-Cyano- <i>N</i> -(4-{2-[4-(3-methylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	132	IIA
183		2-Cyano- <i>N</i> -(4-{2-[4-(naphthalen-1-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	174	IIA
184		<i>N</i> -(4-{2-[4-(3,5-Bistrifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	166	IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
185		<i>N</i> -(4-{2-[4-(3-Chloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	183	IIA
186		<i>N</i> -(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamide	255	IIA
187		<i>N</i> -(4-{2-[4-(4-Phenylpiperazin-1-yl)ethyl]cyclohexyl)succinamide	252	IIA
188		3,3,3-Trifluoro- <i>N</i> -(4-{2-[4-(4-phenylpiperazin-1-yl)ethyl]cyclohexyl}propanamide	185	IIA
189		<i>N</i> -(4-{2-[4-(2-Chloro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	203-204	IIA
190		<i>N</i> -(4-{2-[4-(5-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamide	237-240	IIA
191		4-Oxo-pentanoic acid (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amide	159	IIA
192		2-cyano- <i>N</i> -(4-{2-[4-(2-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	178	IIA
193		<i>N</i> -(4-{2-[4-(2-Chloro-5-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	165	IIA
194		2-Cyano- <i>N</i> -(4-{2-[4-(2-methylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	146	IIA
195		2-Cyano- <i>N</i> -(4-{2-[4-(2-methoxy-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	178	IIA
196		2-Cyano- <i>N</i> -(4-{2-[4-(5-fluoro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	159	IIA
197		<i>N</i> -(4-{2-[4-(5- <i>tert</i> -Butyl-2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	163	IIA
198		2-Cyano- <i>N</i> -(4-{2-[4-(5-methoxy-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	178-180	IIA
199		<i>N</i> -(4-{2-[4-(3,5-Bistrifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	174	IIA

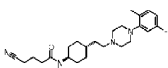
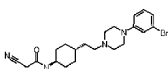
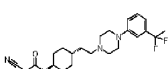
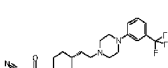
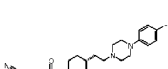
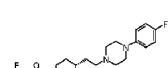
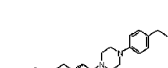
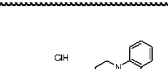
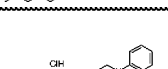
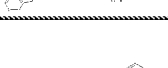
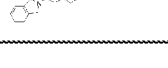
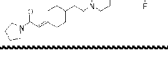
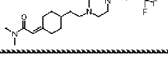
Ex	Structure	Name	M.P. (°C)	Synthetic Path
200		<i>N</i> -4-{2-[4-(3,5-Bis-trifluoromethylphenyl)piperidin-1-yl]ethyl}cyclohexyl-2-cyanoacetamide	164	IIA
201		1-(4-{2-[4-(2,3-Dichlorophenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}piperidin-1-yl)propan-2-one	296- 297	IIIB
202		5-Oxo-hexanoic acid (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amide	158	IIA
203		4-Cyano- <i>N</i> -(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide, hydrochloride trans/cis 85/15	205	IIA
204		4-Cyano- <i>N</i> -(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	170	IIA
205		<i>N</i> -(4-{2-[4-(3-Chloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	186	IIA
206		4-Cyano- <i>N</i> -(4-{2-[4-(3-trifluoromethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	133- 134	IIA
207		4-Cyano- <i>N</i> -(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	138- 139	IIA
208		2-Cyano- <i>N</i> -(4-{2-[4-(2-cyano-3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	187- 189	IIA
209		4-Cyano- <i>N</i> -(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-1-yl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	148	IIA
210		4-Cyano- <i>N</i> -(4-{2-[4-(2,3-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	192	IIA
211		2-Cyano- <i>N</i> -(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-2-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	200	IIA
212		2-Cyano- <i>N</i> -(4-{2-[4-indan-5-ylpiperazin-1-yl]ethyl}cyclohexyl)acetamide	210	IIA
213		<i>N</i> -(4-{2-[4-(3,5-Bistrifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-cyanopropanamide	158- 159	IIA
214		3-cyano- <i>N</i> -(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide trans/cis 95/5	153	IIA
215		<i>N</i> -(4-{2-[4-(3-Chloro-2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	122	IIA

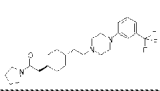
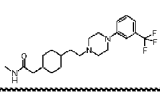
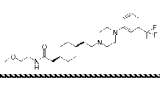
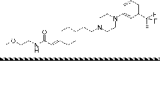
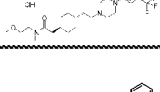
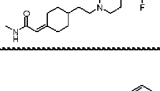
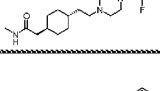
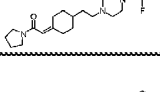
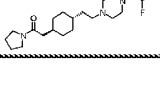
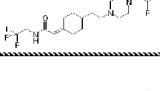
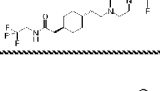
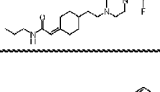
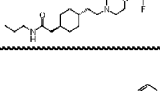
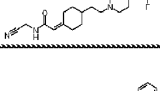
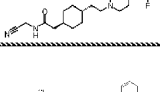
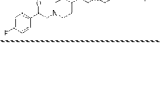
Ex	Structure	Name	M.P. (°C)	Synthetic Path
216		<i>N</i> -(4-{2-[4-(3-Benzylphenyl)-piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	168	IIA
217		[3-(4-{2-[4-(2-Cyanoacetylaminocyclohexyl)ethyl]phenyl}piperazin-1-yl)phenyl]carbamic acid ethyl ester	170	IIA
218		2-Cyano- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperidin-1-yl]ethyl}cyclohexyl)acetamide	129	IIA
219		2-Cyano- <i>N</i> -(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	166	IIA
220		2-Cyano- <i>N</i> -(4-{2-[4-(o-tolyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	150	IIA
221		2-Cyano- <i>N</i> -(4-{2-[4-(2,5-dimethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	171-173	IIA
222		4-Oxopentanoic acid (4-{2-[4-(3,5-bis-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amide	172-174	IIA
223		4-Dimethylamino- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	128	IIA
224		2-(4-Fluorophenoxy)- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)-piperazin-1-yl]ethyl}cyclohexyl)-acetamide	119	IIA
225		2-Cyano- <i>N</i> -(4-{2-[4-(2-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, hydrochloride	278	IIA
226		2-Cyano- <i>N</i> -(4-{2-[4-(2,5-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	198	IIA
227		<i>N</i> -(4-{2-[4-(2-Chloro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	174	IIA
228		2-Cyano- <i>N</i> -(4-{2-[4-(2,5-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	182-184	IIA
229		<i>N</i> -(4-{2-[4-(3-Chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	171-173	IIA
230		4-Cyano- <i>N</i> -(4-{2-[4-(2-methyl-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	162	IIA
231		4-Oxopentanoic acid (4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amide	178	IIA

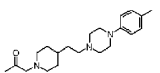
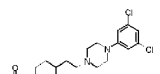
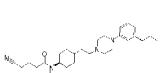
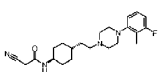
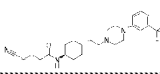
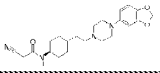
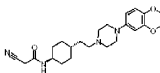
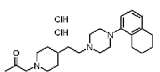
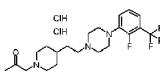
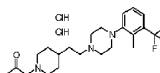
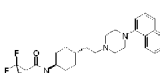
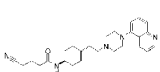
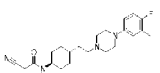
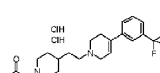
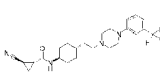
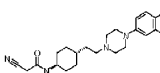
Ex	Structure	Name	M.P. (°C)	Synthetic Path
232		2-Cyano- <i>N</i> -(4-{2-[4-(3,5-di- <i>tert</i> -butylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	168	IIA
233		<i>N</i> -(4-{2-[4-(2-Chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	142	IIA
234		4-Cyano- <i>N</i> -(4-{2-[4-(4-m-tolyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	150	IIA
235		3,3,3-Trifluoro- <i>N</i> -(4-{2-[4-(4-m-tolyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	170	IIA
236		4-Cyano- <i>N</i> -(4-{2-[4-(2-methylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	130	IIA
237		2-Cyano- <i>N</i> -(4-{2-[4-(quinolin-8-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	225	IIA
238		4-Cyano- <i>N</i> -(4-{2-[4-(3-methylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	127	IIA
239		2-Cyano- <i>N</i> -(4-{2-[4-(quinolin-5-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	220	IIA
240		2-Cyano- <i>N</i> -(4-{2-[4-(3-methanesulfonylamino)phenyl]piperazin-1-yl]ethyl}cyclohexyl)-acetamide	194	IIA
241		2-Cyano- <i>N</i> -(4-{2-[4-(4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	209	IIA
242		2-Cyano- <i>N</i> -(4-{2-[4-(4-p-tolyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	237	IIA
243		2-Cyano- <i>N</i> -(4-{2-[4-(2-ethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	138	IIA
244		<i>N</i> -(4-{2-[4-(2- <i>tert</i> -Butyl-6-trifluoromethylpyrimidin-4-yl)piperazin-1-yl]ethyl}cyclohexyl)-3-cyanopropanamide trans/cis 80/20	151	IIA
245		2-Cyano- <i>N</i> -(4-{2-[4-(2-phenoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	169	IIA
246		<i>N</i> -(4-{2-[4-(3-Chloro-2-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	232-233	IIA

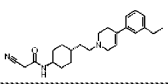
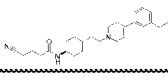
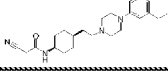
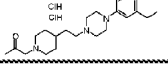
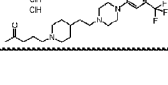
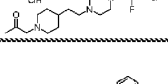
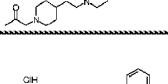
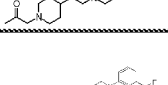
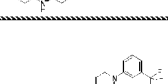
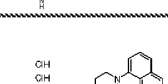
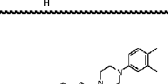
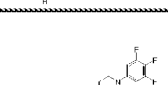
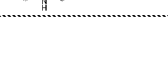
Ex	Structure	Name	M.P. (°C)	Synthetic Path
247		2-Cyano- <i>N</i> -(4-{2-[4-(2-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	142-143	IIA
248		<i>N</i> -(4-{2-[4-(5-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	152-153	IIA
249		4-Cyano- <i>N</i> -(4-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	169	IIA
250		<i>N</i> -(4-{2-[4-(3-Ethylphenyl)-piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide	154	IIA
251		3-Cyano- <i>N</i> -(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	143	IIA
252		1-(4-{2-[4-(5-Methoxy-2-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	283	IIIB
253		4-Cyano- <i>N</i> -(4-{2-[4-(6-trifluoromethylbenzo[b]thiophen-3-yl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	169	IA
254		4-Cyano- <i>N</i> -(4-{2-[4-(3,5-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	165	IIA
255		2-Cyano- <i>N</i> -(4-{2-[4-(2,4-diethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	183	IIA
256		3,3,3-Trifluoro- <i>N</i> -(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-propanamide	198	IIA
257		<i>N</i> -(4-{2-[4-(5-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-cyanopropanamide	133-134	IIA
258		<i>N</i> -(4-{2-[4-(3-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	180-183	IIA
259		<i>N</i> -(4-{2-[4-(3-Chloro-5-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	158-159	IIA
260		<i>N</i> -(4-{2-[4-(2-Fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	142	IIA
261		4-Cyano- <i>N</i> -(4-{2-[4-(3,5-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide trans/cis 98/2	179	IIA
262		4-Cyano- <i>N</i> -(4-{2-[4-(quinolin-8-yl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	180	IIA

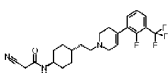
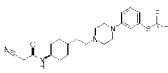
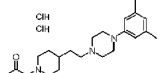
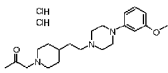
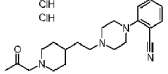
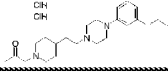
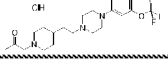
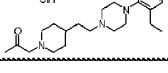
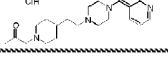
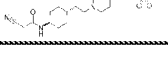
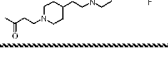
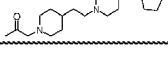
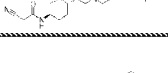
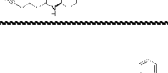
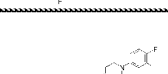
Ex	Structure	Name	M.P. (°C)	Synthetic Path
263		1-(4-{2-[4-(2,3-Dimethylphenyl)-3,6-dihydro-2H-pyridin-1-yl]ethyl}piperidin-1-yl)propan-2-one	310	IIIB
264		1-(4-{2-[4-(4-Benzothiazol-5-yl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	110	IIIB
265		4,4,4-Trifluoro-N-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	152	IIA
266		3-Cyano-N-(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	164	IIA
267		2-Cyano-N-(4-{2-[4-(2,6-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	143	IIA
268		2-Cyano-N-(4-{2-[4-(3-hydroxymethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	180	IIA
269		3-Cyano-N-(4-{2-[4-(3-methylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-propanamide	98	IIA
270		2-Cyano-N-(4-{2-[4-(3-methoxymethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	117	IIA
271		2-Cyano-N-(4-{2-[4-(3-propylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	132	IIA
272		2-Cyano-N-(4-{2-[4-(3,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	216	IIA
273		2-Cyano-N-(4-{2-[4-[3-(1-hydroxyethyl)phenyl]piperazin-1-yl]ethyl}cyclohexyl)acetamide trans/cis 80/20	160	IIA
274		2-Cyano-N-(4-{2-[4-(4-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	240	IIA
275		N-(4-{2-[4-(4-Chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	247	IIA
276		N-(4-{2-[4-(4-Biphenyl-3-yl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	157	IIA
277		2-Cyano-N-(4-{2-[4-(4-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	181	IIA
278		3-Cyano-N-(4-{2-[4-(5-fluoro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	146	IIA

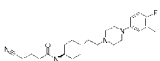
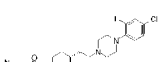
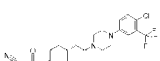
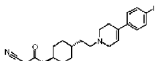
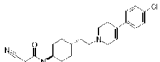
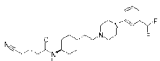
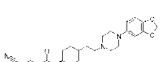
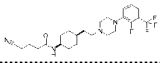
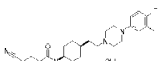
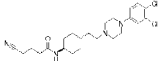
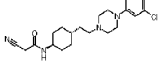
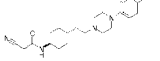
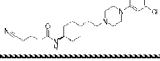
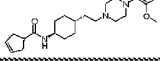
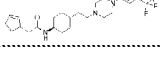
Ex	Structure	Name	M.P. (°C)	Synthetic Path
279		4-Cyano- <i>N</i> -(4-{2-[4-(5-fluoro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	155	IIA
280		<i>N</i> -(4-{2-[4-(3-Bromophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	168	IIA
281		2-Cyano- <i>N</i> -[4-{2-[4-[3-(1,1-difluoroethyl)phenyl]piperazin-1-yl]ethyl}cyclohexyl]acetamide trans/cis 90/10	150	IIA
282		2-Cyano-2,2-dimethyl- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-acetamide	150	IIA
283		4-Cyano- <i>N</i> -(4-{2-[4-(4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	154	IIA
284		3,3,3-Trifluoro- <i>N</i> -(4-{2-[4-(4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	200	IIA
285		2-Cyano- <i>N</i> -(4-{2-[4-(4-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	210	IIA
286		4-Cyano- <i>N</i> -(4-{2-[4-(2-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	124	IIA
287		1-(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexylidene)propan-2-one, hydrochloride	226-8	IIC
288		1-(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-propan-2-one, hydrochloride trans/cis 80/20	233-236	IIC
289		1-(1,3-Dihydroisindol-2-yl)-2-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexylidene)ethanone, hydrochloride	260	IIC
290		1-(1,3-Dihydroisindol-2-yl)-2-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)ethanone, hydrochloride 60/40 mixture of isomers		IIC
291		1-Pyrrolidin-1-yl-2-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexylidene)ethanone	87	IIC
292		<i>N,N</i> -Dimethyl-2-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexylidene)acetamide	66	IIC
293		<i>N,N</i> -Dimethyl-2-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide trans/cis 80/20		IIC

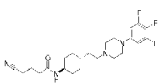
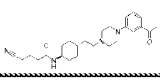
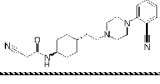
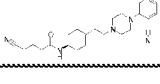
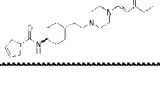
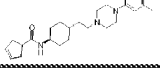
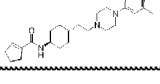
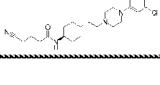
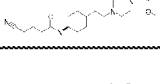
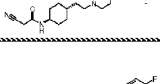
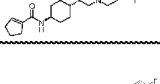
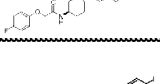
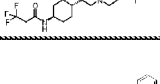
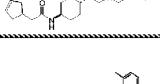
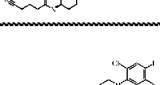
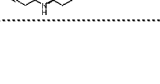
Ex	Structure	Name	M.P. (°C)	Synthetic Path
294		1-Pyrrolidin-1-yl-2-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)ethanone	131	IIC
295		<i>N</i> -Methyl-2-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide cis/trans 50/50	196	IIC
296		<i>N</i> -(2-Methoxyethyl)-2-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide		IIC
297		<i>N</i> -(2-Methoxyethyl)-2-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexylidene) acetamide		IIC
298		<i>N</i> -(2-Methoxyethyl)-2-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, hydrochloride	143	IIC
299		2-(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexylidene)- <i>N</i> -methylacetamide	135	IIC
300		2-(4-{2-[4-(2-Fluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)- <i>N</i> -methylacetamide	165-166	IIC
301		2-(4-{2-[4-(2-Fluorophenyl)-piperazin-1-yl]ethyl}cyclohexylidene)-1-pyrrolidin-1-ylethanone	109-110	IIC
302		2-(4-{2-[4-(2-Fluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-1-pyrrolidin-1-ylethanone	92-93	IIC
303		2-(4-{2-[4-(2-Fluorophenyl)-piperazin-1-yl]ethyl}cyclohexylidene)- <i>N</i> -(2,2,2-trifluoroethyl)acetamide	125	IIC
304		2-(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)- <i>N</i> -(2,2,2-trifluoroethyl)acetamide	158-9	IIC
305		2-(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexylidene)- <i>N</i> -propylacetamide	120-121	IIC
306		2-(4-{2-[4-(2-Fluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)- <i>N</i> -propylacetamide	150	IIC
307		<i>N</i> -Cyanomethyl-2-(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexylidene)acetamide	140-142	IIC
308		<i>N</i> -Cyanomethyl-2-(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide trans/cis 90/10	164-167	IIC
309		1-(4-Fluorophenyl)-2-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)ethanone, dihydrochloride	265	IIIB

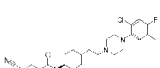
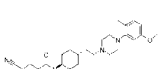
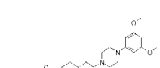
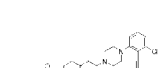
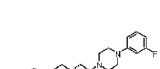
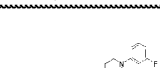
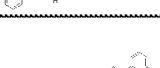
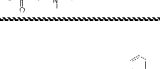
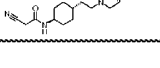
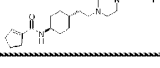
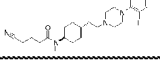
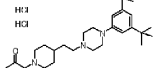
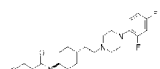
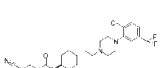
Ex	Structure	Name	M.P. (°C)	Synthetic Path
310		1-(4-[2-(4-p-Tolyl)piperazin-1-yl]ethyl)piperidin-1-ylpropan-2-one	92	IIIB
311		1-(4-[2-[4-(3,5-Dichlorophenyl)-piperazin-1-yl]ethyl]piperidin-1-yl)propan-2-one	126	IIIB
312		4-Cyano-N-(4-[2-[4-(3-propylphenyl)piperazin-1-yl]ethyl]cyclohexyl)butanamide	142	IIA
313		2-Cyano-N-(4-[2-[4-(3-fluoro-2-methylphenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide	174	IIA
314		4-Cyano-N-(4-[2-[4-[3-(1,1-difluoroethyl)phenyl]piperazin-1-yl]ethyl]cyclohexyl)butanamide	179	IIA
315		N-(4-[2-(4-Benzo[1,3]dioxol-5-yl)piperazin-1-yl]ethyl)cyclohexyl]-2-cyanoacetamide	226	IIA
316		2-Cyano-N-(4-[2-[4-(2,3-dihydrobenzo[1,4]dioxin-6-yl)piperazin-1-yl]ethyl]cyclohexyl)acetamide	208	IIA
317		1-(4-[2-[4-(5,6,7,8-Tetrahydronaphthalen-1-yl)piperazin-1-yl]ethyl]piperidin-1-yl)propan-2-one	320	IIIB
318		1-(4-[2-[4-(2-Fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl]piperidin-1-yl)propan-2-one, dihydrochloride	270	IIIB
319		1-(4-[2-[4-(2-Methyl-3-trifluoromethylphenyl)piperazin-1-yl]ethyl]piperidin-1-yl)propan-2-one, dihydrochloride	300	IIIB
320		3,3,3-Trifluoro-N-(4-[2-(4-quinolin-5-yl)piperazin-1-yl]ethyl]cyclohexyl)propanamide	207	IIA
321		4-Cyano-N-(4-[2-(4-quinolin-5-yl)piperazin-1-yl]ethyl]cyclohexyl)butanamide	155	IIA
322		2-Cyano-N-(4-[2-[4-(4-fluoro-3-methylphenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide	192	IIA
323		1-(4-[2-[4-(3-Trifluoromethylphenyl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]piperidin-1-yl)propan-2-one, dihydrochloride	268	IIIB
324		2-Cyano-cyclopropanecarboxylic acid (4-[2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl]cyclohexyl) amide	159	IIA
325		2-Cyano-N-(4-[2-[4-(3,4-difluorophenyl)piperazin-1-yl]ethyl]cyclohexyl)acetamide	197	IIA

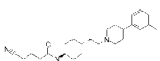
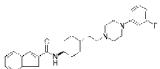
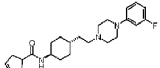
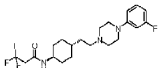
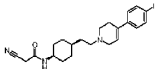
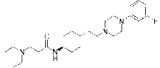
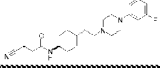
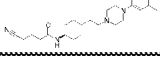
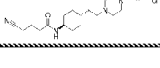
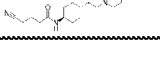
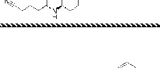
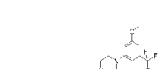
Ex	Structure	Name	M.P. (°C)	Synthetic Path
326		2-Cyano- <i>N</i> -(4-{2-[4-(3-ethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-acetamide	158	IIA
327		4-Cyano- <i>N</i> -(4-{2-[4-(3-ethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)butanamide	147	IIA
328		2-Cyano- <i>N</i> -(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	101	IIA
329		1-(4-{2-[4-(3-Ethylphenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	266	IIIB
330		5-(4-{2-[4-(3-Trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)pentan-2-one, dihydrochloride	315	IIIB
331		1-(4-{2-[4-(3-Chloro-2-fluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	270	IIIB
332		1-(4-{2-[4-(3-m-Tolylpiperazin-1-yl)ethyl]piperidin-1-yl}propan-2-one, dihydrochloride	260	IIIB
333		1-(4-{2-[4-(3-Fluoro-2-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	317	IIIB
334		2-Methanesulfinyl- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	153	IIA
335		2-Cyano- <i>N</i> -(4-{2-[4-(3-isopropylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	153	IIA
336		2-Cyano- <i>N</i> -(4-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	119	IIA
337		2-Methanesulfonyl- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	158	IIA
338		1-(4-{2-[4-(4-Quinolin-8-yl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	270	IIIB
339		2-Cyano- <i>N</i> -(4-{2-[4-(3-fluoro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	208	IIA
340		2-Cyano- <i>N</i> -(4-{2-[4-(3,4-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	210	IIA
341		2-Cyano- <i>N</i> -(4-{2-[4-(3,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	209	IIA

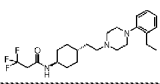
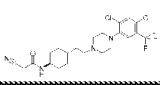
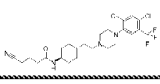
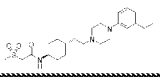
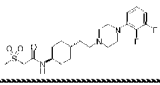
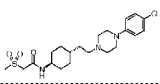
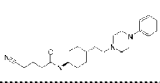
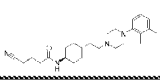
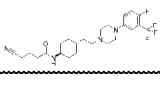
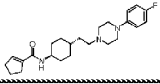
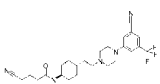
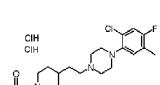
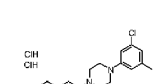
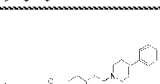
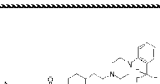
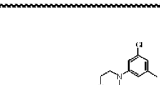
Ex	Structure	Name	M.P. (°C)	Synthetic Path
342		2-Cyano- <i>N</i> -(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)acetamide	171	IIA
343		2-Cyano- <i>N</i> -(4-{2-[4-(3-trifluoromethylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-acetamide	165	IIA
344		1-(4-{2-[4-(3,5-Dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	275	IIIB
345		1-(4-{2-[4-(3-Methoxyphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	265	IIIB
346		2-(4-{2-[1-(2-Oxopropyl)piperidin-4-yl]ethyl}piperazin-1-yl)benzonitrile, dihydrochloride	290	IIIB
347		1-(4-{2-[4-(3-Propylphenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	256	IIIB
348		1-(4-{2-[4-(3-Trifluoromethoxyphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	275	IIIB
349		1-(4-{2-[4-(2-Ethylphenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	291	IIIB
350		1-(4-{2-[4-(4-Quinolin-5-yl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	295	IIIB
351		2-Cyano- <i>N</i> -(4-{2-[4-(3-methanesulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	195	IIA
352		4-(4-{2-[4-(3-Trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-one, dihydrochloride		IIIB
353		1-(4-{2-[4-(4-Indan-4-yl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	295	IIIB
354		2-Cyano- <i>N</i> -(4-{2-[4-(3-difluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	185	IIA
355		4-Cyano- <i>N</i> -(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)butanamide	130	IIA
356		4-Cyano- <i>N</i> -(4-{2-[4-(3-fluoro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	159	IIA
357		4-Cyano- <i>N</i> -(4-{2-[4-(3,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	141	IIA

