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Background of the Invention

[0001] The present invention relates to bicyclic[3.1.0]amines and to pharmaceutical compositions containing them useful for the treatment of central nervous system disorders, cognitive disorders, schizophrenia, dementia and other disorders in mammals, including humans. These compounds exhibit activity as inhibitors of the glycine type-1 transporter.

[0002] Schizophrenia, a progressive neurological disease, is manifested in its early stages as thought disorders such as hallucinations, paranoid delusions, and bizarre thought patterns, collectively known as positive symptoms. These easily recognizable symptoms gave the disease the historical name "madness". As the disease progresses, negative symptoms, such as social withdrawal and anhedonia, and cognitive symptoms such as dementia become more apparent. Only about one-third of schizophrenic patients can be treated successfully and returned to society, while the remainder is generally institutionalized. The burden on society of this devastating illness and the toll it takes on family members of affected patients make it one of the most costly of all CNS diseases.

[0003] Pharmacological treatment for schizophrenia has traditionally involved blockade of the dopamine system, which is thought to be responsible for its positive symptoms. Such treatment, however, ignores the negative and cognitive aspects of the disease. Another neurotransmitter system believed to play a role in schizophrenia is the glutamate system, the major excitatory transmitter system in the brain. This hypothesis is based on the observation that blockade of the glutamate system by compounds such as PCP ("angel dust") can replicate many of the symptoms of schizophrenia, including its positive, negative, and cognitive aspects. If schizophrenia involves a deficit of glutamatergic transmission, augmentation of the glutamate system, and specifically the NMDA receptor, can be beneficial. While glutamate is the principle agonist at NMDA receptors, glycine is required as a co-agonist to set the "tone" of the receptor for its response to glutamate. Enhancing this "tone" by increasing the effect of glycine would augment NMDA neurotransmission, and provide potential benefit in the treatment of schizophrenia.

[0004] A specific mechanism for augmenting the glycinergic "tone" of the NMDA receptor was disclosed recently by Bergeron, et al. (Proc. Natl. Acad. Sci. USA, 95, 15730, (1998)). This group showed that a specific and potent inhibitor of the glycine type-1 transporter (GlyT1) responsible for removing glycine from the synapse at the NMDA receptor, termed NFPS (WO 97/45115), could enhance NMDA receptor function. For example, NFPS increased the postsynaptic current driven by the NMDA receptor, an effect blocked by both a specific NMDA-site antagonist and a glycine-site antagonist. Even though glycine levels in the brain are high relative to the amount required to act as an NMDA receptor co-agonist, this work shows that GlyT1 removes glycine efficiently at the synapse, and that inhibition of GlyT1 can augment NMDA receptor function. The present invention provides GlyT1 inhibitors as a treatment for disorders or conditions such as schizophrenia through its augmentation of glutamatergic neurotransmission.

Summary of the Invention

[0005] The present invention relates to compounds of the Formula I,
wherein:

- Y is \((R^{100})_k-R^1-(R^6)_m\);
- k is 0 or 1;
- l = 0, 1, 2 or 3;
- m = 1, 2 or 3;
- n is 0, 1, 2, 3 or 4;
- o is 0 or 1;
- p is 0, 1, 2, or 3;
- q is 0, 1, 2, 3 or 4;
- r is 1 or 2;
- s is 0, 1, 2, 3 or 4;
- t is 0 or 1;
- u is 1, 2, or 3;
- v is 1, 2, or 3;
- \(R^{100}\) is \(-\text{CH}_2-, -\text{CH}(\text{C}_1-\text{C}_3)\text{alkyl}-, -\text{C}(=\text{O})-\) or \(-\text{SO}_2-\);
- \(R^1\) is \(-(\text{C}_1-\text{C}_6)\text{alkyl}, -(\text{C}_3-\text{C}_8)\text{cycloalkyl}, -(4 to 7 membered) heterocycloalkyl, -(\text{CH}_2)_r-(\text{C}_6-\text{C}_{10}\text{aryl})\) or -(5 to 10 membered) heteroaryl, or -(5 to 10 membered) tetrahydro-heteroaryl;
- each \(R^6\) can be the same or different and is independently selected from \(\text{H, halo, -(C}_1-\text{C}_6\text{alkyl, -(C}_3-\text{C}_7\text{alkoxy, -(C}_2-\text{C}_4\text{alkenoxy, -(C}_1-\text{C}_6\text{alkyl-OH, -OH, -CN, -NO}_2, -\text{CR}^7\text{R}^8\text{R}^9, -\text{N}\text{R}^{20}\text{R}^{21}, -\text{NHCOC}_{1-\text{C}_3}\text{alkyl, NHSO}_2\text{alkyl(C}_1-\text{C}_3\text{), C}(=\text{O})\text{OR}^{22}, -\text{R}^{23}\text{C}(=\text{O})\text{OR}^{22}, -\text{C}(=\text{O})\text{NH}_2, \text{phenyl-E, phenoxy-F, morpholine, -NR}^{20}\text{R}^{21}, \text{aryl, heteroaryl, -S-R}^{24}, \text{and -SO}_2\text{R}^{25};}\)
- \(B\) and \(D\) are each independently \(\text{H, OH, phenyl, diphenyl or trifluoro;}\)
- \(E\) and \(F\) are each independently \(\text{H, alkyl, or halo;}\)
- \(R^7, R^8\) and \(R^9\) are each independently \(\text{H, (C}_1-\text{C}_4\text{) alkyl, -OH, -(C}_1-\text{C}_4\text{)alkyl, -CN, -NR}^{26}\text{R}^{27}\) and \(-\text{NHC}(=\text{O})\) \((\text{C}_1-\text{C}_3)\)alkyl, wherein said alkyl groups are optionally substituted with \(\text{OH, OCH}_3, \text{NH}_2, \text{NHC}(=\text{O})(\text{C}_1-\text{C}_3)\)alkyl, or \(R^7\) and \(R^8\) together with the carbon atom to which they are attached optionally form a \((\text{C}_3-\text{C}_7)\)cycloalkyl ring, or a \((\text{C}_4-\text{C}_7)\)heterocycloalkyl ring which contains 1-3 heteroatoms selected from \(\text{N, O, S and optionally contains a C=O group;}\)
- \(R^{20}\) and \(R^{21}\) are each independently \(\text{H or (C}_1-\text{C}_3\text{) alkyl;}\)
- or \(R^{20}\) and \(R^{21}\) can be connected by 4 to 7 carbon atoms wherein from one to three of said carbon atoms can optionally be replaced with \(\text{O, N or S, to form a heterocycloalkyl ring;}\)
or R20 and R21 can be connected by 3 to 7 atoms selected from C, N, O or S to form a 5 to 10 membered heteroaryl ring;
R22, R23 and R24 are each independently H, or (C1-C3)alkyl;
R25 is (C1-C2)alkyl;
R26 and R27 are each independently H or (C1-C3)alkyl;
or R26 and R27 can be connected by 4 to 7 carbon atoms to form a heterocycloalkyl ring;
R2 and R3 are each independently H or (C1-C3)alkyl;
R4 and R5 are each independently H or (C1-C3) alkyl;
A is H;
R12 and R13 are each independently H or -(C1-C4)alkyl; or
R12 and R13 can be connected by 4 to 7 carbon atoms to form a heterocycloalkyl ring;
X is a bond, -CH2-(R29)p, -C(=O) or -SO2;
R29 is -(C1-C3)alkyl;
W is -(C3-C6)cycloalkyl, -(3 to 7 membered) heterocycloalkyl, -(3 to 7 membered) heterocycloalkyl with 1 or 2 C=O groups, phenyl, or -(5 to 7 member) heteroaryl;
R30 is -(C1-C4)alkyl, -(C1-C3)alkoxy, CN, -F, -Cl, -Br, -I, -NR18R19, -NHC(=O)R18, -SCH3 or -C(=O)CH3;
R18 and R19 are each independently H or -(C1-C3)alkyl;
Q is a bond, -CH-(R31)r, -C(=O) or -SO2;
R31 is independently H or -(C1-C3)alkyl;
Z is -(C3-C8)cycloalkyl, -(4 to 8 member) heterocycloalkyl, phenyl or -(5 to 7 membered) heteroaryl;
R14 is F, Cl, Br, I, V, H, -NR16R17, -OR16, -C(=O)NR16R17, -(SO2)NR16R17, or -NR32C=O-R33;
R15 is -(C1-C2)alkyl, -(C1-C3)alkoxy, -F, -Br, -Cl, -I-OH or -CN;
V is -(C3-C6)cycloalkyl, -(C1-C3)alkyl, (5 to 7 membered) heterocycloalkyl, (5 to 7 membered)heterocycloalkyl substituted with 1 or 2 C=O groups or 1, 2, or 3 (C1-C3)alkyl groups;
R16 and R17 are each independently H, -(C1-C4)alkyl-(R34)u, or -(C3-C6)alkycyloalkyl-(R35)v;
or R16 and R17 together with the nitrogen atom to which they are attached form a 4 to 7 membered heterocycloalkyl ring optionally containing from 1 to 3 additional heteroatoms independently selected from N, S and O, and contain C=O, wherein said heterocycloalkyl ring is optionally and independently substituted with 1 to 3 substituents independently selected from (C1-C2)alkyl, OH, (C1-C3)alkoxy, NH2, -NH(C=O)alkyl, -N(C1-C3)alkyl, CONH2, COH2, CH2OH, CH2Oalkyl(C2-C4), and (5 to 7 membered) heterocycloalkyl;
R32 and R33 are each independently H or (C1-C3)alkyl;
or R32 and R33 can be taken together to form a 3-7 membered cycloalkyl ring, a 3-7 member heterocycloalkyl ring with 1 to 3 heteroatoms, or a 5-7 member heterocycloalkyl ring with 1 to 3 heteroatoms;
R34 and R35 are each independently H, OH, (C1-C3)alkyl, (C2-C4)alkoxy, NH2, NH(C=O)(C1-C3)alkyl, or a 5 to 7 membered heterocycloalkyl;
or R34 and R35 can be taken together to form a bridge containing 1-2 carbon atoms;
or pharmaceutically acceptable salts thereof.

This invention also relates to a compound of the formula I, or a pharmaceutically acceptable salt thereof for use in treating a disorder or condition selected from psychosis, schizophrenia, conduct disorder, disruptive behavior disorder, bipolar disorder, psychotic episodes of anxiety, anxiety associated with psychosis, psychotic mood disorders such as severe major depressive disorder; mood disorders associated with psychotic disorders such as acute mania or depression associated with bipolar disorder and mood disorders associated with schizophrenia, behavioral manifestations of mental retardation, conduct disorder and autistic disorder; movement disorders such as Tourette’s syndrome, akinetic-rigid syndrome, movement disorders associated with Parkinson’s disease, tardive dyskinesia and other drug induced and neurodegeneration based dyskinesias; attention deficit hyperactivity disorder; cognitive disorders such as dementias (including age related dementia, and senile dementia of the Alzheimer’s type) and memory disorders in a mammal, including a human.

This invention also relates to a pharmaceutical composition comprising a compound of the formula I, or a pharmaceutically acceptable salt thereof for use in treating a disorder or condition selected from psychosis, schizophrenia, conduct disorder, disruptive behavior disorder, bipolar disorder, psychotic episodes of anxiety, anxiety associated with psychosis, psychotic mood disorders such as severe major depressive disorder; mood disorders associated with psychotic disorders such as acute mania or depression associated with bipolar disorder and mood disorders associated with schizophrenia, behavioral manifestations of mental retardation, conduct disorder and autistic disorder; movement disorders such as Tourette’s syndrome, akinetic-rigid syndrome, movement disorders associated with Parkinson’s disease, tardive dyskinesia and other drug induced and neurodegeneration based dyskinesias; attention deficit hyperactivity disorder; cognitive disorders such as dementias (including age related dementia and senile dementia of the Alzheimer’s type) and memory disorders in a mammal, including a human.

This invention also relates to a glycine transport-inhibiting amount of a compound of the formula I, or a phar-
Detailed Description of the Invention

[0010] The term "alkyl", as used herein, unless otherwise indicated, includes saturated monovalent hydrocarbon radicals having straight or branched moieties or combinations thereof. Examples of "alkyl" groups include, but are not limited to, methyl, ethyl, propyl, isopropyl, butyl, iso-butyl, sec-butyl, tert-butyl, pentyl, hexyl, heptyl, 3-ethylbutyl, and the like.

[0011] The term "halo", as used herein, means chloro, fluoro, iodo or bromo.

[0012] The term "alkoxy", as used herein, means "alkyl-O-", wherein "alkyl" is defined as above.

[0013] The term "treating", as used herein, refers to reversing, alleviating, inhibiting the progress of, or preventing the disorder or condition to which such term applies, or one or more symptoms of such condition or disorder. The term "treatment", as used herein, refers to the act of "treating" is defined immediately above.

[0014] The term "bridge", as used herein, refers to a bridge, containing 1 or 2 carbons, linking two bridgeheads in a cyclic system to form a bicyclic compound.

[0015] As used herein, the expression "reaction inert solvent" refers to a solvent system in which the components do not interact with starting materials, reagents, or intermediates of products in a manner which adversely affects the yield of the desired product.

[0016] The compounds of formula I can have optical centers and therefore can occur in different enantiomeric configurations. Formula I, as depicted above, includes all enantiomers, diastereomers, and other stereoisomers of the compounds depicted in structural formula I, as well as racemic and other mixtures thereof. Individual isomers can be obtained by known methods, such as optical resolution, optically selective reaction, or chromatographic separation in the preparation of the final product or its intermediate.

[0017] Another embodiment of the invention relates to compounds of formula I, wherein the stereochemistry is defined as in formula II.
Still another embodiment of the invention relates to compounds of formula I, wherein the stereochemistry is defined as in formula III:

Yet another embodiment of the invention relates to compounds of formula I, wherein examples of C₆-C₁₀ aryl include phenyl, indenyl, indanyl and naphthyl; examples of heterocycloalkyl include saturated nonaromatic monocyclic or bicyclic ring systems, wherein said monocyclic ring systems contain from four to seven ring carbon atoms, from one to three of which are replaced with O, N, or S; examples of heteroaryl include pyridinyl, pyridazinyl, imidazolyl, pyrimidinyl, pyrazolyl, triazolyl, pyrazinyl, quinolyl, isoquinolyl, tetrazolyl, furyl, thienyl, isoxazolyl, thiazolyl, oxazolyl, isothiazolyl, pyrrolyl, indolyl, benzimidazolyl, benzofuranyl, cinnolinyl, indazolyl, indoliziny, phthalazinyl, triazinyl, isoindolyl, purinyl, oxadiazolyl, thiazolyl, furazanyl, benzofurazanly, benzothiophenyl, benzotriazolyl, benzothiazolyl, benzoxazolyl, quinazolinyl, quinoxalinyl, naphthyridinyl, dihydroquinolinyl, tetrahydroquinolyl, dihydroisoquinolyl, tetrahydroisoquinolyl, benzofuryl, furopyridinyl, pyrolopirimidinyl, and azaindolyl.
In the definitions of hereinabove, Y can be (R^{100})_k\cdot R^1\cdot (R^6)^m, wherein k is equal to 0 or 1. It is to be understood that when k is 0, R^{100} is a bond so that R^1 is attached directly to the nitrogen atom of the bicyclic ring. As defined herein, R^1 is a bridging group connecting the N atom of the bicyclic ring with R^6. The portion of R^1 that is attached directly to R^6 can be mono, di-, or tri-substituted with R^6 depending upon whether m is one, two or three, respectively. For example, when m is equal to 2, Y is (R^{100})_k\cdot R^1\cdot (R^6)^2.

Compounds of formula I, above, and their pharmaceutically acceptable salts, can be prepared according to the following reaction Schemes I through VIII as discussed herein below. Unless otherwise indicated A, B, D, Q, V, W, X, Y, Z, R^1\cdot R^{35} and R^{100} are defined as above. Isolation and purification of the products is accomplished by standard procedures, which are known to a chemist of ordinary skill.

The compounds of formula I, above, and the intermediates shown in the following reaction schemes can be isolated and purified by conventional procedures, such as recrystallization or chromatographic separation.

Insofar as the compounds of formula I of this invention can contain basic substituents, they are capable of forming a wide variety of different salts with various inorganic and organic acids. Although such salts must be pharmaceutically acceptable for administration to animals, it is often desirable in practice to initially isolate the base compound from the reaction mixture as a pharmaceutically unacceptable salt and then simply convert to the free base compound by treatment with an alkaline reagent and thereafter convert the free base to a pharmaceutically acceptable acid addition salt. The acid addition salts of the base compounds of this invention are readily prepared by treating the base compound with a substantially equivalent amount of the chosen mineral or organic acid in an aqueous solvent or in a suitable organic solvent, such as methanol or ethanol. Upon careful evaporation of the solvent, the desired solid salt is readily obtained.

The acids which are used to prepare the pharmaceutically acceptable acid addition salts of the aforementioned base compounds of this invention are those which form non-toxic acid addition salts, i.e., salts containing pharmaceutically acceptable anions, such as the hydrochloride, hydrobromide, hydroiodide, nitrate, sulfate or bisulfate, phosphate or acid phosphate, acetate, lactate, citrate or acid citrate, tartrate or bi-tartrate, succinate, maleate, fumarate, gluconate, saccharate, benzoate, methanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate and pamoate (i.e., 1,1'-methylene-bis-(2-hydroxy-3-naphthoate)) salts.

The compounds of the present invention exhibit significant glycine transport inhibiting activity and therefore are of value in the treatment of a wide variety of clinical conditions that are characterized by the deficit of glutamatergic neurotransmission in mammalian subjects, especially humans. Such conditions include the positive and negative symptoms of schizophrenia and other psychoses, and cognitive deficits.

