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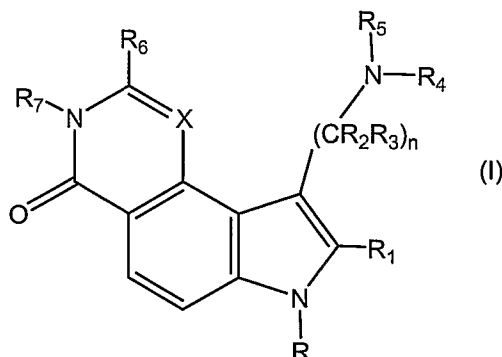
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(54) Title: PYRROLOQUINOLINONE DERIVATIVES AS 5-HYDROXYTRYPTAMINE-6 LIGANDS



(57) Abstract: The present invention provides a compound of formula (I) and the use thereof in the therapeutic treatment of a central nervous system disorder related to or affected by the 5-HT6 receptor.

5

PYRROLOQUINOLINONE DERIVATIVES
AS 5-HYDROXYTRYPTAMINE-6 LIGANDS

FIELD OF THE INVENTION

10 The present invention is directed to substituted pyrroloquinolinones, the use thereof in the treatment of a central nervous system disorder related to or affected by the 5-HT₆ receptor and pharmaceutical compositions comprising said substituted pyrroloquinolinones.

15

BACKGROUND OF THE INVENTION

 Serotonin (5-hydroxytryptamine)(5-HT) receptors play a critical role in many physiological and behavioral functions in humans and animals. These functions are mediated through various 5-HT receptors distributed throughout the body. There are now approximately fifteen different human 5-HT receptor subtypes that have been
20 cloned, many with well-defined roles in humans. The 5-HT₆ receptor was first cloned from rat tissue in 1993 (Monsma et al., *Molecular Pharmacology* 1993, 43, 320-327) and subsequently from human tissue (Kohen et al., *Journal of Neurochemistry* 1996, 66, 47-56). The receptor is a G-protein coupled receptor (GPCR) positively coupled to adenylate cyclase (Ruat et al., *Biochemical Biophysical Research*
25 *Communications* 1993, 193, 268-276). The receptor is found almost exclusively in the central nervous system (CNS) areas both in rat and in human. *In situ* hybridization studies of the 5-HT₆ receptor in rat brain using mRNA indicate principal localization in the areas of 5-HT projection including striatum, nucleus accumbens, olfactory tubercle, and hippocampal formation (Ward et al., *Neuroscience* 1995, 64,
30 1105-1111).

 There are many potential therapeutic uses for 5-HT₆ ligands in humans based on direct effects and on indications from available scientific studies. These studies include the localization of the receptor, the affinity of ligands with known *in vivo* activity, and various animal studies conducted so far.

One potential therapeutic use of modulators of 5-HT₆ receptor function is in the enhancement of cognition and memory in human diseases such as Alzheimer's Disease. The high levels of receptor found in important structures in the forebrain, including the caudate/putamen, hippocampus, nucleus accumbens, and cortex suggest a role for the receptor in memory and cognition, since these areas are known to play a vital role in memory (Gerard et al., *Brain Research* 1997, 746, 207-219). The ability of known 5-HT₆ receptor ligands to enhance cholinergic transmission also supported the potential cognition use (Bentley et al., *British Journal of Pharmacology* 1999, 126(7), 1537-1542). Studies have found that a known 5-HT₆ selective antagonist significantly increased glutamate and aspartate levels in the frontal cortex without elevating levels of noradrenaline, dopamine, or 5-HT. This selective elevation of neurochemicals known to be involved in memory and cognition strongly suggests a role for 5-HT₆ ligands in cognition (Dawson et al., *British Journal of Pharmacology* 2000, 130(1), 23-26). Animal studies of memory and learning with a known selective 5-HT₆ antagonist have found positive indications (Rogers et al., *Society of Neuroscience, Abstracts* 2000, 26, 680 and Foley et al., *Neuropsychopharmacology* 2004, 29(1), 93-100).