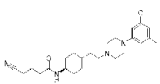
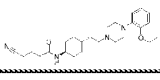
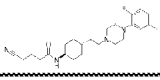
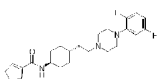
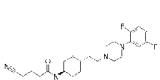
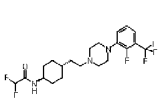
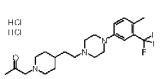
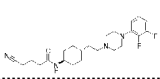
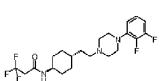
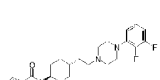
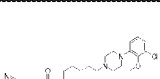
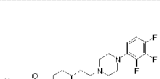
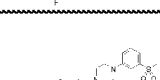
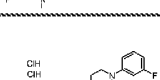
Ex	Structure	Name	M.P. (°C)	Synthetic Path
358		4-Cyano- <i>N</i> -(4-{2-[4-(4-fluoro-3-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	160	IIA
359		<i>N</i> -(4-{2-[4-(4-Chloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	218	IIA
360		<i>N</i> -(4-{2-[4-(4-Chloro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	187	IIA
361		2-Cyano- <i>N</i> -(4-{2-[4-(4-fluorophenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-acetamide	202	IIA
362		<i>N</i> -(4-{2-[4-(4-Chlorophenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	220	IIA
363		4-Cyano- <i>N</i> -(4-{2-[4-(3-trifluoromethylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	150	IIA
364		4-Cyano- <i>N</i> -(4-{2-[4-(3-difluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	155	IIA
365		<i>N</i> -(4-{2-[4-(Benzo[1,3]dioxol-5-yl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	189	IIA
366		4-Cyano- <i>N</i> -(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	95	IIA
367		4-Cyano- <i>N</i> -(4-{2-[4-(4-fluoro-3-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide, hydrochloride		IIIB
368		4-Cyano- <i>N</i> -(4-{2-[4-(3,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	151	IIA
369		<i>N</i> -(4-{2-[4-(3-Chloro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	220	IIA
370		2-Cyano- <i>N</i> -(4-{2-[4-(4-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	228	IIA
371		4-Cyano- <i>N</i> -(4-{2-[4-(2,5-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	179	IIA
372		Cyclopent-3-enecarboxylic acid (4-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	202	IIA
373		2-Cyclopent-2-enyl- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	154	IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
374		4-Cyano- <i>N</i> -(4-{2-[4-(3,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	156	IIA
375		<i>N</i> -(4-{2-[4-(3-Acetylphenyl)-piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	181	IIA
376		2-Cyano- <i>N</i> -(4-{2-[4-(2-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	190	IIA
377		4-Cyano- <i>N</i> -(4-{2-[4-(2-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	160	IIA
378		Cyclopent-3-enecarboxylic acid (4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	185	IIA
379		Cyclopent-3-enecarboxylic acid {4-[2-(4-m-tolylpiperazin-1-yl)ethyl]cyclohexyl}	200	IIA
380		Cyclopent-1-enecarboxylic acid {4-[2-(4-m-tolylpiperazin-1-yl)ethyl]cyclohexyl} amide	188	IIA
381		<i>N</i> -(4-{2-[4-(3-Chloro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	168	IIA
382		4-Cyano- <i>N</i> -(4-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	147	IIA
383		2-Cyano- <i>N</i> -(4-{2-[4-(2-methyl-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	192	IIA
384		Cyclopent-1-enecarboxylic acid (4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	205	IIA
385		<i>N</i> -(4-{2-[4-(2,4-Difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-(4-fluorophenoxy)acetamide	162	IIA
386		<i>N</i> -(4-{2-[4-(2,4-Difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide	184	IIA
387		2-Cyclopent-3-enyl- <i>N</i> -(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	188	IIA
388		4-Cyano- <i>N</i> -(4-{2-[4-(2-methyl-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butyramide	153	IIA
389		<i>N</i> -(4-{2-[4-(2-Chloro-4-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	177	IIA

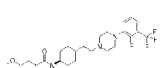
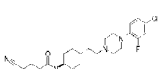
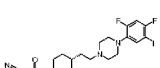
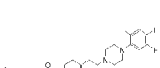
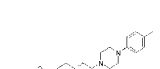
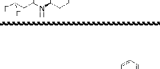
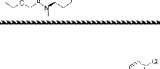
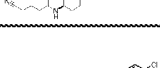
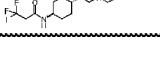
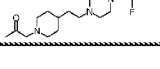
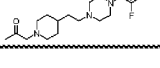
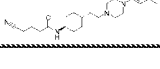
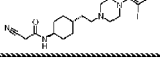
Ex	Structure	Name	M.P. (°C)	Synthetic Path
390		<i>N</i> -(4-{2-[4-(2-Chloro-4-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	158	IIA
391		4-Cyano- <i>N</i> -(4-{2-[4-(5-methoxy-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	170	IIA
392		4-Cyano- <i>N</i> -(4-{2-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	147	IIA
393		<i>N</i> -(4-{2-[4-(3-Chloro-2-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	189	IIA
394		Cyclohex-1-enecarboxylic acid (4-{2-[4-(3-fluorophenyl)-piperazin-1-yl]ethyl}cyclo-hexylamide	195	IIA
395		4-Cyano- <i>N</i> -(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	170	IIA
396		<i>N</i> -(4-{2-[4-(3-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-phenoxyacetamide	150	IIA
397		<i>N</i> -(4-{2-[4-(3-Fluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-succinamide	255	IIA
398		<i>N</i> -(4-{2-[4-(3-Fluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-succinamide	169	IIA
399		2-Cyano- <i>N</i> -(4-{2-[4-(3,5-dimethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-acetamide	182	IIA
400		Cyclopent-1-enecarboxylic acid (4-{2-[4-(3-fluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl) amide	202	IIA
401		4-Cyano- <i>N</i> -(4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	167	IIA
402		1-(4-{2-[4-(3,5-Di- <i>tert</i> -butylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	308	IIIB
403		3-Cyano- <i>N</i> -(4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	165	IIA
404		<i>N</i> -(4-{2-[4-(2-Chloro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	168	IIA
405		4-Cyano- <i>N</i> -(4-{2-[4-(2-methoxy-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	136	IIA

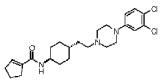
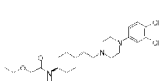
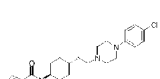
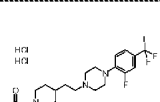
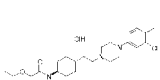
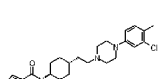
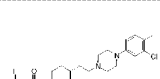
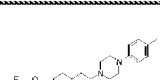
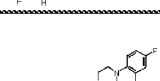
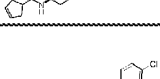
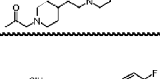
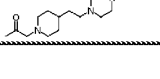
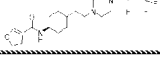
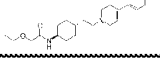
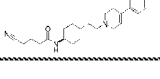
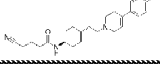
Ex	Structure	Name	M.P. (°C)	Synthetic Path
406		4-Cyano- <i>N</i> -(4-{2-[4-(3,5-dimethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-butanamide	166	IIA
407		1 <i>H</i> -Indene-2-carboxylic acid (4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	242	IIA
408		Cyclopent-3-enecarboxylic acid (4-{2-[4-(3-fluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl) amide	215	IIA
409		3,3,3-Trifluoro- <i>N</i> -(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	195	IIA
410		2-Cyano- <i>N</i> -(4-{2-[4-(4-fluorophenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-acetamide	147	IIA
411		3-Diethylamino- <i>N</i> -(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	118	IIA
412		3-Cyano- <i>N</i> -(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	186	IIA
413		4-Cyano- <i>N</i> -(4-{2-[4-(2,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	158	IIA
414		<i>N</i> -(4-{2-[4-(5-Chloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	165	IIA
415		<i>N</i> -(4-{2-[4-(5-Chloro-2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	152	IIA
416		4-Cyano- <i>N</i> -(4-{2-[4-(3-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	145	IIA
417		Cyclopent-1-enecarboxylic acid (4-{2-[4-(3-methoxyphenyl)-piperazin-1-yl]ethyl}cyclohexyl) amide	160	IIA
418		3-Cyano- <i>N</i> -(4-{2-[4-(3-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	140	IIA
419		<i>N</i> -(4-{2-[4-(3-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	165	IIA
420		2-Cyclopent-2-enyl- <i>N</i> -(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	188	IIA
421		4-Cyano- <i>N</i> -(4-{2-[4-(3-methoxy-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	147	IIA

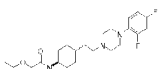
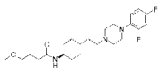
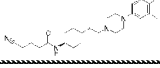
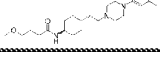
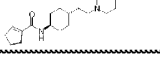
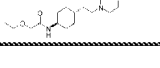
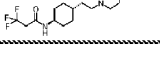
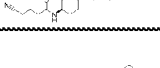
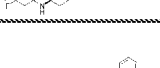
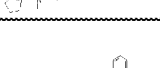
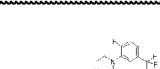
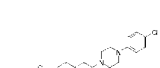
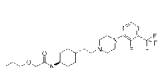
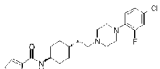
Ex	Structure	Name	M.P. (°C)	Synthetic Path
422		<i>N</i> -(4-{2-[4-(2-Ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide	135	IIA
423		2-Cyano- <i>N</i> -(4-{2-[4-(2,4-dichloro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	193	IIA
424		4-Cyano- <i>N</i> -(4-{2-[4-(2,4-dichloro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	188	IIA
425		<i>N</i> -(4-{2-[4-(3-Ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methanesulfonylacetamide	185	IIA
426		<i>N</i> -(4-{2-[4-(2,3-Difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methanesulfonylacetamide	214	IIA
427		<i>N</i> -(4-{2-[4-(4-Chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methanesulfonylacetamide	214	IIA
428		4-Cyano- <i>N</i> -(4-{2-[4-(4-o-tolyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	160	IIA
429		4-Cyano- <i>N</i> -(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	162	IIA
430		4-Cyano- <i>N</i> -(4-{2-[4-(4-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	149	IIA
431		Cyclopent-1-enecarboxylic acid (4-{2-[4-(4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	227	IIA
432		4-Cyano- <i>N</i> -(4-{2-[4-(3-cyano-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	174	IIA
433		1-(4-{2-[4-(2-Chloro-4-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	344	IIIB
434		1-(4-{2-[4-(3-Chloro-5-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	300	IIIB
435		4-Cyano- <i>N</i> -(4-{2-[4-(phenyl-3,6-dihydro-2H-pyridin-1-yl)ethyl]cyclohexyl)butanamide	171	IIA
436		4-Cyano- <i>N</i> -(4-{2-[4-(2-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide, hydrochloride	248	IIA
437		<i>N</i> -(4-{2-[4-(3-Chloro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	185	IIA

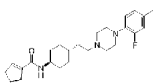
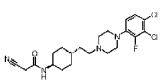
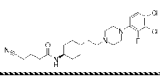
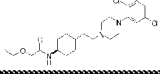
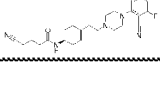
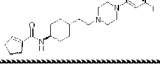
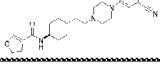
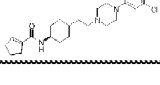
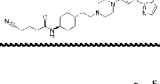
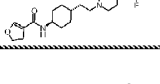
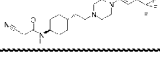
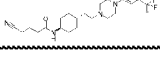
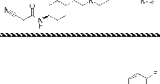
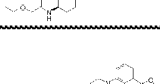
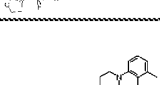
Ex	Structure	Name	M.P. (°C)	Synthetic Path
438		<i>N</i> -(4-{2-[4-(3-Chloro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	165	IIA
439		4-Cyano- <i>N</i> -(4-{2-[4-(2-ethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	137	IIA
440		4-Cyano- <i>N</i> -(4-{2-[4-(2-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	156	IIA
441		Cyclopent-1-enecarboxylic acid (4-{2-[4-(2,5-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	209	IIA
442		4-Cyano- <i>N</i> -(4-{2-[4-(2,5-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	159	IIA
443		2,2-Difluoro- <i>N</i> -(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	156	IIA
444		1-(4-{2-[4-(4-Methyl-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	325	IIIB
445		4-Cyano- <i>N</i> -(4-{2-[4-(2,3-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	197	IIA
446		<i>N</i> -(4-{2-[4-(2,3-Difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide	220	IIA
447		Cyclopent-1-enecarboxylic acid (4-{2-[4-(2,3-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	225	IIA
448		4-Cyano- <i>N</i> -(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	184	IIA
449		<i>N</i> -(4-{2-[4-(3-Chloro-2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	118	IIA
450		2-Cyano- <i>N</i> -(4-{2-[4-(2,3,4-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	207	IIA
451		4-Cyano- <i>N</i> -(4-{2-[4-(2,3,4-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	178	IIA
452		3,3,3-Trifluoro- <i>N</i> -(4-{2-[4-(3-methanesulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-propanamide	173	IIA
453		1-(4-{2-[4-(3-Fluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	268	IIIB

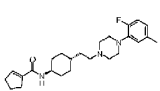
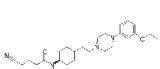
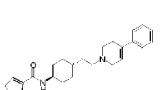
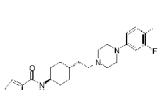
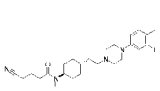
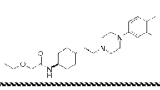
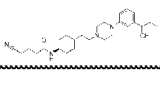
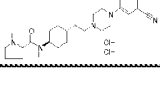
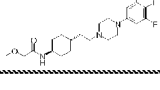
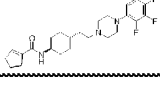
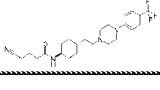
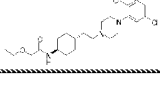
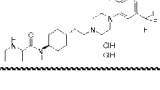
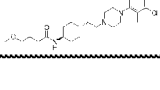
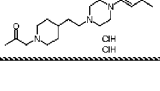
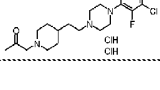
Ex	Structure	Name	M.P. (°C)	Synthetic Path
454		1-(4-{2-[4-(3-Ethoxyphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	246	IIIB
455		1-(4-{2-[4-(2,4-Difluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	260	IIIB
456		2-Cyano- <i>N</i> -{4-[2-(4-indan-4-yl)piperazin-1-yl]ethyl}cyclohexyl}acetamide	175	IIIB
457		4-Cyano- <i>N</i> -{4-[2-(4-indan-4-yl)piperazin-1-yl]ethyl}cyclohexyl}butanamide	157	IIA
458		Cyclopent-1-enecarboxylic acid (4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	190	IIA
459		<i>N</i> -(4-{2-[4-(2-Fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamide	244	IIA
460		4-Cyano-2,2-difluoro- <i>N</i> -(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	151	IIA
461		2,2,2-Trifluoro- <i>N</i> -(4-{2-[4-(3-methanesulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	132	IIA
462		<i>N</i> -(4-{2-[4-(4-Biphenyl-3-yl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	119	IIA
463		Cyclopent-1-enecarboxylic acid (4-{2-[4-(3,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	208	IIA
464		2-Methyl-5-(4-{2-[1-(2-oxopropyl)piperidin-4-yl]ethyl}piperazin-1-yl)benzonitrile	107	IIIB
465		2-Ethoxy- <i>N</i> -(4-{2-[4-(3,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	133	IIA
466		Cyclopent-3-enecarboxylic acid (4-{2-[4-(3,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	224	IIA
467		4-Cyano- <i>N</i> -(4-{2-[4-(p-tolyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	189	IIA
468		1-(4-{2-[4-(3-Methoxy-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	277- 278	IIIB
469		4,4,4-Trifluoro- <i>N</i> -(4-{2-[4-(3-methanesulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	205	IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
470		<i>N</i> -(4-{2-[4-(2-Fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	175	IIA
471		<i>N</i> -(4-{2-[4-(4-Chloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	171	IIA
472		2-Cyano- <i>N</i> -(4-{2-[4-(2,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	188	IIA
473		4-Cyano- <i>N</i> -(4-{2-[4-(2,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	153	IIA
474		2-Ethoxy- <i>N</i> -(4-{2-[4-(p-tolyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	130	IIA
475		Cyclopent-1-enecarboxylic acid {4-[2-(4-p-tolyl)piperazin-1-yl]ethyl}cyclohexyl amide	227	IIA
476		5,6-Dihydro-4 <i>H</i> -pyran-3-carboxylic acid (4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl amide	207	IIA
477		3,3,3-Trifluoro- <i>N</i> -(4-{2-[4-[3-(1-hydroxyethyl)phenyl]piperazin-1-yl]ethyl}cyclohexyl)propanamide	190	IIA
478		2-Ethoxy- <i>N</i> -(4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	125	IIA
479		<i>N</i> -(4-{2-[4-(4-Chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	190	IIA
480		<i>N</i> -(4-{2-[4-(4-Chlorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide	234	IIA
481		1-(4-{2-[4-(4-Chloro-2-fluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	206	IIIB
482		1-(4-{2-[4-(2-Fluoro-4-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	65	IIIB
483		4-Cyano- <i>N</i> -(4-{2-[4-(2-methoxy-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	164	IIA
484		2-Cyano- <i>N</i> -(4-{2-[4-(2-fluoro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	197	IIA
485		4-Cyano- <i>N</i> -(4-{2-[4-(2-fluoro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	173	IIA

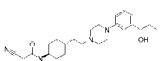
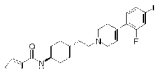
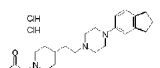
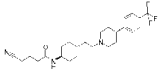
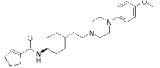
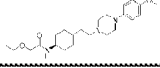
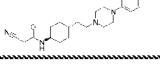
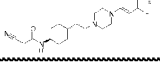
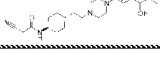
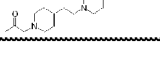
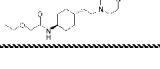
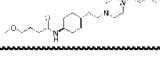
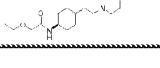
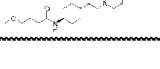
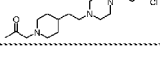
Ex	Structure	Name	M.P. (°C)	Synthetic Path
486		Cyclopent-1-enecarboxylic acid (4-{2-[4-(3,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	202	IIA
487		<i>N</i> -(4-{2-[4-(3,4-Dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	112	IIA
488		Cyclopent-1-enecarboxylic acid (4-{2-[4-(4-chlorophenyl)-piperazin-1-yl]ethyl}cyclohexyl) amide	237	IIA
489		1-(4-{2-[4-(2-Fluoro-4-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	278-279	IIIB
490		<i>N</i> -(4-{2-[4-(3-Chloro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	162	IIA
491		Cyclopent-1-enecarboxylic acid (4-{2-[4-(3-chloro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	197	IIA
492		<i>N</i> -(4-{2-[4-(3-Chloro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide	192	IIA
493		3,3,3-Trifluoro- <i>N</i> -(4-[2-(4-p-tolyl)piperazin-1-yl]ethyl)cyclohexyl}propanamide	217	IIA
494		Cyclopent-3-enecarboxylic acid (4-{2-[4-(2,4-difluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl) amide	199	IIA
495		1-(4-{2-[4-(3,4-Dichlorophenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	114	IIIB
496		1-(4-{2-[4-(4-Fluorophenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	270	IIIB
497		4,5-Dihydrofuran-3-carboxylic acid (4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	192	IIA
498		<i>N</i> -(4-{2-[4-(4-Chlorophenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	149	IIA
499		<i>N</i> -(4-{2-[4-(4-Chlorophenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	198	IIA
500		4-Cyano- <i>N</i> -(4-{2-[4-(4-fluorophenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-butanamide	180	IIA
501		Pyrrolidine-2-carboxylic acid (4-{2-[4-(2-fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	140	IIA

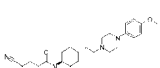
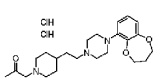
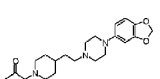
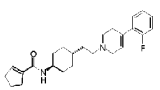
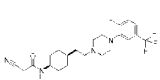
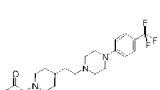
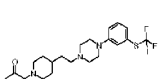
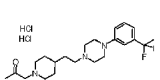
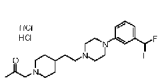
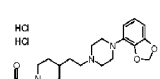
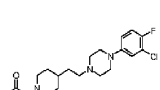
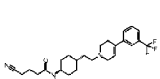
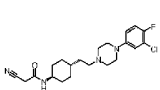
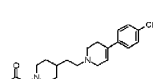
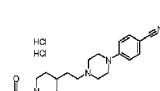
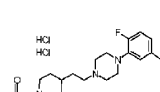
Ex	Structure	Name	M.P. (°C)	Synthetic Path
502		<i>N</i> -(4-{2-[4-(3,4-Dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	175	IIA
503		<i>N</i> -(4-{2-[4-(2,4-Difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	130	IIA
504		<i>N</i> -(4-{2-[4-(2,4-Difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	185	IIA
505		4-Cyano- <i>N</i> -(4-{2-[4-(3,4-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	172	IIA
506		<i>N</i> -(4-{2-[4-(3,4-Dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	161	IIA
507		Cyclopent-1-enecarboxylic acid (4-{2-[4-(3,4-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	201	IIA
508		<i>N</i> -(4-{2-[4-(3,4-Dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	122	IIA
509		<i>N</i> -(4-{2-[4-(3,4-Dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide	199	IIA
510		4-Cyano- <i>N</i> -(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-2-yl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	170	IIA
511		<i>N</i> -(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide	180	IIA
512		Cyclopent-1-enecarboxylic acid (4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	191	IIA
513		<i>N</i> -(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	168	IIA
514		2-Ethoxy- <i>N</i> -(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	128	IIA
515		<i>N</i> -(4-{2-[4-(4-Chloro-phenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	154	IIA
516		<i>N</i> -(4-{2-[4-(2-Fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-propoxyacetamide	102	IIA
517		Cyclopent-1-enecarboxylic acid (4-{2-[4-(4-chloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	216	IIA

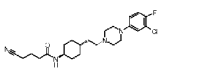
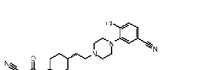
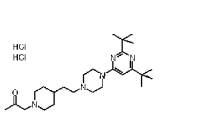
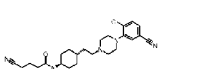
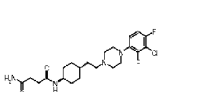
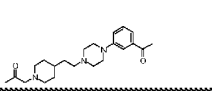
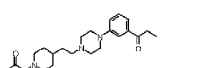
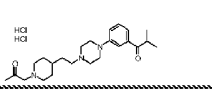
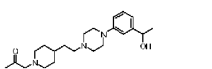
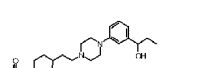
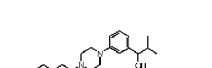
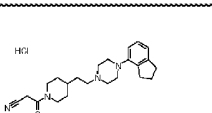
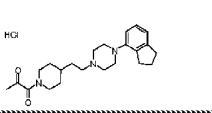
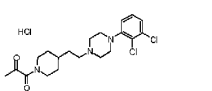
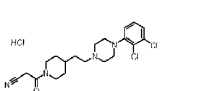
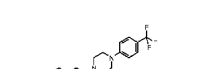
Ex	Structure	Name	M.P. (°C)	Synthetic Path
518		Cyclopent-1-enecarboxylic acid (4-{2-[4-(2-fluoro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	202	IIA
519		2-Cyano- <i>N</i> -(4-{2-[4-(3,4-dichloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	237	IIA
520		4-Cyano- <i>N</i> -(4-{2-[4-(3,4-dichloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	199	IIA
521		<i>N</i> -(4-{2-[4-(2,5-Dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	128	IIA
522		4-Cyano- <i>N</i> -(4-{2-[4-(2-cyano-3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	175	IIA
523		Cyclopent-1-enecarboxylic acid (4-{2-[4-(2,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	199	IIA
524		4,5-Dihydrofuran-3-carboxylic acid (4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	165	IIA
525		Cyclopent-1-enecarboxylic acid (4-{2-[4-(5-chloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	198	IIA
526		4-Cyano- <i>N</i> -(4-{2-[4-(3-oxazol-2-ylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	192	IIA
527		4,5-Dihydrofuran-3-carboxylic acid (4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	192	IIA
528		<i>N</i> -(4-{2-[4-(3-Chloro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	172	IIA
529		<i>N</i> -(4-{2-[4-(3-Chloro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	152	IIA
530		2-Cyano- <i>N</i> -(4-{2-[4-(3-oxazol-2-ylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	185	IIA
531		2-Ethoxy- <i>N</i> -(4-{2-[4-(4-fluorophenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-acetamide	122	IIA
532		4,5-Dihydrofuran-3-carboxylic acid(4-{2-[4-(3-oxazol-2-ylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	202	IIA
533		(4-{2-[4-(2,3-Dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)acetic acid ethyl ester	82	IIIB