The compounds of this invention can be administered via either the oral, parenteral (such as subcutaneous, intravenous, intramuscular, intrasternal and infusion techniques), rectal, intranasal or topical routes to mammals. In general, these compounds are most desirably administered to humans in doses ranging from about 1 mg to about 2000 mg per day, although variations will necessarily occur depending upon the weight and condition of the subject being treated and the particular route of administration chosen. However, a dosage level that is in the range of from about 0.1 mg to about 20 mg per kg of body weight per day is most desirably employed. Nevertheless, variations can still occur depending upon the species of animal being treated and its individual response to said medicament, as well as on the type of pharmaceutical formulation chosen and the time period and interval at which such administration is carried out. In some instances, dosage levels below the lower limit of the aforesaid range can be more than adequate, while in other cases still larger doses can be employed without causing any harmful side effects provided that such higher dose levels are first divided into several small doses for administration throughout the day.

In one embodiment, the compounds of this invention are administered as adjunctive therapy with known antipsychotics such as Geodon.

The compounds of this invention can be administered alone or in combination with pharmaceutically acceptable carriers or diluents by either of the above routes previously indicated, and such administration can be carried out in single or multiple doses. More particularly, the novel therapeutic agents of the invention can be administered in a wide variety of different dosage forms, i.e., they can be combined with various pharmaceutically acceptable inert carriers in the form of tablets, capsules, lozenges, troches, hard candies, powders, sprays, creams, salves, suppositories, jellies, gels, pastes, lotions, ointments, aqueous suspensions, injectable solutions, elixirs, syrups, and the like. Such carriers include solid diluents or fillers, sterile aqueous media and various nontoxic organic solvents, etc. Moreover, oral pharmaceutical compositions can be suitably sweetened and/or flavored. In general, the therapeutically effective compounds of this invention are present in such dosage forms at concentration levels ranging about 5.0% to about 70% by weight.

For oral administration, tablets containing various excipients such as microcrystalline cellulose, sodium citrate, calcium carbonate, dicalcium phosphate and glycerin can be employed along with various disintegrants such as starch and preferably corn, potato or tapioca starch, alginic acid and certain complex silicates, together with granulation binders like polyvinylpyrrolidone, sucrose, gelatin and acacia. Additionally, lubricating agents such as magnesium stearate, sodium lauryl sulfate and talc are often very useful for tabletting purposes. Solid compositions of a similar type can also...
be employed as fillers in gelatine capsules; preferred materials in this connection also include lactose or milk sugar as well as high molecular weight polyethylene glycols. When aqueous suspensions and/or elixirs are desired for oral administration, the active ingredient can be combined with various sweetening or flavoring agents, coloring matter or dyes, and, if so desired, emulsifying and/or suspending agents as well, together with such diluents as water, ethanol, propylene glycol, glycerin and various like combinations thereof.

[0030] For parenteral administration, solutions of a compound of the present invention in either sesame or peanut oil or in aqueous propylene glycol can be employed. The aqueous solutions should be suitably buffered (preferably pH>8) if necessary and the liquid diluent first rendered isotonic. These aqueous solutions are suitable for intravenous injection purposes. The oily solutions are suitable for intra-articular, intra-muscular and subcutaneous injection purposes. The preparation of all these solutions under sterile conditions is readily accomplished by standard pharmaceutical techniques well-known to those skilled in the art. Additionally, it is also possible to administer the compounds of the present invention topically when treating inflammatory conditions of the skin and this can preferably be done by way of creams, jellies, gels, pastes, ointments and the like, in accordance with standard pharmaceutical practice.

[0031] The compounds of the present invention were assayed for their activity in inhibiting glycine reuptake in synaptosomes by first preparing synaptosomes and then measuring neurotransmitter reuptake activity as follows, the results of which are presented in Table 1 above: Male Sprague Dawley rats were decapitated and the brains removed. The whole brains were dissected out and placed in ice cold sucrose buffer; 1 gram in 20 mls (320 mM sucrose containing 1 mg/ml glucose, 0.1 mM EDTA and brought up to pH 7.4 with Tris base). The tissue was homogenized in a glass homogenizing tube with a teflon pestle at 350 RPMS using a Potters homogenizer. The homogenate was centrifuged at 1000 x g for 10 min at 4°C. The resulting supernatant was recentrifuged at 17,000 x g for 20 min at 4 °C. The final pellet was resuspended in an appropriate volume of sucrose buffer containing 5 mM alanine, to yield less than 10 % uptake.

[0032] The uptake assays were conducted in 96 well matrix plates. Each well contained 25μL of solvent, inhibitor or 10 mM glycine for nonspecific uptake, 200 μL of [3H]-glycine (40 nM final), made up in modified Krebs containing 5 mM alanine and glucose (1mg/ml) and 25 μL of synaptosomes. The plates were then incubated at room temperature for the 15 min. The incubation was terminated by filtration through GF/B filters, using a 96 well Brandel Cell Harvester. The filters were washed with modified Krebs buffer and either counted in a liquid scintillation counter or in a LKB Beta Plate counter. Compounds of the invention analyzed by this assay have been found to have significant activity in inhibiting glycine reuptake in synaptosomes, having IC50 values more potent than 10 μM.

[0033] The present invention is illustrated by the examples shown in tables 1 & 2 and preparations below. However, it should be understood that the invention is not limited to the specific details of these examples. Melting points were taken with a Buchi micro melting point apparatus and uncorrected. Infrared Ray absorption spectra (IR) were measured by a Shimazu infrared spectrometer (IR-470). 1H and 13C nuclear magnetic resonance spectra (NMR) were measured at 400 MHz for 1H, 100MHz for 13C.)

A pharmaceutical composition for treating a disorder or condition selected from psychosis, schizophrenia, conduct disorder, disruptive behavior disorder, bipolar disorder, psychotic episodes of anxiety, anxiety associated with psychosis, psychotic mood disorders selected from severe major depressive disorder; mood disorders associated with psychotic disorders selected from acute mania and depression associated with bipolar disorder, and mood disorders associated with schizophrenia; behavioral manifestations of mental retardation, conduct disorder and autistic disorder; movement disorders selected from Tourette’s syndrome, akinetic-rigid syndrome, movement disorders associated with Parkinson’s disease, tardive dyskinesia and other drug-induced and neurodegeneration-based dyskinesias; attention deficit hyperactivity disorder; cognitive disorders selected from dementias, age-related dementia and senile dementia of the Alzheimer’s type; and memory disorders in a mammal, comprising an amount of a compound according to claim 1 that is effective in treating such disorder or condition.

[0035] During any of the following synthetic sequences it can be necessary and/or desirable to protect sensitive or reactive groups on any of the molecules concerned. This can be achieved by means of conventional protecting groups, such as those described in T. W. Greene, Protective Groups in Organic Chemistry, John Wiley & Sons, 1981; and T. W. Greene and P. G. M. Wuts, Protective Groups in Organic Chemistry, John Wiley & Sons, 1991.

[0036] Compounds of formula I, above, and their pharmaceutically acceptable salts, can be prepared according to the following reaction Schemes I through VII as discussed herein below. Unless otherwise indicated A, B, D, Q, V, W, X, Y, Z, R1-R35 and R100 are defined as above. Isolation and purification of the products is accomplished by standard procedures, which are known to a chemist of ordinary skill.

[0037] The following schemes are exemplary of the processes for making compounds of formula I.

[0038] Scheme I illustrates a method for the preparation of reference compounds having the basic structure of formula I, where A is hydrogen, X is C=O or SO2, W is 2-thiophene, Q is a single bond or a methylene group, Y is H, R2 and R3 are H, and Z, R14, R15, and V are described as above.

[0039] Referring to Scheme I, a compound of formula (I) [SynLett, 1996, 1097] can be treated with (BOC)2O in the
presence of a suitable base such as triethylamine, in solvents such as CH$_2$Cl$_2$, to produce the desired carbamate of formula (II). Oxidation of the primary alcohol under Swern conditions with DMSO and oxayl chloride, in the presence of a suitable base such as triethyl amine (TEA) or disopropylethylamine (DIEA), in solvents such as CH$_2$Cl$_2$ or 1,2-dichloroethane (DCE), at temperatures ranging from -78 °C to room temperature, preferably at about room temperature, to produce the corresponding aldehyde (not depicted). Other suitable oxidation reagents for this transformation include TPAP/NMO or PCC.

[0040] Treatment of the aldehyde with an appropriately substituted amine or aniline reagent of formula (III) and a suitable reducing agent such as NaCNBH$_3$, in a solvent such as MeOH, at temperatures ranging from -5 °C to room temperature, preferably at about room temperature, produced the desired amine of formula (IV). Other suitable reducing agents for this reaction include NaBH$_4$ or NaHB(OAc)$_3$, in solvents such as MeOH, CH$_2$Cl$_2$ or DCE. Other suitable conditions for this transformation include treatment of the corresponding aldehyde with the amine reagent (III) in CH$_2$Cl$_2$ or DCE in the presence of 4 A molecular sieves and a base such as TEA at room temperature, followed by treatment with NaHB(OAc)$_3$.

Compounds of formula (VI) can be prepared by treatment of an amine of formula (IV) with an appropriately substituted acid chloride or sulfonyl chloride reagent of formula (V) in the presence of a suitable base such as DIEA, pyridine or TEA, in solvents such as DCE or CH$_2$Cl$_2$, at temperatures ranging from room temperature to about the reflux temperature, preferably at about room temperature, to produce the corresponding compound of formula (VI). Finally, compounds of formula (VII) can be prepared by treatment of a carbamate of formula (VI) with TFA, in solvents such as CH$_2$Cl$_2$ or DCE, at temperatures ranging from 0 °C to about room temperature, preferably at about room temperature, to produce the corresponding amine of formula (VII).

[0041] Compounds of formula (VI) can be prepared by treatment of an amine of formula (IV) with an appropriately substituted amine or aniline reagent of formula (III) and a suitable reducing agent such as NaCNBH$_3$, in a solvent such as MeOH, at temperatures ranging from -5 °C to room temperature, preferably at about room temperature, produced the desired amine of formula (IV). Other suitable reducing agents for this reaction include NaBH$_4$ or NaHB(OAc)$_3$, in solvents such as MeOH, CH$_2$Cl$_2$ or DCE. Other suitable conditions for this transformation include treatment of the corresponding aldehyde with the amine reagent (III) in CH$_2$Cl$_2$ or DCE in the presence of 4 A molecular sieves and a base such as TEA at room temperature, followed by treatment with NaHB(OAc)$_3$.

Scheme II illustrates a method for the preparation of compounds having the basic structure of formula I, where A is hydrogen, X is C=O or SO$_2$, W is 2-thiophene, Q is a single bond or a methylene group, R$_{100}$ is a methylene (CH$_2$) or substituted methylene, R$^2$ and R$^3$ are H, and Z, R$^{14}$, R$^{15}$, R$_1$, R$_6$, m, V and Y are described as above.

[0042] Scheme II illustrates a method for the preparation of compounds having the basic structure of formula I, where A is hydrogen, X is C=O or SO$_2$, W is 2-thiophene, Q is a single bond or a methylene group, R$_{100}$ is a methylene (CH$_2$) or substituted methylene, R$^2$ and R$^3$ are H, and Z, R$^{14}$, R$^{15}$, R$_1$, R$_6$, m, V and Y are described as above.

[0043] Referring to scheme II below, compounds of formula (VIII) can be prepared by treatment of an amine of formula (VII) with an appropriately substituted aldehyde or ketone and a reducing agent such as NaHB(OAc)$_3$, in solvents such as CH$_2$Cl$_2$ or DCE, at temperatures ranging from 0 °C to about room temperature, preferably at about room temperature, to produce the corresponding amine of formula (VIII). Other suitable conditions for this process include treatment of the amine of formula (VII) with an aldehyde in toluene, at about the reflux temperature; followed by treatment with NaBH$_4$,
in solvents such as MeOH, produce the corresponding amine of formula (VIII). Also, treatment of an amine of formula (VII) with an aldehyde and NaCNBH₃ in a solvent such as MeOH, produce the corresponding amine of formula (VIII).

Scheme II

Scheme III illustrates a method for the preparation of compounds having the basic structure of formula I, where A is hydrogen, X is C=O or SO₂, W is 2-thiophene, Q is a single bond or a methylene group, R₁₀⁰ is C=O or SO₂, R² and R³ are H, and Z, R¹₄, R¹₅, R¹, R², V and Y are described as above.

Scheme IV illustrates a method for the preparation of compounds having the basic structure of formula I, where A is hydrogen, X is C=O, Q is a single bond or a methylene group, R₁₀⁰ is C=O, CH₂ or SO₂, R² and R³ are H, and W, q, Z, R¹₄, R¹₅, R¹, R², V and Y are described as above.

[0044] Referring to scheme III below, compounds of formula (VIII), where R₁₀⁰ = C=O, can be prepared by treatment of compounds of formula (VII) with an appropriately substituted acid chloride (R₁₀⁰ = C=O) reagent of formula (IX) in the presence of a suitable base such as DIEA, in solvents such as CH₂Cl₂ or DCE, at temperature ranging from 0 °C to about room temperature, preferably at about room temperature, to produce the corresponding compounds of formula (VIII). Furthermore, compounds of formula (VIII), where R₁₀⁰ = SO₂, can be prepared by treatment of compounds of formula (VII) with an appropriately substituted sulfonyle chloride (R₁₀⁰ = SO₂) reagent of formula (IX), in the presence of a suitable base such as DIEA or TEA, in solvents such as CH₂Cl₂ or DCE, at temperatures ranging from room temperature to about the reflux temperature, preferably at about the reflux temperature, to produce compounds of formula (VIII).

Scheme IV

[0046] Referring to scheme IV below, compounds of formula (XII) can be prepared by treatment of compounds of formula (X) with an appropriately substituted acid chloride reagent of formula (XI) in the presence of a suitable base such as pyridine, DIEA or TEA, in solvents such as CH₂Cl₂ or DCE, at temperature ranging from 0 °C to about room temperature, preferably at about room temperature, to produce the corresponding compounds of formula (XII).
Scheme IV

[0048] Scheme V illustrates a method for the preparation of compounds having the basic structure of formula I, where A is hydrogen, X is a methylene (CH2), Q is a single bond or a methylene group, R100 is C=O or SO2, R2 and R3 are H, and W, o, q, R30, Z, R14, R15, R1, R6, V and Y are described as above.

[0049] Referring to scheme V below, compounds of formula (X) can be treated with a suitable base such as NaH or KH, and an appropriately substituted alkylating agent of formula (XIII), where L is a suitable leaving group such as Cl, Br, I, OMs, OTs, in solvents such as THF or ether, at temperatures ranging from 0 °C to about room temperature, preferably at about room temperature, to produce the compounds of formula (XIV).

Scheme V

[0050] Scheme VI illustrates a method for the preparation of compounds having the basic structure of formula I, where A is hydrogen, Q is a single bond or a methylene group, R100 is C=O, CH2 or SO2, R2 and R3 are H, and X, W, o, q, R30, Z, R14, R15, R1, R6, V and Y are described as above.

[0051] Referring to scheme VI below, treatment of a compound of formula (XV) with an appropriately substituted primary or secondary amine (HNR16R17), a suitable catalyst such as palladium (II) acetate and BINAP, and a base, such as sodium tert-butoxide, in solvents such as toluene, at temperatures ranging from room temperature to about the reflux temperature, preferably, at about the reflux temperature, produces the desired compound of formula (XVI).
Alternatively, compounds of formula (XVI), wherein the Z group is a heteroaryl moiety, such as pyridine group, can be prepared by the alternative method described below. Referring to scheme VII below, treatment of a compound of formula (XVII), wherein halogen is bromo or chloro, neat in an appropriately substituted primary or secondary amine reagent (HNR16R17), at temperatures ranging from 50 °C to about 180 °C, preferably, at about 150 °C, produces the desired compound of formula (XVI). Alternative conditions for this reaction can include treatment of compounds of formula (XVII) with an amine reagent (HNR16R17) in solvents such as DMF or DMP, at temperatures ranging from room temperature to about the reflux temperature to produce the corresponding compounds of formula (XVI).

In the above schemes it is noted that R6 is H. However, the present invention contemplates schemes when R6 is other than H, as defined herein. The chemistry shown in the above schemes is applicable in those cases where R6 is other than hydrogen. However, if any of the substituents in R6 are reactive with the reactants or intermediates, then R6 can be protected with a protecting group using techniques known to skilled in the art such as those described above.

The following Examples illustrate the present invention. It is to be understood, however, that the invention, as fully described herein and as recited in the claims, is not intended to be limited by the details of the following examples.

EXAMPLES
PREPARATION 1
6-Hydroxymethyl-3-aza-bicyclo[3.1.0]hexane-3-carboxylic acid tert-butyl ester

To a solution of (3-Aza-bicyclo[3.1.0]hex-6-yl)-methanol-HCl (11.8gm, 78.7 mmol) in 350 mL of anhydrous CH2Cl2 at room temperature was added Et3N (32.9 mL, 236 mmol), followed by (BOC)2O (18.9 gm, 86.6 mmol) in portions. The reaction was stirred at room temperature for 18 hours. The mixture was washed with saturated NaHCO3, water, brine and dried over anhydrous MgSO4. The mixture was filtered and concentrated under reduced pressure to
yield the crude material, which was purified via flash chromatography with 10 % MeOH/EtOAc. The product containing fractions were collected and concentrated to yield the desired product (15.6 gm). 400 MHz ¹H NMR (CDCl₃) δ 3.42-3.56 (m, 4H), 3.24-3.37 (m, 2H), 1.72 (brs, 1 H), 1.37-1.41 (m, 10 H), 0.87-0.93 (m, 1 H); MS (M+1) 213.2.