A related potential therapeutic use for 5-HT₆ ligands is the treatment of attention deficit disorders (ADD, also known as Attention Deficit Hyperactivity Disorder or ADHD) in both children and adults. Because 5-HT₆ antagonists appear to enhance the activity of the nigrostriatal dopamine pathway and because ADHD has been linked to abnormalities in the caudate (Ernst et al., *Journal of Neuroscience* 1998, 18(15), 5901-5907), 5-HT₆ antagonists may attenuate attention deficit disorders.

Early studies examining the affinity of various CNS ligands with known therapeutic utility or a strong structural resemblance to known drugs suggests a role for 5-HT₆ ligands in the treatment of schizophrenia and depression. For example, clozapine (an effective clinical antipsychotic) has high affinity for the 5-HT₆ receptor subtype. Also, several clinical antidepressants have high affinity for the receptor as well and act as antagonists at this site (Branchek, et al., *Annual Reviews in Pharmacology and Toxicology* 2000, 40, 319-334).

Further, recent *in vivo* studies in rats indicate 5-HT₆ modulators may be useful in the treatment of movement disorders including epilepsy (Stean et al., *British Journal of Pharmacology* 1999, 127 Proc. Supplement 131P and Routledge et al., *British Journal of Pharmacology* 2000, 130(7), 1606-1612).

Taken together, the above studies strongly suggest that compounds which are 5-HT₆ receptor modulators, i.e., ligands, may be useful for therapeutic indications including: the treatment of diseases associated with a deficit in memory, cognition, and learning such as Alzheimer's and attention deficit disorder; the treatment of personality disorders such as schizophrenia; the treatment of behavioral disorders, e.g., anxiety, depression and obsessive-compulsive disorders; the treatment of motion or motor disorders such as Parkinson's disease and epilepsy; the treatment of diseases associated with neurodegeneration such as stroke and head trauma; or withdrawal from drug addiction including addiction to nicotine, alcohol, and other substances of abuse.

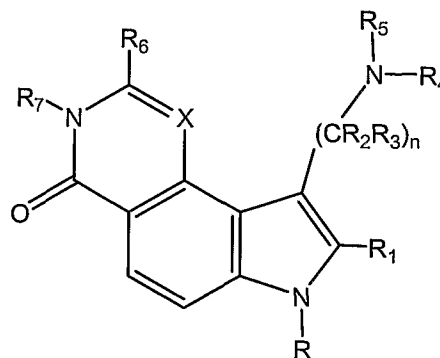
Therefore, it is an object of this invention to provide compounds which are useful as therapeutic agents in the treatment of a variety of central nervous system disorders related to or affected by the 5-HT₆ receptor.

It is another object of this invention to provide therapeutic methods and pharmaceutical compositions useful for the treatment of central nervous system disorders related to or affected by the 5-HT₆ receptor.

It is a feature of this invention that the compounds provided may also be used to further study and elucidate the 5-HT₆ receptor.

SUMMARY OF THE INVENTION

The present invention provides a pyrroloquinolinone compound of formula I



(I)

wherein

- 25 X is N or CR₈;
 n is an integer of 1, 2, 3, 4, 5, or 6;

R is H, SO₂R₉ or an alkyl, cycloalkyl, alkenyl or alkynyl group each optionally substituted;

R₁ is H, halogen or an alkyl, aryl or heteroaryl group each optionally substituted;

5 R₂ and R₃ are each independently H or an optionally substituted alkyl group;

R₄ and R₅ are each independently H or an alkyl, alkenyl, cycloalkyl, cycloheteroalkyl, aryl or heteroaryl group each optionally substituted, or R₄ and R₅ may be taken together with the atom to which they are attached to form an optionally substituted 5- to 8-membered ring
10 optionally containing an additional heteroatom selected from O, S or NR₇;