Ex	Structure	Name	M.P. (°C)	Synthetic Path
534		Cyclopent-1-enecarboxylic acid (4-{2-[4-(2-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	174	IIA
535		4-Cyano-N-(4-{2-[4-(3-ethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	121	IIA
536		Cyclopent-1-enecarboxylic acid {4-[2-(4-phenyl-3,6-dihydro-2H-pyridin-1-yl)ethyl]cyclohexyl} amide	202	IIA
537		Cyclopent-1-enecarboxylic acid (4-{2-[4-(3-fluoro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	220	IIA
538		4-Cyano-N-(4-{2-[4-(3-fluoro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	180	IIA
539		2-Ethoxy-N-(4-{2-[4-(3-fluoro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	124	IIA
540		4-Cyano-N-[4-{2-[4-[3-(1-hydroxypropyl)phenyl]piperazin-1-yl]ethyl}cyclohexyl]butanamide	151	IIA
541		Pyrrolidine-2-carboxylic acid (4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl) amide, dihydrochloride	314	IIA
542		2-Methoxy-N-(4-{2-[4-(3,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	153	IIA
543		Cyclopent-1-enecarboxylic acid (4-{2-[4-(2,3,4-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	213	IIA
544		4-Cyano-N-(4-{2-[4-(4-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	207	IIA
545		N-(4-{2-[4-(2,5-Dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	128	IIA
546		Pyrrolidine-2-carboxylic acid (4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	274	IIA
547		N-(4-{2-[4-(3-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	188	IIA
548		1-(4-{2-[4-(3,4-Dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	275	IIIB
549		1-(4-{2-[4-(3,4-Dichloro-2-fluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	230	IIIB

Ex	Structure	Name	M.P. (°C)	Synthetic Path
550		Pyrrolidine-2-carboxylic acid (4-{2-[4-(2,4-difluorophenyl)-piperazin-1-yl]ethyl}cyclohexyl) amide, dihydrochloride	260	IIA
551		<i>N</i> -(4-{2-[4-(3-Chloro-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	198	IIA
552		<i>N</i> -(4-{2-[4-(3-Chloro-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	192	IIA
553		1-(4-{2-[4-(2-Fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	230	IIIB
554		1-(4-{2-[4-(3-Chloro-2-methoxyphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	270	IIIB
555		2-Cyano- <i>N</i> -(4-{2-[4-(4-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)acetamide	217	IIA
556		Cyclopent-1-enecarboxylic acid {4-[2-(4-o-tolylpiperazin-1-yl)ethyl]cyclohexyl} amide	181	IIA
557		2-Ethoxy- <i>N</i> -(4-{2-[4-(4-o-tolylpiperazin-1-ylethyl]cyclohexyl)acetamide	101	IIA
558		4-Cyano- <i>N</i> -(4-{2-[4-(6-cyano-3,4-dihydro-1 <i>H</i> -isoquinolin-2-yl)ethyl]cyclohexyl)butanamide	177	IIA
559		2-Cyano- <i>N</i> -(4-{2-[4-(6-cyano-3,4-dihydro-1 <i>H</i> -isoquinolin-2-yl)ethyl]cyclohexyl)acetamide	206	IIA
560		<i>N</i> -(4-{2-[4-(3-Ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	130	IIA
561		5,6-Dihydro-4 <i>H</i> -pyran-2-carboxylic acid (4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	135	IIA
562		5,6-Dihydro-4 <i>H</i> -pyran-2-carboxylic acid (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	142	IIA
563		2-Ethoxy- <i>N</i> -(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	100	IIA
564		4,5-Dihydrofuran-3-carboxylic acid (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	175	IIA
565		5,6-Dihydro-4 <i>H</i> -pyran-2-carboxylic acid (4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	160	IIA

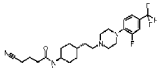
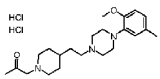
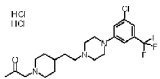
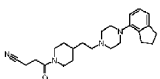
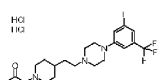
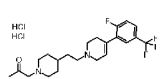
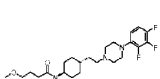
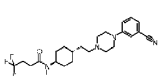
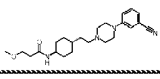
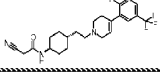
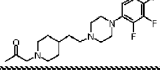
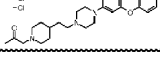
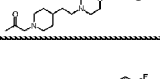
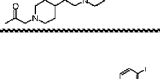
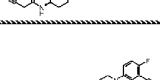
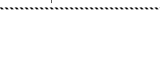
Ex	Structure	Name	M.P. (°C)	Synthetic Path
566		2-Cyano- <i>N</i> -[4-(2-{4-[3-(1-hydroxypropyl)phenyl]piperazin-1-yl}ethyl)cyclohexyl]acetamide	157	IIA
567		Cyclopent-1-enecarboxylic acid (4-{2-[4-(2,4-difluorophenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl) amide	166	IIA
568		4-Methoxy- <i>N</i> -(4-{2-[4-(3,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	194	IIA
569		1-(4-[2-(4-Indan-5-yl)piperazin-1-yl]ethyl)piperidin-1-yl)propan-2-one, dihydrochloride	291	IIIB
570		4-Cyano- <i>N</i> -(4-{2-[4-(4-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)butanamide	185	IIA
571		Cyclopent-1-enecarboxylic acid (4-{2-[4-(4-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	205	IIA
572		2-Ethoxy- <i>N</i> -(4-{2-[4-(4-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	132	IIA
573		2-Cyano- <i>N</i> -(4-{2-[4-(4-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	227	IIA
574		2-Cyano- <i>N</i> -(4-{2-[4-(3,5-difluoro-4-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	231	IIA
575		2-Cyano- <i>N</i> -[4-(2-{4-[3-(1-hydroxy-2-methylpropyl)phenyl]piperazin-1-yl}ethyl)cyclohexyl]acetamide	119	IIA
576		1-(4-[2-[4-(5,6,7,8-Tetrahydro-naphthalen-2-yl)piperazin-1-yl]ethyl]piperidin-1-yl)propan-2-one	75	IIIB
577		<i>N</i> -(4-{2-[4-(3-Chloro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	100	IIA
578		<i>N</i> -(4-{2-[4-(3-Chloro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	167	IIA
579		<i>N</i> -(4-{2-[4-(2-Chloro-4-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamide	132	IIA
580		<i>N</i> -(4-{2-[4-(2-Chloro-4-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	171	IIA
581		1-(4-[2-[4-(3-Chloro-5-fluorophenyl)piperazin-1-yl]ethyl]piperidin-1-yl)propan-2-one	107	IIIB

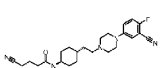
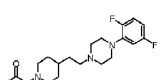
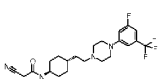
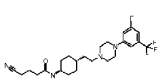
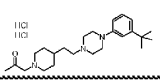
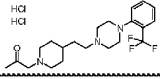
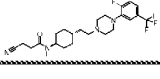
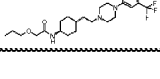
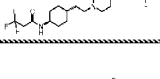
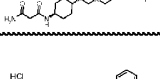
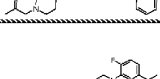
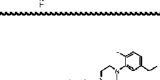
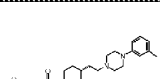
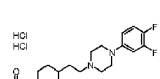
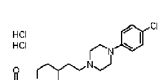
Ex	Structure	Name	M.P. (°C)	Synthetic Path
582		4-Cyano- <i>N</i> -(4-{2-[4-(4-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	200	IIA
583		1-(4-{2-[4-(3,4-Dihydro-2 <i>H</i> -benzo[<i>b</i>][1,4]dioxepin-6-yl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	280	IIIB
584		1-(4-{2-[4-(Benzo[1,3]dioxol-5-yl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	113	IIIB
585		Cyclopent-1-enecarboxylic acid (4-{2-[4-(2-fluorophenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl) amide	192	IIA
586		2-Cyano- <i>N</i> -(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	152	IIA
587		1-(4-{2-[4-(4-Trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	104	IIIB
588		1-(4-{2-[4-(3-Trifluoromethylsulfanylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	67	IIIB
589		1-(4-{2-[4-(3-(1,1-Difluoroethyl)phenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	256	IIIB
590		1-(4-{2-[4-(3-Difluoromethyl-phenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	265	IIIB
591		1-(4-{2-[4-(Benzo[1,3]dioxol-4-yl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	264	IIIB
592		1-(4-{2-[4-(3-Chloro-4-fluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	92	IIIB
593		4-Cyano- <i>N</i> -(4-{2-[4-(3-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)butanamide	102	IIA
594		<i>N</i> -(4-{2-[4-(3-Chloro-4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	176	IIA
595		1-(4-{2-[4-(4-Chlorophenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}piperidin-1-yl)propan-2-one	101	IIIB
596		4-(4-{2-[1-(2-Oxopropyl)piperidin-4-yl]ethyl}piperazin-1-yl)benzonitrile, dihydrochloride	295	IIIB
597		1-(4-{2-[4-(2-Fluoro-5-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	275	IIIB

Ex	Structure	Name	M.P. (°C)	Synthetic Path
598		<i>N</i> -(4-{2-[4-(3-Chloro-4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	142	IIA
599		<i>N</i> -(4-{2-[4-(2-Chloro-5-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamide	225	IIA
600		1-(4-{2-[4-(2,6-Di- <i>tert</i> -butylpyrimidin-4-yl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	310	IIIB
601		<i>N</i> -(4-{2-[4-(2-Chloro-5-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	206	IIA
602		<i>N</i> -(4-{2-[4-(3-Chloro-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamide	257	IIA
603		1-(4-{2-[4-(3-Acetylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	85	IIIB
604		1-[3-(4-{2-[1-(2-Oxopropyl)piperidin-4-yl]ethyl}piperazin-1-yl)phenyl]propan-1-one	68	IIIB
605		2-Methyl-1-[3-(4-{2-[1-(2-oxopropyl)piperidin-4-yl]ethyl}piperazin-1-yl)phenyl]propan-1-one, dihydrochloride	250	IIIB
606		1-[4-(2-{4-[3-(1-Hydroxyethyl)phenyl]piperazin-1-yl}ethyl)piperidin-1-yl]propan-2-one	97	IIIB
607		1-[4-(2-{4-[3-(1-Hydroxypropyl)phenyl]piperazin-1-yl}ethyl)piperidin-1-yl]propan-2-one	83	IIIB
608		1-[4-(2-{4-[3-(1-Hydroxy-2-methylpropyl)phenyl]piperazin-1-yl}ethyl)piperidin-1-yl]propan-2-one	78	IIIB
609		3-[4-[2-(4-Indan-4-yl)piperazin-1-yl]ethyl]piperidin-1-yl]-3-oxopropanenitrile, hydrochloride	210	IIIA
610		1-[4-[2-(4-Indan-4-yl)piperazin-1-yl]ethyl]piperidin-1-yl]propane-1,2-dione, hydrochloride	225	IIIA
611		1-[4-(2-[4-(2,3-Dichlorophenyl)piperazin-1-yl]ethyl)piperidin-1-yl]propane-1,2-dione, hydrochloride	244	IIIA
612		3-[4-[2-[4-(2,3-Dichlorophenyl)piperazin-1-yl]ethyl]piperidin-1-yl]-3-oxopropanenitrile, hydrochloride	228	IIIA
613		2-Cyano- <i>N</i> -(4-{2-[4-(4-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	156	IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
614		1-(4-{2-[4-(2-Ethoxyphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	271	IIIB
615		1-(4-{2-[4-(4-Fluorophenyl)-3,6-dihydro-2H-pyridin-1-yl]ethyl}piperidin-1-yl)propan-2-one	72	IIIB
616		<i>N</i> -(4-{2-[4-(2-Fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	177	IIA
617		1-(4-{2-[4-(2,5-Dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	172	IIIB
618		1-(4-{2-[4-(3-Chloro-4-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	103	IIIB
619		1-(4-{2-[4-(4-Indan-4-yl-3,6-dihydro-2H-pyridin-1-yl)ethyl]piperidin-1-yl}propan-2-one, dihydrochloride	291	IIIB
620		4-{4-[2-(4-Indan-4-ylpiperazin-1-yl)ethyl]piperidin-1-yl}-4-oxobutanamide	137	IIIA
621		1-(4-{2-[4-(4-Indan-4-ylpiperazin-1-yl)ethyl]piperidin-1-yl}butane-1,2-dione, hydrochloride	202	IIIA
622		1-(4-{2-[4-(3-Methanesulfonylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	260	IIIB
623		1-(4-{2-[4-(3-Chloro-2,4-difluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	82	IIIB
624		1-(4-{2-[4-(4-Phenyl-3,6-dihydro-2H-pyridin-1-yl)ethyl]piperidin-1-yl}propan-2-one	80	IIIB
625		2-Cyano- <i>N</i> -(4-{2-[4-(3,5-dimethylphenyl)-3,6-dihydro-2H-pyridin-1-yl]ethyl}cyclohexyl)acetamide, hydrochloride	220	IIA
626		1-(4-{2-[4-(3-Fluoro-4-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	276	IIIB
627		2-[2-[1-(2-Oxopropyl)piperidin-4-yl]ethyl]-1,2,3,4-tetrahydroisoquinoline-6-carbonitrile, dihydrochloride	249	IIIB
628		1-(4-{2-[4-(4-Chloro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	263	IIIB
629		1-(4-{2-[4-(4-Biphenyl-3-yl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	235	IIIB

Ex	Structure	Name	M.P. (°C)	Synthetic Path
630		1-(4-{2-[4-(4-Fluoro-2-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	283	IIIB
631		<i>N</i> -(4-{2-[4-(2-Fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamide	238	IIA
632		1-(4-{2-[4-(2,5-Dimethoxyphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	268	IIIB
633		1-(4-{2-[4-(2-Indan-4-yl)piperidin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	339	IIIB
634		1-(4-{2-[4-(4-Fluorophenyl)piperidin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride		IIIB
635		1-(4-{2-[4-(2-Methoxy-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	260	IIIB
636		1-(4-{2-[4-(2-Indan-4-yl)piperazin-1-yl]ethyl}piperidin-1-yl)pentan-2-one, dihydrochloride	270	IIIB
637		1-(4-{2-[4-(4-Fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	266	IIIB
638		1-(4-{2-[4-(2,6-Dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	249	IIIB
639		1-(4-{2-[4-(2-Chloro-5-methoxyphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	263	IIIB
640		1-(4-{2-[4-(3-Hydroxymethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	84	IIIB
641		1-(4-{2-[4-(6,7,8,9-Tetrahydro-5H-benzocyclohepten-1-yl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	300	IIIB
642		1-(4-{2-[4-(6,7,8,9-Tetrahydro-5H-benzocyclohepten-2-yl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	98	IIIB
643		3-Cyano- <i>N</i> -(4-{2-[4-(4-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	207	IIA
644		3-Cyano- <i>N</i> -(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	160	IIA
645		2-Cyano- <i>N</i> -(4-{2-[4-(2-fluoro-4-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	212	IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
646		4-Cyano- <i>N</i> -(4-{2-[4-(2-fluoro-4-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-butanamide	165	IIA
647		1-(4-{2-[4-(2-Methoxy-5-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	260	IIIB
648		1-(4-{2-[4-(3-Chloro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	289	IIIB
649		4-{4-[2-(4-Indan-4-yl)piperazin-1-yl]ethyl}piperidin-1-yl-4-oxo-butanonitrile		IIIA
650		1-(4-{2-[4-(3-Fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	295	IIIB
651		1-(4-{2-[4-(2-Fluoro-5-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	282	IIIB
652		4-Methoxy- <i>N</i> -(4-{2-[4-(2,3,4-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	203	IIA
653		<i>N</i> -(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4,4,4-trifluorobutanamide	176	IIA
654		<i>N</i> -(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-methoxypropanamide	145	IIA
655		2-Cyano- <i>N</i> -(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)acetamide	168	IIA
656		1-(4-{2-[4-(2,3,4-Trifluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	88	IIIB
657		1-(4-{2-[4-(3-Phenoxyphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	241	IIIB
658		1-(4-{2-[4-(3-Isopropoxyphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	237	IIIB
659		2-Fluoro-5-(4-{2-[1-(2-oxopropyl)piperidin-4-yl]ethyl}piperazin-1-yl)benzonitrile	102	IIIB
660		2-Cyano- <i>N</i> -(4-{2-[4-(3-cyano-4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	185	IIA
661		<i>N</i> -(4-{2-[4-(3-Cyano-4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	197	IIA

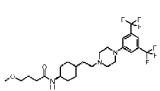
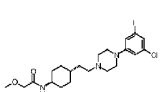
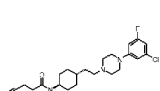
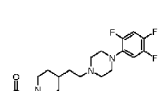
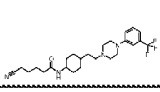
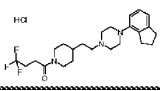
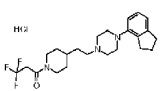
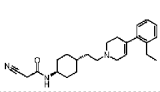
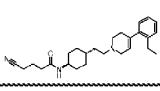
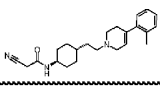
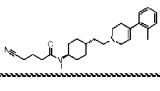
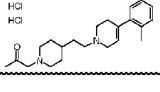
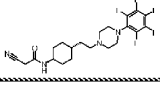
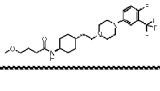
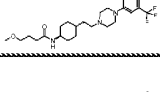
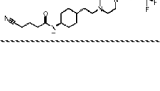
Ex	Structure	Name	M.P. (°C)	Synthetic Path
662		4-Cyano- <i>N</i> -(4-{2-[4-(3-cyano-4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	158	IIA
663		1-(4-{2-[4-(2,5-Difluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	90	IIIB
664		2-cyano- <i>N</i> -(4-{2-[4-(3-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	178	IIA
665		4-Cyano- <i>N</i> -(4-{2-[4-(3-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	163	IIA
666		1-(4-{2-[4-(3- <i>tert</i> -Butylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	257	IIIB
667		1-(4-{2-[4-(2-Trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	290	IIIB
668		3-cyano- <i>N</i> -(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	164	IIA
669		<i>N</i> -(4-{2-[4-(2-Fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-propoxyacetamide, hydrochloride	240	IIA
670		3,3,3-Trifluoro- <i>N</i> -(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	177	IIA
671		<i>N</i> -(4-{2-[4-(2-Fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-malonamide	185	IIA
672		1-(4-{2-[4-(3-Benzylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	253	IIIB
673		2-Cyano- <i>N</i> -(4-{2-[4-(5-ethyl-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	180	IIA
674		4-Cyano- <i>N</i> -(4-{2-[4-(5-ethyl-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	153	IIA
675		4-Methoxy- <i>N</i> -(4-{2-[4-(<i>m</i> -tolyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	148	IIA
676		1-(4-{2-[4-(3,4-Difluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	249	IIIB
677		1-(4-{2-[4-(4-Chlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	277	IIIB

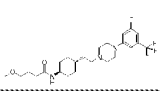
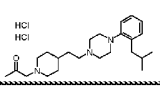
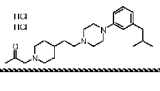
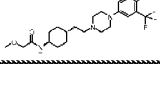
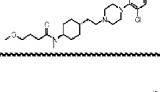
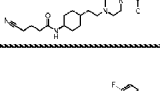
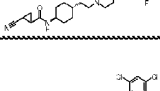
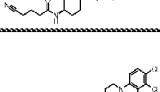
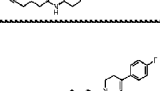
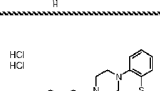
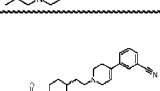
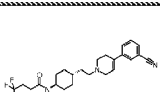
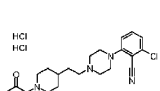
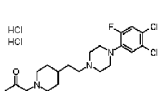
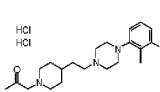
Ex	Structure	Name	M.P. (°C)	Synthetic Path
678		1-(4-{2-[4-(3-Isopropylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	252	IIIB
679		5-{4-[2-(4-Indan-4-yl)piperazin-1-yl]ethyl}piperidin-1-yl-5-oxo-pentanenitrile, hydrochloride	210	IIA
680		2-Ethoxy-1-{4-[2-(4-indan-4-yl)piperazin-1-yl]ethyl}piperidin-1-yl}ethanone, hydrochloride	270	IIA
681		3-{1-[2-[1-(2-Oxopropyl)piperidin-4-yl]ethyl]-1,2,3,6-tetrahydropyridin-4-yl}benzonitrile	94	IIIB
682		2-Cyano-N-(4-{2-[4-(3-cyanophenyl)-3,6-dihydro-2H-pyridin-1-yl]ethyl}cyclohexyl)acetamide	185	IIA
683		N-(4-{2-[4-(3-cyanophenyl)-3,6-dihydro-2H-pyridin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	178	IIA
684		N-(4-{2-[4-(3,4-Dichloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	210	IIA
685		1-(4-{2-[4-(5-Chloro-2-fluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	270	IIIB
686		1-(4-{2-[4-(3-Methylsulfanyl-phenyl)piperazin-1-yl]ethyl}-piperidin-1-yl)propan-2-one	113	IIIB
687		2-Cyano-N-(4-{2-[4-(3-cyano-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	210	IIA
688		4-Cyano-N-(4-{2-[4-(3-cyano-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	203	IIA
689		N-(4-{2-[4-(3-Fluoro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	172	IIA
690		2,6-Difluoro-3-(4-{2-[1-(2-oxo-propyl)piperidin-4-yl]ethyl}piperazin-1-yl)benzonitrile	108	IIIB
691		N-(4-{2-[4-(3,5-Dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	184	IIA
692		N-(4-{2-[4-(3-Cyano-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	211	IIA
693		4-(4-{2-[4-(3-Fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-4-oxobutanitrile		IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
694		1-(4-{2-[4-(3-Methoxymethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	255	IIIB
695		1-(4-{2-[4-(2,3,4,5-Tetrafluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	235	IIIB
696		1-(4-{2-[4-(2-Chloro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	299	IIIB
697		1-(4-{2-[4-(3,4,5-Trifluorophenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	86	IIIB
698		N-(4-{2-[4-(4-Chlorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	204	IIA
699		1-(4-{2-[4-(3,5-Difluoro-4-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	80	IIIB
700		1-(4-{2-[4-(2-tert-Butyl-6-trifluoromethylpyrimidin-4-yl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, trihydrochloride	287	IIIB
701		N-(4-{2-[4-(2-Fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	139	IIA
702		1-(4-{2-[4-(2,4-Dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	283	IIIB
703		1-(4-{2-[4-(2,4,5-Trichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	261	IIIB
704		4-(4-{2-[4-(3-Chloro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-4-oxobutanonitrile, hydrochloride	128	IIIA
705		Cyclopent-1-enecarboxylic acid (4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	199	IIA
706		N-(4-{2-[4-(2-Fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methanesulfonylacetamide	192	IIA
707		N-(4-{2-[4-(2-Fluoro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide		IIA
708		2-Cyano-N-(4-{2-[4-(2,3,4,5-tetrafluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	214	IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
709		2-Cyano- <i>N</i> -(4-{2-[4-(2,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	189	IIA
710		1-(4-{2-[4-(5-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	259	IIIB
711		1-(4-{2-[4-(2,3-Dihydrobenzo[1,4]dioxin-6-yl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	126	IIIB
712		4-Cyano- <i>N</i> -(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)butanamide	153	IIA
713		<i>N</i> -(4-{2-[4-(2-Fluoro-5-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	164	IIA
714		1-(4-{2-[4-(2,5-Dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	350	IIIB
715		<i>N</i> -(4-{2-[4-(3,5-Dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	195	IIA
716		3-Cyano- <i>N</i> -(4-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	175	IIA
717		2-Cyano- <i>N</i> -(4-{2-[4-(2,4,5-trichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	200	IIA
718		1-(4-{2-[4-(3-Fluoro-5-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	273	IIIB
719		<i>N</i> -(4-{2-[4-(3,4-Dichloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	172	IIIB
720		3-Cyano- <i>N</i> -(4-{2-[4-(3,4-dichloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	210	IIIB
721		1-(4-{2-[4-(3-Fluoro-5-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	287	IIIB
722		4-(4-{2-[4-(2-Fluoro-5-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}piperidin-1-yl)-4-oxobutanonitrile, hydrochloride	150	IIIA
723		2-cyano- <i>N</i> -(4-{2-[4-(3-fluoro-5-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)acetamide	163	IIA
724		4-cyano- <i>N</i> -(4-{2-[4-(3-fluoro-5-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)butanamide	114	IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
725		2-cyano- <i>N</i> -(4-{2-[4-(3-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	180	IIA
726		4-cyano- <i>N</i> -(4-{2-[4-(3-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	150	IIA
727		1-(4-{2-[4-(2,3,4-Trichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	275	IIIB
728		1-(4-{2-[4-(4-Fluoro-3-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	258	IIIB
729		2-Cyano- <i>N</i> -(4-{2-[4-(2,3,4-trichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	217	IIA
730		1-(4-{2-[4-(Pentafluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride		IIIB
731		5-Cyano-pentanoic acid (4-{2-[4-(2-fluoro-5-trifluoromethyl-phenyl)piperazin-1-ylethyl}cyclohexyl)amide	158	IIA
732		<i>N</i> -(4-{2-[4-(3-Chloro-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-cyanopropanamide	190	IIA
733		4-(4-{2-[4-(2,3-Dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-4-oxobutanonitrile	94	IIIA
734		2-Methoxy- <i>N</i> -(4-{2-[4-(2-methyl-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	159	IIA
735		4-Methoxy- <i>N</i> -(4-{2-[4-(2-methyl-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	173	IIA
736		4,4,4-Trifluoro- <i>N</i> -(4-{2-[4-(2-fluoro-5-trifluoromethyl-phenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	182	IIA
737		1-(4-{2-[4-(2,3-Dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	281	IIIB
738		<i>N</i> -(4-{2-[4-(3,5-Bistrifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)malonamide	165	IIA
739		1-(4-{2-[4-(2-Ethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	316	IIIB
740		<i>N</i> -(4-{2-[4-(3-Chloro-5-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	177	IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
741		<i>N</i> -(4-{2-[4-(3,5-Bistrifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	168	IIA
742		<i>N</i> -(4-{2-[4-(3-Chloro-5-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	132	IIA
743		<i>N</i> -(4-{2-[4-(3-Chloro-5-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-cyanopropanamide	148	IIA
744		1-(4-{2-[4-(2,4,5-Trifluorophenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	68	IIIB
745		5-Cyano-pentanoic acid (4-{2-[4-(3-trifluoromethylphenyl)-piperazin-1-yl]ethyl}cyclohexyl) amide	90	IIA
746		4,4,4-Trifluoro-1-{4-[2-(4-indan-4-yl)piperazin-1-yl]ethyl}piperidin-1-yl}butan-1-one, hydrochloride	219	IIIA
747		3,3,3-Trifluoro-1-{4-[2-(4-indan-4-yl)piperazin-1-yl]ethyl}piperidin-1-yl}propan-1-one, hydrochloride	206	IIIA
748		2-Cyano- <i>N</i> -(4-{2-[4-(2-ethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)acetamide	158	IIA
749		4-Cyano- <i>N</i> -(4-{2-[4-(2-ethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-butanamide	120	IIA
750		2-Cyano- <i>N</i> -(4-{2-[4-(2-o-tolyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)acetamide	166	IIA
751		4-Cyano- <i>N</i> -(4-{2-[4-(2-o-tolyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-butanamide	140	IIA
752		1-{4-[2-(4-o-Tolyl-3,6-dihydro-2 <i>H</i> -pyridin-1-yl)ethyl]piperidin-1-yl}propan-2-one, dihydrochloride	292	IIIB
753		2-Cyano- <i>N</i> -(4-{2-[4-(pentafluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	202	IIA
754		<i>N</i> -(4-{2-[4-(4-Fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	177	IIA
755		<i>N</i> -(4-{2-[4-(4-Chloro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	171	IIA
756		<i>N</i> -(4-{2-[4-(4-Chloro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	126	IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
757		<i>N</i> -(4-{2-[4-(3-Fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	177	IIA
758		1-(4-{2-[4-(2-Isobutylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	285	IIIB
759		1-(4-{2-[4-(3-Isobutylphenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	240	IIIB
760		<i>N</i> -(4-{2-[4-(4-Fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	146	IIA
761		<i>N</i> -(4-{2-[4-(2,4-Dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	171	IIA
762		4-Cyano- <i>N</i> -(4-{2-[4-(2,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	162	IIA
763		2-Cyano-cyclopropanecarboxylic acid (4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	196	IIA
764		4-Cyano- <i>N</i> -(4-{2-[4-(2,4,5-trichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	179	IIA
765		4-Cyano- <i>N</i> -(4-{2-[4-(2,3,4-trichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	176	IIA
766		<i>N</i> -(4-{2-[4-(4-Fluorophenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	201	IIA
767		1-(4-{2-[4-(2-Methylsulfanylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	280	IIIB
768		<i>N</i> -(4-{2-[4-(3-Cyanophenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	117	IIA
769		<i>N</i> -(4-{2-[4-(3-Cyanophenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-4,4,4-trifluorobutanamide	177	IIA
770		2-Chloro-6-(4-{2-[1-(2-oxopropyl)piperidin-4-yl]ethyl}piperazin-1-yl)benzonitrile, dihydrochloride	284	IIIB
783		1-(4-{2-[4-(4,5-Dichloro-2-fluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	309 (dec)	IIIB
784		1-(4-{2-[4-(3-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	320- 325	IIIB