PREPARATION 2

6-[(3-Fluoro-4-morpholin-4-yl-phenylamino)-methyl]-3-aza-bicyclo[3.1.0]hexane-3-carboxylic acid tert-butyl ester

To a stirring solution of oxalyl chloride (0.49 mL, 5.63 mmol) in 30 mL of anhydrous CH₂Cl₂ at -78 °C was added DMSO (0.87 mL, 12.2 mmol) dropwise. After 10 minutes, 6-Hydroxymethyl-3-aza-bicyclo[3.1.0]hexane-3-carboxylic acid tert-butyl ester (1.0 gm, 4.69 mmol) in 10 mL anhydrous CH₂Cl₂ was added. After the mixture stirred 30 minutes, triethylamine (3.24 mL, 23.4 mmol) was added and the mixture was allowed to slowly warm to 0 °C over 1 hour. The mixture was concentrated, the resulting solid was taken up in saturated NaHCO₃ and EtOAc, the layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were dried, filtered and concentrated to yield the crude aldehyde, which was used in the next step without purification.

To a stirring solution of the aldehyde prepared above (991 mg, 4.69 mmol) in 30 mL of MeOH was added 3-fluoro-4-morpholinoaniline (920 mg, 4.69 mmol), AcOH (0.38 mL, 6.56 mmol) and NaCNBH₃ (295 mg, 4.69 mmol). The reaction mixture was stirred at room temperature for 90 minutes. The mixture was concentrated under reduced pressure and the resulting material was taken up in saturated NaHCO₃ and extracted with CH₂Cl₂. The combined organic layers were dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash chromatography with 50 % EtOAc/hexanes. The product containing fractions were collected and concentrated to yield 1.3 gm of the desired amine. 400 MHz ¹H NMR (CDCl₃) δ 6.74-6.81 (m, 1 H), 6.30-6.42 (m, 2H), 3.81-3.83 (m, 4H), 3.61 (brs, 1H), 3.59 (d, J = 10.8 Hz, 1H), 3.51 (d, J = 10.8 Hz, 1H), 3.32 (t, J = 9.5 Hz, 2H), 2.93 (brs, 6H), 1.40 (s, 11 H), 0.87-0.92 (m, 1 H); MS (M+1) 392.2.

PREPARATION 3

6-[(3-Fluoro-4-morpholin-4-yl-phenyl)-(thiophene-2-carbonyl)-amino]-methyl]-3-aza-bicyclo[3.1.0]hexane-3-carboxylic acid tert-butyl ester

To a stirring solution of 6-[(3-Fluoro-4-morpholin-4-yl-phenylamino)-methyl]-3-aza-bicyclo[3.1.0]hexane-3-carboxylic acid tert-butyl ester prepared above (500 mg, 1.28 mmol) in 10 mL of DCE at room temperature was added DIEA (0.33 mL, 1.92 mmol) and 2-thiophencarbonylchloride (0.21 mL, 1.92 mmol). After 2 hours, saturated NaHCO₃ was added, and the mixture was extracted with CH₂Cl₂. The combined extracts were dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. The resulting crude material was taken up in 50 % EtOAc/hexanes and the white solids were filtered off. The remaining filtrate was concentrated under reduced pressure to yield 640 mg of the desired product. 400 MHz ¹H NMR (CDCl₃) δ 7.26-7.28 (m, 1H), 6.83-7.15 (m, 4H), 6.76-6.78 (m, 1 H), 3.79-3.85 (m, 5H), 3.54-3.59 (m, 1 H), 3.44 (d, J = 11.0 Hz, 1 H), 3.39 (d, J = 11.0 Hz, 1 H), 3.21-3.26 (m, 4H), 3.08-3.10 (m, 4H), 1.36-1.38 (m, 11 H), 0.81-0.86 (m, 1H); MS (M+1) 402.1

PREPARATION 4

Thiophene-2-carboxylic acid (3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluoro-4-morpholin-4-yl-phenyl)-amide trifluoroacetic acid salt

To a stirring solution of 6-[(3-Fluoro-4-morpholin-4-yl-phenyl)-(thiophene-2-carbonyl)-amino]-methyl]-3-aza-bicyclo[3.1.0]hexane-3-carboxylic acid tert-butyl ester prepared above (640 mg, 1.28 mmol) in 6 mL of CH₂Cl₂ at room temperature was added 6 mL of TFA. The reaction stirred at room temperature for 1 hour. The mixture was concentrated under reduced pressure, taken up in toluene and concentrated again to yield 854 mg of the desired product. 400 MHz ¹H NMR (CDCl₃) δ 9.06 (brs, 1H), 8.62 (brs, 1H), 7.33-7.35 (m, 1H), 7.21-7.25 (m, 1H), 6.94-7.11 (m, 2H), 6.88-6.92 (m, 1H), 6.81-6.84 (m, 1 H), 3.89-3.91 (m, 4H), 3.72 (d, J = 7.05 Hz, 2H), 3.39-3.46 (m, 4H), 3.16-3.18 (m, 4H), 1.77 (brs, 2H), 1.35-1.37 (m, 1 H); MS (M+1) 402.1
EXAMPLE 1

**Thiophene-2-carboxylic acid (3-benzyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluoro-4-morpholin-4-yl-phenyl)-amide**

[0060] To a stirring solution of the Thiophene-2-carboxylic acid (3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluoro-4-morpholin-4-yl-phenyl)-amide trifluoroacetic acid salt prepared above (100 mg, 0.16 mmol) in 4 mL of CH$_2$Cl$_2$ at room temperature was added benzaldehyde (0.02 mL, 0.24 mmol) and NaHB(OAc)$_3$ (50 mg, 0.24 mmol). The reaction stirred at room temperature for 2 hours. The reaction was quenched by the addition of saturated NaHCO$_3$, the layers were separated, and the aqueous layer was extracted with CH$_2$Cl$_2$. The combined organic layers were dried over anhydrous MgSO$_4$, filtered, and concentrated under reduced pressure. The resulting crude material was purified via flash chromatography with 75% EtOAc/hexanes. The product containing fractions were collected and concentrated to yield 32 mg of the desired product. 400 MHz $^1$H NMR (CDCl$_3$) $\delta$ 7.17-7.29 (m, 6H), 6.94-6.98 (m, 4H), 6.78-6.80 (m, 1H), 3.86-3.88 (m, 4H), 3.65 (d, $J$ = 7.47 Hz, 2H), 3.52 (brs, 2H), 3.09-3.12 (m, 4H), 2.86-2.88 (m, 2H), 2.26-2.28 (m, 2H), 1.63 (brs, 1 H), 1.47 (brs, 1 H), 1.21-1.25 (m, 1 H); MS (M+1) 492.2.

**General procedure for the reductive alkylation preparation of compounds of Formula VIII**

[0061] To a stirring solution of 1.0 equiv. of a compound of formula (VII) in methylene chloride (0.2 M) at room temperature was added the appropriately substituted aldehyde reagent (2.0 equiv.), acetic acid (2.0 equiv.) and sodium triacetoxyborohydride (2.0 equiv.). The reaction mixtures were stirred at room temperature for up to 24 hours. The mixtures were then quenched by the addition of saturated sodium bicarbonate solution and extracted with methylene chloride. The combined organic layers were dried over anhydrous MgSO$_4$ and concentrated under reduced pressure. The resulting crude material was purified by flash chromatography to yield the desired tertiary amines in 40-95 % yield.

[0062] The following compounds were made using the above procedure of Example 1, starting with the appropriate starting amine of formula (VII) and the appropriate aldehyde reagent. Furthermore, pharmaceutically acetable salts of the compounds listed below can be prepared as follows. To a stirring solution of compounds of the general formula (VIII) (prepared as described above in Example 1, 1.0 equiv.) in a suitable solvent such as methyl ethyl ketone, methylene chloride/methanol (1:1) or methanol (0.1 M) at room temperature was added the appropriate acid, such as hydrochloric acid, citric acid, p-toluene-sulfonic acid, methanesulfonic acid or benzene sulfonic acid (2-3 equiv) in one portion. The resulting mixture was stirred at room temperature for up to 18 hours, during which time a precipitate formed. Filtration of the solid and drying under reduced pressure afforded the desired salts.

**Thiophene-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide**

[0063] 400 MHz $^1$H NMR (CDCl$_3$) $\delta$ 7.27-7.29 (m, 1H), 7.07-7.13 (m, 4H), 6.90-6.98 (m, 2H), 6.84-6.89 (m, 2H), 6.78-6.80 (m, 1H), 3.86-3.88 (m, 4H), 3.65 (d, $J$ = 7.47 Hz, 2H), 3.50 (brs, 2H), 3.09-3.11 (m, 4H), 2.86-2.89 (m, 2H), 2.59 (q, 2H), 2.28-2.29 (m, 2H), 1.47 (brs, 1H), 1.17-1.27 (m, 5H); MS (M+1) 520.2.

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<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-fluoro-4-morpholin-4-yl-phenyl)-amide</td>
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<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-fluoro-4-morpholin-4-yl-phenyl)-amide</td>
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<td>46</td>
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<td>47</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-fluoro-4-morpholin-4-yl-phenyl)-amide</td>
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<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-fluoro-4-morpholin-4-yl-phenyl)-amide</td>
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<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-fluoro-4-morpholin-4-yl-phenyl)-amide</td>
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(continued)
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<tr>
<td>51</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-methylsulfanyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>52</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-phenoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>4-(6-[[3-Fluoro-4-morpholin-4-yl-phenyl]-(thiophene-2-carbonyl)-amino]-methyl)-3-aza-bicyclo[3.1.0]hex-3-ylmethyl]-benzoic acid methyl ester</td>
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<td>54</td>
<td>Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>55</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-isobutyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>56</td>
<td>Thiophene-2-carboxylic acid [3-(4-acetylamino-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>57</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-imidazol-1-yl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>58</td>
<td>Thiophene-2-carboxylic acid [3-(4-benzyloxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>59</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-pyridin-2-yl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-morpholin-4-yl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>61</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-allyloxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>62</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>63</td>
<td>Thiophene-2-carboxylic acid [3-(4-propoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>64</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-propoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>65</td>
<td>Thiophene-2-carboxylic acid [3-(5-ethyl-thiophen-2-ylmethyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<tr>
<td>66</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-propoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
</tr>
<tr>
<td>67</td>
<td>Thiophene-2-carboxylic acid [3-(4-allyloxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<tr>
<td>68</td>
<td>Thiophene-2-carboxylic acid [3-(4-allyloxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<tr>
<td>69</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-propoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<tr>
<td>70</td>
<td>Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[4-morpholin-4-yl-phenyl]-amide</td>
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<td>71</td>
<td>Thiophene-2-carboxylic acid (4-tert-butyl-phenyl)-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>72</td>
<td>Thiophene-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[4-piperidin-1-yl-phenyl]-amide</td>
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</table>
EXAMPLE 2

Thiophene-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide

[0064] To a stirring solution of thiophene-2-carboxylic acid (3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluoro-4-morpholin-4-yl-phenyl)-amide (50 mg, 0.13 mmol) in 3 mL of anhydrous CH₂Cl₂, was added DIEA (0.065 mL, 0.37 mmol), followed by 4-ethylbenzoyl chloride (0.02 mL, 0.14 mmol). The reaction was stirred at room temperature for 1 hour, quenched with saturated NaHCO₃, and extracted with CH₂Cl₂. The combined extracts were dried over anhydrous MgSO₄, filtered and concentrated. The resulting crude material was purified via flash chromatography with 75% EtOAc/hexanes. The product containing fractions were collected and concentrated to yield 50 mg of a clear colorless oil. 400 MHz ¹H NMR (CDCl₃) δ 7.25-7.28 (m, 3H), 7.14-7.16 (m, 2H), 6.42-6.92 (m, 4H), 6.76-6.78 (m, 1H), 4.02-4.09 (m, 1H), 3.84-3.91 (m, 5H), 3.48-3.54 (m, 2H), 3.08-3.11 (m, 4H), 2.60 (q, 2H), 1.45 (s, 2H), 1.16-1.19 (m, 3H), 0.82-0.85 (m, 1H); MS (M+1) 534.2.

General procedure for the acid chloride preparation of compounds of Formula (VIII), where R¹₀⁰=R=C=O

[0065] To a stirring solution of 1.0 equiv. of a compound of formula (VII) in methylene chloride (0.2 M) at room temperature was added DIEA (2.8 equiv.), followed by the acid chloride reagent of formula (IX) (1.1 equiv.). The reaction mixtures were stirred at room temperature for up to 24 hours. The mixtures were then quenched by the addition of saturated sodium bicarbonate solution and extracted with methylene chloride. The combined organic layers were dried over anhydrous MgSO₄ and concentrated under reduced pressure. The resulting crude material was purified by flash chromatography to yield the desired tertiary amines in 35-95% yield.

[0066] The following compounds were made using the above procedure of Example 2, starting with the appropriate
Furthermore, pharmaceutically acceptable salts of the compounds listed below can be prepared as follows. To a stirring solution of compounds of the general formula (VIII) (prepared as described above in Example 2, 1.0 equiv.) in a suitable solvent such as methyl ethyl ketone, methylene chloride/methanol (1:1) or methanol (0.1 M) at room temperature was added the appropriate acid, such as hydrochloric acid, citric acid, p-toluenesulfonic acid, methansulfonic acid or benzene sulfonic acid (1.0 equiv) in one portion. The resulting mixture was stirred at room temperature for up to 18 hours, during which time a precipitate formed. Filtration of the solid and drying under reduced pressure afforded the desired salts.

<table>
<thead>
<tr>
<th>Compound ID</th>
<th>IUPAC NAME</th>
</tr>
</thead>
<tbody>
<tr>
<td>85</td>
<td>Thiophene-2-carboxylic acid [3-[4-(cyano-dimethyl-methyl)-benzoyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
</tr>
<tr>
<td>86</td>
<td>Thiophene-2-carboxylic acid [3-[4-(cyano-dimethyl-methyl)-benzoyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide</td>
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<tr>
<td>87</td>
<td>Thiophene-2-carboxylic acid [3-[4-(4-tert-butyl-benzoyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[4-(tetrahydro-pyran-4-yl)-phenyl]-amide</td>
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<td>88</td>
<td>Thiophene-2-carboxylic acid [3-[4-(4-tert-butyl-benzoyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[4-(2-oxo-pyrrolidin-1-yl)-phenyl]-amide</td>
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<td>(reference)</td>
<td>Thiophene-2-carboxylic acid [3-[4-(4-tert-butyl-benzoyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[2-[2-ethoxy-ethyl]-1,2,3,4-tetrahydro-isoquinolin-7-yl]-amide</td>
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<td>3-Chloro-thiophene-2-carboxylic acid [3-[4-(4-tert-butyl-benzoyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide</td>
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<td>91</td>
<td>Thiophene-2-carboxylic acid [3-[4-(4-tert-butyl-benzoyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[4-(morpholine-4-carbonyl)-phenyl]-amide</td>
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<td>92</td>
<td>Thiophene-2-carboxylic acid [3-[4-(4-tert-butyl-benzoyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[4-(morpholin-4-ylmethyl)-phenyl]-amide</td>
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<td>93</td>
<td>Thiophene-2-carboxylic acid [3-[4-(4-tert-butyl-benzoyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-thiomorpholin-4-yl-pyridin-3-yl]-amide</td>
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<td>94</td>
<td>Thiophene-2-carboxylic acid [3-[4-(4-tert-butyl-benzoyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-chloro-pyridin-3-yl]-amide</td>
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<td>95</td>
<td>5-Fluoro-thiophene-2-carboxylic acid [3-[4-(4-tert-butyl-benzoyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide</td>
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<td>96</td>
<td>5-Methyl-thiophene-2-carboxylic acid [3-[4-(4-tert-butyl-benzoyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide</td>
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<td>97</td>
<td>Thiophene-2-carboxylic acid [3-[4-(4-tert-butyl-benzoyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[1-(tetrahydro-pyran-4-yl)-pyrrolidin-3-yl]-amide</td>
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<td>98</td>
<td>N-[3-(4-Tert-Butyl-benzoyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-4-methyl-N-(6-morpholin-4-yl-pyridin-3-yl)-benzamide</td>
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<td>Thiophene-2-carboxylic acid [3-[4-(4-tert-butyl-benzoyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-[3,6-dihydro-2H-pyran-4-yl]-pyrrolidin-3-yl]]-amide</td>
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<td>100</td>
<td>Thiophene-2-carboxylic acid [3-[4-(4-tert-butyl-benzoyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>Thiophene-2-carboxylic acid [3-[4-(4-tert-butyl-benzoyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(tetrahydro-pyran-4-yl)-pyridin-3-yl]-amide</td>
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<td>Furan-2-carboxylic acid [3-[4-(4-tert-butyl-benzoyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide</td>
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<td>1-Methyl-1 H-pyrrrole-2-carboxylic acid [3-[4-(4-tert-butyl-benzoyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide</td>
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</table>
**EXAMPLE 3**

Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide

[0068] To a stirring solution of thiophene-2-carboxylic acid (3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluoro-4-morpholin-4-yl-phenyl)-amide (60 mg, 0.15 mmol) in 3 mL of DCE was added DIEA (0.026 mL, 0.45 mmol), DMAP (cat.) and 4-tert-butylbenzene sulfonyl chloride (0.10 mL, 0.45 mmol). The resulting mixture was heated to 80 °C for 1.5 hours, cooled to room temperature and quenched with saturated NaHCO₃. The layers were separated, the aqueous layer was extracted with CH₂Cl₂, and the combined organic layers were dried and concentrated. The resulting crude material was purified via flash chromatography with 40% EtOAc/hexanes. The product containing fractions were collected and concentrated to yield 70 mg of a white foam. 400 MHz ¹H NMR (CDCl₃) δ 7.62-7.66 (m, 2H), 7.47-7.50 (m, 2H), 7.29-7.31 (m, 1 H), 7.17-7.20 (m, 2H), 7.02-7.08 (m, 2H), 6.91-6.95 (m, 2H), 6.77-6.80 (m, 1H), 6.65-6.70 (m, 1H), 6.47-6.50 (m, 1H), 6.35-6.40 (m, 1H), 5.85-5.90 (m, 1H), 5.59-5.64 (m, 1H), 5.35-5.40 (m, 1H), 4.90-4.95 (m, 1H), 4.80-4.85 (m, 1H), 4.70-4.75 (m, 1H), 4.60-4.65 (m, 1H), 4.50-4.55 (m, 1H), 4.40-4.45 (m, 1H), 4.30-4.35 (m, 1H), 4.20-4.25 (m, 1H), 4.10-4.15 (m, 1H), 4.00-4.05 (m, 1H), 3.90-3.95 (m, 1H), 3.80-3.85 (m, 1H), 3.70-3.75 (m, 1H), 3.60-3.65 (m, 1H), 3.50-3.55 (m, 1H), 3.40-3.45 (m, 1H), 3.30-3.35 (m, 1H), 3.20-3.25 (m, 1H), 3.10-3.15 (m, 1H), 3.00-3.05 (m, 1H), 2.90-2.95 (m, 1H), 2.80-2.85 (m, 1H), 2.70-2.75 (m, 1H), 2.60-2.65 (m, 1H), 2.50-2.55 (m, 1H), 2.40-2.45 (m, 1H), 2.30-2.35 (m, 1H), 2.20-2.25 (m, 1H), 2.10-2.15 (m, 1H), 2.00-2.05 (m, 1H), 1.90-1.95 (m, 1H), 1.80-1.85 (m, 1H), 1.70-1.75 (m, 1H), 1.60-1.65 (m, 1H), 1.50-1.55 (m, 1H), 1.40-1.45 (m, 1H), 1.30-1.35 (m, 1H), 1.20-1.25 (m, 1H), 1.10-1.15 (m, 1H), 1.00-1.05 (m, 1H), 0.90-0.95 (m, 1H), 0.80-0.85 (m, 1H), 0.70-0.75 (m, 1H), 0.60-0.65 (m, 1H), 0.50-0.55 (m, 1H), 0.40-0.45 (m, 1H), 0.30-0.35 (m, 1H), 0.20-0.25 (m, 1H), 0.10-0.15 (m, 1H), 0.00-0.05 (m, 1H), 0.00 ppm (s, 3H).
6.79-6.95 (m, 5H), 3.87-3.89 (m, 4H), 3.68 (d, J = 7.47 Hz, 2H), 3.46 (d, J = 9.13 Hz, 2H), 3.13-3.15 (m, 4H), 2.94-2.96 (m, 2H), 1.64 (s, 2H), 1.31 (s, 9H), 1.12-1.14 (m, 1 H); MS (M+1) 598.2.

General procedure for the sulfonyl chloride preparations of compounds of Formula (VIII), where R100 = SO2

[0069] To a stirring solution of 1.0 equiv. of a compound of formula (VII) in DCE (0.2 M) at room temperature was added DIEA (3.0 equiv.), followed by the sulfonyl chloride reagent of formula (IX) (3.0 equiv.). The reaction mixtures were heated at 80 °C for up to 18 hours. The mixtures were then cooled to room temperature, quenched by the addition of saturated sodium bicarbonate solution and extracted with methylene chloride. The combined organic layers were dried over anhydrous MgSO4 and concentrated under reduced pressure. The resulting crude material was purified by flash chromatography to yield the desired tertiary amines in 55-95 % yield.

[0070] The following compounds were made using the above procedure of Example 3, starting with the appropriate starting amine of formula (VII) and the appropriate sulfonyl chloride reagent of formula (IX).

Furthermore, pharmaceutically acceptable salts of the compounds listed below can be prepared as follows. To a stirring solution of compounds of the general formula (VIII) (prepared as described above in Example 3, 1.0 equiv.) in a suitable solvent such as methyl ethyl ketone, methylene chloride/methanol (1:1) or methanol (0.1 M) at room temperature was added the appropriate acid, such as hydrochloric acid, citric acid, p-toluenesulfonic acid, methansulfonic acid or benzene sulfonic acid (1.0 equiv) in one portion. The resulting mixture was stirred at room temperature for up to 18 hours, during which time a precipitate formed. Filtration of the solid and drying under reduced pressure afforded the desired salts.

<table>
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<th>IUPAC NAME</th>
</tr>
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<td>121 (reference)</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-{3-(3-trifluoromethylphenyl)aminomethanesulfonyl}-3-aza-bicyclo[3.1.0]hex-6-ylmethyl-amide</td>
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<tr>
<td>122</td>
<td>Thiophene-2-carboxylic acid {3-[3-[3-(4-chloro-phenoxy)benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-3-fluoro-4-morpholin-4-yl-phenyl}amide</td>
</tr>
<tr>
<td>123</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-{3-[3-(3-trifluoromethoxybenzenesulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-3-fluoro-4-morpholin-4-yl-phenyl}amide</td>
</tr>
<tr>
<td>124</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-{3-(3-cyano-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-3-fluoro-4-morpholin-4-yl-phenyl}amide</td>
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<td>125 (reference)</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-{3-[3-(4-pyridin-2-ylxy]-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-3-fluoro-4-morpholin-4-yl-phenyl}amide</td>
</tr>
<tr>
<td>126</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-{3-[3-(4-butyl-benzenesulfonyl)])-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-3-fluoro-4-morpholin-4-yl-phenyl}amide</td>
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<td>127 (reference)</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-{3-[3-(4-pyridin-3-ylxy]-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-3-fluoro-4-morpholin-4-yl-phenyl}amide</td>
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<td>128</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-{3-[3-(4-pyridin-3-ylxy]-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-3-fluoro-4-morpholin-4-yl-phenyl}amide</td>
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<td>129</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-{3-[3-(4-(4'-fluorobenzensulfonyl))-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-3-fluoro-4-morpholin-4-yl-phenyl}amide</td>
</tr>
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<td>130</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-{3-[3-(1-methyl-1H-imidazole-4-sulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-3-fluoro-4-morpholin-4-yl-phenyl}amide</td>
</tr>
<tr>
<td>131</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-{3-[3-(1-methyl-1H-imidazole-4-sulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-3-fluoro-4-morpholin-4-yl-phenyl}amide</td>
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<td>132</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-{3-[3-(2-acetylamino-4-methyl-thiazole-5-sulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-3-fluoro-4-morpholin-4-yl-phenyl}amide</td>
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<td>Compound ID</td>
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<td>135</td>
<td>Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[4-diethylcarbamoyl-phenyl]-amide</td>
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<td>136</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-methyl-thiophene-2-sulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>137</td>
<td>Thiophene-2-carboxylic acid [3-(4-chloro-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>138</td>
<td>3-Chloro-thiophene-2-carboxylic acid [3-(4-tert-butyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>139</td>
<td>Thiophene-2-carboxylic acid [3-(4-fluoro-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[4-(2-oxo-pyrrolidin-1-yl)-phenyl]-amide</td>
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<td>140</td>
<td>Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>141</td>
<td>Thiophene-2-carboxylic acid [3-(benzo[b]thiophene-2-sulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>142</td>
<td>Thiophene-2-carboxylic acid [3-(biphenyl-3-sulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>143</td>
<td>Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>144</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-phenylmethanesulfonyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide</td>
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<td>145</td>
<td>3-Chloro-thiophene-2-carboxylic acid [3-(4-tert-butyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide</td>
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<td>146</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-phenylmethanesulfonyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide</td>
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<td>147</td>
<td>5-Fluoro-thiophene-2-carboxylic acid [3-(4-tert-butyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide</td>
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<td>148</td>
<td>Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[4-(morpholine-4-carbonyl)-phenyl]-amide</td>
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<td>149</td>
<td>4-Methyl-[1,2,3]thiadiazole-5-carboxylic acid [3-(4-tert-butyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide</td>
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<td>150</td>
<td>1-Methyl-1H-pyrrole-2-carboxylic acid [3-(4-tert-butyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide</td>
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<td>151</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-quinoline-8-sulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide</td>
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<td>152</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-propyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>153</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-methoxy-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>154</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(2-methoxy-4-methyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>155</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-trifluoromethyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>156</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(isoquinoline-5-sulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>157</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-3-(4-isopropyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>158</td>
<td>Thiophene-2-carboxylic acid [3-(5-bromo-6-chloro-pyridine-3-sulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>159</td>
<td>Thiophene-2-carboxylic acid [3-(4-ethyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<tr>
<td>160 (reference)</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(2-oxo-2H-chromene-6-sulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>161</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-fluoro-phenylmethanesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>162</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-nitro-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>163 (reference)</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-trifluoromethyl-phenylmethanesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<tr>
<td>164 (reference)</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-[4-(pyridin-4-oxo)-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>165</td>
<td>4-(6-[[3-Fluoro-4-morpholin-4-yl-phenyl]-(thiophene-2-carbonyl)-amino]-methyl]-3-aza-bicyclo[3.1.0]hexane-3-sulfonyl]-benzoic acid</td>
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<td>166</td>
<td>Thiophene-2-carboxylic acid [3-(biphenyl-4-sulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>167</td>
<td>Thiophene-2-carboxylic acid [3-(4-butoxy-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>168</td>
<td>Thiophene-2-carboxylic acid [3-[4'-chloro-biphenyl-3-sulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>169 (reference)</td>
<td>Thiophene-2-carboxylic acid [3-(4-acetyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<tr>
<td>170</td>
<td>Cyclopropanecarboxylic acid [3-(4-acetylamino-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide</td>
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<tr>
<td>171</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-tert-butyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide</td>
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<td>172</td>
<td>Cyclopentanecarboxylic acid [3-(4-tert-butyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide</td>
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<td>173</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-phenoxy-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide</td>
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<td>174</td>
<td>Cyclobutanecarboxylic acid [3-(4-tert-butyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide</td>
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<td>175</td>
<td>3-[4-(6-[[3-Fluoro-4-morpholin-4-yl-phenyl]-(thiophene-2-carbonyl)-amino]-methyl]-3-aza-bicyclo[3.1.0]hexan-3-sulfonyl]-phenoxy-propionic acid methyl ester</td>
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<tr>
<td>176</td>
<td>Thiophene-2-carboxylic acid [3-(4-acetylamino-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<tr>
<td>177</td>
<td>N-[3-(4-tert-Butyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-4-methyl-N-(6-morpholin-4-yl-pyridin-3-yl)-benzamide</td>
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<tr>
<td>178</td>
<td>Thiophene-2-carboxylic acid [3-(4-1,1-dimethyl-propyl)-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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</tbody>
</table>
**PREPARATION 5**

**[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl]-methanol**

To a stirring solution of (3-Aza-bicyclo[3.1.0]hex-6-yl)-methanol (18.4 gm, 123 mmol) in 450 mL of MeOH at room temperature was added 4-ethylbenzaldehyde (18.5 mL, 135 mmol) and NaCNBH 3 (8.5 gm, 135 mmol). After stirring 3 hours, the reaction mixture was concentrated under reduced pressure, taken up in water, treated with 1 M NaOH, and diluted with CH 2Cl2. The layers were separated, the aqueous layer was extracted with CH 2Cl2 and the combined organic layers were dried and concentrated under reduced pressure. The crude material was dissolved in CH 2Cl2, treated with 1 M HCl and concentrated. This material was taken up in water and extracted with Et 2O, the aqueous layer was basified with NH 4OH and extracted with CH 2Cl2. The combined extracts were dried, filtered and concentrated under reduce pressure to yield 22.4 gm of the desired amine.

400 MHz 1H NMR (CDCl 3) δ 7.14-7.16 (m, 2H), 7.08-7.10 (m, 2H), 3.54 (s, 2H), 3.38-3.40 (m, 2H), 2.95 (d, J = 8.7 Hz, 2H), 2.59 (q, 2H), 2.33 (d, J = 8.7 Hz, 2H), 1.55-1.59 (m, 1 H), 1.42 (brs, 1 H), 1.25-1.26 (m, 2H), 1.18-1.23 (m, 3H); MS (M+1) 232.2.

**PREPARATION 6**

**[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amine**

To a stirring solution of oxalyl chloride (0.45 mL, 5.19 mmol) in 25 mL of anhydrous CH 2Cl2 at -78 °C was added DMSO (0.79 mL, 11.2 mmol) dropwise. After 10 minutes [3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl]-methanol-(1.0 gm, 4.32 mmol) in 10 mL anhydrous CH 2Cl2 was added. After the mixture stirred 30 minutes, triethylamine (3.01 mL, 21.6 mmol) was added and the mixture was allowed to slowly warm to 0 °C over 1 hour. The mixture was concentrated, the resulting solid was taken up in saturated NaHCO 3 and EtOAc, the layers were separated and the aqueous layer was extracted with EtOAc. The combined extracts were dried, filtered and concentrated under reduce pressure to yield 22.4 gm of the desired amine.

400 MHz 1H NMR (CDCl 3) δ 7.18-7.20 (m, 2H), 7.12-7.14 (m, 2H), 6.80-6.84 (m, 1H), 6.29-6.35 (m, 2H), 3.84-3.86 (m, 4H), 3.62 (brs, 1 H), 3.53-3.57 (m, 2H), 3.00 (d, J = 8.70 Hz, 2H), 2.95-2.97 (m, 4H), 2.85 (d, J = 7.05 Hz, 2H), 2.63 (q, 2H), 2.38 (d, J = 8.40 Hz, 2H), 1.59 (s, 1 H), 1.26-1.30 (m, 2H), 1.23 (t, 3H); MS (M+1) 412.2.

The following compounds were made using the above procedure of Preparation 6.

<table>
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<th>Compound ID</th>
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<tbody>
<tr>
<td>179</td>
<td>Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(naphthalene-2-sulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
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<td>180</td>
<td>Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide</td>
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</table>

**[4-Bromo-3-fluoro-phenyl]-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amine**

400 MHz 1H NMR (CDCl 3) δ 7.13-7.23 (m, 4H), 6.27-6.38 (m, 2H), 6.20-6.22 (m, 1H), 3.58 (s, 2H), 3.01 (d, J = 8.70 Hz, 2H), 2.82 (d, J = 7.05 Hz, 2H), 2.62 (q, 2H), 2.39 (d, J = 8.70 Hz, 2H), 1.53-1.57 (m, 1 H), 1.29 (s, 2H), 1.23 (t, 3H); MS (M+1) 405.0.
EXAMPLE 4

Benzo[b]thiophene-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide

[0077] To a stirring solution of [3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amine prepared above (50 mg, 0.12 mmol) in 2 mL of DCE at room temperature was added DIEA (0.03 mL, 0.18 mmol) and 2-benzthiophene carboxylic chloride (0.02 mL, 0.18 mmol). After 1 hour, saturated NaHCO₃ was added, and the mixture was extracted with CH₂Cl₂. The combined extracts were dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. The resulting crude material was taken up in 50 % EtOAc/hexanes and the white solids were filtered off. The remaining filtrate was concentrated under reduced pressure to yield 58 mg of the desired product.

400 MHz ¹H NMR (CDCl₃) δ 7.60-7.68 (m, 2H), 7.24-7.31 (m, 2H), 7.08-7.18 (m, 5H), 6.99-7.02 (m, 2H), 6.86-6.91 (m, 1 H), 3.82-3.88 (m, 4H), 3.68 (d, J = 7.47 Hz, 2H), 3.50 (brs, 2H), 3.10-3.12 (m, 4H), 2.88 (brd, J = 7.47 Hz, 2H), 2.49 (q, 2H), 2.28, (brs, 2H), 1.49 (brs, 1 H), 1.22-1.24 (m, 2H), 1.19 (t, 3H); MS (M+1) 570.2.

[0078] The following compounds were made using the above procedure of Example 4, starting with the appropriate starting amine of formula (X) and the acid chloride reagent of formula (XI).

Furthermore, pharmaceutically acceptable salts of the compounds listed below can be prepared as follows. To a stirring solution of compounds of the general formula (XII) (prepared as described above in Example 4, 1.0 equiv.) in a suitable solvent such as methyl ethyl ketone, methylene chloride/methanol (1:1) or methanol (0.1 M) at room temperature was added the appropriate acid, such as hydrochloric acid, citric acid, p-toluenesulfonic acid, methansulfonic acid or benzene sulfonic acid (1.0 equiv) in one portion. The resulting mixture was stirred at room temperature for up to 18 hours, during which time a precipitate formed. Filtration of the solid and drying under reduced pressure afforded the desired salts.

Thiophene-2-carboxylic acid (4-bromo-3-fluoro-phenyl)-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide

[0080] 400 MHz ¹H NMR (CDCl₃) δ 7.54 (t, 1H), 7.31-7.32 (m, 1H), 7.04-7.12 (m, 5H), 6.93-6.95 (m, 1H), 6.80-6.84 (m, 2H), 3.67 (d, J = 7.47 Hz, 2H), 3.49 (s, 2H), 2.85 (d, J = 8.71 Hz, 2H), 2.59 (q, 2H), 2.25 (d, J = 8.31 Hz, 2H), 1.46 (brs, 1H), 1.18-1.24 (m, 5H); MS (M+1) 513.0, 514.8.