R₆ and R₈ are each independently H, halogen or an alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, cycloheteroalkyl, aryl or heteroaryl group each optionally substituted;

15 R₇ is H or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloheteroalkyl, aryl, or heteroaryl group each optionally substituted; and

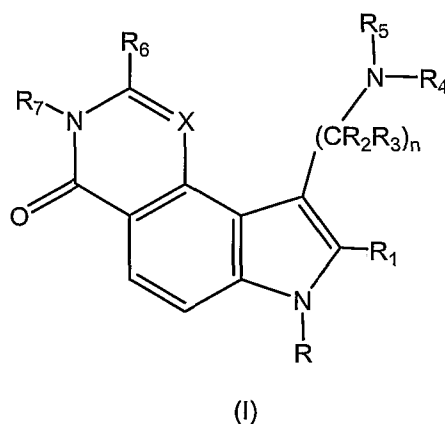
R₉ is an alkyl, aryl or heteroaryl group each optionally substituted; or a stereoisomer thereof or a pharmaceutically acceptable salt thereof.

The present invention also provides methods and compositions useful in the
20 treatment of central nervous system disorders.

DETAILED DESCRIPTION OF THE INVENTION

The 5-hydroxytryptamine-6 (5-HT₆) receptor has been identified by molecular cloning. Its ability to bind a wide range of therapeutic compounds used in psychiatry,
25 coupled with its intriguing distribution in the brain has stimulated significant interest in new compounds which are capable of interacting with or affecting said receptor. Significant efforts are being made to understand the possible role of the 5-HT₆ receptor in psychiatry, cognitive dysfunction, motor function and control, memory, mood and the like. To that end, compounds which demonstrate a binding affinity for
30 the 5-HT₆ receptor are earnestly sought both as an aid in the study of the 5-HT₆ receptor and as potential therapeutic agents in the treatment of central nervous system disorders, for example, see Reavill et al., *Current Opinion in Investigational Drugs* 2001, 2(1), 104-109.

Surprisingly, it has now been found that a pyrroloquinolinone compound of formula I demonstrates 5-HT₆ affinity along with significant sub-type selectivity. Advantageously, said formula I compounds are effective therapeutic agents for the treatment of central nervous system (CNS) disorders associated with or affected by the 5-HT₆ receptor. Accordingly, the present invention provides a pyrroloquinolinone compound of formula I



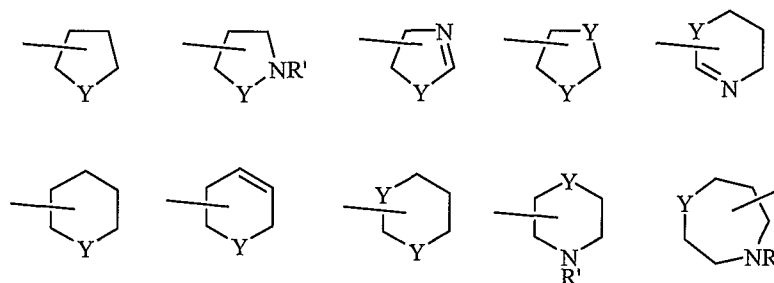
wherein

- 10 X is N or CR₈;
- n is an integer of 1, 2, 3, 4, 5, or 6;
- R is H, SO₂R₉ or an alkyl, cycloalkyl, alkenyl or alkynyl group each optionally substituted;
- R₁ is H, halogen or an alkyl, aryl or heteroaryl group each optionally substituted;
- 15 R₂ and R₃ are each independently H or an optionally substituted alkyl group;
- R₄ and R₅ are each independently H or an alkyl, alkenyl, cycloalkyl, cycloheteroalkyl, aryl or heteroaryl group each optionally substituted, or R₄ and R₅ may be taken together with the atom to which they are attached to form an optionally substituted 5- to 8-membered ring optionally containing an additional heteroatom selected from O, S or NR₇;
- 20 R₆ and R₈ are each independently H, halogen or an alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, cycloheteroalkyl, aryl or heteroaryl group each optionally substituted;
- 25

R_7 is H or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloheteroalkyl, aryl, or heteroaryl group each optionally substituted; and

R_9 is an alkyl, aryl or heteroaryl group each optionally substituted; or a stereoisomer thereof or a pharmaceutically acceptable salt thereof.