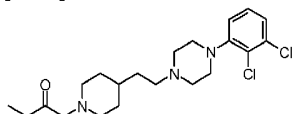
[0287] Further characterisation by ¹H NMR of some representative examples and comparative examples is given in the following table:

Ex	Structure	¹ H NMR
13		7.3 (t, 1H, J=7.5); 7.15 to 7.0 (ms, 3H); 3.35 (s, 2H) ; 3.25 (m, 4H) ; 2.9 (m, 2H) ; 2.6 (m, 4H) ; 2.45 (m, 2H) ; 2.0 (m, 2H) ; 1.8 to 1.55 (ms, 2H) ; 1.55 to 1.2 (ms, 5H) ; 1.15 (s, 9H)
37		7.45 to 7.25 (ms, 6H) ; 7.2 to 7.0 (ms, 3H) ; 5.1 (s, 2H) ; 4.6 (broad d, 1H) ; 3.45 (m, 1H) ; 3.25 (m, 4H) ; 2.6 (m, 4H) ; 2.4 (m, 2H) ; 2.05 (m, 2H) ; 1.8 (m, 2H) ; 1.7 to 1.0 (ms, 7H)
46		7.5 (t, 1H, J = 7.5) ; 7.4 to 7.25 (ms, 3H) ; 4.05 (s, 2H) ; 4.0 to 3.8 (ms, 2H) ; 3.8 to 3.5 (ms, 3H) ; 3.35 to 3.05 (ms, 6H) ; 1.95 to 1.5 (ms, 7H) ; 1.5 to 1.0 (ms, 4H) (D ₂ O)
59		7.7 to 7.35 (ms, 4H) ; 6.35 (broad d, 1H) ; 6.15 (s, 1H) ; 3.9 (s, 2H) ; 3.8 (m, 1H) ; 3.4 (s, 3H) ; 3.2 (m, 2H) ; 2.7 (m, 2H) ; 2.6 (m, 2H) ; 2.5 (m, 2H) ; 2.0 (m, 2H) ; 1.8 (m, 2H) ; 1.75 to 1.4 (ms, 2H) ; 1.4 to 1.0 (ms, 5H)
62		7.45 to 7.25 (ms, 4H) ; 7.2 to 7.0 (ms, 3H) ; 7.0 to 6.85 (ms, 2H) ; 6.4 (broad d, 1H) ; 4.45 (s, 2H) ; 3.85 (m, 1H) ; 3.3 (m, 4H) ; 2.65 (m, 4H) ; 2.45 (m, 2H) ; 2.0 (m, 2H) ; 1.9 to 1.4 (ms, 4H) ; 1.4 to 1.0 (ms, 5H)
79		7.15 to 6.85 (ms, 4H) ; 5.85 (broad d, 1H) ; 3.75 (m, 1H) ; 3.4 (s, 2H) ; 3.15 (m, 4H) ; 2.65 (m, 4H) ; 2.45 (m, 2H) ; 2.0 (m, 2H) ; 1.85 (m, 2H) ; 1.8 to 1.4 (ms, 3H) ; 1.4 to 1.0 (ms, 4H)
85		11.2 (broad s, 1H) ; 7.55 to 7.35 (ms, 2H) ; 7.3 (d, 1H, J = 5) ; 7.25 (s, 1H) ; 7.15 (d, 1H, J = 5) ; 4.0 to 3.7 (ms, 5H) ; 3.7 to 3.4 (ms, 4H) ; 3.4 to 2.95 (ms, 9H) ; 1.85 to 1.85 (ms, 13) (DMSO D ₆)
94		10.8 (broad s, 1H) ; 8.4 (d, 1H, J = 7.5) ; 7.35 to 7.2 (ms, 2H) ; 7.15 (d, 1H, J = 7.5) ; 3.9 (m, 2H) ; 3.5 (m, 2H) ; 3.4 to 3.05 (ms, 7H) ; 2.9 (q, 2H, J = 7.5) ; 1.85 to 1.55 (ms, 5H) ; 1.55 to 1.15 (ms, 4H) ; 1.15 to 1.85 (ms, 5H) (DMSO D ₆)
95		11.05 (broad s, 1H) ; 8.35 (d, 1H, J = 7.5) ; 7.4 (t, 1H, J = 7.5) ; 7.35 to 7.2 (ms, 2H) ; 7.1 (d, 1H, J = 7.5) ; 3.9 (m, 2H) ; 3.75 to 3.4 (ms, 3H) ; 3.4 to 2.9 (ms, 6H) ; 2.3 (s, 3H) ; 1.9 to 1.15 (ms, 9H) ; 1.15 to 0.85 (ms, 2H) (DMSO D ₆)
96		7.35 (t, 1H, J = 7.5) ; 7.15 to 7.0 (ms, 3H) ; 6.95 (broad d, 1H) ; 3.75 (m, 1H) ; 3.25 (m, 4H) ; 2.9 (s, 2H) ; 2.65 (m, 4H) ; 2.45 (m, 2H) ; 2.25 (s, 6H) ; 2.0 (m, 2H) ; 1.8 (m, 2H) ; 1.5 (m, 2H) ; 1.4 to 1.0 (ms, 5H)
100		7.35 (t, 1H, J = 7.5) ; 7.2 to 7.0 (ms, 3H) ; 6.4 (broad d, 1H) ; 3.9 (s, 2H) ; 3.8 (m, 1H) ; 3.65 (m, 1 H) ; 3.25 (m, 4H) ; 2.6 (m, 4H) ; 2.45 (m, 2H) ; 2.05 (m, 2H) ; 1.85 (m, 2H) ; 1.7 (m, 1H) ; 1.5 (m, 2H) ; 1.4 to 1.0 (ms, 10H)
107		7.35 to 7.2 (ms, 2H) ; 5.85 (broad d, 1H) ; 3.75 (m, 1H) ; 3.4 (s, 2H) ; 3.3 (m, 4H) ; 2.6 (m, 4H) ; 2.45 (m, 2H) ; 2.05 (m, 2H) ; 1.85 (m, 2H) ; 1.6 (m, 1H) ; 1.5 (m, 2H) ; 1.4 to 1.0 (ms, 4H)
109		7.35 (t, 1H, J = 7.5) ; 7.2 to 7.0 (ms, 3H) ; 6.75 (broad d, 1H) ; 3.7 (m, 1H) ; 3.4 (s, 2H) ; 3.25 (m, 4H) ; 2.6 (m, 4H) ; 2.45 (m, 2H) ; 2.3 (s, 3H) ; 2.05 (m, 2H) ; 1.85 (m, 2H) ; 1.75 to 1.4 (ms, 3H) ; 1.4 to 1.0 (ms, 4H)
120		8.25 (d, 2H, J = 7.5) ; 6.65 (d, 2H, J = 7.5) ; 6.45 (broad s, 1H) ; 4.0 (0.35H equatorial) ; 3.7 (0.65H axial) ; 3.35 to 3.25 (ms, 6H) ; 2.55 (m, 4H) ; 2.4 (m, 2H) ; 2.3 (1.7H) ; 2.0 (m, 1.4H) ; 1.8 (m, 1.4H) ; 1.75 to 0.9 (ms, 7.5H)
141		7.5 to 7.15 (ms, 5H) ; 6.1 (m, 1H) ; 5.85 (broad d, 1H) ; 3.75 (m, 1H) ; 3.35 (s, 2H) ; 3.2 (m, 2H) ; 2.7 (m, 2H) ; 2.6 (m, 2H) ; 2.5 (m, 2H) ; 2.05 (m, 2H) ; 1.9 (m, 2H) ; 1.5 (m, 2H) ; 1.4 to 1.0 (ms, 5H)

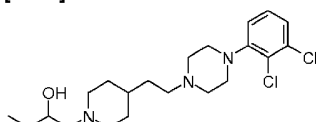
Ex	Structure	¹ H NMR
149		7.25 (t, 1H, J = 7.5); 6.85 to 6.65 (ms, 3H); 5.85 (broad d, 1H); 3.75 (m, 1H); 3.35 (s, 2H); 3.2 (m, 4H); 2.7 to 2.5 (ms, 6H); 2.4 (m, 2H); 2.05 (m, 2H); 1.85 (m, 2H); 1.45 (m, 2H); 1.4 to 1.0 (ms, 7H)
154		7.35 (t, 1H, J = 7.5); 7.2 to 7.0 (ms, 3H); 6.05 (broad s, 1H); 5.65 (broad d, 1H); 5.35 (broad s, 1H); 4.0 (m, 0.35H equatorial); 3.7 (m, 0.65H axial); 3.25 (m, 4H); 2.7 to 2.45 (ms, 8H); 2.4 (m, 2H); 2.0 (m, 2H); 1.8 (m, 2H); 1.55 (m, 1H); 2.5 (m, 2H); 2.4 to 1.0 (ms, 4H)
172		7.25 to 7.05 (ms, 3H); 5.3 (broad d, 1H); 3.7 (m, 1H); 3.15 (m, 4H); 2.65 (m, 4H); 2.55 to 2.4 (ms, 4H); 2.3 (t, 2H, J = 7.5); 2.0 (m, 4H); 1.8 (m, 2H); 1.45 (m, 2H); 1.4 to 1.0 (ms, 5H)
175		10.4 (broad s, 1H); 8.2 (d, 1H, J = 7.5); 7.0 (t, 1H, J = 7.5); 6.4 (d, 1H, J = 7.5); 6.35 (s, 1H); 6.25 (d, 1H, J = 7.5); 3.7 (m, 2H); 3.65 (s, 2H); 3.6 to 3.3 (ms, 3H); 3.2 to 2.9 (ms, 6H); 1.9 to 1.5 (ms, 6H); 1.4 to 0.9 (ms, 5H) (DMSO D ₆)
290		10.3 (broad s, 1H); 7.4 (t, 1H, J = 7.5); 7.4 to 7.0 (ms, 7H); 4.8 (s, 2H); 4.6 (s, 2H); 3.9 (m, 2H); 3.5 (m, 2H); 3.3 to 2.8 (ms, 7H); 2.3 (d, 0.8H, J = 7.5); 2.2 (d, 1.2H, J = 7.5); 1.9 to 0.8 (ms, 11H) trans/cis 60/40 (DMSO D ₆)
293		7.35 (t, 1H, J = 7.5); 7.2 to 7.0 (m, 3H); 3.25 (m, 4H); 3.2 (s, 3H); 2.95 (s, 3H); 2.45 (m, 4H); 2.2 (t, 2H, J = 7.5); 2.2 (d, 2H, J = 7.5); 1.9 to 1.6 (ms, 4H); 1.6 to 1.15 (ms, 5H); 1.15 to 0.75 (ms, 3H)
296		7.35 (t, 1H, J = 7.5); 7.15 to 7.0 (ms, 3H); 5.8 (broad t, 1H); 3.45 (m, 4H); 3.35 (s, 3H); 3.25 (m, 4H); 2.6 (m, 4H); 2.41 (t, 2H, J = 7.5); 2.05 (d, 2H, J = 7.5); 1.9 to 1.7 (ms, 5H); 1.6 to 1.1 (ms, 4H); 1.1 to 0.8 (ms, 3H)
297		7.35 (t, 1H); 7.15 to 7.0 (ms, 3H); 5.75 (broad t, 1H); 5.25 (s, 1H); 3.75 (m, 1H); 3.45 (m, 4H); 3.35 (s, 3H); 3.25 (m, 4H); 3.6 (m, 4H); 2.45 (t, 2H, J = 7.5); 2.3 to 1.85 (ms, 5H); 1.6 to 1.4 (ms, 2H); 1.3 to 1.0 (ms, 3H)
352		7.5 (t, 1H, J = 7.5); 7.4 to 7.2 (ms, 3H); 4.75 (2H); 3.9 (m, 2H); 3.7 (m, 2H); 3.55 (m, 2H); 3.45 to 3.05 (ms, 10H); 2.95 (m, 2H); 2.2 (s, 3H); 2.0 (m, 2H); 1.9 to 1.6 (3H); 1.5 (m, 2H) (D ₂ O)
367		13.4 (broad s, 1H); 7.75 to 7.5 (ms, 2H); 7.1 (t, 1H, J = 7.5); 5.85 (d, 1H); 4.55 (m, 2H); 4.3 to 3.95 (ms, 3H); 3.7 (m, 4H); 3.15 (m, 2H); 2.6 to 2.15 (ms, 7H); 2.1 to 1.05 (ms, 13H)
634		7.35 to 7.2 (ms, 2H); 7.05 (t, 1H, J = 7.5); 4.85 (s, 2H); 4.25 (s, 2H); 3.65 (m, 2H); 3.5 (m, 2H); 3.35 to 2.85 (ms, 7H); 2.2 (s, 3H); 2.15 to 1.9 (ms, 6H); 1.9 to 1.5 (ms, 5H)
649		7.15 (t, 1H, J = 7.5); 6.95 (d, 1H, J = 7.5); 6.75 (d, 1H, J = 7.5); 4.6 (m, 1H); 3.75 (m, 1H); 3.25 to 3.0 (ms, 5H); 2.9 (t, 2H, J = 7.5); 2.85 (t, 2H, J = 7.5); 2.8 to 2.5 (ms, 7H); 2.45 (m, 2H); 2.05 (m, 2H); 1.8 (m, 2H); 1.7 to 1.45 (ms, 5H); 2.15 (m, 2H)
693		6.9 (s, s, 1H); 6.8 to 6.6 (m, 2H); 4.6 (m, 1H); 3.8 (m, 1H); 3.25 (m, 4H); 3.05 (m, 2H); 2.75 to 2.65 (ms, 3H); 2.5 to 2.35 (ms, 5H); 2.45 (m, 2H); 1.8 (m, 2H); 1.7 to 1.4 (ms, 3H); 1.2 (m, 2H)
707		6.9 to 6.75 (ms, 3H); 5.45 (d, 1H, J = 7.5); 3.75 (m, 1H); 3.45 (t, 1H, J = 7.5); 3.4 (s, 3H); 3.1 (m, 4H); 2.65 (m, 4H); 2.45 (m, 2H); 2.3 (s, 3H); 2.25 (t, 2H, J = 7.5); 2.1 to 1.7 (ms, 6H); 1.45 (m, 2H); 1.35 to 1.0 (ms, 5H)
730		4.75 (s, 2H); 4.2 (s, 2H); 3.65 to 3.1 (ms, 12H); 3.0 (m, 2H); 2.2 (s, 3H); 2.0 (m, 2H); 1.85 to 1.4 (ms, 5H) (D ₂ O)

Example 771: 1-(4-{2-[4-(2,3-dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-one

[0288]

**Step a: 1-(4-{2-[4-(2,3-dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-ol**

[0289]



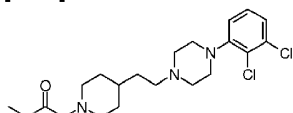
[0290] A suspension of 0.41 g (1 mmol) of 1-(2,3-dichlorophenyl)-4-(2-piperidin-4-ylethyl)piperazine, dihydrochloride in 25 mL of isopropanol and 0.29 g (2.1 mmol) of potassium carbonate is stirred for 30 minutes then 0.08 g (1.1 mmol) of 2-ethyloxirane is added. The suspension is stirred to reflux overnight. The precipitate is filtered and the solution is concentrated under reduced pressure. The residue is dissolved in ethyl acetate, washed with water and with brine, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue is purified over 10 g of silica gel (dichloromethane/methanol 90/10) to give 0.2 g (50%) of 1-(4-{2-[4-(2,3-dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-ol as an oil that crystallizes upon standing.

Melting point: 94°C

¹H NMR: 7.2 to 7.05 (ms, 2H) ; 7.0 to 6.9 (m, 1 H) ; 3.7 (m, 1 H) ; 3.1 (m, 6H) ; 2.9 (m, 2H) ; 2.65 (m, 4H) ; 2.55 to 2.2 (ms, 4H) ; 2.05 (m, 1 H) ; 1.7 (m, 2H) ; 1.65 to 1.25 (ms, 7H) ; 1.0 (t, 3H, J = 7.5)

Step b: 1-(4-{2-[4-(2,3-dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-one

[0291]



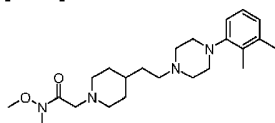
[0292] The 1-(4-{2-[4-(2,3-dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-one is obtained by Swern oxydation of 1-(4-{2-[4-(2,3-dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-ol according to the procedure described in example 7.

Melting point: 68°C

¹H NMR: 7.2 to 7.1 (m, 2H) ; 6.95 (m, 1 H) ; 3.2 (s, 2H) ; 3.15 (m, 4H) ; 2.85 (m, 2H) ; 2.7 (m, 4H) ; 2.6 to 2.4 (ms, 4H) ; 2.05 (m, 2H) ; 1.7 (m, 2H) ; 1.65 to 1.2 (ms, 5H) ; 1.1 (t, 3H, J = 7.5)

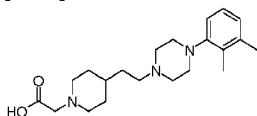
Example 772: 2-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-N-methoxy-N-methylacetamide

[0293]



Step a: (4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)acetic acid

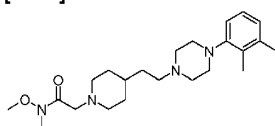
[0294]



[0295] The (4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)acetic acid is prepared from (4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)acetic acid ethyl ester using the procedure described in preparation F, step 1.

Step b: 2-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-N-methoxy-N-methylacetamide

[0296]

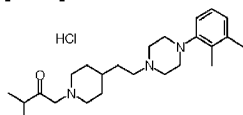


[0297] The 2-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-N-methoxy-N-methylacetamide is prepared from 4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)acetic acid using the procedure described in preparation F, step 2.
Melting point: 66°C

¹H NMR: 7.1 (t, 1H, J = 7.5) ; 7.0 to 6.85 (ms, 2H) ; 3.7 (s, 3H) ; 3.35 (s, 2H) ; 3.3 to 2.6 (ms, 17H) ; 2.4 to 2.15 (ms, 8H) ; 1.9 to 1.65 (ms, 3H), 1.65 to 1.35 (ms, 2H)

Example 773: 1-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-3-methylbutan-2-one, hydrochloride

[0298]



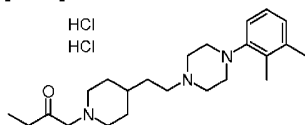
[0299] The 1-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-3-methylbutan-2-one, hydrochloride is prepared by addition of a solution of isopropylmagnesium bromide on 2-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-N-methoxy-N-methylacetamide using the procedure described in preparation F, step 3.

Melting point: 182°C

¹H NMR: 7.1 (t, 1H, J = 7.5) ; 7.0 to 6.85 (ms, 2H) ; 6.4 (broad s, 1H) ; 3.0 to 2.7 (ms, 8H) ; 2.7 to 2.5 (ms, 4H) ; 2.45 (m, 2H) ; 2.3 (s, 3H) ; 2.25 (s, 3H) ; 2.2 to 2.0 (ms, 3H) ; 1.7 (m, 2H) ; 1.5 (m, 2H) ; 1.4 to 1.1 (ms, 3H) ; 1.0 (d, 3H) ; 0.85 (d, 3H, J = 7.5)

Example 774: 1-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-one, dihydrochloride

[0300]

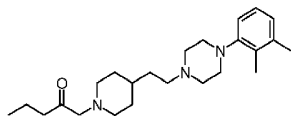


[0301] The 1-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-one, dihydrochloride is prepared by addition of a solution of ethylmagnesium bromide on 2-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-*N*-methoxy-*N*-methylacetamide using the procedure described in preparation F, step 3.

Melting point: 315°C

Example 775: 1-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)pentan-2-one

[0302]

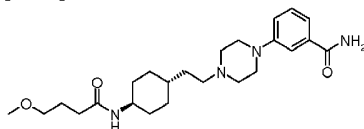


[0303] The 1-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl) pentan-2-one is prepared by addition of a solution of propylmagnesium bromide on 2-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-*N*-methoxy-*N*-methylacetamide using the procedure described in preparation F, step 3.

Melting point: 47°C

Example 776: 3-(4-{2-[4-(4-methoxybutanoylamino)cyclohexyl]ethyl}piperazin-1-yl)benzamide

[0304]



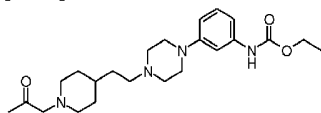
[0305] A mixture of 85 mg (0.2 mmol) of *N*-(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide, 2 mL of dimethyl sulfoxide, 16.5 mg of potassium carbonate and 0.12 mL of an aqueous 30% hydrogen peroxide solution is stirred for 2 hours at room temperature. The suspension is poured into 50 mL of water. The solid is filtered, washed with water, dried under reduced pressure to give 15 mg (17%) of 3-(4-{2-[4-(4-methoxybutanoylamino)cyclohexyl]ethyl}piperazin-1-yl)benzamide as a white solid.

Melting point: 202°C

¹H NMR (DMSO D₆): 7.85 (s, 1 H) ; 7.6 (d, 1 H, J = 7.5) ; 7.35 (s, 1 H) ; 7.3 to 7.15 (ms, 3H) ; 7.05 (m, 1 H) ; 3.4 (m, 1 H) ; 3.25 (t, 2H, J = 7.5) ; 3.2 (s, 3H) ; 3.15 (m, 4H) ; 2.45 (m, 4H) ; 2.3 (m, 2H) ; 2.05 (m, 2H) ; 1.8 to 1.55 (ms, 6H) ; 1.35 (m, 2H) ; 1.25 to 0.8 (ms, 5H)

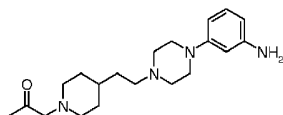
Example 777: [3-(4-{2-[1-(2-oxopropyl)piperidin-4-yl]ethyl}piperazin-1-yl)phenyl]carbamic acid ethyl ester

[0306]



Step a: 1-(4-{2-[4-(3-aminophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one

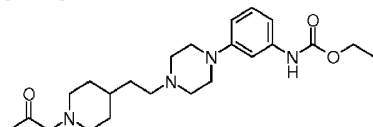
[0307]



[0308] The 1-(4-{2-[4-(3-aminophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one is prepared from 1-(4-{2-[4-(3-nitrophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one using the procedure described in preparation D, step 2 to give the title compound in 49% crude yield, used without further purification.

Step b: [3-(4-{2-[1-(2-oxopropyl)piperidin-4-yl]ethyl}piperazin-1-yl)phenyl]carbamic acid ethyl ester

[0309]



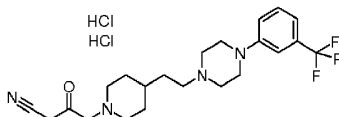
[0310] To a cooled solution of 0.1 g (0.3 mmol) of 1-(4-{2-[4-(3-aminophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one in 5 mL of dichloromethane and 0.03 g (0.3 mmol) of triethylamine, is slowly added 0.032 g (0.3 mmol) of ethyl chloroformate. The mixture is stirred overnight at room temperature then concentrated under reduced pressure. The product is dissolved in ethyl acetate, washed twice with water, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The oily residue is purified over 10 g of silica gel (eluant dichloromethane/methanol 95/5) to give 0.025 g (20%) of [3-(4-{2-[1-(2-oxopropyl)piperidin-4-yl]ethyl}piperazin-1-yl)phenyl]carbamic acid ethyl ester as a solid.