<table>
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<th>Compound ID</th>
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<tr>
<td>181</td>
<td>N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-isonicotinamide</td>
</tr>
<tr>
<td>182 (reference)</td>
<td>Benzofuran-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide</td>
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<td>183</td>
<td>Furan-3-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide</td>
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<td>184 (reference)</td>
<td>N-{1-[[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-carbamoyl]-ethyl}-benzamide</td>
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<td>185</td>
<td>3-Bromo-thiophene-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide</td>
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<td>186</td>
<td>3-Methyl-furan-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide</td>
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<td>187</td>
<td>5-Methyl-isoxazole-3-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide</td>
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<td>188</td>
<td>N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-2-methoxy-benzamide</td>
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<td>189</td>
<td>3-Methyl-thiophene-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide</td>
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<tr>
<td>190</td>
<td>N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-4-methoxy-benzamide</td>
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<td>IUPAC NAME</td>
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<td>191</td>
<td>2,5-Dimethyl-furan-3-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>192</td>
<td>N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-4-methyl-benzamide</td>
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<td>193</td>
<td>5-Methyl-thiophene-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>194</td>
<td>5-tert-Butyl-2-methyl-2H-pyrazole-3-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>195</td>
<td>N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-3,5-dimethoxy-benzamide</td>
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<td>196</td>
<td>N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-3-methoxy-benzamide</td>
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<td>197</td>
<td>1,5-Dimethyl-1H-pyrazole-3-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
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<td>198</td>
<td>3-Ethoxy-thiophene-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
</tr>
<tr>
<td>199</td>
<td>Isoxazole-5-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
</tr>
<tr>
<td>200</td>
<td>1-Methyl-1H-imidazole-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
</tr>
<tr>
<td>201</td>
<td>Furan-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
</tr>
<tr>
<td>202</td>
<td>N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-2-methyl-benzamide</td>
</tr>
<tr>
<td>203 (reference)</td>
<td>Benzo[b]thiophene-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
</tr>
<tr>
<td>204</td>
<td>4-Cyano-N-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-benzamide</td>
</tr>
<tr>
<td>205</td>
<td>4-Ethyl-N-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-benzamide</td>
</tr>
<tr>
<td>206</td>
<td>3-Chloro-thiophene-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
</tr>
<tr>
<td>207</td>
<td>N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-2-methylsulfonyl-nicotinamide</td>
</tr>
<tr>
<td>208</td>
<td>1-Methyl-1H-pyrazole-3-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
</tr>
<tr>
<td>209</td>
<td>N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-2,4-difluoro-N-(3-fluoro-4-morpholin-4-yl-phenyl)-benzamide</td>
</tr>
<tr>
<td>210</td>
<td>N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-nicotinamide</td>
</tr>
<tr>
<td>211</td>
<td>3,5-Dimethyl-1H-pyrazole-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
</tr>
<tr>
<td>212</td>
<td>1-Methyl-1H-pyrole-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide</td>
</tr>
</tbody>
</table>
EXAMPLE 5

Thiophene-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-methyl-piperazin-1-yl)-phenyl]-amide

[0081] To a stirring solution of the (4-Bromo-3-fluoro-phenyl)-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amine prepared above (100 mg, 0.20 mmol) in 3 mL of anhydrous toluene at room temperature was added N-methylpiperazine (0.03 mL, 0.23 mmol), BINAP (9.1 mg, 0.015 mmol), NaOtBu (26 mg, 0.27 mmol) and palladium (II) acetate (2.2 mg, 0.009 mmol). The mixture was evacuated under reduced pressure and purged with N2. The reaction mixture was heated to 100 °C for 18 hours. The mixture was cooled to room temperature, quenched with saturated NaHCO3, and extracted with CH2Cl2. The combined organic layers were dried and concentrated under reduced pressure. Purification of the crude material by flash chromatography with 5% MeOH/ CH2Cl2 produced the desired product (24 mg) as a white foam. 400 MHz 1H NMR (CDCl3) δ 7.27-7.29 (m, 1H), 7.08-7.15 (m, 4H), 6.89-6.98 (m, 3H), 6.77-6.84 (m, 2H), 3.64 (d, J = 7.05 Hz, 2H), 3.53 (s, 2H), 3.15-3.17 (m, 4H), 2.90 (brs, 2H), 2.57-2.62 (m, 6H), 2.29-2.40 (m, 5H), 1.39 (brs, 1H), 1.27 (brs, 2H), 1.19 (t, 3H); MS (M+1) 533.2.

[0082] The following compounds were made using the above procedure of Example 5, starting with the appropriate starting bromide of formula (XV) and the corresponding amine (R16 R17 NH).

<table>
<thead>
<tr>
<th>Compound ID</th>
<th>IUPAC NAME</th>
</tr>
</thead>
<tbody>
<tr>
<td>213</td>
<td>2-Methyl-thiazole-4-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-methyl-phenyl)-amide</td>
</tr>
<tr>
<td>214</td>
<td>4-Bromo-N-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-y1-phenyl)-benzamide</td>
</tr>
<tr>
<td>215</td>
<td>5-Oxo-pyrrolidine-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-y1-phenyl)-amide</td>
</tr>
<tr>
<td>216 (reference)</td>
<td>N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-2-(2-methoxy-phenyl)-acetamide</td>
</tr>
<tr>
<td>217 (reference)</td>
<td>N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-2-(2-fluoro-phenyl)-acetamide</td>
</tr>
<tr>
<td>218</td>
<td>1-Acetyl-pyrrolidine-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide</td>
</tr>
<tr>
<td>219</td>
<td>Thiophene-3-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide</td>
</tr>
<tr>
<td>220 (reference)</td>
<td>N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-2-pyridin-3-yl-acetamide</td>
</tr>
<tr>
<td>221</td>
<td>5-Bromo-thiophene-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide</td>
</tr>
<tr>
<td>222 (reference)</td>
<td>N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-2-o-tolyl-acetamide</td>
</tr>
</tbody>
</table>

Thiophene-2-carboxylic acid [4-(4-acetyl-piperazin-1-yl)-3-fluoro-phenyl]-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide

[0084] 400 MHz 1H NMR (CDCl3) δ 7.27-7.29 (m, 1 H), 6.95-7.09 (m, 4H), 6.88-6.91 (m, 2H), 6.85-6.87 (m, 2H), 6.77-6.84 (m, 2H), 3.64 (d, J = 7.05 Hz, 2H), 3.53 (s, 2H), 3.15-3.17 (m, 4H), 2.90 (brs, 2H), 2.57-2.62 (m, 6H), 2.29-2.40 (m, 5H), 1.39 (brs, 1H), 1.27 (brs, 2H), 1.19 (t, 3H); MS (M+1) 533.2.
EXAMPLE 6

Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3,4,5,6-tetrahydro-2H-[1,2']bipyridylin-5'-yl]-amide

[0085] A stirring solution of the Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-chloro-pyridin-3-yl]-amide prepared above (50 mg, 0.10 mmol) in 1 mL of anhydrous piperidine was heated to 150 °C for 18 hours. The mixture was cooled to room temperature, quenched with water, and extracted with Et₂O. The combined organic layers were dried over anhydrous MgSO₄ and concentrated under reduced pressure to yield the desired compound (40 mg, 73%).

[0086] The following compounds were made using the above procedure of Example 6, starting with the appropriate starting bromo or chloro compounds of formula (XVII) and the corresponding amine (R₁⁶R₁⁷NH). Furthermore, pharmaceutically acceptable salts of the compounds listed below can be prepared as follows. To a stirring solution of compounds of the general formula (XVI) (prepared as described above in Example 6, 1.0 equiv.) in a suitable solvent such as methyl ethyl ketone, methylene chloride/methanol (1:1) or methanol (0.1 M) at room temperature was added the appropriate acid, such as hydrochloric acid, citric acid, p-toluenesulfonic acid, methansulfonic acid or benzene sulfonic acid (1.0 equiv) in one portion. The resulting mixture was stirred at room temperature for up to 18 hours, during which time a precipitate formed. Filtration of the solid and drying under reduced pressure afforded the desired salts.

<table>
<thead>
<tr>
<th>Compound ID</th>
<th>IUPAC NAME</th>
</tr>
</thead>
<tbody>
<tr>
<td>223</td>
<td>Thiophene-2-carboxylic acid [4-(4-acetyl-[1,4]diazepan-1-yl)-3-Tfluoro-phenyl]-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
</tr>
<tr>
<td>224</td>
<td>Thiophene-2-carboxylic acid [6-(4-acetyl-piperazin-1-yl)-pyridin-3-yl]-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
</tr>
<tr>
<td>225</td>
<td>Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3,4,5,6-tetrahydro-2H-[1,2']bipyridinylin-5'-yl]-amide</td>
</tr>
<tr>
<td>226 (reference)</td>
<td>Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(5-methyl-2,5-diaza-bicyclo[2.2.1]hept-2-yl)-pyridin-3-yl]-amide</td>
</tr>
<tr>
<td>227</td>
<td>Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-amide</td>
</tr>
<tr>
<td>228</td>
<td>Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-[ethyl-(2-methoxy-ethyl)-amino]-pyridin-3-yl]-amide</td>
</tr>
<tr>
<td>229</td>
<td>Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-[[1H-imidazol-2-ylmethyl]-methyl-amino]-pyridin-3-yl]-amide</td>
</tr>
<tr>
<td>230</td>
<td>Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(3-oxo-piperazin-1-yl)-pyridin-3-yl]-amide</td>
</tr>
<tr>
<td>231</td>
<td>Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-[[2-methoxy-ethyl]-methyl-amino]-pyridin-3-yl]-amide</td>
</tr>
<tr>
<td>232</td>
<td>Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-[[3-dimethylamino-pyrrolidin-1-yl]-pyridin-3-yl]-amide</td>
</tr>
<tr>
<td>233</td>
<td>Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(4-methyl-[1,4]diazepan-1-yl)-pyridin-3-yl]-amide</td>
</tr>
<tr>
<td>234</td>
<td>Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(3-diethylamino-pyrrolidin-1-yl)-pyridin-3-yl]-amide</td>
</tr>
<tr>
<td>235</td>
<td>Thiophene-2-carboxylic acid [6-[1,3']bipyrrrolidinyl-1'-yl-pyridin-3-yl]-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide</td>
</tr>
</tbody>
</table>
Claims

1. A compound of formula I:

wherein:

- Y is \((R^{100})_k-R^1-(R^8)_m\);
- \(k\) is 0 or 1;
- \(l = 0, 1, 2\) or 3;
- \(m = 1, 2\) or 3;
- \(n\) is 0, 1, 2, 3 or 4;
- \(o\) is 0 or 1;
- \(p\) is 0, 1, 2, or 3;
- \(q\) is 0, 1, 2, 3 or 4;
- \(r\) is 1 or 2;
- \(s\) is 0, 1, 2, 3 or 4;
- \(t\) is 0 or 1;
- \(u\) is 1, 2, or 3;
- \(v\) is 1, 2, or 3;
- \(R^{100}\) is \(-\text{CH}_2\), \(-\text{CH}(\text{C}_1\text{C}_3)\text{alkyl}\), \(-\text{C}(=\text{O})\)- or \(-\text{SO}_2\)-;
R1 is -(C1-C6)alkyl, -(C3-C8)cycloalkyl, -(4 to 7 membered) heterocycloalkyl, -(CH2)-((C6-C10)aryl) or -(5 to 10 membered) heteroaryl, or -(5 to 10 membered) tetrahydro-heteroaryl;
each R6 can be same or different and is independently selected from H, halo, -(C1-C6)alkyl-B, (C1-C7) alkoxy-D, (C2-C4)alkenoxycycloalkyl-ONH2, -(CR7R8R9)-alkyl heteroaryl, -S-R24, and -SO2-R25;
B and D are each independently H, OH, phenyl, diphenyl or trifluoro;
E and F are each independently H, alkyl, or halo;
R7, R8 and R9 are each independently H, (C1-C6)alkyl, -(C1-C7)alkoxy-D, (C2-C4)alkenoxycycloalkyl-ONH2, -(CR7R8R9)-alkyl heteroaryl, -S-R24, and -SO2-R25;
E and F are each independently H, alkyl, or halo;
R7, R8 and R9 are each independently H, (C1-C6)alkyl, -(C1-C7)alkoxy-D, (C2-C4)alkenoxycycloalkyl-ONH2, -(CR7R8R9)-alkyl heteroaryl, -S-R24, and -SO2-R25;
or R20 and R21 can be connected by 4 to 7 carbon atoms wherein one to three of said carbon atoms can optionally be replaced with O, N or S, to form a heterocycloalkyl ring;
or R20 and R21 can be connected by 3 to 7 atoms selected from C, N, O or S to form a 5 to 10 membered heteroaryl ring;
R22, R23 and R24 are each independently H, or (C1-C5)alkyl;
R25 is (C1-C5)alkyl;
R26 and R27 are each independently H or (C1-C3)alkyl;
or R26 and R27 can be connected by 4 to 7 carbon atoms to form a heterocycloalkyl ring;
R2 and R3 are each independently H or (C1-C3)alkyl;
or R2 and R3 can be connected by 4 to 7 carbon atoms wherein one to two of said carbon atoms can optionally be replaced with O, N or S, to form a heterocycloalkyl ring;
or R2 and R3 can be connected by 3 to 7 atoms selected from C, N, O or S to form a 5 to 10 membered heteroaryl ring;
R2 and R3 are each independently H or (C1-C6)alkyl;
or R2 and R3 can be connected by 3 to 7 atoms selected from C, N, O or S to form a 5 to 10 membered heteroaryl ring;
A is H;
R12 and R13 are each independently H or -(C1-C4)alkyl; or
R12 and R13 can be connected by 4 to 7 carbon atoms to form a heterocycloalkyl ring;
Z is -(C3-C8)cycloalkyl, -(4 to 8 membered) heterocycloalkyl, -(3 to 7 membered) heterocycloalkyl with 1 or 2 C=O groups, phenyl, or -(5 to 7 member) heteroaryl;
V is -(C3-C8)cycloalkyl, -(C1-C5)alkyl, and (5 to 7 membered) heterocycloalkyl, (5 to 7 membered) heterocycloalkyl substituted with 1 or 2 C=O groups or 1, 2, or 3 (C1-C5)alkyl groups;
or R16 and R17 together with the nitrogen atom to which they are attached form a 4 to 7 membered heterocycloalkyl ring optionally containing from 1 to 3 additional heteroatoms independently selected from N, S and O, and contain C=O, wherein said heterocycloalkyl ring is optionally and independently substituted with 1 to 3 substituents independently selected from (C1-C6)alkyl, OH, (C1-C6)alkoxy, NH2, -(NH(C=O)alkyl, -(N(C1-C3)alkyl)2, -(C=O)CH2, CONH2, CO2H, CH2OH, CH2Oalkyl(C2-C4), and (5 to 7 membered) heterocycloalkyl;
or R32 and R33 are each independently H or (C1-C5)alkyl;
or R32 and R33 can be taken together to form a bridge containing 1-2 carbon atoms; or
or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1, wherein the stereochemistry is as in formula II:
3. A compound according to claim 1, wherein the stereochemistry is as in formula III:

4. A compound according to claim 1, selected from the group consisting of:

- Thiophene-2-carboxylic acid (3-cyclohexylmethyl-3-aza-bicyclo[3.1.0]hex-6-yl)-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
- Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-methylbenzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
- Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-methoxybenzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
- Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(1-hydroxy-cyclohexylmethyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
- Thiophene-2-carboxylic acid [3-(4-butyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-pyridin-3-ylmethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid [3-(4-chloro-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
Thiophene-2-carboxylic acid [3-(4-fluoro-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-pyridin-3-ylmethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-quinolin-2-ylmethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-quinolin-3-ylmethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-naphthalen-1-ylmethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-naphthalen-2-ylmethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-quinoxalin-6-ylmethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-phenethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-naphthalen-1-ylmethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-phenethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-naphthalen-1-ylmethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-phenethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-naphthalen-1-ylmethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-phenethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-naphthalen-1-ylmethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-phenethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-phenethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-phenethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-phenethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-phenethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(2-fluoro-3-trifluoromethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-(2-hydroxy-ethoxy)-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-methanesulfonyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(1-methyl-1H-pyrrol-2-ylmethyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-furan-3-ylmethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-thiophen-3-ylmethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-trifluoromethoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-tert-butoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-bromo-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-isopropyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-methylsulfanyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-phenoxybenzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-isobutyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-imidazol-1-yl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-benzyloxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-pyridin-2-yl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-morpholin-4-yl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-pyrimidin-5-yl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4,5,6,7-tetrahydro-benzothiazol-2-ylmethyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-(3-propoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid [3-(5-ethyl-thiophen-2-ylmethyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid [3-(3-ethoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid [3-fluoro-4-morpholin-4-yl-phethyl]-amide;
Thiophene-2-carboxylic acid [3-(4-allyloxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid [3-(3-ethoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-propoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-propoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-allyloxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-propoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-allyloxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-propoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
5-Methyl-thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[1-(tetrahydro-pyran-4-yl)-pyrrolidin-3-yl]-amide;
N-[3-(4-tert-Butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-4-methyl-N-(6-morpholin-4-yl-pyridin-3-yl)-benzamide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(3,6-dihydro-2H-pyran-4-yl)-pyrindin-3-yl]-amide;
Thiophene-2-carboxylic acid [3-(4-ethyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(tetrahydro-pyran-4-yl)-pyrindin-3-yl]-amide;
Furan-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide;
1-Methyl-1H-pyrrole-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide;
4-Methyl-[1,2,3]thiadiazole-5-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide;
Pyridine-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide;
2-Methyl-thiazole-4-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[4-morpholin-4-yl-cyclohexyl]-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[4-morpholin-4-yl-cyclohexyl]-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-methyl-pyridin-3-yl]-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide;
Thiophene-2-carboxylic acid [3-(2-(4-tert-butyl-phenyl)-acetyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[4-diethylcarbamoyl-phenyl]-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[1-(tetrahydro-pyran-4-yl)-piperidin-4-yl]-amide;
3-Chloro-thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-(tetrahydro-pyran-4-yl)-3-aza-bicyclo[3.1.0]hex-6-yl]-amide;
N-[3-(4-tert-Butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-6-morpholin-4-yl-N-thiophen-2-ylmethyl-nicotinamide;
Thiophene-2-carboxylic acid [3-(4-chloro-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide;
Thiophene-2-carboxylic acid [3-(4-trifluoromethoxy-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluoro-4-morpholin-4-yl-phenyl]-amide;
Thiophene-2-carboxylic acid \{3\-[4-(4-chloro-phenoxy)-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-3-fluoro-4-morpholin-4-yl-phenyl\}-amide;
Thiophene-2-carboxylic acid \{3\-[4\-fluoro-biphenyl-4-sulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-3-fluoro-4-morpholin-4-yl-phenyl\}-amide;
Thiophene-2-carboxylic acid \{3\-[4\-bromo-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-3-fluoro-4-morpholin-4-yl-phenyl\}-amide;
Thiophene-2-carboxylic acid \{3\-[2-acetylamino-4-methyl-thiazole-5-sulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-amid;
Thiophene-2-carboxylic acid \{3\-[4-tert-butyl-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-4-diethylcarbamoyl-phenyl\}-amide;
Thiophene-2-carboxylic acid \{3\-[4-tert-butyl-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-[4-(2-oxo-pyrrolidin-1-yl)-phenyl\}-amide;
Thiophene-2-carboxylic acid \{3\-[benzo[b]thiophene-2-sulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-3-fluoro-4-morpholin-4-yl-phenyl\}-amide;
Thiophene-2-carboxylic acid \{3\-[biphenyl-3-sulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-3-fluoro-4-morpholin-4-yl-phenyl\}-amide;
Thiophene-2-carboxylic acid \{3\-[3-phenylmethanesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-3-fluoro-4-morpholin-4-yl-phenyl\}-amide;
3-Chloro-thiophene-2-carboxylic acid \{3\-[4-tert-butyl-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-3-fluoro-4-morpholin-4-yl-phenyl\}-amide;
Thiophene-2-carboxylic acid \{3\-[4-tert-butyl-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-[4-(morpholine-4-carbonyl)-phenyl\}-amide;
4-Methyl-[1,2,3]thiadiazole-5-carboxylic acid \{3\-[4-tert-butyl-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-[4-(morpholine-4-carbonyl)-phenyl\}-amide;
1-Methyl-1H-pyrrole-2-carboxylic acid \{3\-[4-tert-butyl-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-[6-morpholin-4-yl-pyridin-3-yl\}-amide;
Thiophene-2-carboxylic acid \{3\-[quinoline-8-sulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-3-fluoro-4-morpholin-4-yl-phenyl\}-amide;
Thiophene-2-carboxylic acid \{3\-[4-propyl-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-3-fluoro-4-morpholin-4-yl-phenyl\}-amide;
Thiophene-2-carboxylic acid \{3\-[4-methoxybenzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-3-fluoro-4-morpholin-4-yl-phenyl\}-amide;
Thiophene-2-carboxylic acid \{3\-[2-methoxy-4-methyl-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-3-fluoro-4-morpholin-4-yl-phenyl\}-amide;
Thiophene-2-carboxylic acid \{3\-[4-trifluoromethyl-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-3-fluoro-4-morpholin-4-yl-phenyl\}-amide;
Thiophene-2-carboxylic acid \{3\-[isoquinoline-5-sulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-3-fluoro-4-morpholin-4-yl-phenyl\}-amide;
Thiophene-2-carboxylic acid \{3\-[4-isopropyl-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-3-fluoro-4-morpholin-4-yl-phenyl\}-amide;
Thiophene-2-carboxylic acid \{3\-[4 chloro-benzenesulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl\}-3-fluoro-4-morpholin-4-yl-phenyl\}-amide;
Thiophene-2-carboxylic acid [3-(4-ethyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl](3-fluoro-4-morpholin-4-yl-phenyl)-amide;

Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)[3-(4-fluorobenzenesulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;

Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)[3-(4-nitrobenzenesulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;

4-(6-[[3-Fluoro-4-morpholin-4-yl-phenyl]-[thiophene-2-carbonyl]-amino]-methyl]-3-aza-bicyclo[3.1.0]hexane-3-sulfonic acid;

Thiophene-2-carboxylic acid (3-(biphenyl-4-sulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)(3-fluoro-4-morpholin-4-yl-phenyl)-amide;

Thiophene-2-carboxylic acid [3-(4-butoxyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl](3-fluoro-4-morpholin-4-yl-phenyl)-amide;

Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-fluorobenzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;

Thiophene-2-carboxylic acid (3-fluoro-4-morpholin-4-yl-phenyl)-[3-(4-ethyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;

5-Methyl-isoxazole-3-carboxylic acid [3-(4-ethyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;

N-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-isonicotinamide;
5-tert-Butyl-2-methyl-2H-pyrazole-3-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-3,5-dimethoxy-benzamide;
N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-3-methoxy-benzamide;
1.5-dimethyl-1H-pyrazole-3-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
3-Ethoxy-thiophene-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
Isoxazole-5-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
1-Methyl-1H-imidazole-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
Furan-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-2-methyl-benzamide;
4-Cyano-N-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-benzamide;
4-Ethyl-N-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-benzamide;
3-Chloro-thiophene-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-2-methylsulfonyl-nicotinamide;
1-Methyl-1H-pyrazole-3-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-benzamide;
N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-2,4-difluoro-N-(3-fluoro-4-morpholin-4-yl-phenyl)-benzamide;
N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-nicotinamide;
3,5-Dimethyl-1H-pyrrole-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
1-Methyl-1H-pyrrole-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
2-Methyl-thiazole-4-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
4-Bromo-N-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluoro-4-morpholin-4-yl-phenyl)-benzamide;
5-Oxo-pyrrolidine-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
1-Acetyl-pyrrolidine-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
Thiophene-3-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
5-Bromo-thiophene-2-carboxylic acid [3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluoro-4-morpholin-4-yl-phenyl)-amide;
Thiophene-2-carboxylic acid [4-(4-acetyl-[1,4]diazepan-1-yl)-3-fluoro-phenyl]-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid [6-(4-acetyl-piperazin-1-yl)-pyridin-3-yl]-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3,4,5,6-tetrahydro-2H-[1,2]bipyrindinyl-5'-yl)-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(ethyl-2-methoxy-ethyl)-aminol-pyridin-3-yl]-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-[[1H-imidazol-2-

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ylmethyl)-methyl-amino]-pyridin-3-yl]-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(3-oxo-piperazin-1-yl)-pyridin-3-yl]-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-[(2-methoxyethyl)-methyl-amino]-pyridin-3-yl]-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(3-dimethylamino-pyrrolidin-1-yl)-pyridin-3-yl]-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(3-morpholin-4-yl-azetidin-1-yl)-pyridin-3-yl]-amide;
Thiophene-2-carboxylic acid [3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(3-morpholin-4-yl-pyrrolidin-1-yl)-pyridin-3-yl]-amide;
or a pharmaceutically acceptable salt thereof.

5. A pharmaceutical composition comprising a compound of claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

6. A compound of claim 1, or a pharmaceutically acceptable salt thereof, for use as a medicament.

7. A compound of claim 1, or a pharmaceutically acceptable salt thereof, for use in the treatment of a disorder or condition selected from psychosis, schizophrenia, conduct disorder, disruptive behavior disorder, bipolar disorder, psychotic episodes of anxiety, anxiety associated with psychosis, psychotic mood disorders, severe major depressive disorder, mood disorders associated with psychotic disorders, acute mania, depression associated with bipolar disorder, mood disorders associated with schizophrenia, behavioral manifestations of mental retardation, conduct disorder, autistic disorder, movement disorders, Tourette’s syndrome, akinetic-rigid syndrome, movement disorders associated with Parkinson’s disease, tardive dyskinesia, other drug induced and neurodegeneration based dyskinesias, attention deficit hyperactivity disorder, cognitive disorders, dementias, and memory disorders.

Patentansprüche

1. Verbindung der Formel I:
worin:

Y gleich (R100)k-R1-(R6)m ist;
k gleich 0 oder 1 ist;
l = 0, 1, 2 oder 3 ist;
m = 1, 2 oder 3 ist;
n gleich 0, 1, 2, 3 oder 4 ist;
o gleich 0 oder 1 ist;
p gleich 0, 1, 2, oder 3 ist;
q gleich 0, 1, 2, oder 4 ist;
r gleich 1 oder 2 ist;
s gleich 0, 1, 2, oder 4 ist;
t gleich 0 oder 1 ist;
u gleich 1, 2, oder 3 ist;
v gleich 1, 2, oder 3 ist;
R100 gleich -CH2-, -CH(C1-C3)Alkyl-, -C(=O)- oder -SO2- ist;
R1 gleich -(C1-C6)Alkyl, -(C3-C8)Cycloalkyl, -(4- bis 7-gliedrigen) Heterocycloalkyl, -(CH2)-(C6-C10-Aryl) oder -(5-bis 10-gliedrigen) Heteroaryl ist;
B und D jeweils unabhängig H, OH, Phenyl, Diphenyl oder Trifluor sind;
E und F jeweils unabhängig H, Alkyl oder Halogen sind;
R7, R8 und R9 jeweils unabhängig H, -OH, -(C1-C4)Alkyl, -CN, -NR26R27 und -NHCO-Alkyl sind, wobei die Alkylgruppen gegebenenfalls substituiert sind mit OH, OCH3, NH2, NHC(=O)(C1-C3)Alkyl, oder R7 und R8 bilden zusammen mit dem Kohlenstoffatom an das sie gebunden sind, gegebenenfalls einen (C3-C7)Cycloalkylring oder einen (C4-C7)Heterocycloalkylring, der 1-3 Heteroatome enthält, ausgewählt aus N, O, S und gegebenenfalls eine C==O-Gruppe enthält;
R20 und R21 jeweils unabhängig H oder -(C1-C6)Alkyl sind;
oder R20 und R21 können verbunden sein durch 4 bis 7 Kohlenstoffatome, wobei eines bis drei der Kohlenstoffatome gegebenenfalls ersetzt sein kann durch O, N oder S, um einen Heterocycloalkylring zu bilden;
ooder R20 und R21 können verbunden sein durch 3 bis 7 Atome, ausgewählt aus C, N, O oder S, um einen 5-bis 10-gliedrigen Heteroarylring zu bilden;
R22, R23 und R24 jeweils unabhängig H oder -(C1-C6)Alkyl sind;
R²⁵ (C₁-C₅)Alkyl ist;  
R²⁶ und R²⁷ jeweils unabhängig H oder (C₁-C₃)Alkyl sind;  
or R²⁶ und R²⁷ können verbunden sein durch 4 bis 7 Kohlenstoffatome, um einen Heterocycloalkylyring zu bilden;  
R² und R³ jeweils unabhängig H oder (C₁-C₅)Alkyl sind;  
R⁴ und R⁵ jeweils unabhängig H oder (C₁-C₅)Alkyl sind;  
A gleich H ist;  
R¹² und R¹³ jeweils unabhängig H oder -(C₁-C₅)Alkyl sind;  
or R¹² und R¹³ können verbunden sein durch 4 bis 7 Kohlenstoffatome, um einen Heterocycloalkylyring zu bilden;  
X eine Bindung, -CH₂-(R²⁹)p, -C(=O) oder -SO₂ ist;  
R²⁹-(C₁-C₃)Alkyl ist;  
W -(C₂-C₅)Cycloalkyl, -(3- bis 7-gliedriges) Heterocycloalkyl, -(3- bis 7-gliedriges) Heterocycloalkyl mit 1 oder 2 C=O-Gruppen, Phenyl, oder -(5- bis 7-gliedriges) Heteroaryl ist;  
R³⁰-(C₁-C₅)Alkyl, -(C₁-C₅)Alkoxy, CN, -F, -Cl, -Br, -I, -NR¹⁸R¹⁹, -NHC(=O)R¹⁸, -SCH₃ oder -C(=O)CH₃ ist;  
R¹⁸ und R¹⁹ jeweils unabhängig H oder -(C₁-C₅)Alkyl sind;  
Q eine Bindung, -CH-(R³¹)q, -C(=O) oder -SO₂ ist;  
R³¹ unabhängig H oder -(C₁-C₅)Alkyl ist;  
Z -(C₂-C₅)Cycloalkyl, -(4- bis 8-gliedriges) Heterocycloalkyl, Phenyl oder -(5- bis 7-gliedriges) Heteroaryl ist;  
R¹⁴ F, Cl, Br, I, V, H, -NR¹⁶R¹⁷, -OR¹⁶, -C(=O)NR¹⁶R¹⁷, -(SO₂)NR¹⁶R¹⁷, oder -NR³²-C=O-R³³ ist;  
R¹⁵-(C₁-C₅)Alkyl, -(C₁-C₅)Alkoxy, -F, -Br, -Cl, -I -OH oder -CN ist;  
V -(C₂-C₅)Cycloalkyl, -(C₁-C₅)Alkyl, -(5- bis 7-gliedriges) Heterocycloalkyl, -(5- bis 7-gliedriges) Heterocycloalkyl substituiert mit 1 oder 2 C=O-Gruppen oder 1, 2 oder 3 (C₁-C₅)Alkylgruppen ist;  
R¹⁶ und R¹⁷ jeweils unabhängig H, -(C₁-C₅)Alkyl-(R³⁴)u oder -(C₂-C₅)Cycloalkyl-(R³⁵)v ist;  
or R¹⁶ und R¹⁷ bilden zusammen mit dem Stickstoffatom, an das sie gebunden sind, einen 4- bis 7-gliedrigen Heterocycloalkylyring, gegebenenfalls enthaltend von 1 bis 3 weiteren Heteroatomen, unabhängig ausgewählt aus N, S und O, und enthalten C=O, wobei der Heterocycloalkylyring gegebenenfalls und unabhängig substituiert ist mit 1 bis 3 Substituenten, unabhängig ausgewählt aus (C₁-C₅)Alkyl, (C₁-C₅)Alkoxy, NH₂, -NH(C=O)Alkyl, -N(C₁-C₅)Alkyl)-₂, -(C=O)CH₂, CONH₂, CO₂H, CH₂OH, CH₂O-Alkyl(C₂-C₄) und (5- bis 7-gliedrigem) Heterocycloalkyl;  
R³² und R³³ jeweils unabhängig H oder -(C₁-C₅)Alkyl sind;  
or R³² und R³³ können zusammen einen 3-7-gliedrigen Cycloalkylyring, einen 3-7-gliedrigen Heterocycloalkylyring mit 1 bis 3 Heteroatomen, oder einen 5-7-gliedrigen Heteroarylring mit 1 bis 3 Heteroatomen bilden;  
R³⁴ und R³⁵ sind jeweils unabhängig H, OH, (C₁-C₅)Alkyl, (C₂-C₄)Alkoxy, NH₂, NH(C=O) (C₁-C₅)Alkyl, oder ein 5- bis 7-gliedriges Heterocycloalkyl;  
or R³⁴ und R³⁵ können zusammengenommen eine Brücke bilden, enthaltend 1-2 Kohlenstoffatome;  
or ein pharmazeutisch annehmbares Salz davon.