- 5 As used in the specification and claims, the term halogen designates F, Cl, Br or I and the term cycloheteroalkyl designates a five- to seven-membered cycloalkyl ring system containing 1 or 2 heteroatoms, which may be the same or different, selected from N, O or S and optionally containing one double bond. Exemplary of the cycloheteroalkyl ring systems included in the term as designated herein are the
- 10 following rings wherein Y is NR' , O or S; and R' is H or an optional substituent as described herein:



- 15 Similarly, as used in the specification and claims, the term heteroaryl designates a five- to ten-membered aromatic ring system containing 1, 2 or 3 heteroatoms, which may be the same or different, selected from N, O or S. Such heteroaryl ring systems include pyridinyl, pyrrolyl, azolyl, oxazolyl, thiazolyl, imidazolyl, furyl, thienyl, quinolinyl, isoquinolinyl, indolyl, indazolyl, azaindazolyl,
- 20 benzothienyl, benzofuranyl, benzisoxazolyl or the like. The term aryl designates a carbocyclic aromatic ring system, e.g. of 6 to 14 carbon atoms such as phenyl, naphthyl, anthracenyl or the like.

- As used herein, the term "alkyl" as a group or part of a group eg alkoxy, alkylamino, alkylcarbonyl (=alkanoyl), includes both (C_1 - C_{12}) straight chain or
- 25 branched-chain (unless defined otherwise) monovalent saturated hydrocarbon moiety. Examples of saturated hydrocarbon alkyl moieties include, but are not limited to, chemical groups of 1-6 carbon atoms such as methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, *tert*-butyl, isobutyl, *sec*-butyl; higher homologs such as *n*-

hexyl, and the like. Specifically included within the definition of "alkyl" are those alkyl groups that are optionally substituted, eg =. Suitable alkyl substitutions include, but are not limited to, CN, OH, halogen, phenyl, carbamoyl, carbonyl, alkoxy or aryloxy.

As used herein the term "haloalkyl" designates a C_nH_{2n+1} group having from
5 one to $2n+1$ halogen atoms which may be the same or different. Examples of haloalkyl groups include CF_3 , CH_2Cl , C_2H_3BrCl , $C_3H_5F_2$, or the like.

The term "alkenyl", as used herein, refers to either a (C_2 - C_{10}) straight chain or branched-chain monovalent hydrocarbon moiety containing at least one double bond. Such hydrocarbon alkenyl moieties may be mono or polyunsaturated, and may exist
10 in the E or Z configurations. The compounds of this invention are meant to include all possible E and Z configurations. Examples of mono or polyunsaturated hydrocarbon alkenyl moieties include, but are not limited to, chemical groups such as vinyl, 2-propenyl, isopropenyl, crotyl, 2-isopentenyl, butadienyl, 2-(butadienyl), 2,4-pentadienyl, 3-(1,4-pentadienyl), and higher homologs, isomers, or the like.

15 The term "alkynyl", as used herein, refers to either a (C_2 - C_{10}) straight chain or branched-chain monovalent hydrocarbon moiety containing at least one triple bond.

The term "cycloalkyl", as used herein, refers to a monocyclic, bicyclic, tricyclic, fused, bridged, or spiro monovalent saturated hydrocarbon moiety of 3-10 carbon atoms, unless otherwise specified. Any suitable ring position of the
20 cycloalkyl moiety may be covalently linked to the defined chemical structure. Examples of cycloalkyl moieties include, but are not limited to, chemical groups such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, norbornyl, adamantyl, spiro[4.5]decanyl, and homologs, isomers, or the like.