Melting point: 118°C

¹H NMR: 7.25 to 7.1 (ms, 2H) ; 6.75 (d, 1 H, J = 7.5) ; 6.65 (d, 1 H, J = 7.5) ; 6.55 (s, 1H) ; 4.25 (q, 2H, J = 7.5) ; 3.25 (m, 4H) ; 3.15 (s, 2H) ; 2.85 (m, 2H) ; 2.6 (m, 4H) ; 2.45 (m, 2H) ; 2.2 (s, 3H) ; 2.05 (m, 2H) ; 1.8 to 1.2 (ms, 10H)

Example 778: 3-oxo-4-(4-{2[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butanenitrile, dihydrochloride

[0311]



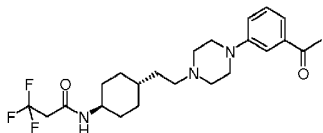
[0312] A solution of 0.77 mL (1.3 mmol) of potassium *tert*-pentyxide solution (1.7M in toluene) is added dropwise at room temperature to a stirred solution of 52 mg (1,27 mmol) of acetonitrile in 2.5 mL of tetrahydrofuran followed by dropwise addition of 0.19 g (0.44 mmol) of (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)acetic acid ethyl ester in 1 mL of tetrahydrofuran. After 30 minutes at room temperature, the reaction mixture is diluted with 10 mL of an aqueous 0.2N aqueous hydrochloric acid solution and 50 mL of ethyl acetate forming an emulsion. The mixture is concentrated under reduced pressure and the product is purified over 10 g of silica gel (eluant dichloromethane/methanol 95/5). The oily product is dissolved in 2 mL of diethyl ether and acidified with a hydrochloric acid diethyl ether solution. The precipitate is filtered, washed with diethyl ether and dried under reduced pressure to give 30 mg (14%) of 3-oxo-4-(4-{2[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butanenitrile, dihydrochloride.

Melting point: 160°C

¹H NMR (DMSO D₆): 11.2 (broad s, 1 H) ; 10.2 (broad s, 1 H) ; 7.45 (t, 1 H, J = 7.5) ; 7.3 (d, 1 H, J = 7.5) ; 7.25 (s, 1 H) ; 7.1 (d, 1 H, J = 7.5) ; 4.35 (s, 2H) ; 4.2 (s, 2H) ; 3.95 (m, 2H) ; 2.55 (m, 2H) ; 2.45 to 2.9 (ms, 10H) ; 2.0 to 2.45 (ms, 7H)

Example 779: N-(4-{2-[4-(3-acetylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide

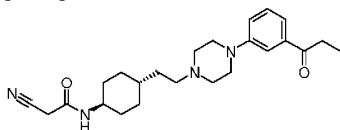
[0313]



[0314] The *N*-(4-(2-[4-(3-acetylphenyl)piperazin-1-yl]ethyl)cyclohexyl)-3,3,3-trifluoro-propanamide is prepared by oxidation of 3,3,3-trifluoro-*N*-(4-(2-[4-(3-(1-hydroxyethyl)phenyl]piperazin-1-yl)ethyl)cyclohexyl)propanamide (example 477) using the procedure described in example 7 to give the title compound.
Melting point 165°C.

Example 780: 2-cyano-*N*-(4-(2-[4-(3-propanoylphenyl)piperazin-1-yl]ethyl)cyclohexyl)acetamide

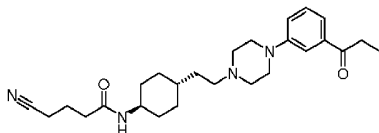
[0315]



[0316] The 2-cyano-*N*-(4-(2-[4-(3-propanoylphenyl)piperazin-1-yl]ethyl)cyclohexyl)-acetamide is prepared by oxidation of 2-cyano-*N*-(4-(2-[4-(3-(1-hydroxypropyl)-phenyl]piperazin-1-yl)ethyl)cyclohexyl)acetamide (example 566) using the procedure described in example 7 to give the title compound.
Melting point 178°C.

Example 781: 4-cyano-*N*-(4-(2-[4-(3-propanoylphenyl)piperazin-1-yl]ethyl)cyclohexyl)butanamide

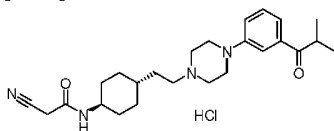
[0317]



[0318] The 4-cyano-*N*-(4-(2-[4-(3-propanoylphenyl)piperazin-1-yl]ethyl)cyclohexyl)-butanamide is prepared by oxidation of 4-cyano-*N*-(4-(2-[4-(3-(1-hydroxy-propyl)phenyl]piperazin-1-yl)ethyl)cyclohexyl)butanamide (example 540) using the procedure described in example 7 to give the title compound.
Melting point 158°C.

Example 782: 2-cyano-*N*-(4-(2-[4-(3-isobutanylphenyl)piperazin-1-yl]ethyl)cyclohexyl)acetamide, dihydrochloride

[0319]



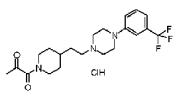
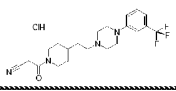
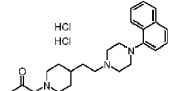
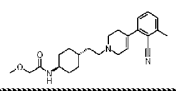
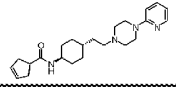
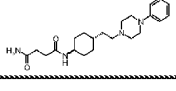
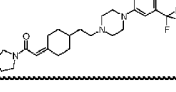
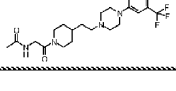
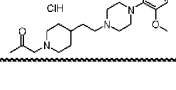
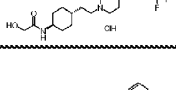
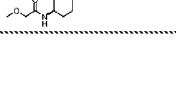
[0320] The 2-cyano-*N*-(4-(2-[4-(3-isobutanylphenyl)piperazin-1-yl]ethyl)cyclohexyl)-acetamide, dihydrochloride is prepared by oxidation of 2-cyano-*N*-(4-(2-[4-(3-(1-hydroxy-2-methylpropyl)phenyl]piperazin-1-yl)ethyl)cyclohexyl)acetamide (example 575) using the procedure described in example 7 to give the title compound.
Melting point 185°C.

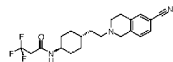
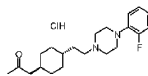
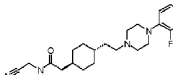
Affinity of compounds for the human D₃ receptor can be determined by [³H] spiperone binding

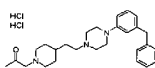
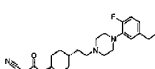
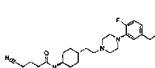
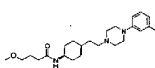
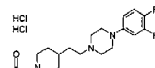
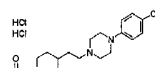
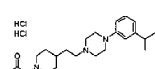
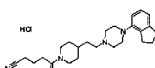
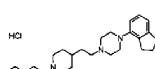
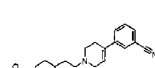
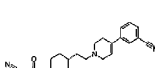
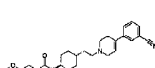
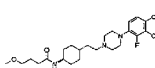
[0321] CHO cells have been transfected by the cDNA coding for the human D₃ receptor (hD₃). [³H]Spiperone (0,5 à 2 nM) binding is performed in the presence of 2.5 to 5 µg of membrane proteins in a medium containing 120 mM NaCl, 5 mM KCl, and 50 mM Tris HCl pH 7.4; incubation for 60 minutes at room temperature is performed. Non specific binding is estimated in the presence of 10µM haloperidol. Non transfected cells are devoid of any specific binding.

[0322] Exemplified compounds all display an inhibitory constant below 1µM, most of them are below 50nM.

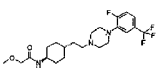
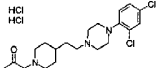
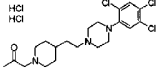
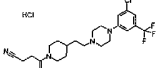
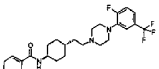
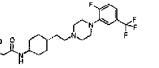
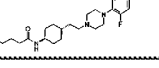
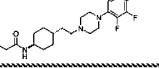
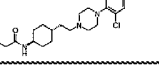
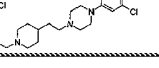
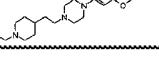
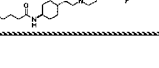
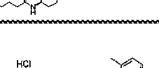
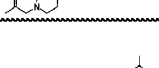
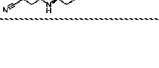
[0323] Affinities for the human D₃ receptor of some representative examples and comparative examples are given in the following table:

Ex	Structure	Ki (nM)
2 comparative		6.6
15 comparative		15.1
36 comparative		1.32
54 comparative		18.3
65 comparative		31.6
187		3.9
291 comparative		4.4
14 comparative		15.1
20 comparative		9.5
46		12.0
61 comparative		8.5

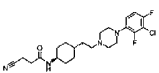
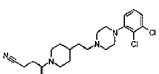
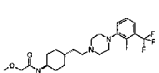
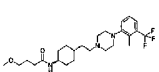
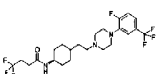
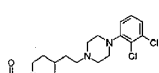
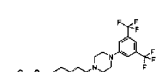
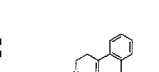
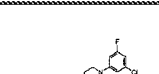
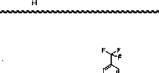
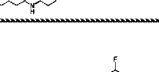
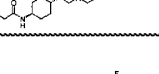
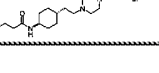
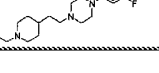
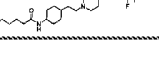
Ex	Structure	Ki (nM)
110 comparative		10.6
288 comparative		2.1
308 comparative		3.5

Ex	Structure	Name	M.P. (°C)	Synthetic Path
672		1-(4-{2-[4-(3-Benzylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	253	IIIB
673		2-Cyano- <i>N</i> -(4-{2-[4-(5-ethyl-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	180	IIA
674		4-Cyano- <i>N</i> -(4-{2-[4-(5-ethyl-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	153	IIA
675		4-Methoxy- <i>N</i> -(4-{2-[4-(m-tolyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	148	IIA
676		1-(4-{2-[4-(3,4-Difluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	249	IIIB
677		1-(4-{2-[4-(4-Chlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	277	IIIB
678		1-(4-{2-[4-(3-Isopropylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	252	IIIB
679		5-(4-{2-[4-(Indan-4-yl)piperazin-1-yl]ethyl}piperidin-1-yl)-5-oxopentanenitrile, hydrochloride	210	IIIA
680		2-Ethoxy-1-(4-{2-[4-(indan-4-yl)piperazin-1-yl]ethyl}piperidin-1-yl)ethanone, hydrochloride	270	IIIA
681		3-(1-{2-[1-(2-Oxopropyl)piperidin-4-yl]ethyl}-1,2,3,6-tetrahydropyridin-4-yl)benzonitrile	94	IIIB
682		2-Cyano- <i>N</i> -(4-{2-[4-(3-cyanophenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)acetamide	185	IIA
683		<i>N</i> -(4-{2-[4-(3-Cyanophenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	178	IIA
684		<i>N</i> -(4-{2-[4-(3,4-Dichloro-2-fluoro-phenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	210	IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
685		1-(4-{2-[4-(5-Chloro-2-fluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	270	IIIB
686		1-(4-{2-[4-(3-Methylsulfonyl-phenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	113	IIIB
687		2-Cyano-N-(4-{2-[4-(3-cyano-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	210	IIA
688		4-Cyano-N-(4-{2-[4-(3-cyano-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	203	IIA
689		N-(4-{2-[4-(3-Fluoro-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	172	IIA
690		2,6-Difluoro-3-(4-{2-[1-(2-oxo-propyl)piperidin-4-yl]ethyl}piperazin-1-yl)benzonitrile	108	IIIB
691		N-(4-{2-[4-(3,5-Dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	184	IIA
692		N-(4-{2-[4-(3-Cyano-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	211	IIA
693		4-(4-{2-[4-(3-Fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-4-oxobutanonitrile		IIIA
694		1-(4-{2-[4-(3-Methoxymethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	255	IIIB
695		1-(4-{2-[4-(2,3,4,5-Tetrafluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	235	IIIB
696		1-(4-{2-[4-(2-Chloro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	299	IIIB
697		1-(4-{2-[4-(3,4,5-Trifluorophenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	86	IIIB
698		N-(4-{2-[4-(4-chlorophenyl)-piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	204	IIA
699		1-(4-{2-[4-(3,5-Difluoro-4-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	80	IIIB
700		1-(4-{2-[4-(2- <i>tert</i> -Butyl-6-trifluoromethylpyrimidin-4-yl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, trihydrochloride	287	IIIB

Ex	Structure	Name	M.P. (°C)	Synthetic Path
701		<i>N</i> -(4-{2-[4-(2-Fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	139	IIA
702		1-(4-{2-[4-(2,4-Dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	283	IIIB
703		1-(4-{2-[4-(2,4,5-Trichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	261	IIIB
704		4-(4-{2-[4-(3-Chloro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-4-oxobutanonitrile, hydrochloride	128	IIIA
705		Cyclopent-1-enecarboxylic acid (4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	199	IIA
706		<i>N</i> -(4-{2-[4-(2-Fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methanesulfonylacetamide	192	IIA
707		<i>N</i> -(4-{2-[4-(2-Fluoro-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide		IIA
708		2-Cyano- <i>N</i> -(4-{2-[4-(2,3,4,5-tetrafluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	214	IIA
709		2-Cyano- <i>N</i> -(4-{2-[4-(2,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	189	IIA
710		1-(4-{2-[4-(5-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	259	IIIB
711		1-(4-{2-[4-(2,3-Dihydrobenzo[1,4]dioxin-6-yl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	126	IIIB
712		4-Cyano- <i>N</i> -(4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)butanamide	153	IIA
713		<i>N</i> -(4-{2-[4-(2-Fluoro-5-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	164	IIA
714		1-(4-{2-[4-(2,5-Dimethylphenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	350	IIIB
715		<i>N</i> -(4-{2-[4-(3,5-Dimethylphenyl)-piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	195	IIA
716		3-Cyano- <i>N</i> -(4-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	175	IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
717		2-Cyano- <i>N</i> -(4-{2-[4-(2,4,5-trichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	200	IIA
718		1-(4-{2-[4-(3-Fluoro-5-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	273	IIIB
719		<i>N</i> -(4-{2-[4-(3,4-Dichloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	172	IIIB
720		3-Cyano- <i>N</i> -(4-{2-[4-(3,4-dichloro-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide	210	IIIB
721		1-(4-{2-[4-(3-Fluoro-5-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	287	IIIB
722		4-(4-{2-[4-(2-Fluoro-5-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}piperidin-1-yl)-4-oxobutanonitrile, hydrochloride	150	IIIA
723		2-Cyano- <i>N</i> -(4-{2-[4-(3-fluoro-5-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)acetamide	163	IIA
724		4-Cyano- <i>N</i> -(4-{2-[4-(3-fluoro-5-trifluoromethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}cyclohexyl)butanamide	114	IIA
725		2-Cyano- <i>N</i> -(4-{2-[4-(3-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	180	IIA
726		4-Cyano- <i>N</i> -(4-{2-[4-(3-fluoro-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	150	IIA
727		1-(4-{2-[4-(2,3,4-Trichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	275	IIIB
728		1-(4-{2-[4-(4-Fluoro-3-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	258	IIIB
729		2-Cyano- <i>N</i> -(4-{2-[4-(2,3,4-trichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	217	IIA
730		1-(4-{2-[4-(Pentafluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride		IIIB
731		5-Cyano-pentanoic acid (4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-ylethyl}cyclohexyl)amide	158	IIA

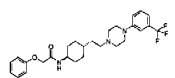
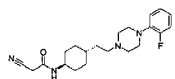
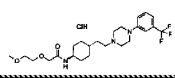
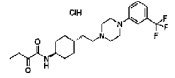
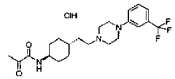
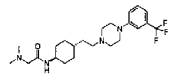
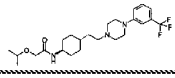
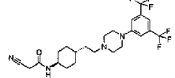
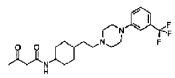
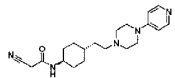
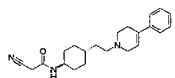
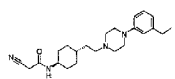
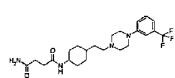
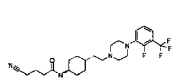
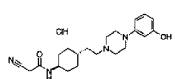
Ex	Structure	Name	M.P. (°C)	Synthetic Path
732		<i>N</i> -(4-{2-[4-(3-Chloro-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-cyanopropanamide	190	IIA
733		4-(4-{2-[4-(2,3-Dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-4-oxobutanonitrile	94	IIIA
734		2-Methoxy- <i>N</i> -(4-{2-[4-(2-methyl-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	159	IIA
735		4-Methoxy- <i>N</i> -(4-{2-[4-(2-methyl-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	173	IIA
736		4,4,4-Trifluoro- <i>N</i> -(4-{2-[4-(2-fluoro-5-trifluoromethyl-phenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	182	IIA
737		1-(4-{2-[4-(2,3-Dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	281	IIIB
738		<i>N</i> -(4-{2-[4-(3,5-Bistrifluoromethyl-phenyl)piperazin-1-yl]ethyl}cyclohexyl)malonamide	165	IIA
739		1-(4-{2-[4-(2-Ethylphenyl)-3,6-dihydro-2 <i>H</i> -pyridin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	316	IIIB
740		<i>N</i> -(4-{2-[4-(3-Chloro-5-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	177	IIA
741		<i>N</i> -(4-{2-[4-(3,5-Bistrifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	168	IIA
742		<i>N</i> -(4-{2-[4-(3-Chloro-5-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	132	IIA
743		<i>N</i> -(4-{2-[4-(3-Chloro-5-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-cyanopropanamide	148	IIA
744		1-(4-{2-[4-(2,4,5-Trifluorophenyl)-piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	68	IIIB
745		5-Cyano-pentanoic acid (4-{2-[4-(3-trifluoromethylphenyl)-piperazin-1-yl]ethyl}cyclohexyl) amide	90	IIA
746		4,4,4-Trifluoro-1-{4-[2-(4-indan-4-ylpiperazin-1-yl)ethyl]piperidin-1-yl}butan-1-one, hydrochloride	219	IIIA

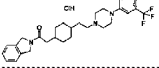
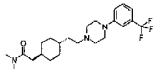
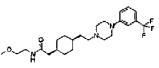
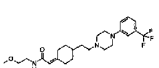
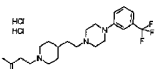
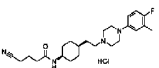
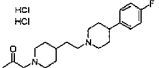
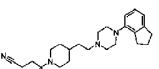
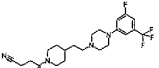
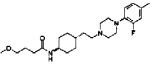
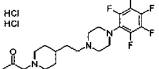
Ex	Structure	Name	M.P. (°C)	Synthetic Path
747		3,3,3-Trifluoro-1-{4-[2-(4-indan-4-yl)piperazin-1-yl]ethyl}piperidin-1-yl}propan-1-one, hydrochloride	206	IIA
748		2-Cyano-N-(4-{2-[4-(2-ethylphenyl)-3,6-dihydro-2H-pyridin-1-yl]ethyl}cyclohexyl)acetamide	158	IIA
749		4-Cyano-N-(4-{2-[4-(2-ethylphenyl)-3,6-dihydro-2H-pyridin-1-yl]ethyl}cyclohexyl)-butanamide	120	IIA
750		2-Cyano-N-(4-{2-[4-(2-o-tolyl-3,6-dihydro-2H-pyridin-1-yl]ethyl}cyclohexyl)acetamide	166	IIA
751		4-Cyano-N-(4-{2-[4-(2-o-tolyl-3,6-dihydro-2H-pyridin-1-yl]ethyl}cyclohexyl)butanamide	140	IIA
752		1-(4-[2-(4-o-Tolyl-3,6-dihydro-2H-pyridin-1-yl)ethyl]piperidin-1-yl}propan-2-one, dihydrochloride	292	IIIB
753		2-Cyano-N-(4-{2-[4-(pentafluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide	202	IIA
754		N-(4-{2-[4-(4-Fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	177	IIA
755		N-(4-{2-[4-(4-Chloro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	171	IIA
756		N-(4-{2-[4-(4-Chloro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamide	126	IIA
757		N-(4-{2-[4-(3-Fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	177	IIA
758		1-(4-[2-[4-(2-Isobutylphenyl)piperazin-1-yl]ethyl]piperidin-1-yl)propan-2-one, dihydrochloride	285	IIIB
759		1-(4-[2-[4-(3-Isobutylphenyl)piperazin-1-yl]ethyl]piperidin-1-yl)propan-2-one, dihydrochloride	240	IIIB
760		N-(4-{2-[4-(4-Fluoro-3-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	146	IIA
761		N-(4-{2-[4-(2,4-Dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	171	IIA
762		4-Cyano-N-(4-{2-[4-(2,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	162	IIA

Ex	Structure	Name	M.P. (°C)	Synthetic Path
763		2-Cyano-cyclopropanecarboxylic acid (4-{2-[4-(2-fluoro-5-trifluoromethylphenyl)piperazin-1-yl]ethyl}cyclohexyl) amide	196	IIA
764		4-Cyano-N-(4-{2-[4-(2,4,5-trichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	179	IIA
765		4-Cyano-N-(4-{2-[4-(2,3,4-trichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide	176	IIA
766		N-(4-{2-[4-(4-Fluorophenyl)-3,6-dihydro-2H-pyridin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide	201	IIA
767		1-(4-{2-[4-(2-Methylsulfanyphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	280	IIIB
768		N-(4-{2-[4-(3-Cyanophenyl)-3,6-dihydro-2H-pyridin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamide	117	IIA
769		N-(4-{2-[4-(3-Cyanophenyl)-3,6-dihydro-2H-pyridin-1-yl]ethyl}cyclohexyl)-4,4,4-trifluorobutanamide	177	IIA
770		2-Chloro-6-(4-{2-[1-(2-oxopropyl)piperidin-4-yl]ethyl}piperazin-1-yl)benzonitrile, dihydrochloride	284	IIIB
783		1-(4-{2-[4-(4,5-Dichloro-2-fluorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one	309 (dec)	IIIB
784		1-(4-{2-[4-(3-Chloro-2-methylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one, dihydrochloride	320- 325	IIIB

[0324] Further characterisation by ^1H NMR of some representative examples is given in the following table:

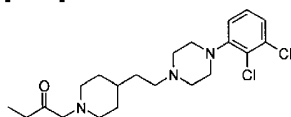
Ex	Structure	^1H NMR
13		7.3 (t, 1H, J = 7.5) ; 7.15 to 7.0 (ms, 3H) ; 3.35 (s, 2H) ; 3.25 (m, 4H) ; 2.9 (m, 2H) ; 2.6 (m, 4H) ; 2.45 (m, 2H) ; 2.0 (m, 2H) ; 1.8 to 1.55 (ms, 2H) ; 1.55 to 1.2 (ms, 5H) ; 1.15 (s, 9H)
37		7.45 to 7.25 (ms, 6H) ; 7.2 to 7.0 (ms, 3H) ; 5.1 (s, 2H) ; 4.6 (broad d, 1H) ; 3.45 (m, 1H) ; 3.25 (m, 4H) ; 2.6 (m, 4H) ; 2.4 (m, 2H) ; 2.05 (m, 2H) ; 1.8 (m, 2H) ; 1.7 to 1.0 (ms, 7H)
46		7.5 (t, 1H, J = 7.5) ; 7.4 to 7.25 (ms, 3H) ; 4.05 (s, 2H) ; 4.0 to 3.8 (ms, 2H) ; 3.8 to 3.5 (ms, 3H) ; 3.35 to 3.05 (ms, 6H) ; 1.95 to 1.5 (ms, 7H) ; 1.5 to 1.0 (ms, 4H) (D ₂ O)
59		7.7 to 7.35 (ms, 4H) ; 6.35 (broad d, 1H) ; 6.15 (s, 1H) ; 3.9 (s, 2H) ; 3.8 (m, 1H) ; 3.4 (s, 3H) ; 3.2 (m, 2H) ; 2.7 (m, 2H) ; 2.6 (m, 2H) ; 2.5 (m, 2H) ; 2.0 (m, 2H) ; 1.8 (m, 2H) ; 1.75 to 1.4 (ms, 2H) ; 1.4 to 1.0 (ms, 5H)