2. Verbindung nach Anspruch 1, worin die Stereochemie wie in Formel II dargestellt ist:
3. Verbindung nach Anspruch 1, wobei die Stereochemie wie in Formel III dargestellt ist:

4. Verbindung nach Anspruch 1, ausgewählt aus der Gruppe, bestehend aus:

- Thiophen-2-carbonsäure-(3-cyclohexylmethyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluor-4-morpholin-4-yl-phenyl)-amid;
- Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-(3-(4-methyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amid;
- Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-(3-(4-methoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amid;
- Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-(3-(1-hydroxy-cyclohexylmethyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amid;
- Thiophen-2-carbonsäure-(3-(4-butyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluor-4-morpholin-4-yl-
phenyl)-amid;
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-(3-pyridin-3-ylmethyl-3-aza-bicyclo[3.1.0]hex-6-yl-
phenyl)-amid;
Thiophen-2-carbonsäure-[3-(4-chlor-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-
phenyl]-amid;
Thiophen-2-carbonsäure-[3-(4-fluor-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-
phenyl]-amid;
Thiophen-2-carbonsäure-[3-(2-ethyl-5-methyl-3H-imidazol-4-ylmethyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-
fluor-4-morpholin-4-yl-phenyl]-amid;
Thiophen-2-carbonsäure-[3-(2-fluor-4-morpholin-4-yl-phenyl)][3-(2-p-tolyl-ethyl)-3-aza-bicyclo[3.1.0]hex-6-
ylmethyl]-amid;
Thiophen-2-carbonsäure-[3-(4-chlor-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-
phenyl]-amid;
Thiophen-2-carbonsäure-[3-(4-fluor-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-
phenyl]-amid;
Thiophen-2-carbonsäure-[3-(2-ethyl-5-methyl-3H-imidazol-4-ylmethyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-
fluor-4-morpholin-4-yl-phenyl]-amid;
Thiophen-2-carbonsäure-[3-(2-fluor-4-morpholin-4-yl-phenyl)][3-(2-p-tolyl-ethyl)-3-aza-bicyclo[3.1.0]hex-6-
ylmethyl]-amid;
Thiophen-2-carbonsäure-[3-(4-chlor-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-
phenyl]-amid;
Thiophen-2-carbonsäure-[3-(4-fluor-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-
phenyl]-amid;
Thiophen-2-carbonsäure-[3-(2-ethyl-5-methyl-3H-imidazol-4-ylmethyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-
fluor-4-morpholin-4-yl-phenyl]-amid;
Thiophen-2-carbonsäure-[3-(2-fluor-4-morpholin-4-yl-phenyl)][3-(2-p-tolyl-ethyl)-3-aza-bicyclo[3.1.0]hex-6-
ylmethyl]-amid;
Thiophen-2-carbonsäure-[3-(4-chlor-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-
phenyl]-amid;
Thiophen-2-carbonsäure-[3-(4-fluor-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-
phenyl]-amid;
Thiophen-2-carbonsäure-[3-(2-ethyl-5-methyl-3H-imidazol-4-ylmethyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-
fluor-4-morpholin-4-yl-phenyl]-amid;
Thiophen-2-carbonsäure-[3-(2-fluor-4-morpholin-4-yl-phenyl)][3-(2-p-tolyl-ethyl)-3-aza-bicyclo[3.1.0]hex-6-
ylmethyl]-amid;
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-tert-butoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;  
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-brom-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;  
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-isobutyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;  
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-acetylamino-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;  
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-imidazol-1-yl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;  
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-benzyloxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;  
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-pyridin-2-yl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;  
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-morpholin-4-yl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;  
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-pyrimidin-5-yl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;  
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(3-propoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;  
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(3-phenyl-propyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
methyl]-amid;
Thiophen-2-carbonsäure-[3-{5-ethyl-thiophen-2-ylmethyl}-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{3-fluor-4-morpholin-4-yl-phenyl]-amid;
Thiophen-2-carbonsäure-[3-(3-ethoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{3-fluor-4-morpholin-4-yl-phenyl]-amid;
Thiophen-2-carbonsäure-[3-fluor-4-morpholin-4-yl-phenyl]-{3-(4-propoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-[3-(4-allyloxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{3-fluor-4-morpholin-4-yl-phenyl]-amid;
Thiophen-2-carbonsäure-[3-fluor-4-morpholin-4-yl-phenyl]-{3-hexyl-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-[3-(4-ethylbenzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{3-fluor-4-morpholin-4-yl-phenyl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{4-(4-ethyl-2,6-dioxo-piperidin-4-yl)-phenyl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{4-(4-ethyl-2-hydroxy-ethyl)-amino-phenyl}-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{4-(4-ethylbenzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{4-oxo-pyrrolidin-1-yl-phenyl]-amid;
Thiophen-2-carbonsäure-{3-[2-fluor-4-(1-hydroxy-1-methyl-ethyl)-benzyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{4-(4-ethyl-2-hydroxy-ethyl)-amino-phenyl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{4-(tetrahydro-pyran-4-yl)-phenyl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{4-(2-oxo-pyrrolidin-1-yl)-phenyl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{4-(morpholin-4-carbonyl)-phenyl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{4-(morpholin-4-carbonyl)-phenyl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{4-(thiomorpholin-4-yl)-phenyl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{4-(morpholin-4-carbonyl)-phenyl]-amid;
3-Chlor-thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{6-morpholin-4-yl-pyridin-3-yl]-amid;
3-Chlor-thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{6-morpholin-4-yl-pyridin-3-yl]-amid;
3-Chlor-thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{6-morpholin-4-yl-pyridin-3-yl]-amid;
3-Chlor-thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{6-morpholin-4-yl-pyridin-3-yl]-amid;
3-Chlor-thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{6-morpholin-4-yl-pyridin-3-yl]-amid;
3-Chlor-thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{6-morpholin-4-yl-pyridin-3-yl]-amid;
3-Chlor-thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{6-morpholin-4-yl-pyridin-3-yl]-amid;
3-Chlor-thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{6-morpholin-4-yl-pyridin-3-yl]-amid;
3-Chlor-thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{6-morpholin-4-yl-pyridin-3-yl]-amid;
3-Chlor-thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-{6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[1-(tetrahydro-pyran-4-yl)-pyrrolidin-3-yl]-amid;
N-[3-(4-tert-Butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-4-methyl-N-(6-morpholin-4-yl-pyridin-3-yl)-benzamid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(3,6-dihydro-2H-pyran-4-yl)-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-ethyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-(fluor-4-morpholin-4-yl-phenyl)]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(tetrahydro-pyran-4-yl)-pyridin-3-yl]-amid;
Furan-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
1-Methyl-1H-pyrrol-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
4-Methyl-[1,2,3]thiadiazol-5-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Pyrindin-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
2-Methyl-thiazol-4-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-morpholin-4-yl-pyridin-3-yl]-amide;
Thiophen-2-carbonsäure-[3-(4-fluor-biphenyl-4-sulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluor-4-morpholin-4-yl-phenyl)-amid;
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(1-methyl-1H-imidazol-4-sulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-[3-(4-brom-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluor-4-morpholin-4-yl-phenyl)-amid;
Thiophen-2-carbonsäure-[3-(4-brom-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluor-4-morpholin-4-yl-phenyl)-amid;
Thiophen-2-carbonsäure-[3-(4-fluor-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluor-4-morpholin-4-yl-phenyl)-amid;
3-Chlor-thiophen-2-carbonsäure-[3-(4-tert-butyl-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluor-4-morpholin-4-yl-phenyl)-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(4-diethylcarbamoyl-phenyl)-amid;
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-methyl-thiophen-2-sulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-[3-(4-chlor-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(3-fluor-4-morpholin-4-yl-phenyl)-amid;
3-Chlor-thiophen-2-carbonsäure-[3-(4-tert-butyl-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(6-morpholin-4-yl-pyridin-3-yl)-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(6-morpholin-4-yl-pyridin-3-yl)-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(6-morpholin-4-yl-pyridin-3-yl)-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(4-morpholin-4-carbonyl)-phenyl]-amid;
4-Methyl-[1,2,3]thiadiazol-5-carbonsäure-[3-(4-tert-butyl-benzensulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(6-morpholin-4-yl-pyridin-3-yl)-amid;
1-Methyl-1H-pyrrol-2-carbonsäure-[3-(4-tert-butyl-benzensulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-(6-morpholin-4-yl-pyridin-3-yl)-amid;
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(chinoxalin-8-sulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-propyl-benzensulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-methoxy-benzensulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(2-methoxy-4-methyl-benzensulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-trifluormethyl-benzensulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(isochinolin-5-sulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-isopropyl-benzensulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-[3-(5-brom-6-chlor-pyridin-3-sulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-[3-(4-propyl-benzensulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-[3-(4-ethyl-benzensulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-fluor-methylsulfonyl)-3-aza-bicyclo[3.1.0]hexan-3-yl]-amid;
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-nitro-benzensulfonyl)-3-aza-bicyclo[3.1.0]hexan-3-yl]-amid;
4-(6-[(3-Fluor-4-morpholin-4-yl-phenyl)-(thiophen-2-carbonyl)-amino]-methyl)-3-aza-bicyclo[3.1.0]hexan-3-sulfonyl]-benzoesäure;
Thiophen-2-carbonsäure-[3-(biphenyl-4-sulfondl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-[3-(4-butoxy-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-[3-(4'-chlor-biphenyl-3-sulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Cyclopropancarbonsäure-[3-(4-tert-butyl-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-pentyl-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Cyclopentancarbonsäure-[3-(4-tert-butyl-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(4-phenoxy-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Cyclobutancarbonsäure-[3-(4-tert-butyl-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
3-[4-(6-[(3-Fluor-4-morpholin-4-yl-phenyl)-(thiophen-2-carbonyl)-amino]-methyl]-3-aza-bicyclo[3.1.0]hexan-3-sulfonyl]-phenyl]-propionsäuremethylester;
Thiophen-2-carbonsäure-[3-(4-acetylamino-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
N-[3-(4-tert-Butyl-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-4-methyl-N-(6-morpholin-4-yl-pyridin-3-yl)-benzamid;
Thiophen-2-carbonsäure-[3-[4-(1,1-dimethyl-propyl)-benzensulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-(3-fluor-4-morpholin-4-yl-phenyl)-[3-(naphthalen-2-sulfonyl)-3-aza-bicyclo[3.1.0]hexan-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzensulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluor-4-morpholin-4-yl-phenyl)-isonicotinamid;
Furan-3-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
3-Brom-thiophen-2-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
3-Methyl-furan-2-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
5-Methyl-isoxazol-3-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluor-4-morpholin-4-yl-phenyl)-3,5-dimethoxybenzamid;
3-Methyl-thiophen-2-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hexan-3-sulfonyl]-amid;
3-Methyl-thiophen-2-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hexan-3-sulfonyl]-amid;
N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hexan-3-sulfonyl]-benzoesäure;
3,5-Dimethyl-furan-3-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hexan-3-sulfonyl]-amid;
N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hexan-3-sulfonyl]-benzoesäure;
5-Methyl-thiophen-2-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hexan-3-sulfonyl]-amid;
5-tert-Butyl-2-methyl-2H-pyrrozol-3-carbonsäure-[3-(4-ethylbenzyl)-3-aza-bicyclo[3.1.0]hexan-3-sulfonyl]-amid;
N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hexan-3-sulfonyl]-benzoesäure;
benzamid;
N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluor-4-morpholin-4-yl-phenyl)-3-methoxybenzamid;
1,5-Dimethyl-1H-pyrazol-3-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-phenyl]-amid;
3-Ethoxy-thiophen-2-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-phenyl]-amid;
Isoxazol-5-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-phenyl]-amid;
1-Methyl-1H-imidazol-2-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-phenyl]-amid;
Furan-2-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-phenyl]-amid;
N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluor-4-morpholin-4-yl-phenyl)-2-methyl-benzamid;
4-Cyano-N-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluor-4-morpholin-4-yl-phenyl)-benzamid;
3-Chlor-thiophen-2-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-phenyl]-amid;
N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluor-4-morpholin-4-yl-phenyl)-2-methylsulfanyl-nicotinamid;
1-Methyl-1H-pyrazol-3-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-phenyl]-amide;
N-[3-(4-Ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluor-4-morpholin-4-yl-phenyl)-2-methylbenzamid;
4-Ethyl-N-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-N-(3-fluor-4-morpholin-4-yl-phenyl)-benzamid;
1-Acetyl-pyrrolidin-2-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-phenyl]-amide;
7-Methyl-thiophen-2-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-phenyl]-amide;
5-Oxo-pyrrolidin-2-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-phenyl]-amide;
1-Acetyl-pyrrolidin-2-carbonsäure-[3-(4-ethyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[3-fluor-4-morpholin-4-yl-phenyl]-amide;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-[(2-methoxy-ethyl)-methyl-amino]-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(3-dimethylamino-pyrrolidin-1-yl)-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(4-methyl-[1,4]diazepan-1-yl)-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(3-diethylamino-pyrrolidin-1-yl)-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-(6-[1,3′]bipyridinyl-1′-yl-pyridin-3-yl)-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(3-morpholin-4-yl-azetidin-1-yl)-pyridin-3-yl]-amid;
Thiophen-2-carbonsäure-[3-(4-tert-butyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl]-[6-(3-morpholin-4-yl-pyrrolidin-1-yl)-pyridin-3-yl]-amid;
oder ein pharmazeutisch verträgliches Salz davon.

5. Pharmazeutische Zusammensetzung, umfassend eine Verbindung nach Anspruch 1 oder ein pharmazeutisch annehmbares Salz davon, und einen pharmazeutisch annehmbaren Trägerstoff oder ein pharmazeutisch annehmbares Verdünnungsmittel.

6. Verbindung nach Anspruch 1 oder ein pharmazeutisch annehmbares Salz davon zur Verwendung als ein Medikament.


Revendications

1. Composé de formule I :
dans laquelle :

Y est un groupe \((R^{100})_k-R^l-(R^6)_m\);

dans laquelle :

k vaut 0 ou 1 ;

l = 0, 1, 2 ou 3 ;

m = 1, 2 ou 3 ;

n vaut 0, 1, 2, 3 ou 4 ;

o vaut 0 ou 1 ;

p vaut 0, 1, 2 ou 3 ;

q vaut 0, 1, 2, 3 ou 4 ;

r vaut 1 ou 2 ;

s vaut 0, 1, 2, 3 ou 4 ;

t vaut 0 ou 1 ;

u vaut 1, 2 ou 3 ;

v vaut 1, 2 ou 3 ;

R^{100} est un groupe -CH2-, -CH(alkyle en C1 à C3)-, -C(=O)- ou -SO2- ;

R^l est un groupe alkyle en C1 à C6, cycloalkyle en C3 à C8, hétérocycloalkyle(tétra- à heptagonal), -(CH2)_l-(aryle en C6 à C10 ou hétéroaryle(penta- à décagonal) ou tétrahydro-hétéroaryle(penta- à décagonal) ;

dans laquelle :

echape R^l peut être identique ou différent et est choisi indépendamment parmi H, un groupe halogéné, (alkyle en C1 à C6)-B, (alkoxy en C1 à C7)-D, alcénoxy en C2 à C4, (alkyle en C1 à C6)-OH, -OH, CN, -NO2, -CR7R8R9, -NR20R21, -NHCOalkyle en C1 à C3, NHSO2-alkyle en C1 à C3, C(=O)OR22, -R23-C(=O)OR22, -C(=O)NH2, phényle-E, phénolxy-F, morpholine, -NR20R21, aryle, hétéroaryl, -S-R24 et -SO2-R25 ;

B et D sont chacun indépendamment H, un groupe OH, phényle, diphényle ou trifluoro ;

E et F sont chacun indépendamment H, un groupe alkyle ou halogéné ;

R^7, R^8 et R^9 sont chacun indépendamment H, un groupe alkyle en C1 à C4, -OH, -O-(alkyle en C1 à C4), -CN, -NR26R27 et -NHC(=0)alkyle en C1 à C3, où lesdits groupes alkyle sont éventuellement substitués avec des groupes OH, OCH3, NH2, NH=C(O)alkyle en C1 à C3, ou R^7 et R^9, conjointement avec l’atome de carbone auquel ils sont attachés, forment éventuellement un noyau cycloalkyle en C3 à C7, ou un noyau hétérocycloalkyle en C4 à C7 qui contient 1 à 3 hétéroatomes choisis parmi N, 0, S et contient éventuellement un groupe C=O ;

R^20 et R^21 sont chacun indépendamment H ou un groupe alkyle en C1 à C6 ;

ou R^20 et R^21 peuvent être connectés par 4 à 7 atomes où de un à trois desdits atomes de carbone peuvent éventuellement être remplacés avec 0, N ou S, pour former un cycle hétérocycloalkyle ;

ou R^20 et R^21 peuvent être connectés par 3 à 7 atomes de carbone choisis parmi C, N, 0 ou S pour former un noyau hétéroaryle penta- à décagonal ;

R^22, R^23 et R^24 sont chacun indépendamment H ou un groupe alkyle en C1 à C5 ;

R^25 est un groupe alkyle en C1 à C5 ;
R26 et R27 sont chacun indépendamment H ou un groupe alkyle en C1 à C3 ;
or R26 et R27 peuvent être connectés par 4 à 7 atomes de carbone pour former un noyau hétérocycloalkyle ;
R2 et R3 sont chacun indépendamment H ou un groupe alkyle en C1 à C3 ;
R4 et R5 sont chacun indépendamment H ou un groupe alkyle en C1 à C3 ;
A est H ;
R12 et R13 sont chacun indépendamment H ou un groupe alkyle en C1 à C4 ; ou
R12 et R13 peuvent être connectés par 4 à 7 atomes de carbone pour former un noyau hétérocycloalkyle ;
X est une liaison, un groupe -CH2-(R29)p, -C(=O) ou -SO2- ;
R29 est un groupe alkyle en C1 à C3 ;
W est un groupe cycloalkyle en C3 à C6, hétérocycloalkyle(tri- à heptagonal), hétérocycloalkyle(tri- à heptagonal)
avec 1 ou 2 groupes C=O, phényle ou hétéroaryle(penta- à heptagonal) ;
R30 est un groupe alkyle en C1 à C2, alkoxy en C1 à C3, CN, -F, -Cl, -Br, -l, -NR18R19, -NHC(=O)R18, -SCH3
ou -C(=O)CH3 ;
R18 et R19 sont chacun indépendamment H ou un groupe alkyle en C1 à C3 ;
Q est une liaison, un groupe -CH(R31)r, -C(=O) ou -SO2 ;
R31 est indépendamment H ou un groupe alkyle en C1 à C3 ;
Z est un groupe cycloalkyle en C3 à C6, hétérocycloalkyle(tétra- à octagonal), phényle ou hétéroaryle(penta- à
heptagonal) ;
R14 est F, Cl, Br, I, V, H, un groupe -NR16R17, -OR16, -C(=O)NR16R17, -(SO2)NR16R17 ou -NR32-C=O-R33 ;
V est un groupe cycloalkyle en C3 à C6, alkyle en C1 à C6, hétérocycloalkyle(penta- à heptagonal), hétérocycloalkyle(penta- à heptagonal) substitué avec 1 ou 2 groupes C=O ou 1, 2 ou 3 groupes alkyle en C1 à C5 ;
R16 et R17 sont chacun indépendamment H, un groupe -(alkyle en C1 à C6) - (R34)u, ou cycloalkyle en C3 à
C6-(R35)v ;
ou R16 et R17, conjointement avec l’atome d’azote auquel ils sont attachés, forment un noyau hétérocycloalkyle
tétra- à heptagonal contenant éventuellement de 1 à 3 hétéroatomes supplémentaires choisis indépendamment
parmi N, S et 0, et contiennent C=O, ledit noyau hétérocycloalkyle étant éventuellement et indépendamment
substitué avec 1 à 3 substituants choisis indépendamment parmi des groupes alkyle en C1 à C5, OH, alkoxy en
C1 à C4, NH2, NH(C=O)alkyle, -N (alkyle en C1 à C3)2, -C(=O)-CH3, CONH2, CO2H, CH2OH, CH2O-alkyle en
C1 à C4, et hétérocycloalkyle(penta- à heptagonal) ;
R32 et R33 sont chacun indépendamment H ou un groupe alkyle en C1 à C5 ;
or R32 et R33 peuvent être pris conjointement pour former un noyau cycloalkyle tri- à heptagonal, un noyau
hétérocycloalkyle tri- à heptagonal avec 1 à 3 hétéroatomes, ou un groupe hétéroaryle penta- à heptagonal
avec 1 à 3 hétéroatomes ;
R34 et R35 sont chacun indépendamment H, un groupe OH, alkyle en C1 à C6, alkoxy en C2 à C4, NH2, 
NH(C=O)alkyle en C1 à C3, ou un groupe hétérocycloalkyle penta- à heptagonal ;
or R34 et R35 peuvent être pris conjointement pour former un pont contenant 1 à 2 atomes de carbone ;
or un de ses sels pharmaceutiquement acceptables.