In the specification and claims, when the terms alkyl, alkenyl,
25 alkynyl, cycloalkyl, cycloheteroalkyl, aryl or heteroaryl are designated as being optionally substituted, the substituent groups which are optionally present may be one or more of those customarily employed in the development of pharmaceutical compounds, or the modification of such compounds, to influence their structure/activity, persistence, absorption, stability or other beneficial property.
30 Specific examples of optional substituents include halogen atoms, nitro, cyano, thiocyanato, cyanato, hydroxyl, alkyl, haloalkyl, alkoxy, haloalkoxy, amino, alkylamino, dialkylamino, formyl, alkoxycarbonyl, carboxyl, alkanoyl, alkylthio, alkylsulphanyl, alkylsulphonyl, carbamoyl, alkylaminocarbonyl, cycloalkyl, aryl, phenyl,

phenoxy, benzyl, benzyloxy, heteroaryl, indolyl, heterocyclyl, (e.g., 5-10 membered heteroaryl or heterocycloalkyl moieties containing 1-3 ring heteroatoms selected from O, S and N) or cycloalkyl groups, preferably halogen atoms or lower alkyl or lower alkoxy groups where 'lower' denotes 1-6 carbon atoms. Typically, 0-3 substituents
5 may be present. When any of the foregoing substituents represents or contains an alkyl substituent group, e.g., alkoxy, alkylsulfonyl, alkanoyl, this may be linear or branched and may contain up to 12, preferably up to 6, more preferably up to 4 carbon atoms.

Pharmaceutically acceptable salts may be any acid addition salt formed by a
10 compound of formula I and a pharmaceutically acceptable acid such as phosphoric, sulfuric, hydrochloric, hydrobromic, citric, maleic, malonic, mandelic, succinic, fumaric, acetic, lactic, nitric, sulfonic, p-toluene sulfonic, tartaric, malic, methane sulfonic acid or the like.

Compounds of the invention include esters, carbamates or other conventional
15 prodrug forms, which in general, are functional derivatives of the compounds of the invention and which are readily converted to the inventive active moiety *in vivo*. Correspondingly, the method of the invention embraces the treatment of the various conditions described hereinabove with a compound of formula I or with a compound which is not specifically disclosed but which, upon administration, converts to a
20 compound of formula I *in vivo*. Also included are metabolites of the compounds of the present invention defined as active species produced upon introduction of these compounds into a biological system.

Compounds of the invention may exist as one or more stereoisomers. The various stereoisomers include enantiomers, diastereomers, atropisomers and
25 geometric isomers. One skilled in the art will appreciate that one stereoisomer may be more active or may exhibit beneficial effects when enriched relative to the other stereoisomer(s) or when separated from the other stereoisomer(s). Additionally, the skilled artisan knows how to separate, enrich or selectively prepare said stereoisomers. Accordingly, the present invention comprises compounds of formula
30 I, the stereoisomers thereof and the pharmaceutically acceptable salts thereof. The compounds of the invention may be present as a mixture of stereoisomers, individual stereoisomers, or as an optically active or enantiomerically pure form.

Examples of the variables in the formulae I are as follows:

An example of X is CH or N.

Examples of R₄ are

H;

alkyl (such as methyl, pentyl,) optionally substituted, eg by hydroxy;

5 arylalkyl (such as benzyl),

cycloalkylalkyl or

heteroarylalkyl (such as heteroarylmethyl)

for example where the said aryl (eg phenyl), cycloalkyl or heteroaryl (eg
indolyl, furanyl, pyridyl, pyrrolyl, thienyl, benzofuranyl, imidazolyl, quinolyl)
10 group is optionally substituted for example by one to three optional
substituents selected from one or more of aryloxy, alkoxy, alkoxycarbonyl,
halogen, dialkylamino, alkyl, alkylendioxy, cyano, hydroxyl, CF₃.