Ex	Structure	¹ H NMR
62		7.45 to 7.25 (ms, 4H); 7.2 to 7.0 (ms, 3H); 7.0 to 6.85 (ms, 2H); 6.4 (broad d, 1H); 4.45 (s, 2H); 3.85 (m, 1H); 3.3 (m, 4H); 2.65 (m, 4H); 2.45 (m, 2H); 2.0 (m, 2H); 1.9 to 1.4 (ms, 4H); 1.4 to 1.0 (ms, 5H)
79		7.15 to 6.85 (ms, 4H); 5.85 (broad d, 1H); 3.75 (m, 1H); 3.4 (s, 2H); 3.15 (m, 4H); 2.65 (m, 4H); 2.45 (m, 2H); 2.0 (m, 2H); 1.85 (m, 2H); 1.8 to 1.4 (ms, 3H); 1.4 to 1.0 (ms, 4H)
85		11.2 (broad s, 1H); 7.55 to 7.35 (ms, 2H); 7.3 (d, 1H, J = 5); 7.25 (s, 1H); 7.15 (d, 1H, J = 5); 4.0 to 3.7 (ms, 5H); 3.7 to 3.4 (ms, 4H); 3.4 to 2.95 (ms, 9H); 1.85 to 1.85 (ms, 13) (DMSO D ₆)
94		10.8 (broad s, 1H); 8.4 (d, 1H, J = 7.5); 7.35 to 7.2 (ms, 2H); 7.15 (d, 1H, J = 7.5); 3.9 (m, 2H); 3.5 (m, 2H); 3.4 to 3.05 (ms, 7H); 2.9 (q, 2H, J = 7.5); 1.85 to 1.55 (ms, 5H); 1.55 to 1.15 (ms, 4H); 1.15 to 1.85 (ms, 5H) (DMSO D ₆)
95		11.05 (broad s, 1 H); 8.35 (d, 1 H, J = 7.5); 7.4 (t, 1H, J = 7.5); 7.35 to 7.2 (ms, 2H); 7.1 (d, 1 H, J = 7.5); 3.9 (m, 2H); 3.75 to 3.4 (ms, 3H); 3.4 to 2.9 (ms, 6H); 2.3 (s, 3H); 1.9 to 1.15 (ms, 9H); 1.15 to 0.85 (ms, 2H) (DMSO D ₆)
96		7.35 (t, 1H, J = 7.5); 7.15 to 7.0 (ms, 3H); 6.95 (broad d, 1H); 3.75 (m, 1H); 3.25 (m, 4H); 2.9 (s, 2H); 2.65 (m, 4H); 2.45 (m, 2H); 2.25 (s, 6H); 2.0 (m, 2H); 1.8 (m, 2H); 1.5 (m, 2H); 1.4 to 1.0 (ms, 5H)
100		7.35 (t, 1H, J = 7.5); 7.2 to 7.0 (ms, 3H); 6.4 (broad d, 1H); 3.9 (s, 2H); 3.8 (m, 1H); 3.65 (m, 1H); 3.25 (m, 4H); 2.6 (m, 4H); 2.45 (m, 2H); 2.05 (m, 2H); 1.85 (m, 2H); 1.7 (m, 1H); 1.5 (m, 2H); 1.4 to 1.0 (ms, 10H)
107		7.35 to 7.2 (ms, 2H); 5.85 (broad d, 1H); 3.75 (m, 1H); 3.4 (s, 2H); 3.3 (m, 4H); 2.6 (m, 4H); 2.45 (m, 2H); 2.05 (m, 2H); 1.85 (m, 2H); 1.6 (m, 1H); 1.5 (m, 2H); 1.4 to 1.0 (ms, 4H)
109		7.35 (t, 1H, J = 7.5); 7.2 to 7.0 (ms, 3H); 6.75 (broad d, 1H); 3.7 (m, 1H); 3.4 (s, 2H); 3.25 (m, 4H); 2.6 (m, 4H); 2.45 (m, 2H); 2.3 (s, 3H); 2.05 (m, 2H); 1.85 (m, 2H); 1.75 to 1.4 (ms, 3H); 1.4 to 1.0 (ms, 4H)
120		8.25 (d, 2H, J = 7.5); 6.65 (d, 2H, J = 7.5); 6.45 (broad s, 1H); 4.0 (0.35H equatorial); 3.7 (0.65H axial); 3.35 to 3.25 (ms, 6H); 2.55 (m, 4H); 2.4 (m, 2H); 2.3 (1.7H); 2.0 (m, 1.4H); 1.8 (m, 1.4H); 1.75 to 0.9 (ms, 7.5H)
141		7.5 to 7.15 (ms, 5H); 6.1 (m, 1H); 5.85 (broad d, 1 H); 3.75 (m, 1 H); 3.35 (s, 2H); 3.2 (m, 2H); 2.7 (m, 2H); 2.6 (m, 2H); 2.5 (m, 2H); 2.05 (m, 2H); 1.9 (m, 2H); 1.5 (m, 2H); 1.4 to 1.0 (ms, 5H)
149		7.25 (t, 1 H, J = 7.5); 6.85 to 6.65 (ms, 3H); 5.85 (broad d, 1 H); 3.75 (m, 1 H); 3.35 (s, 2H); 3.2 (m, 4H); 2.7 to 2.5 (ms, 6H); 2.4 (m, 2H); 2.05 (m, 2H); 1.85 (m, 2H); 1.45 (m, 2H); 1.4 to 1.0 (ms, 7H)
154		7.35 (t, 1H, J = 7.5); 7.2 to 7.0 (ms, 3H); 6.05 (broad s, 1H); 5.65 (broad d, 1H); 5.35 (broad s, 1H); 4.0 (m, 0.35H equatorial); 3.7 (m, 0.65H axial); 3.25 (m, 4H); 2.7 to 2.45 (ms, 8H); 2.4 (m, 2H); 2.0 (m, 2H); 1.8 (m, 2H); 1.55 (m, 1 H); 2.5 (m, 2H); 2.4 to 1.0 (ms, 4H)
172		7.25 to 7.05 (ms, 3H); 5.3 (broad d, 1H); 3.7 (m, 1H); 3.15 (m, 4H); 2.65 (m, 4H); 2.55 to 2.4 (ms, 4H); 2.3 (t, 2H, J = 7.5); 2.0 (m, 4H); 1.8 (m, 2H); 1.45 (m, 2H); 1.4 to 1.0 (ms, 5H)
175		10.4 (broad s, 1H); 8.2 (d, 1H, J = 7.5); 7.0 (t, 1H, J = 7.5); 6.4 (d, 1H, J = 7.5); 6.35 (s, 1H); 6.25 (d, 1H, J = 7.5); 3.7 (m, 2H); 3.65 (s, 2H); 3.6 to 3.3 (ms, 3H); 3.2 to 2.9 (ms, 6H); 1.9 to 1.5 (ms, 6H); 1.4 to 0.9 (ms, 5H) (DMSO D ₆)

Ex	Structure	¹ H NMR
290		10.3 (broad s, 1H); 7.4 (t, 1H, J = 7.5); 7.4 to 7.0 (ms, 7H); 4.8 (s, 2H); 4.6 (s, 2H); 3.9 (m, 2H); 3.5 (m, 2H); 3.3 to 2.8 (ms, 7H); 2.3 (d, 0.8H, J = 7.5); 2.2 (d, 1.2H, J = 7.5); 1.9 to 0.8 (ms, 11H) trans/cis 60/40 (DMSO D ₆)
293		7.35 (t, 1H, J = 7.5); 7.2 to 7.0 (m, 3H); 3.25 (m, 4H); 3.2 (s, 3H); 2.95 (s, 3H); 2.45 (m, 4H); 2.2 (t, 2H, J = 7.5); 2.2 (d, 2H, J = 7.5); 1.9 to 1.6 (ms, 4H); 1.6 to 1.15 (ms, 5H); 1.15 to 0.75 (ms, 3H)
296		7.35 (t, 1H, J = 7.5); 7.15 to 7.0 (ms, 3H); 5.8 (broad t, 1H); 3.45 (m, 4H); 3.35 (s, 3H); 3.25 (m, 4H); 2.6 (m, 4H); 2.41 (t, 2H, J = 7.5); 2.05 (d, 2H, J = 7.5); 1.9 to 1.7 (ms, 5H); 1.6 to 1.1 (ms, 4H); 1.1 to 0.8 (ms, 3H)
297		7.35 (t, 1H); 7.15 to 7.0 (ms, 3H); 5.75 (broad t, 1H); 5.25 (s, 1H); 3.75 (m, 1H); 3.45 (m, 4H); 3.35 (s, 3H); 3.25 (m, 4H); 3.6 (m, 4H); 2.45 (t, 2H, J = 7.5); 2.3 to 1.85 (ms, 5H); 1.6 to 1.4 (ms, 2H); 1.3 to 1.0 (ms, 3H)
352		7.5 (t, 1H, J = 7.5); 7.4 to 7.2 (ms, 3H); 4.75 (2H); 3.9 (m, 2H); 3.7 (m, 2H); 3.55 (m, 2H); 3.45 to 3.05 (ms, 10H); 2.95 (m, 2H); 2.2 (s, 3H); 2.0 (m, 2H); 1.9 to 1.6 (3H); 1.5 (m, 2H) (D ₂ O)
367		13.4 (broad s, 1H); 7.75 to 7.5 (ms, 2H); 7.1 (t, 1H, J = 7.5); 5.85 (d, 1H); 4.55 (m, 2H); 4.3 to 3.95 (ms, 3H); 3.7 (m, 4H); 3.15 (m, 2H); 2.6 to 2.15 (ms, 7H); 2.1 to 1.05 (ms, 13H)
634		7.35 to 7.2 (ms, 2H); 7.05 (t, 1H, J = 7.5); 4.85 (s, 2H); 4.25 (s, 2H); 3.65 (m, 2H); 3.5 (m, 2H); 3.35 to 2.85 (ms, 7H); 2.2 (s, 3H); 2.15 to 1.9 (ms, 6H); 1.9 to 1.5 (ms, 5H)
649		7.15 (t, 1H, J = 7.5); 6.95 (d, 1H, J = 7.5); 6.75 (d, 1H, J = 7.5); 4.6 (m, 1H); 3.75 (m, 1H); 3.25 to 3.0 (ms, 5H); 2.9 (t, 2H, J = 7.5); 2.85 (t, 2H, J = 7.5); 2.8 to 2.5 (ms, 7H); 2.45 (m, 2H); 2.05 (m, 2H); 1.8 (m, 2H); 1.7 to 1.45 (ms, 5H); 2.15 (m, 2H)
693		6.9 (s, s, 1H); 6.8 to 6.6 (m; 2H); 4.6 (m, 1H); 3.8 (m, 1H); 3.25 (m, 4H); 3.05 (m, 2H); 2.75 to 2.65 (ms, 3H); 2.5 to 2.35 (ms, 5H); 2.45 (m, 2H); 1.8 (m, 2H); 1.7 to 1.4 (ms, 3H); 1.2 (m, 2H)
707		6.9 to 6.75 (ms, 3H); 5.45 (d, 1H, J = 7.5); 3.75 (m, 1H); 3.45 (t, 1H, J = 7.5); 3.4 (s, 3H); 3.1 (m, 4H); 2.65 (m, 4H); 2.45 (m, 2H); 2.3 (s, 3H); 2.25 (t, 2H, J = 7.5); 2.1 to 1.7 (ms, 6H); 1.45 (m, 2H); 1.35 to 1.0 (ms, 5H)
730		4.75 (s, 2H); 4.2 (s, 2H); 3.65 to 3.1 (ms, 12H); 3.0 (m, 2H); 2.2 (s, 3H); 2.0 (m, 2H); 1.85 to 1.4 (ms, 5H) (D ₂ O)

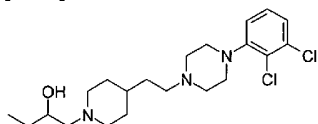
Example 771: 1-(4-{2-[4-(2,3-dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-one

[0325]



Step a: 1-(4-{2-[4-(2,3-dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-ol

[0326]



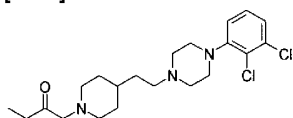
[0327] A suspension of 0.41 g (1 mmol) of 1-(2,3-dichlorophenyl)-4-(2-piperidin-4-ylethyl)piperazine, dihydrochloride in 25 mL of isopropanol and 0.29 g (2.1 mmol) of potassium carbonate is stirred for 30 minutes then 0.08 g (1.1 mmol) of 2-ethyloxirane is added. The suspension is stirred to reflux overnight. The precipitate is filtered and the solution is concentrated under reduced pressure. The residue is dissolved in ethyl acetate, washed with water and with brine, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue is purified over 10 g of silica gel (dichloromethane/methanol 90/10) to give 0.2 g (50%) of 1-(4-{2-[4-(2,3-dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-ol as an oil that crystallizes upon standing.

Melting point: 94°C

¹H NMR: 7.2 to 7.05 (ms, 2H) ; 7.0 to 6.9 (m, 1 H) ; 3.7 (m, 1 H) ; 3.1 (m, 6H) ; 2.9 (m, 2H) ; 2.65 (m, 4H) ; 2.55 to 2.2 (ms, 4H) ; 2.05 (m, 1 H) ; 1.7 (m, 2H) ; 1.65 to 1.25 (ms, 7H) ; 1.0 (t, 3H, J = 7.5)

Step b: 1-(4-{2-[4-(2,3-dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-one

[0328]



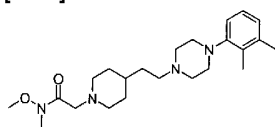
[0329] The 1-(4-{2-[4-(2,3-dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-one is obtained by Swern oxydation of 1-(4-{2-[4-(2,3-dichlorophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-ol according to the procedure described in example 7.

Melting point: 68°C

¹H NMR: 7.2 to 7.1 (m, 2H) ; 6.95 (m, 1H) ; 3.2 (s, 2H) ; 3.15 (m, 4H) ; 2.85 (m, 2H) ; 2.7 (m, 4H) ; 2.6 to 2.4 (ms, 4H) ; 2.05 (m, 2H) ; 1.7 (m, 2H) ; 1.65 to 1.2 (ms, 5H) ; 1.1 (t, 3H, J = 7.5)

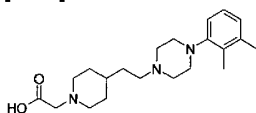
Example 772: 2-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-N-methoxy-N-methylacetamide

[0330]

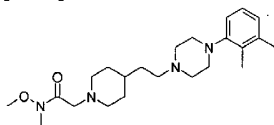


Step a: (4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)acetic acid

[0331]



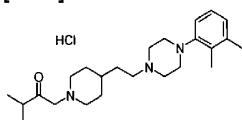
[0332] The (4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)acetic acid is prepared from (4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)acetic acid ethyl ester using the procedure described in preparation F, step 1.

Step b: 2-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-*N*-methoxy-*N*-methylacetamide**[0333]**

[0334] The 2-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-*N*-methoxy-*N*-methylacetamide is prepared from 4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)acetic acid using the procedure described in preparation F, step 2.

Melting point: 66°C

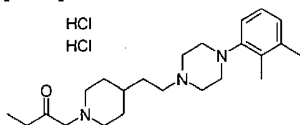
¹H NMR: 7.1 (t, 1H, J = 7.5) ; 7.0 to 6.85 (ms, 2H) ; 3.7 (s, 3H) ; 3.35 (s, 2H) ; 3.3 to 2.6 (ms, 17H) ; 2.4 to 2.15 (ms, 8H) ; 1.9 to 1.65 (ms, 3H), 1.65 to 1.35 (ms, 2H)

Example 773: 1-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-3-methylbutan-2-one, hydrochloride**[0335]**

[0336] The 1-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-3-methyl-butan-2-one, hydrochloride is prepared by addition of a solution of isopropylmagnesium bromide on 2-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-*N*-methoxy-*N*-methylacetamide using the procedure described in preparation F, step 3.

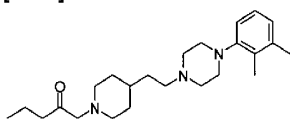
Melting point: 182°C

¹H NMR: 7.1 (t, 1H, J = 7.5) ; 7.0 to 6.85 (ms, 2H) ; 6.4 (broad s, 1H) ; 3.0 to 2.7 (ms, 8H) ; 2.7 to 2.5 (ms, 4H) ; 2.45 (m, 2H) ; 2.3 (s, 3H) ; 2.25 (s, 3H) ; 2.2 to 2.0 (ms, 3H) ; 1.7 (m, 2H) ; 1.5 (m, 2H) ; 1.4 to 1.1 (ms, 3H) ; 1.0 (d, 3H) ; 0.85 (d, 3H, J = 7.5)

Example 774: 1-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-one, dihydrochloride**[0337]**

[0338] The 1-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butan-2-one, dihydrochloride is prepared by addition of a solution of ethylmagnesium bromide on 2-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-*N*-methoxy-*N*-methylacetamide using the procedure described in preparation F, step 3.

Melting point: 315°C

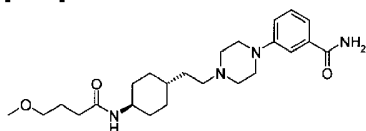
Example 775: 1-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)pentan-2-one**[0339]**

[0340] The 1-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl) pentan-2-one is prepared by addition of a solution of propylmagnesium bromide on 2-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)-*N*-methoxy-*N*-methylacetamide using the procedure described in preparation F, step 3.

Melting point: 47°C

Example 776: 3-(4-{2-[4-(4-methoxybutanoylamino)cyclohexyl]ethyl}piperazin-1-yl)benzamide

[0341]



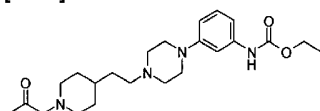
[0342] A mixture of 85 mg (0.2 mmol) of *N*-(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamide, 2 mL of dimethyl sulfoxide, 16.5 mg of potassium carbonate and 0.12 mL of an aqueous 30% hydrogen peroxide solution is stirred for 2 hours at room temperature. The suspension is poured into 50 mL of water. The solid is filtered, washed with water, dried under reduced pressure to give 15 mg (17%) of 3-(4-{2-[4-(4-methoxybutanoylamino)cyclohexyl]ethyl}piperazin-1-yl)benzamide as a white solid.

Melting point: 202°C

¹H NMR (DMSO D₆): 7.85 (s, 1H) ; 7.6 (d, 1H, J = 7.5) ; 7.35 (s, 1H) ; 7.3 to 7.15 (ms, 3H) ; 7.05 (m, 1H) ; 3.4 (m, 1H) ; 3.25 (t, 2H, J = 7.5) ; 3.2 (s, 3H) ; 3.15 (m, 4H) ; 2.45 (m, 4H) ; 2.3 (m, 2H) ; 2.05 (m, 2H) ; 1.8 to 1.55 (ms, 6H) ; 1.35 (m, 2H) ; 1.25 to 0.8 (ms, 5H)

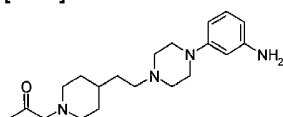
Example 777: [3-(4-{2-[1-(2-oxopropyl)piperidin-4-yl]ethyl}piperazin-1-yl)phenyl]carbamic acid ethyl ester

[0343]



Step a: 1-(4-{2-[4-(3-aminophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one

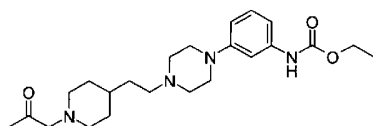
[0344]



[0345] The 1-(4-{2-[4-(3-aminophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one is prepared from 1-(4-{2-[4-(3-nitrophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one using the procedure described in preparation D, step 2 to give the title compound in 49% crude yield, used without further purification.

Step b: [3-(4-{2-[1-(2-oxopropyl)piperidin-4-yl]ethyl}piperazin-1-yl)phenyl]carbamic acid ethyl ester

[0346]



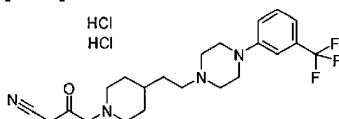
[0347] To a cooled solution of 0.1 g (0.3 mmol) of 1-(4-{2-[4-(3-aminophenyl)piperazin-1-yl]ethyl}piperidin-1-yl)propan-2-one in 5 mL of dichloromethane and 0.03 g (0.3 mmol) of triethylamine, is slowly added 0.032 g (0.3 mmol) of ethyl chloroformate. The mixture is stirred overnight at room temperature then concentrated under reduced pressure. The product is dissolved in ethyl acetate, washed twice with water, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The oily residue is purified over 10 g of silica gel (eluant dichloromethane/methanol 95/5) to give 0.025 g (20%) of [3-(4-{2-[1-(2-oxopropyl)piperidin-4-yl]ethyl}piperazin-1-yl)phenyl]carbamic acid ethyl ester as a solid.

Melting point: 118°C

¹H NMR: 7.25 to 7.1 (ms, 2H) ; 6.75 (d, 1 H, J = 7.5) ; 6.65 (d, 1 H, J = 7.5) ; 6.55 (s, 1 H) ; 4.25 (q, 2H, J = 7.5) ; 3.25 (m, 4H) ; 3.15 (s, 2H) ; 2.85 (m, 2H) ; 2.6 (m, 4H) ; 2.45 (m, 2H) ; 2.2 (s, 3H) ; 2.05 (m, 2H) ; 1.8 to 1.2 (ms, 10H)

Example 778: **3-oxo-4-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butanenitrile, dihydrochloride**

[0348]



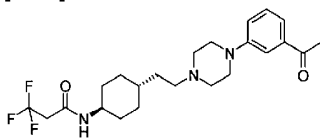
[0349] A solution of 0.77 mL (1.3 mmol) of potassium *tert*-pentyxide solution (1.7M in toluene) is added dropwise at room temperature to a stirred solution of 52 mg (1.27 mmol) of acetonitrile in 2.5 mL of tetrahydrofuran followed by dropwise addition of 0.19 g (0.44 mmol) of (4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)acetic acid ethyl ester in 1 mL of tetrahydrofuran. After 30 minutes at room temperature, the reaction mixture is diluted with 10 mL of an aqueous 0.2N aqueous hydrochloric acid solution and 50 mL of ethyl acetate forming an emulsion. The mixture is concentrated under reduced pressure and the product is purified over 10 g of silica gel (eluant dichloromethane/methanol 95/5). The oily product is dissolved in 2 mL of diethyl ether and acidified with a hydrochloric acid diethyl ether solution. The precipitate is filtered, washed with diethyl ether and dried under reduced pressure to give 30 mg (14%) of 3-oxo-4-(4-{2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethyl}piperidin-1-yl)butanenitrile, dihydrochloride.

Melting point: 160°C

¹H NMR (DMSO D₆): 11.2 (broad s, 1 H) ; 10.2 (broad s, 1 H) ; 7.45 (t, 1 H, J = 7.5) ; 7.3 (d, 1 H, J = 7.5) ; 7.25 (s, 1 H) ; 7.1 (d, 1 H, J = 7.5) ; 4.35 (s, 2H) ; 4.2 (s, 2H) ; 3.95 (m, 2H) ; 2.55 (m, 2H) ; 2.45 to 2.9 (ms, 10H) ; 2.0 to 2.45 (ms, 7H)

Example 779: **N-(4-{2-[4-(3-acetylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamide**

[0350]

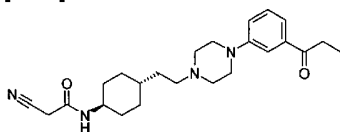


[0351] The *N*-(4-{2-[4-(3-acetylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoro-propanamide is prepared by oxidation of 3,3,3-trifluoro-*N*-(4-{2-[4-(3-(1-hydroxyethyl)phenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamide (example 477) using the procedure described in example 7 to give the title compound.

Melting point 165°C.

Example 780: **2-cyano-N-(4-{2-[4-(3-propanoylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide**

[0352]

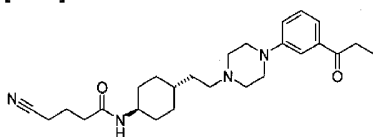


[0353] The 2-cyano-*N*-(4-{2-[4-(3-propanoylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-acetamide is prepared by oxidation of 2-cyano-*N*-(4-{2-[4-(3-(1-hydroxypropyl)-phenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide (example 566) using the procedure described in example 7 to give the title compound.

Melting point 178°C.

Example 781: 4-cyano-*N*-(4-{2-[4-(3-propanoylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide

[0354]

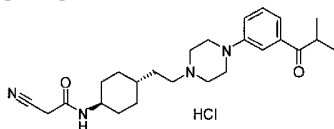


[0355] The 4-cyano-*N*-(4-{2-[4-(3-propanoylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-butanamide is prepared by oxidation of 4-cyano-*N*-(4-{2-[4-(3-(1-hydroxy-propyl)phenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamide (example 540) using the procedure described in example 7 to give the title compound.

Melting point 158°C.

Example 782: 2-cyano-*N*-(4-{2-[4-(3-isobutanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide, dihydrochloride

[0356]



[0357] The 2-cyano-*N*-(4-{2-[4-(3-isobutanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-acetamide, dihydrochloride is prepared by oxidation of 2-cyano-*N*-(4-{2-[4-(3-(1-hydroxy-2-methylpropyl)phenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamide (example 575) using the procedure described in example 7 to give the title compound.

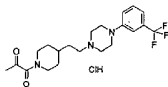
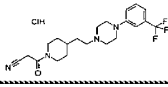
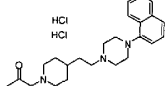
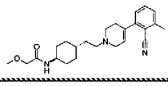
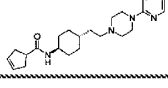
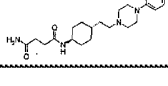
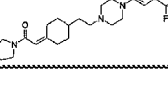
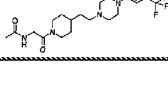
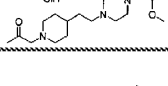
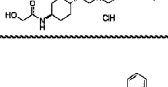
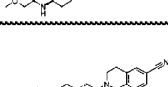
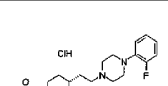
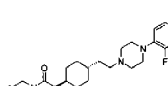
Melting point 185°C.

Affinity of compounds for the human D₃ receptor can be determined by [³H] spiperone binding

[0358] CHO cells have been transfected by the cDNA coding for the human D₃ receptor (hD₃). [³H]Spiperone (0,5 à 2 nM) binding is performed in the presence of 2.5 to 5 µg of membrane proteins in a medium containing 120 mM NaCl, 5 mM KCl, and 50 mM Tris HCl pH 7.4; incubation for 60 minutes at room temperature is performed. Non specific binding is estimated in the presence of 10 µM haloperidol. Non transfected cells are devoid of any specific binding.

[0359] Exemplified compounds all display an inhibitory constant below 1 µM, most of them are below 50 nM.