2. Composé selon la revendication 1, dans lequel la stéréochimie est comme dans la formule II :
3. Composé selon la revendication 1, dans lequel la stéréochimie est comme dans la formule III :

4. Composé selon la revendication 1, choisi dans le groupe constitué par
   le (3-cyclohexylméthyl-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl)-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide thiophène-2-carboxylique ;
   le (3-fluoro-4-morpholine-4-yl-phényl)-(3-(4-méthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl)-amide d’acide thiophène-2-carboxylique ;
   le (3-fluoro-4-morpholine-4-yl-phényl)-(3-(4-méthoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl)-amide d’acide thiophène-2-carboxylique ;
   le (3-fluoro-4-morphonoline-4-yl-phényl)-(3-(1-hydroxy-cyclohexylméthyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl)-amide d’acide thiophène-2-carboxylique ;
   le [3-(4-butyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide thiophène-2-carboxylique ;
   le (3-fluoro-4-morpholine-4-yl-phényl)-(3-pyridine-3-yl-méthyl-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl)-amide d’acide thiophène-2-carboxylique ;
le [3-(4-chloro-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide thiophène-2-carboxylique ;
le [3-(4-fluoro-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide thiophène-2-carboxylique ;
le [3-(2-éthyl-5-méthyl-3H-imidazole-4-ylméthyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-[3-(2-p-tolyl-éthyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-(3-thiophène-2-ylméthyl-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-(3-quinoléine-2-ylméthyl-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-[3-(4-nitro-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-[3-(3-méthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-[3-(3,4,5-tri-méthoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-(3-pyridine-2-ylméthyl-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-[3-(4-dichloro-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-[3-(3-méthoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-[3-(5-hydroxy-méthyl-furanne-2-ylméthyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-[3-(1H-indole-3-ylméthyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-(3-pyridine-4-ylméthyl-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-[3-(2-méthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-[3-(3-phénoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-(3-naphtalène-1-ylméthyl-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-(3-naphtalène-2-ylméthyl-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-[3-(3-trifluoro-méthoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-[3-(3-méthyl-benzo[b]thiophène-2-ylméthyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-(3-quinoxaline-6-ylméthyl-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-(3-quinoléine-4-ylméthyl-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-(3-quinoléine-3-ylméthyl-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-y1-phényl)-[3-(2-fluoro-5-trifluorométhyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-amide d’acide thiophène-2-carboxylique ;

le (3-fluoro-4-morpholine-4-yl-phényl)-(3-[4-(2-hydroxy-éthoxy)-benzyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-(3-[4-méthane-sulfonyl-benzyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-(3-[1-méthyl-1H-pyrrole-2-ylméthyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-(3-[4-hydroxy-benzyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-(3-[4-trifluoro-méthoxy-benzyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-(3-[4-trifluoro-méthyl-benzyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluo-4-morpholine-4-yl-phényl)-(3-[4-isopropyl-benzyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-(3-[4-isobutyl-benzyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-(3-[4-imidazole-1-yl-benzyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-(3-[4-pyridine-2-yl-benzyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-(3-[4-morpholine-4-yl-benzyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-(3-[4,5,6,7-tétrahydro-benzothiazole-2-ylméthyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-(3-[3-prooxy-benzyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-(3-[5-éthyl-thiophène-2-ylméthyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-(3-[3-phényl-propyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-(3-[5-éthyl-thiophène-2-ylméthyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le [3-(3-éthoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-[3-(4-proproxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-allyoxy-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-(3-hexyl-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobuty1-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-(4-morpholine-4-yl-benzyl)-amide d’acide thiophène-2-carboxylique ;
le (4-tertiobutyl-phényl)-[3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-(3-hexyl-3-aza-bicyclo[3.1.0]hex-6-ylméthyl)-amide d’acide thiophène-2-carboxylique ;
le (4-tertiobutyl-amino-phényl)-[3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-déthylamino-phényl)-3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-(4-pipéridine-1-yl-phényl)-amide d’acide thiophène-2-carboxylique ;
le (4-diéthylamino-phényl)-[3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-cyclohexylméthyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-amide d’acide thiophène-2-carboxylique ;
le {3-[2-fluoro-4-(1-hydroxy-1-méthyl-éthyl)-benzyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl}-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-(6-morpholine-4-yl-pyridine-3-yl)-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-(6-morpholine-4-yl-pyridine-3-yl)-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-(4-morpholine-4-carbonyl)-amide d’acide thiophène-2-carboxylique ;
le {3-[4-(cyano-diméthyl-méthyl)-benzoyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl}-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide thiophène-2-carboxylique ;
le [3-[4-(cyano-diméthyl-méthyl)-benzoyl]-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-(6-morpholine-4-yl-pyridine-3-yl)-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-(4-(tétrahydro-pyranne-4-yl)-phényl)-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-(4-(2-oxo-pyrrolidine-1-yl)-phényl)-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-(6-thiomorpholine-4-yl-pyridine-3-yl)-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-(6-chloro-pyridine-3-yl)-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-(6-morpholine-4-yl-pyridine-3-yl)-amide d’acide 5-fluoro-thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-(6-morpholine-4-yl-pyridine-3-yl)-amide d’acide 5-méthyl-thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-[1-(téthrahydro-pyranne-4-yl)-pipéridine-3-yl]-ami
5 de d’acide thiophène-2-carboxylique ;
le N-[3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-4-méthyl-N-(6-morpholine-4-yl-pyridine-3-yl)-benzamide ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[6-(3,6-dihydro-2H-pyranne-4-yl)-pyridine-3-yl]-ami
de d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[6-tétrahydro-pyranne-4-yl]-pyridine-3-yl]-ami
de d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[6-morpholine-4-yl-pyridine-3-yl]-amide d’acide fu
ranne-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[6-morpholine-4-yl-pyridine-3-yl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[4-morpholine-4-yl-cyclohexyl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-yl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[4-diéthylcarbamoyl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[6-morpholine-4-yl-pyridine-3-yl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[1-(téthrahydro-pyranne-4-yl)-pipéridine-4-yl]-ami
de d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-yl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-yl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[6-morpholine-4-yl-pyridine-3-yl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[6-morpholine-4-yl-pyridine-3-yl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-yl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[4-morpholine-4-yl-cyclohexyl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-yl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-yl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[6-morpholine-4-yl-pyridine-3-yl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[6-morpholine-4-yl-pyridine-3-yl]-amide d’acide thiophène-2-carboxylique ;
le N-[3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-6-morpholine-4-yl-N-thiophène-2-ylmethyl-
icotinamide ;
le [3-(4-chloro-phénocy)-benzènesulfonyl]-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-(téthrahydro-pyranne-4-yl)-pipérdine-4-yl]-ami
de d’acide thiophène-2-carboxylique ;
le [3-(4-trifluoro-méthoxy-benzènesulfonyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-yl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-cyano-benzènesulfonyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-yl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-butyl-benzènesulfonyl)-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-yl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-chloro-phénocy)-benzènesulfonyl]-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-toluène-4-sulfonyl]-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-ami
de d’acide thiophène-2-carboxylique ;
le [3-(4-chloro-phénocy)-benzènesulfonyl]-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-yl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-chloro-phénocy)-benzènesulfonyl]-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-yl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-chloro-phénocy)-benzènesulfonyl]-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-yl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-chloro-phénocy)-benzènesulfonyl]-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-yl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-chloro-phénocy)-benzènesulfonyl]-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-yl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-chloro-phénocy)-benzènesulfonyl]-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-yl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-chloro-phénocy)-benzènesulfonyl]-3-aza-bicyclo[3.1.0]-hex-6-ylméthyl]-[3-fluoro-4-morpholine-4-yl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4'-fluoro-biphenyl-4-sulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phenyl)-(3-[1-methyl-1H-imidazole-4-sulfonyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-amide d'acide thiophène-2-carboxylique ;
le [3-(4-bromo-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le [3-(4-bromo-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le [3-(2-acetylamino-4-methoxy-thiazole-5-sulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le [3-(2-acetylamino-4-methoxy-thiazole-5-sulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le [3-(4-fluoro-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzenesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(6-morpholine-4-yl-pyridine-3-yl)-amide d'acide thiophène-2-carboxylique ;
le [3-(4-fluoro-3-chloro-phénylméthanesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le [3-(4-fluoro-3-chloro-phénylméthanesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(6-morpholine-4-yl-pyridine-3-yl)-amide d'acide thiophène-2-carboxylique ;
le [3-(4-fluoro-3-chloro-phénylméthanesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(6-morpholine-4-yl-pyridine-3-yl)-amide d'acide thiophène-2-carboxylique ;
le [3-(4-fluoro-3-chloro-phénylméthanesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(6-morpholine-4-yl-pyridine-3-yl)-amide d'acide thiophène-2-carboxylique ;
le [3-(4-fluoro-3-chloro-phénylméthanesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(6-morpholine-4-yl-pyridine-3-yl)-amide d'acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phenyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le [3-(4-fluoro-3-chloro-phénylméthanesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(6-morpholine-4-yl-pyridine-3-yl)-amide d'acide thiophène-2-carboxylique ;
le [3-(4-fluoro-3-chloro-phénylméthanesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(6-morpholine-4-yl-pyridine-3-yl)-amide d'acide thiophène-2-carboxylique ;
le [3-(4-fluoro-3-chloro-phénylméthanesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(6-morpholine-4-yl-pyridine-3-yl)-amide d'acide thiophène-2-carboxylique ;
le [3-(4-fluoro-3-chloro-phénylméthanesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(6-morpholine-4-yl-pyridine-3-yl)-amide d'acide thiophène-2-carboxylique ;
le [3-(4-fluoro-3-chloro-phénylméthanesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(6-morpholine-4-yl-pyridine-3-yl)-amide d'acide thiophène-2-carboxylique ;
le [3-(4-fluoro-3-chloro-phénylméthanesulfonyl)-3-aza-bicyclo[3.1.0]hex-6-ylmethyl)-(6-morpholine-4-yl-pyridine-3-yl)-amide d'acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phenyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phenyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phenyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phenyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phenyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phenyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phenyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phenyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phenyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phenyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phenyl)-(3-fluoro-4-morpholine-4-yl-phenyl)-amide d'acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-[3-(4-fluoro-phénylméthanesulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-[3-(4-nitro-benzènesulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethy]-amide d’acide thiophène-2-carboxylique ;
l’acide 4-[[3-fluoro-morpholine-4-yl-phényl]-pi-2-carbonyl]-[3-morpholine-4-yl-phényl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-butoxy-benzènesulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethy]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-[3-(4-pentyl-benzènesulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-[3-(4-phénoxy-benzènesulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
l’ester méthylique d’acide 3-4-cyclopropanecarboxylique ;
le [3-(4-tertiobutyl-benzènesulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethy]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzènesulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethy]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-[3-(4-tertiobutyl-benzènesulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethy]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-[3-(4-tertiobutyl-benzènesulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylmethy]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-[3-(4-fluoro-4-morpholine-4-yl-phényl)]-N-(3-fluoro-4-morpholine-4-yl-phényl)-isonicotinamide ;
le [3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-amide d’acide furanne-3-carboxylique ;
le N-[3-4-(1,1-diméthyl-propyl)-benzènesulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-[3-(4-phénoxy-benzènesulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-[3-(4-tertiobutyl-benzènesulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-[3-(4-tertiobutyl-benzènesulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le (3-fluoro-4-morpholine-4-yl-phényl)-[3-(4-tertiobutyl-benzènesulfonyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le N-[3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le N-[3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide furanne-3-carboxylique ;
le [3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le N-[3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le N-[3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le N-[3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le N-[3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le N-[3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le N-[3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le N-[3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le N-[3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le N-[3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le N-[3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le N-[3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-éthyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-ylménythyl]-amide d’acide thiophène-2-carboxylique ;
le N-[3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-N-(3-fluoro-4-morpholine-4-yl-phényl)-3,5-diméthoxybenzamide ;
le N-[3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-N-(3-fluoro-4-morpholine-4-yl-phényl)-3-méthoxybenzamide ;
le [3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide 1,5-diméthyl-1H-pyrazole-3-carboxylique ;
le [3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide 3-éthoxy-thiophènes-2-carboxylique ;
le [3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide isoza-5-carboxylique ;
le [3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide furanne-2-carboxylique ;
le N-[3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-N-(3-fluoro-4-morpholine-4-yl-phényl)-2-méthylbenzamide ;
le 4-cyano-N-[3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-N-(3-fluoro-4-morpholine-4-yl-phényl)-benzamide ;
le 4-éthyl-N-[3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-N-(3-fluoro-4-morpholine-4-yl-phényl)-benzamide ;
le [3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide 3-chloro-thiophène-2-carboxylique ;
le N-[3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-N-(3-fluoro-4-morpholine-4-yl-phényl)-2-méthyl-sulfanyl-nicotinamide ;
le [3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide 1-méthyl-1H-pyrazole-3-carboxylique ;
le N-[3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-N-(3-fluoro-4-morpholine-4-yl-phényl)-2-méthylbenzamide ;
le [3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide 1-acétyl-pyrrolidine-2-carboxylique ;
le [3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide 2-méthylthiazole-4-carboxylique ;
le 4-bromo-N-[3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-N-(3-fluoro-4-morpholine-4-yl-phényl)-benzamide ;
le [3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide 5-oxo-pyrrolidine-2-carboxylique ;
le [3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide 1-acétyl-pyrrolidine-2-carboxylique ;
le [3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide thio-phène-3-carboxylique ;
le [3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide thio-phène-3-carboxylique ;
le [3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide 5-bromo-thiophène-2-carboxylique ;
le [4-(4-acétyl-[1,4]diazépane-1-yl)-3-Tfluoro-phényl]-[3-(4-éthyl-benzyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-amide d’acide thio-phène-2-carboxylique ;
le [6-(4-acétyl-pipérazine-1-yl)]-pyridine-3-yl-[3-(4-tertiobutyl-benzyl)]-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-amide d’acide thio-phène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(3-fluoro-4-morpholine-4-yl-phényl)-amide d’acide thio-phène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(6-(4-acétyl-thiophène-3-carboxylique)-amide d’acide thio-phène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(6-(4-acétyl-thiophène-3-carboxylique)-amide d’acide thio-phène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(6-(4-acétyl-thiophène-3-carboxylique)-amide d’acide thio-phène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-yl-méthyl]-(6-(4-acétyl-thiophène-3-carboxylique)-amide d’acide thio-phène-2-carboxylique ;
d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-[6-[(2-méthoxy-éthyl)-méthyl-amino]-pyridine-3-
yl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-[6-(3-diméthylamino-pyrrolidine-1-yl)-pyridine-3-
yl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-[6-[(2-méthoxy-éthyl)-méthyl-amino]-pyridine-3-
yl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-[6-(4-méthyl-[1,4]diazépane-1-yl)-pyridine-3-
yl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-[6-(3-diéthylamino-pyrrolidine-1-yl)-pyridine-3-
yl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-[6-(3-morpholine-4-yl-azétidine-1-yl)-pyridine-3-
yl]-amide d’acide thiophène-2-carboxylique ;
le [3-(4-tertiobutyl-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-ylméthyl]-[6-(3-morpholine-4-yl-pyrrolidine-1-yl)-pyridine-3-
yl]-amide d’acide thiophène-2-carboxylique ;
ou un de ses sels pharmaceutiquement acceptables.

5. Composition pharmaceutique comprenant un composé selon la revendication 1, ou un de ses sels pharmaceuti-
quement acceptables, et un véhicule ou diluant pharmaceutiquement acceptable.

6. Composé selon la revendication 1, ou un de ses sels pharmaceutiquement acceptables, pour une utilisation comme
médicament.

7. Composé selon la revendication 1, ou un de ses sels pharmaceutiquement acceptables, pour une utilisation dans
le traitement d’un trouble ou d’un état choisi parmi la psychose, la schizophrénie, le trouble de la conduite, le trouble
du comportement disruptif, le trouble bipolaire, les épisodes psychotiques d’anxiété, l’anxiété associée à la psychose,
les troubles de l’humeur psychotique, le trouble dépressif majeur sévère, les troubles de l’humeur associés avec
des troubles psychotiques, la manie aigüe, la dépression associée au trouble bipolaire, les troubles de l’humeur
associés à la schizophrénie, les manifestations comportementales du retard mental, le trouble de la conduite, le
trouble autistique, les troubles du mouvement, le syndrome de Tourette, le syndrome acinétique-rigide, les troubles
du mouvement associés avec la maladie de Parkinson, la dyskinésie tardive, d’autres dyskinésies induites par un
médicament et basées sur la neuro-dégénérescence, le trouble d’hyperactivité avec déficit de l’attention, les troubles
cognitifs, les démences et les troubles de la mémoire.
REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

- WO 9745115 A [0004]

Non-patent literature cited in the description

- SynLett, 1996, 1097 [0039]