[0360] Affinities for the human D₃ receptor of some representative examples are given in the following table:

Ex	Structure	Ki (nM)
2		6.6
15		15.1
36		1.32
54		18.3
65		31.6
187		3.9
291		4.4
14		15.1
20		9.5
46		12.0
61		8.5
110		10.6
288		2.1
308		3.5

REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

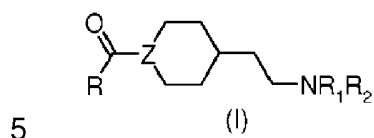
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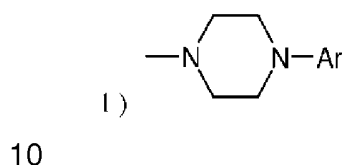
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Patentkrav

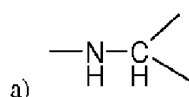
1. Forbindelser med formelen (I):



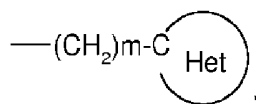
hvor NR_1R_2 er



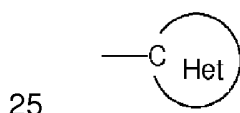
Z er



15 R betegner cyanoalkyl ; monohalogenocyanoalkyl ; polyhalogenocyanoalkyl ;
hydroxyalkyl ; monohalogenoalkyl (hvor halogen er Cl, Br eller I) ; polyhalo-
genoalkyl ; alkoxyalkyl ; monohalogeno-alkoxyalkyl ; polyhalogenoalkoxyal-
kyl; alkoxyalkoxyalkyl ; monohalogeno-alkoxyalkoxyalkyl ; polyhalogeno-
alkoxyalkoxyalkyl ; aryloxyalkyl ; mono- eller polyhalogenoaryloxyalkyl ; cy-
cloalkenylalkyl ; dialkylaminoalkyl ; halodialkylaminoalkyl ; polyhalogenodial-
20 kylaminoalkyl ;



hvor



er en ikke-aromatisk heterocyklus, der eventuelt er kondenseret med aryl
eller eventuelt er substitueret med en eller flere acyl, alkyl eller halogen ; aryl-

aminoalkyl; alkylcarbonylalkyl ; acylaminoalkyl ; aminocarbonylalkyl ; alkylsulfanylalkyl ; alkylsulfinylalkyl ; alkylsulfonylalkyl ;

m er 2 eller 4;

- Ar betegner en aryl; en heteroaryl eller en aryl kondenseret med en cycloalkyl eller en heterocyclus; Ar er eventuelt substitueret med en eller flere alkyl; alkenyl; alkynyl; cyano; halogeno; alkoxy; monohalogenoalkoxy; polyhalogenoalkoxy; alkoxyalkyl; dialkylamino; ikke-aromatisk heterocyclyl bundet af en nitrogen; alkylsulfanyl; alkylsulfinyl; alkylsulfonyl; monohalogenoalkylsulfanyl; monohalogenoalkylsulfinyl; monohalogenoalkylsulfonyl; polyhalogenoalkylsulfanyl; polyhalogenoalkylsulfinyl; polyhalogenoalkylsulfonyl; heteroaryl; aryl; aralkyl; aryloxy; alkoxy-carbonylamino; acyl; acylamino; aminocarbonyl; monoalkylaminocarbonyl; dialkylaminocarbonyl; alkylsulfonylamino; monohalogenoalkyl; polyhalogenoalkyl; hydroxyl; hydroxyalkyl; oxoalkyl; eller deres farmaceutisk acceptable salte, hydrater eller hydrerede salte, eller de polymorfe, krystallinske strukturer af disse forbindelser eller deres optiske isomerer, racemater, diastomerer eller enantiomerer;

hvor :

"Alkyl" betyder en alifatisk hydrocarbongruppe, som kan være lige eller forgrenet, med 1 til 12 carbonatomer i kæden;

- "Alkenyl" betyder en alifatisk hydrocarbongruppe indeholdende en carbon-carbon dobbeltbinding, og som kan være lige eller forgrenet, med 2 til 4 carbonatomer i kæden;

- "Alkynyl" betyder en alifatisk hydrocarbongruppe indeholdende en carbon-carbon tredobbelt binding, og som kan være lige eller forgrenet, med 2 til 4 carbonatomer i kæden;

"Aryl" betyder et aromatisk monocyklisk eller multicyklisk hydrocarbon-ringsystem med 6 til 10 carbonatomer;

"Cycloalkyl" betyder et ikke-aromatisk mono- eller multicyklisk hydrocarbon-ringsystem med 5 til 6 carbonatomer;

- "Cycloalkenyl" betyder et ikke-aromatisk mono- eller multicyklisk ringsystem med ca. 5 til ca. 10 carbonatomer, og som indeholder mindst en carbon-carbon dobbeltbinding;

"Heteroaryl" eller aromatiske heterocyclusser henviser til en 5- til 10-leddet aromatisk hetero-, mono-, bi- eller multicyklisk ring;

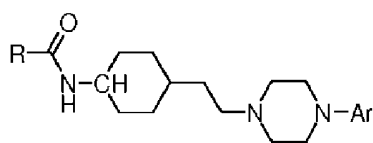
"Heterocyklus" eller "Heterocyklisk" henviser til mættede, delvist umættede eller umættede, ikke-aromatiske stabile 5- til 10-leddede mono-, bi- eller multicykliske ringe, hvor mindst et led af ringen er et heteroatom.

- 5 **2.** Forbindelser ifølge krav 1, hvor R er cyanoalkyl; polyhalogenocyanoalkyl; hydroxyalkyl; polyhalogenoalkyl; alkoxyalkyl; alkoxyalkoxyalkyl; aryloxyalkyl; mono- eller polyhalogenoaryloxyalkyl; ikke-aromatisk heterocyclyl(CH₂)_m, hvor den ikke-aromatiske heterocyklus er eventuelt kondenseret med aryl eller eventuelt substitueret med en eller flere acyl, alkyl eller halogen; alkyl-
10 carbonylalkyl; acylaminoalkyl; aminocarbonylalkyl; alkylsulfanylalkyl; alkylsulfonylalkyl;
m er 2 eller 4.

- 15 **3.** Forbindelser ifølge et af kravene 1 til 2, hvor Ar betegner en aryl.

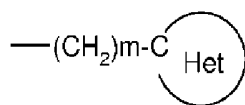
- 4.** Forbindelser ifølge et af kravene 1 til 3, hvor Ar er substitueret med en eller flere alkyl, cyano, halogeno, alkoxy, polyhalogenoalkoxy, alcandiyl, dialkylamino, alkylsulfanyl, aryl, aralkyl, aryloxy, alkoxycarbonylamino, acyl, alkylsulfonylamino, polyhalogenoalkyl, hydroxy, hydroxyalkyl, oxoalkyl.

- 20 **5.** Forbindelser ifølge et af kravene 1 to 4, hvor forbindelserne er dem med formel (A):

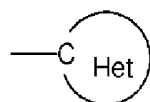


(A)

- 25 hvor
R er valgt blandt cyanoalkyl; monohalogenoalkyl (hvor halogeno er Cl, Br eller I) ; polyhalogenoalkyl; alkoxyalkyl; monohalogenoalkoxyalkyl ; polyhalogenoalkoxyalkyl; alkoxyalkoxyalkyl; monohalogenoalkoxyalkoxyalkyl; polyhalogenoalkoxyalkoxyalkyl; monohalogenocyanoalkyl; polyhalogenocyanoalkyl;
30 aryloxyalkyl; cycloalkenylalkyl; dialkylaminoalkyl; hydroxyalkyl; polyhalogeno-dialkylaminoalkyl;



hvor



5

er en ikke-aromatisk heterocyklus eventuelt kondenseret med aryl eller eventuelt substitueret med en eller flere acyl, alkyl eller halogen; arylaminoalkyl; alkylcarbonylalkyl; acylaminoalkyl; aminocarbonylalkyl; alkylsulfanylalkyl; alkylsulfinylalkyl; alkylsulfonylalkyl; mono- eller polyhalogenoaryloxyalkyl;

10 m er 2 eller 4,

Ar betegner en aryl; en heteroaryl eller en aryl kondenseret med en cycloalkyl eller en heterocyklus; Ar er eventuelt substitueret med en eller flere alkyl; alkenyl; alkynyl; cyano; halogeno; alkoxy; monohalogenoalkoxy; polyhalogenoalkoxy; alkoxyalkyl; dialkylamino; ikke-aromatisk heterocyclyl bundet af en nitrogen; alkylsulfanyl; alkylsulfinyl; alkylsulfonyl; monohalogenoalkylsulfanyl; monohalogenoalkylsulfinyl; monohalogenoalkylsulfonyl; polyhalogenoalkylsulfanyl; polyhalogenoalkylsulfinyl; polyhalogenoalkylsulfonyl; heteroaryl; aryl; aralkyl; aryloxy; alkoxy-carbonylamino; acyl; acylamino; aminocarbonyl; monoalkylaminocarbonyl; dialkylaminocarbonyl; alkylsulfonylamino; monohalogenoalkyl; polyhalogenoalkyl; hydroxyl; hydroxyalkyl; oxoalkyl; eller deres farmaceutisk acceptable salte, hydrater eller hydrerede salte, eller de polymorfe, krystallinske strukturer af disse forbindelser eller deres optiske isomerer, racemater, diastomerer eller enantiomerer.

25 **6.** Forbindelser ifølge et af de foregående krav udvalgt blandt:

- 2-cyano-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,

30 - *N*-(4-{2-[4-(3-acetylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid,

- 2,2,2-Trifluor-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,

- 2-Methoxy-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Methoxy-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid , hydrochlorid,
- 5 - 2,2-Difluor-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Hydroxy-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid , hydrochlorid,
- 3-Methoxy-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid,
- 10 - *N*-(4-{2-[4-(2,4-Difluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid,
- *N*-(4-{2-[4-(2-Cyano-3-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid,
- 15 - *N*-(4-{2-[4-(2-Fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid,
- 2-Ethoxy-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid , hydrochlorid,
- 2-Ethoxy-*N*-(4-{2-[4-(2-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 20 - *N*-(4-{2-[4-(2-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid,
- 2-Methoxy-*N*-(4-{2-[4-(4-phenylpiperazin-1-yl)ethyl]cyclohexyl}acetamid,
- 2-Phenoxy-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 25 - 3,3,3-Trifluor-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid,
- 4-Methoxy-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
- 30 - *N*-(4-{2-[4-(2-Fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxypropanamid,
- *N*-(4-{2-[4-(2-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid,
- *N*-(4-{2-[4-(2-Fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxypropanamid,
- 35

- *N*-(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid,
- 2-Methoxy-2-methyl-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid,
- 5 - *N*-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid,
- 2-Cyano-*N*-(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Methylsulfanyl-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 10 - 2-(2-Methoxyethoxy)-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid, hydrochlorid,
- *N*-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid,
- 3,3,3-Trifluor-*N*-(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid,
- 15 - *N*-(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-phenoxyacetamid,
- 2-Cyano-*N*-(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 20 - *N*-(4-{2-[4-(2,3-Difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid,
- 2-Dimethylamino-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- *N*-(4-{2-[4-(2-Fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-isopropoxyacetamid,
- 25 - 4-Methoxy-*N*-(4-{2-[4-(4-phenylpiperazin-1-yl)ethyl]cyclohexyl})butanamid,
- 2-Isopropoxy-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- *N*-(4-{2-[4-(2-Cyano-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-isopropoxyacetamid,
- 30 - *N*-(4-{2-[4-(2-Cyano-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid,
- 2-Cyano-*N*-(4-{2-[4-(2-cyano-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,

- 2-Cyano-*N*-{4-[2-(4-phenylpiperazin-1-yl)ethyl]cyclohexyl}acetamid, hydrochlorid,
- 2-Acetylamino-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 5 - *N*-(4-{2-[4-(3,5-Bistrifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid,
- *N*-(4-{2-[4-(3,5-Bistrifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid,
- 3-Oxo-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
- 10 - 2-Cyano-*N*-(4-{2-[4-(2,6-di-*tert*-butylpyrimidin-4-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- *N*-(4-{2-[4-(2,3-Difluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid,
- 15 - 2-Cyano-*N*-(4-{2-[4-(2,3-difluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Cyano-*N*-(4-{2-[4-(2-cyano-3-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- *N*-(4-{2-[4-(2-Cyano-3-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-
- 20 trifluorpropanamid,
- 2-Cyano-*N*-(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-1-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Ethoxy-*N*-(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-1-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 25 - *N*-(4-{2-[4-(3,5-Bistrifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid,
- *N*-(4-{2-[4-(2-Cyano-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid,
- 2-Cyano-*N*-{4-[2-(4-pyridin-4-ylpiperazin-1-yl)ethyl]cyclohexyl}acetamid,
- 30 - *N*-(4-{2-[4-(2,6-Di-*tert*-butylpyrimidin-4-yl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid,
- *N*-(4-{2-[4-(2,6-Di-*tert*-butylpyrimidin-4-yl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid,
- 2-Ethoxy-*N*-(4-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 35

- 2-Cyano-*N*-(4-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Methoxy-*N*-(4-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 5 - 2-Cyano-*N*-(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid, hydrochlorid,
- 2-Acetylamino-*N*-(4-{2-[4-(4-phenylpiperazin-1-yl)ethyl]cyclohexyl}acetamid,
- *N*-(4-{2-[4-(2-Chlorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid,
- 10 - 2-Methoxy-*N*-(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-1-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- *N*-(4-{2-[4-(2-Chlorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid,
- *N*-(4-{2-[4-(2-Chlorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid,
- 15 - 2-Cyano-*N*-(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Acetylamino-*N*-(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-*tert*-Butoxy-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 20 - *N*-(4-{2-[4-(3-Chlor-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid,
- *N*-(4-{2-[4-(3-Chlor-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid,
- 2-Cyano-*N*-(4-{2-[4-(3-cyano-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 25 - *N*-(4-{2-[4-(3-Cyano-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid,
- *N*-(4-{2-[4-(3-Cyano-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid,
- 30 - *N*-(4-{2-[4-(2,3-Dichlorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid,
- 2-Cyano-*N*-(4-{2-[4-(2,3-dichlorphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- *N*-(4-{2-[4-(2,3-Dichlorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid,
- 35

- 2-Acetylamino-*N*-(4-{2-[4-(2,3-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- *N*-(4-{2-[4-(2,3-Difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)2-isopropoxyacetamid, hydrochlorid,
- 5 - 2-Cyano-*N*-(4-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Cyano-*N*-(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Cyano-*N*-(4-{2-[4-(3-dimethylaminophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 10 - 2-Cyano-*N*-(4-{2-[4-(3,5-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Cyano-*N*-(4-{2-[4-(2,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- *N*-(4-{2-[4-(3-Trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamid,
- 15 - *N*-(4-{2-[4-(5-Chlor-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid,
- *N*-(4-{2-[4-(3-Chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid,
- 2-Cyano-*N*-(4-{2-[4-(3-trifluormethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 20 - 2-Cyano-*N*-(4-{2-[4-(2-fluor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Cyano-*N*-(4-{2-[4-(3,5-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 25 - 2-Cyano-*N*-(4-{2-[4-(3-methoxy-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 4-Cyano-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
- 2-Cyano-*N*-(4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 30 - 2-Cyano-*N*-(4-{2-[4-(3-isopropoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid , hydrochlorid,
- 2-Cyano-*N*-(4-{2-[4-(3-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid , hydrochlorid,

- 2-Cyano-*N*-(4-{2-[4-(2-methoxy-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Cyano-*N*-(4-{2-[4-(4-m-tolylpiperazin-1-yl)ethyl]cyclohexyl}acetamid,
- 3-Diethylamino-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-
- 5 yl]ethyl}cyclohexyl)propanamid,
- 3-Cyano-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid, hydrochlorid,
- *N*-(4-{2-[4-(3-*tert*-Butylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-
- cyanoacetamid,
- 10 - 2-Cyano-*N*-(4-{2-[4-(3-ethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- *N*-(4-{2-[4-(5-Chlor-2-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-
- cyanoacetamid,
- 4-Cyano-*N*-(4-{2-[4-(2-fluor-3-trifluormethylphenyl)piperazin-1-
- 15 yl]ethyl}cyclohexyl)butanamid,
- 2-Cyano-*N*-(4-{2-[4-(6-trifluormethylbenzo[b]thiophen-3-yl)piperazin-1-
- yl]ethyl}cyclohexyl)acetamid,
- 2-Cyano-*N*-(4-{2-[4-(2-fluor-5-trifluormethylphenyl)piperazin-1-
- yl]ethyl}cyclohexyl)acetamid,
- 20 - 2-Cyano-*N*-(4-{2-[4-(3-hydroxyphenyl)piperazin-1-yl]ethyl}cyclo-
- hexyl)acetamid, hydrochlorid,
- *N*-(4-{2-[4-(5-Chlor-2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-
- cyanoacetamid,
- *N*-(4-{2-[4-(2-*tert* Butyl-6-trifluormethylpyrimidin-4-yl)piperazin-1-
- 25 yl]ethyl}cyclohexyl)-2-cyanoacetamid,
- 2-Cyano-*N*-(4-{2-[4-(2-methyl-3-trifluormethylphenyl)piperazin-1-
- yl]ethyl}cyclohexyl)acetamid,
- *N*-(4-{2-[4-(5-Chlor-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-
- trifluoropropanamid,
- 30 - 2-Cyano-*N*-(4-{2-[4-(3,5-dimethoxyphenyl)piperazin-1-
- yl]ethyl}cyclohexyl)acetamid,
- *N*-(4-{2-[4-(3-Chlor-5-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-
- cyanoacetamid,
- 2-Cyano-*N*-(4-{2-[4-(3-methylsulfanylphenyl)piperazin-1-
- 35 yl]ethyl}cyclohexyl)acetamid,

- 2-Cyano-*N*-(4-[2-(4-naphthalen-1-yl)piperazin-1-yl]ethyl)cyclohexyl)acetamid,
- *N*-(4-{2-[4-(3,5-Bistrifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid,
- 5 - *N*-(4-{2-[4-(3-Chlor-2-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid,
- *N*-(4-{2-[4-(2-Fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamid,
- *N*-(4-{2-[4-(4-Phenylpiperazin-1-yl)ethyl]cyclohexyl)succinamid,
- 3,3,3-Trifluor-*N*-(4-{2-[4-(4-phenylpiperazin-1-yl)ethyl]cyclohexyl}propanamid,
- 10 - *N*-(4-{2-[4-(2-Chlor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid,
- *N*-(4-{2-[4-(5-Chlor-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamid,
- 4-Oxopentansyre (4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amid,
- 15 - 2-Cyano-*N*-(4-{2-[4-(2-fluor-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- *N*-(4-{2-[4-(2-Chlor-5-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid,
- 20 - 2-Cyano-*N*-(4-{2-[4-(2-methylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Cyano-*N*-(4-{2-[4-(2-methoxy-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Cyano-*N*-(4-{2-[4-(5-fluor-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 25 - *N*-(4-{2-[4-(5-*tert*-Butyl-2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid,
- 2-Cyano-*N*-(4-{2-[4-(5-methoxy-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 30 - 5-Oxohexansyre (4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amid,
- 4-Cyano-*N*-(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid, hydrochlorid,
- 4-Cyano-*N*-(4-{2-[4-(2-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
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- *N*-(4-{2-[4-(3-Chlor-2-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid,
- 4-Cyano-*N*-(4-{2-[4-(3-trifluormethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
- 5 - 4-Cyano-*N*-(4-{2-[4-(2-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
- 2-Cyano-*N*-(4-{2-[4-(2-cyano-3-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 4-Cyano-*N*-(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-1-yl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
- 10 - 4-Cyano-*N*-(4-{2-[4-(2,3-dichlorphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
- 2-Cyano-*N*-(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-2-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 15 - 2-Cyano-*N*-(4-{2-[4-(4-indan-5-yl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- *N*-(4-{2-[4-(3,5-Bistrifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-cyanopropanamid,
- 3-Cyano-*N*-(4-{2-[4-(2-fluor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid,
- 20 - *N*-(4-{2-[4-(3-Chlor-2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid,
- *N*-(4-{2-[4-(3-Benzylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid,
- [3-(4-{2-[4-(2-Cyanoacetylaminocyclohexyl)ethyl]piperazin-1-yl}phenyl)carbaminsyreethylester,
- 25 - 2-Cyano-*N*-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Cyano-*N*-(4-{2-[4-(4-o-tolylpiperazin-1-yl)ethyl]cyclohexyl)acetamid,
- 2-Cyano-*N*-(4-{2-[4-(2,5-dimethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 30 - 4-Oxopentansyre (4-{2-[4-(3,5-bis-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amid,
- 4-Dimethylamino-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,

- 2-(4-Fluorophenoxy)-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Cyano-*N*-(4-{2-[4-(2-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid , hydrochlorid,
- 5 - 2-Cyano-*N*-(4-{2-[4-(2,5-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- *N*-(4-{2-[4-(2-Chlor-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid,
- 2-Cyano-*N*-(4-{2-[4-(2,5-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 10 - *N*-(4-{2-[4-(3-Chlorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid,
- 4-Cyano-*N*-(4-{2-[4-(2-methyl-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
- 15 - 4-Oxopentansyre (4-{2-[4-(2-fluor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amid,
- 2-Cyano-*N*-(4-{2-[4-(3,5-di-*tert*-butylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- *N*-(4-{2-[4-(2-Chlorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-
- 20 cyanobutanamid,
- 4-Cyano-*N*-(4-{2-[4-(4-m-tolylpiperazin-1-yl)ethyl]cyclohexyl}butanamid,
- 3,3,3-Trifluor-*N*-(4-{2-[4-(4-m-tolylpiperazin-1-yl)ethyl]cyclohexyl}propanamid,
- 4-Cyano-*N*-(4-{2-[4-(2-methylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
- 25 - 2-Cyano-*N*-(4-{2-[4-(4-quinolin-8-ylpiperazin-1-yl)ethyl]cyclohexyl}acetamid,
- 4-Cyano-*N*-(4-{2-[4-(3-methylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
- 2-Cyano-*N*-(4-{2-[4-(4-quinolin-5-ylpiperazin-1-yl)ethyl]cyclohexyl}acetamid,
- 2-Cyano-*N*-(4-{2-[4-(3-methansulfonfylaminophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 30 - 2-Cyano-*N*-(4-{2-[4-(4-fluor-phenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Cyano-*N*-(4-{2-[4-(4-p-tolylpiperazin-1-yl)ethyl]cyclohexyl}acetamid,
- 2-Cyano-*N*-(4-{2-[4-(2-ethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,

- *N*-(4-{2-[4-(2-*tert*-Butyl-6-trifluormethylpyrimidin-4-yl)piperazin-1-yl]ethyl}cyclohexyl)-3-cyanopropanamid,
- 2-Cyano-*N*-(4-{2-[4-(2-phenoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 5 - *N*-(4-{2-[4-(3-Chlor-2-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid,
- 2-Cyano-*N*-(4-{2-[4-(2-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- *N*-(4-{2-[4-(5-Chlor-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid,
- 10 - 4-Cyano-*N*-(4-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
- *N*-(4-{2-[4-(3-Ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamid,
- 3-Cyano-*N*-(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid,
- 15 - 4-Cyano-*N*-(4-{2-[4-(6-trifluormethylbenzo[b]thiophen-3-yl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
- 4-Cyano-*N*-(4-{2-[4-(3,5-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
- 20 - 2-Cyano-*N*-(4-{2-[4-(2,4-diethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 3,3,3-Trifluor-*N*-(4-{2-[4-(2-fluor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid,
- *N*-(4-{2-[4-(5-Chlor-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-cyanopropanamid,
- 25 - *N*-(4-{2-[4-(3-Chlor-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid,
- *N*-(4-{2-[4-(3-Chlor-5-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid,
- 30 - *N*-(4-{2-[4-(2-Fluor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid,
- 4-Cyano-*N*-(4-{2-[4-(3,5-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
- 4-Cyano-*N*-(4-{2-[4-(quinolin-8-yl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,

- 4,4,4-Trifluor-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
- 3-Cyano-*N*-(4-{2-[4-(2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid,
- 5 - 2-Cyano-*N*-(4-{2-[4-(2,6-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Cyano-*N*-(4-{2-[4-(3-hydroxymethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 3-Cyano-*N*-(4-{2-[4-(3-methylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid,
- 10 - 2-Cyano-*N*-(4-{2-[4-(3-methoxymethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Cyano-*N*-(4-{2-[4-(3-propylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 15 - 2-Cyano-*N*-(4-{2-[4-(3,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Cyano-*N*-(4-{2-[4-[3-(1-hydroxyethyl)phenyl]piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Cyano-*N*-(4-{2-[4-(4-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 20 - *N*-(4-{2-[4-(4-Chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid,
- *N*-(4-{2-[4-(Biphenyl-3-yl-piperazin-1-yl)ethyl]cyclohexyl}-2-cyanoacetamid,
- 2-Cyano-*N*-(4-{2-[4-(4-fluor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 25 - 3-Cyano-*N*-(4-{2-[4-(5-fluor-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid,
- 4-Cyano-*N*-(4-{2-[4-(5-fluor-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
- *N*-(4-{2-[4-(3-Bromophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid,
- 30 - 2-Cyano-*N*-(4-{2-[4-[3-(1,1-difluorethyl)phenyl]piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 2-Cyano-2,2-dimethyl-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 4-Cyano-*N*-(4-{2-[4-(4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid,
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- 3,3,3-Trifluor-*N*-(4-{2-[4-(4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid,
- 2-Cyano-*N*-(4-{2-[4-(4-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid,
- 4-Cyano-*N*-(4-{2-[4-(2-ethylphenyl)piperazin-1-
- 5 yl]ethyl}cyclohexyl)butanamid,
- 4-cyano-*N*-(4-{2-[4-(3-propylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 2-cyano-*N*-(4-{2-[4-(3-fluor-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 10 - 4-cyano-*N*-[4-(2-{4-[3-(1,1-difluorethyl)phenyl]piperazin-1-yl}ethyl)cyclohexyl]butanamid
- *N*-{4-[2-(4-benzo[1,3]dioxol-5-yl)piperazin-1-yl)ethyl}cyclohexyl}-2-cyanoacetamid
- 2-cyano-*N*-(4-{2-[4-(2,3-dihydrobenzo[1,4]dioxin-6-yl)piperazin-1-
- 15 yl]ethyl}cyclohexyl)acetamid
- 3,3,3-trifluor-*N*-(4-{2-[4-(4-quinolin-5-yl)piperazin-1-yl]ethyl}cyclohexyl)propanamid
- 4-cyano-*N*-(4-{2-[4-(4-quinolin-5-yl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 2-cyano-*N*-(4-{2-[4-(4-fluor-3-methylphenyl)piperazin-1-
- 20 yl]ethyl}cyclohexyl)acetamid
- 2-cyano-*N*-(4-{2-[4-(3,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 2-cyano-*N*-(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 2-methansulfinyl-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-
- 25 yl]ethyl}cyclohexyl)acetamid
- 2-cyano-*N*-(4-{2-[4-(3-isopropylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 2-cyano-*N*-(4-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 30 - 2-methansulfonyl-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 2-cyano-*N*-(4-{2-[4-(3-fluor-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 2-cyano-*N*-(4-{2-[4-(3,4-dimethylphenyl)piperazin-1-
- 35 yl]ethyl}cyclohexyl)acetamid

- 2-cyano-*N*-(4-{2-[4-(3,4,5-trifluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 2-cyano-*N*-(4-{2-[4-(3-trifluormethylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 5 - 2-cyano-*N*-(4-{2-[4-(3-methansulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 2-cyano-*N*-(4-{2-[4-(3-difluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 4-cyano-*N*-(4-{2-[4-(3-fluor-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 10 - 4-cyano-*N*-(4-{2-[4-(3,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 4-cyano-*N*-(4-{2-[4-(4-fluor-3-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 15 - *N*-(4-{2-[4-(4-chlor-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid
- *N*-(4-{2-[4-(4-chlor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid
- 4-cyano-*N*-(4-{2-[4-(3-trifluormethylsulfanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 20 - 4-cyano-*N*-(4-{2-[4-(3-difluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- *N*-(4-{2-[4-(4-benzo[1,3]dioxol-5-yl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid
- 25 - 4-cyano-*N*-(4-{2-[4-(2-fluor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 4-cyano-*N*-(4-{2-[4-(4-fluor-3-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid, hydrochlorid
- 4-cyano-*N*-(4-{2-[4-(3,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 30 - *N*-(4-{2-[4-(3-chlor-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid
- 2-cyano-*N*-(4-{2-[4-(4-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 4-cyano-*N*-(4-{2-[4-(2,5-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 35

- 2-cyclopent-2-enyl-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 4-cyano-*N*-(4-{2-[4-(3,4,5-trifluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 5 - *N*-(4-{2-[4-(3-acetylphenyl)piperazin-1-yl]ethylcyclohexyl)-4-cyanobutanamid
- 2-cyano-*N*-(4-{2-[4-(2-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 4-cyano-*N*-(4-{2-[4-(2-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 10 - *N*-(4-{2-[4-(3-chlor-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid
- 4-cyano-*N*-(4-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- *N*-(4-{2-[4-(2,4-difluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-(4-
- 15 fluorphenoxy)acetamid
- *N*-(4-{2-[4-(2,4-difluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluorpropanamid
- 2-cyclopent-3-enyl-*N*-(4-{2-[4-(2-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 20 - *N*-(4-{2-[4-(2-chlor-4-fluor-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid
- *N*-(4-{2-[4-(2-chlor-4-fluor-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid
- 4-cyano-*N*-(4-{2-[4-(5-methoxy-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 25 - 4-cyano-*N*-(4-{2-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- *N*-(4-{2-[4-(3-chlor-2-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid
- 30 - 4-cyano-*N*-(4-{2-[4-(3-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- *N*-(4-{2-[4-(3-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-phenoxyacetamid
- *N*-(4-{2-[4-(3-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamid
- *N*-(4-{2-[4-(3-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamid

- 4-cyano-*N*-(4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 3-cyano-*N*-(4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid
- 5 - *N*-(4-{2-[4-(2-chlor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid
- 4-cyano-*N*-(4-{2-[4-(2-methoxy-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 3,3,3-trifluor-*N*-(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid
- 10 - 3-diethylamino-*N*-(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid
- 3-cyano-*N*-(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid
- 15 - 4-cyano-*N*-(4-{2-[4-(2,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- *N*-(4-{2-[4-(5-chlor-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid
- *N*-(4-{2-[4-(5-chlor-2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid
- 20 - 4-cyano-*N*-(4-{2-[4-(3-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 3-cyano-*N*-(4-{2-[4-(3-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid
- 25 - *N*-(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- 2-cyclopent-2-enyl-*N*-(4-{2-[4-(3-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 4-cyano-*N*-(4-{2-[4-(3-methoxy-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 30 - *N*-(4-{2-[4-(2-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamid
- 2-cyano-*N*-(4-{2-[4-(2,4-dichlor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid

- 4-cyano-*N*-(4-{2-[4-(2,4-dichlor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- *N*-(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methansulfonylacetamid
- 5 - *N*-(4-{2-[4-(2,3-difluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methansulfonylacetamid
- *N*-(4-{2-[4-(4-chlorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methansulfonylacetamid
- 4-cyano-*N*-(4-{2-[4-(4-o-tolyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 10 - 4-cyano-*N*-(4-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 4-cyano-*N*-(4-{2-[4-(4-fluor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 4-cyano-*N*-(4-{2-[4-(3-cyano-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 15 - 4-cyano-*N*-(4-{2-[4-(2-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid, hydrochlorid
- *N*-(4-{2-[4-(3-chlor-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid
- 20 - *N*-(4-{2-[4-(3-chlor-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid
- 4-cyano-*N*-(4-{2-[4-(2-ethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 4-cyano-*N*-(4-{2-[4-(2-fluor-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 25 - 4-cyano-*N*-(4-{2-[4-(2,5-difluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 2,2-difluor-*N*-(4-{2-[4-(2-fluor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 30 - 4-cyano-*N*-(4-{2-[4-(2,3-difluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- *N*-(4-{2-[4-(2,3-difluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluorpropanamid
- 4-cyano-*N*-(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
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- *N*-(4-{2-[4-(3-chlor-2-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid
- 2-cyano-*N*-(4-{2-[4-(2,3,4-trifluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 5 - 4-cyano-*N*-(4-{2-[4-(2,3,4-trifluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 3,3,3-trifluor-*N*-(4-{2-[4-(3-methansulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid
- 2-cyano-*N*-(4-{2-[4-(4-indan-4-ylpiperazin-1-yl)ethyl]cyclohexyl}acetamid
- 10 - 4-cyano-*N*-(4-{2-[4-(4-indan-4-ylpiperazin-1-yl)ethyl]cyclohexyl}butanamid
- *N*-(4-{2-[4-(2-fluor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamid
- 4-cyano-2,2-difluor-*N*-(4-{2-[4-(2-fluor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 15 - 2,2,2-trifluor-*N*-(4-{2-[4-(3-methansulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- *N*-(4-{2-[4-(4-biphenyl-3-ylpiperazin-1-yl)ethyl]cyclohexyl}-4-cyanobutanamid
- 2-ethoxy-*N*-(4-{2-[4-(3,4,5-trifluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 20 - 4-cyano-*N*-(4-{2-[4-(4-p-tolylpiperazin-1-yl)ethyl]cyclohexyl}butanamid
- 4,4,4-trifluor-*N*-(4-{2-[4-(3-methansulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- *N*-(4-{2-[4-(2-fluor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- 25 - *N*-(4-{2-[4-(4-chlor-2-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid
- 2-cyano-*N*-(4-{2-[4-(2,4,5-trifluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 4-cyano-*N*-(4-{2-[4-(2,4,5-trifluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 30 - 2-ethoxy-*N*-(4-{2-[4-(4-p-tolylpiperazin-1-yl)ethyl]cyclohexyl}acetamid
- 3,3,3-trifluor-*N*-(4-{2-[4-(3-(1-hydroxyethyl)phenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid
- 2-ethoxy-*N*-(4-{2-[4-(2-fluor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
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- *N*-(4-{2-[4-(4-chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid
- *N*-(4-{2-[4-(4-chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamid
- 4-cyano-*N*-(4-{2-[4-(2-methoxy-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 5 - 2-cyano-*N*-(4-{2-[4-(2-fluor-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 4-cyano-*N*-(4-{2-[4-(2-fluor-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 10 - *N*-(4-{2-[4-(3,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid
- *N*-(4-{2-[4-(3-chlor-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid
- *N*-(4-{2-[4-(3-chlor-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamid
- 15 - 3,3,3-trifluor-*N*-(4-{2-[4-(*p*-tolylpiperazin-1-yl)ethyl]cyclohexyl})propanamid
- *N*-(4-{2-[4-(3,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- *N*-(4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid
- 20 - *N*-(4-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- 4-cyano-*N*-(4-{2-[4-(3,4-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 25 - *N*-(4-{2-[4-(3,4-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- *N*-(4-{2-[4-(3,4-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid
- *N*-(4-{2-[4-(3,4-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamid
- 30 - 4-cyano-*N*-(4-{2-[4-(5,6,7,8-tetrahydronaphthalen-2-yl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- *N*-(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamid

- *N*-(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- 2-ethoxy-*N*-(4-{2-[4-(2-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 5 - *N*-(4-{2-[4-(4-chlor-phenyl)piperazin-1-yl]ethyl}-cyclohexyl)-2-ethoxyacetamid
- *N*-(4-{2-[4-(2-fluor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-propoxyacetamid
- 2-cyano-*N*-(4-{2-[4-(3,4-dichlor-2-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 10 - 4-cyano-*N*-(4-{2-[4-(3,4-dichlor-2-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- *N*-(4-{2-[4-(2,5-dichlorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid
- 15 - 4-cyano-*N*-(4-{2-[4-(2-cyano-3-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 4-cyano-*N*-(4-{2-[4-(3-oxazol-2-ylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- *N*-(4-{2-[4-(3-chlor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid
- 20 - *N*-(4-{2-[4-(3-chlor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid
- 2-cyano-*N*-(4-{2-[4-(3-oxazol-2-ylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 25 - 4-cyano-*N*-(4-{2-[4-(3-ethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 4-cyano-*N*-(4-{2-[4-(3-fluor-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 2-ethoxy-*N*-(4-{2-[4-(3-fluor-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 30 - 4-cyano-*N*-(4-{2-[4-(3-(1-hydroxypropyl)phenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 2-methoxy-*N*-(4-{2-[4-(3,4,5-trifluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid

- 4-cyano-*N*-(4-{2-[4-(4-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- *N*-(4-{2-[4-(2,5-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid
- 5 - *N*-(4-{2-[4-(3-chlor-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- *N*-(4-{2-[4-(3-chlor-2,4-difluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid
- *N*-(4-{2-[4-(3-chlor-2,4-difluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-
- 10 cyanobutanamid
- 2-ethoxy-*N*-(4-{2-[4-(4-o-tolylpiperazin-1-ylethyl}cyclohexyl}acetamid
- *N*-(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- 2-ethoxy-*N*-(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 15 - 2-cyano-*N*-(4-{2-[4-(3-(1-hydroxypropyl)phenyl]piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 4-methoxy-*N*-(4-{2-[4-(3,4,5-trifluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 2-ethoxy-*N*-(4-{2-[4-(4-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 20 - 2-cyano-*N*-(4-{2-[4-(4-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 2-cyano-*N*-(4-{2-[4-(3,5-difluor-4-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 25 - 2-cyano-*N*-(4-{2-[4-(3-(1-hydroxy-2-methylpropyl)phenyl]piperazin-1-yl]ethyl}cyclohexyl)acetamid
- *N*-(4-{2-[4-(3-chlor-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid
- *N*-(4-{2-[4-(3-chlor-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-
- 30 methoxybutanamid
- *N*-(4-{2-[4-(2-chlor-4-fluor-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid
- *N*-(4-{2-[4-(2-chlor-4-fluor-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid

- 4-cyano-*N*-(4-{2-[4-(4-methoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 2-cyano-*N*-(4-{2-[4-(2-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 5 - *N*-(4-{2-[4-(3-chlor-4-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid
- *N*-(4-{2-[4-(3-chlor-4-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid
- *N*-(4-{2-[4-(2-chlor-5-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid
- 10 - *N*-(4-{2-[4-(2-chlor-5-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid
- *N*-(4-{2-[4-(3-chlor-2,4-difluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamid
- 15 - 2-cyano-*N*-(4-{2-[4-(4-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- *N*-(4-{2-[4-(2-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- *N*-(4-{2-[4-(2-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamid
- 20 - 3-cyano-*N*-(4-{2-[4-(4-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid
- 3-cyano-*N*-(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid
- 25 - 2-cyano-*N*-(4-{2-[4-(2-fluor-4-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 4-cyano-*N*-(4-{2-[4-(2-fluor-4-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-butanamid
- 4-methoxy-*N*-(4-{2-[4-(2,3,4-trifluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 30 - *N*-(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4,4,4-trifluorbutanamid
- *N*-(4-{2-[4-(3-cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-methoxypropanamid

- 2-cyano-*N*-(4-{2-[4-(3-cyano-4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- *N*-(4-{2-[4-(3-cyano-4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- 5 - 4-cyano-*N*-(4-{2-[4-(3-cyano-4-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 2-cyano-*N*-(4-{2-[4-(3-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 4-cyano-*N*-(4-{2-[4-(3-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 10 - 3-cyano-*N*-(4-{2-[4-(2-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid
- *N*-(4-{2-[4-(2-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-propoxyacetamid, hydrochlorid
- 15 - 3,3,3-trifluor-*N*-(4-{2-[4-(2-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid
- *N*-(4-{2-[4-(2-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-malonamid
- 2-cyano-*N*-(4-{2-[4-(5-ethyl-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 20 - 4-cyano-*N*-(4-{2-[4-(5-ethyl-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 4-methoxy-*N*-(4-{2-[4-(*m*-tolylpiperazin-1-yl)ethyl]cyclohexyl})butanamid
- *N*-(4-{2-[4-(3,4-dichlor-2-fluor-phenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- 25 - 2-cyano-*N*-(4-{2-[4-(3-cyano-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 4-cyano-*N*-(4-{2-[4-(3-cyano-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 30 - *N*-(4-{2-[4-(3-fluor-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- *N*-(4-{2-[4-(3,5-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- *N*-(4-{2-[4-(3-cyano-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- 35 methoxybutanamid

- *N*-(4-{2-[4-(4-chlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- *N*-(4-{2-[4-(2-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid
- 5 - *N*-(4-{2-[4-(2-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methansulfonylacetamid
- *N*-(4-{2-[4-(2-fluor-4-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- 2-cyano-*N*-(4-{2-[4-(2,3,4,5-tetrafluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 10 - 2-cyano-*N*-(4-{2-[4-(2,4-dichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- *N*-(4-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- 15 - 3-cyano-*N*-(4-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid
- 2-cyano-*N*-(4-{2-[4-(2,4,5-trichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- *N*-(4-{2-[4-(3,4-dichlor-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid
- 20 - 3-cyano-*N*-(4-{2-[4-(3,4-dichlor-2-fluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid
- 2-cyano-*N*-(4-{2-[4-(3-fluor-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 25 - 4-cyano-*N*-(4-{2-[4-(3-fluor-5-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 2-cyano-*N*-(4-{2-[4-(2,3,4-trichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 5-cyano-pentansyre (4-{2-[4-(2-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amid
- 30 - *N*-(4-{2-[4-(3-chlor-2,4-difluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-cyanopropanamid
- 2-methoxy-*N*-(4-{2-[4-(2-methyl-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid

- 4-methoxy-*N*-(4-{2-[4-(2-methyl-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 4,4,4-trifluor-*N*-(4-{2-[4-(2-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 5 - *N*-(4-{2-[4-(3,5-bistrifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)malonamid
- *N*-(4-{2-[4-(3-chlor-5-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- *N*-(4-{2-[4-(3,5-bistrifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- 10 - *N*-(4-{2-[4-(3-chlor-5-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid
- *N*-(4-{2-[4-(3-chlor-5-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-cyanopropanamid
- 15 - 5-cyano-pentansyre (4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)amid
- 2-cyano-*N*-(4-{2-[4-(4-pentafluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- *N*-(4-{2-[4-(4-fluor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- 20 - *N*-(4-{2-[4-(4-chlor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- *N*-(4-{2-[4-(4-chlor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid
- 25 - *N*-(4-{2-[4-(3-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- *N*-(4-{2-[4-(4-fluor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid
- *N*-(4-{2-[4-(2,4-dichlorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- 30 - 4-cyano-*N*-(4-{2-[4-(2,4-dichlorphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 4-cyano-*N*-(4-{2-[4-(2,4,5-trichlorphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid

- 4-cyano-*N*-(4-{2-[4-(2,3,4-trichlorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 3-(4-{2-[4-(4-methoxybutanoylamino)cyclohexyl]ethyl}piperazin-1-yl)benzamid
- 5 - *N*-(4-{2-[4-(3-acetylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3,3,3-trifluoropropanamid
- 2-cyano-*N*-(4-{2-[4-(3-propanoylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 4-cyano-*N*-(4-{2-[4-(3-propanoylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 10 - 2-cyano-*N*-(4-{2-[4-(3-isobutanylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid, dihydrochlorid
- 4-Methoxy-*N*-(4-{2-[4-(2,3,4,5-tetrafluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butyramid
- 15 - 4-Cyano-*N*-(4-{2-[4-(2,3,4,5-tetrafluorophenyl)piperazin-1-yl]ethyl}cyclohexyl)butyramid
- 2-Cyano-*N*-(4-{2-[4-(2-methyl-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 4-Cyano-*N*-(4-{2-[4-(2-methyl-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butyramid
- 20 eller deres farmaceutisk acceptable salte, hydrater eller hydrerede salte, eller de polymorfe, krystallinske strukturer af disse forbindelser eller deres optiske isomerer, racemater, diastomerer eller enantiomerer.
- 25 **7. Forbindelse ifølge et af de foregående krav valgt blandt:**
- 4-Methoxy-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- *N*-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid
- 30 - *N*-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid
- *N*-(4-{2-[4-(3,5-Bistrifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid

- *N*-(4-{2-[4-(3-Cyano-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid
- *N*-(4-{2-[4-(3-Cyano-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-ethoxyacetamid
- 5 - 2-Cyano-*N*-(4-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 2-Cyano-*N*-(4-{2-[4-(3-ethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 4-Cyano-*N*-(4-{2-[4-(3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 10 - 2-Cyano-*N*-(4-{2-[4-(2-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- *N*-(4-{2-[4-(3-Chlor-5-fluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid
- 4-Cyano-*N*-(4-{2-[4-(2-fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 15 - *N*-(4-{2-[4-(5-Chlor-2-methylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-cyanopropanamid
- 2-Cyano-*N*-(4-{2-[4-(4-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 20 - 2-Cyano-*N*-(4-{2-[4-(4-fluor-3-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 4-Cyano-*N*-(4-{2-[4-(3-(1,1-difluorethyl)phenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 2-Cyano-*N*-(4-{2-[4-(3-methansulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 25 - 2-Cyano-*N*-(4-{2-[4-(3-difluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- *N*-(4-{2-[4-(3-Acetylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid
- 30 - 4-Cyano-*N*-(4-{2-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]ethyl}cyclohexyl)butanamid
- 3,3,3-Trifluor-*N*-(4-{2-[4-(3-methansulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)propanamid
- *N*-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- 35

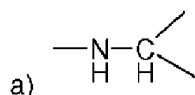
- 4-Cyano-*N*-[4-(2-[4-[3-(1-hydroxypropyl)phenyl]piperazin-1-yl]ethyl)cyclohexyl]butanamid
- *N*-(4-{2-[4-(3-Chlor-2,4-difluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-cyanobutanamid
- 5 - 2-Cyano-*N*-[4-(2-[4-[3-(1-hydroxypropyl)phenyl]piperazin-1-yl]ethyl)cyclohexyl]acetamid
- *N*-(4-{2-[4-(3-Chlor-2,4-difluorphenyl)piperazin-1-yl]ethyl}cyclohexyl)succinamid
- *N*-(4-{2-[4-(2-Fluor-5-trifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-4-methoxybutanamid
- 10 - *N*-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4,4,4-trifluorbutanamid
- *N*-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-methoxypropanamid
- 15 eller deres farmaceutisk acceptable salte, frie former, hydrater eller hydrerede salte, eller de polymorfe, krystallinske strukturer af disse forbindelser eller deres optiske isomerer, racemater, diastomerer eller enantiomerer.

- 8. Forbindelse ifølge et af de foregående krav valgt blandt:
- 20 - *N*-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-methoxyacetamid
- *N*-(4-{2-[4-(3,5-Bistrifluormethylphenyl)piperazin-1-yl]ethyl}cyclohexyl)-2-cyanoacetamid
- 25 - 2-Cyano-*N*-(4-{2-[4-(3-methansulfonylphenyl)piperazin-1-yl]ethyl}cyclohexyl)acetamid
- 2-Cyano-*N*-[4-(2-[4-[3-(1-hydroxypropyl)phenyl]piperazin-1-yl]ethyl)cyclohexyl]acetamid
- *N*-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-4,4,4-trifluorbutanamid
- 30 - *N*-(4-{2-[4-(3-Cyanophenyl)piperazin-1-yl]ethyl}cyclohexyl)-3-methoxypropanamid
- eller deres farmaceutisk acceptable salte, frie former, hydrater eller hydrerede salte, eller de polymorfe, krystallinske strukturer af disse forbindelser

eller deres optiske isomerer, racemater, diastomerer eller enantiomerer.

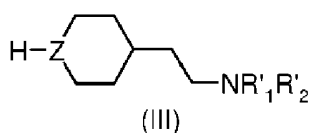
9. Fremgangsmåde til fremstilling af en forbindelse med formel (I) ifølge et af kravene 1 til 8, hvor forbindelserne med formel (I), i hvilken Z er:

5

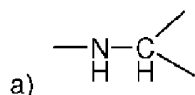


fremstilles :

- ved at forbinde forbindelser med formel (III) med syre eller syrederivater $R'COX$ eller $R'COCOX$, hvor X er udvalgt blandt chlorid ($X = Cl$), en imidazolid ($X = \text{imidazol-1-yl}$), en hydroxysuccinimidoyl ($X = OSu$), en paranitrophenylester ($X = 4\text{-nitrophenoxy}$), en blandet anhydrid eller en symmetrisk anhydrid
- 10



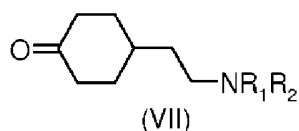
- 15 i hvilken R' og $NR'_1R'_2$ betegner respektivt R og NR_1R_2 som defineret i krav 1, og Z er:



eller

20

- fra forbindelser med formel (VII) ved reduktiv amination:



hvor NR_1R_2 er som defineret i krav 1.

25

10. Farmaceutisk sammensætning, omfattende en terapeutisk virksom mængde af mindst et derivat ifølge krav 1 til 8, med en farmaceutisk acceptabel vehikel eller et farmaceutisk acceptabelt hjælpestof.

11. Anvendelse af en forbindelse med den almene formel (I) som defineret i krav 1 til 8 til fremstilling af farmaceutiske sammensætninger, der er beregnet til at opføre sig som en ligand af dopamin D₃-receptor.

- 5 **12.** Anvendelse af en forbindelse med den almene formel (I) som defineret i krav 1 til 8 til fremstilling af farmaceutiske sammensætninger beregnet til forebyggelse og/eller behandling af sygdomme, der involverer dopamin D₃-receptoren, hvor sygdommen er udvalgt fra gruppen bestående af: neuropsykiatrisk sygdom udvalgt blandt Parkinsons sygdom, skizofreni, demens, psykose eller psykotiske tilstande, depression, mani, angst, dyskinesier, balancelidelser, Tourettes sygdom; afhængighed af stoffer omfattende enhver tilstand associeret med fjernelse, abstinens og/eller afgiftning af et individ, der er afhængigt af et stof, især terapeutisk aktive midler, såsom opioider, amfetaminer og/eller medikamenter såsom kokain, heroin, eller alternativt alkohol og/eller nikotin; seksuelle lidelser omfattende impotens, omfattende mandlig impotens; motoriske lidelser omfattende væsentlig eller iatrogen dyskinesi, og/eller væsentlig eller iatrogen tremor; urolige ben; kardiovaskulære eller metaboliske lidelser omfattende hypertension, hjertefejl; hormonale lidelser omfattende menopausale lidelser eller vækstlidelser ; nyreinsufficiens eller diabetes.
- 10
15
20

13. Anvendelse ifølge krav 12, hvor forbindelsen ifølge et af kravene 1 til 8 kombineres med et eller flere af neuropsychiatriske midler.

- 25 **14.** Anvendelse ifølge krav 13, hvor det neuropsychiatriske middel er udvalgt blandt anxyolitiske, antipsychotiske, antidepressive, prokognitive midler eller antidemensmidler.

- 30 **15.** Anvendelse ifølge krav 12, hvor forbindelsen ifølge et af kravene 1 til 8 kombineres med et eller flere af antihypertensive, cardiotoniske eller antidiabetiske midler.

- 35 **16.** Forbindelse ifølge et af kravene 1 til 8 til anvendelse ved forebyggelse og/eller behandling af sygdomme, der involverer dopamin D₃-receptoren, hvor sygdommen er udvalgt fra gruppen bestående af : neuropsykiatrisk sygdom

- dom udvalgt blandt Parkinsons sygdom, skizofreni, demens, psykose eller psykotiske tilstande, depression, mani, angst, dyskinesier, balancelidelser, Tourettes sygdom; afhængighed af stoffer omfattende enhver tilstand associeret med fjernelse, abstinens og/eller afgiftning af et individ, der er afhængigt af et stof, især terapeutisk aktive midler, såsom opioider, amfetaminer og/eller medikamenter såsom kokain, heroin, eller alternativt alkohol og/eller nikotin; seksuelle lidelser omfattende impotens, omfattende mandlig impotens; motoriske lidelser omfattende væsentlig eller iatrogen dyskinesi, og/eller væsentlig eller iatrogen tremor; urolige ben; kardiovaskulære eller metaboliske lidelser omfattende hypertension, hjertefejl; hormonale lidelser omfattende menopausale lidelser eller vækstlidelser ; nyreinsufficiens eller diabetes.
17. Kombinationer omfattende en forbindelse ifølge et af kravene 1 til 8 med en eller flere aktive bestanddel(e).