Examples of R₇ are H, heteroaryl (such as thienyl), or alkyl (such as methyl,
15 ethyl, propyl, heptyl) which may be optionally substituted, eg by

cycloalkyl (eg cyclopropyl);

alkoxy;

dialkylimino;

optionally substituted heteroaryl (such as thienyl, furanyl);

20 optionally substituted aryl (eg phenyl or naphthyl),

e.g. where the optional substitution on aryl or heteroaryl is by one
or two substituents selected from halogen, alkoxy, alkyl or
haloalkyl.

Examples of R₁ are H, halogen such as Br and optionally substituted phenyl.

25 Examples of R are H and alkyl such as methyl.

Examples of R₈ are H and chlorine.

Preferred compounds of the invention are those compounds of formula I wherein n is
2. Also preferred are those compounds of formula I wherein R is H. Another group
of preferred formula I compounds is those compounds wherein R₇ is H or an
30 optionally substituted alkyl group.

More preferred compounds of the invention are those compounds of formula I
wherein n is 2 and R₁ is H. Another group of more preferred compounds of the
invention is those compounds of formula I wherein n is 2 and R₂ and R₃ are H. A

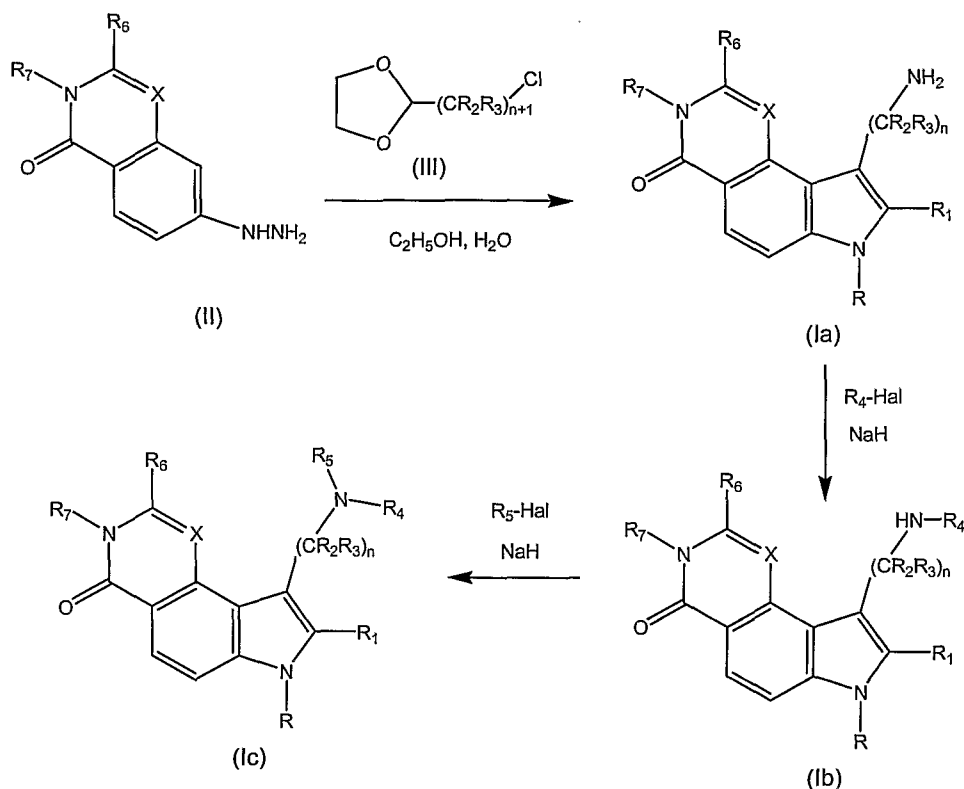
further group of more preferred formula I compounds is those compounds wherein n is 2; R₂ and R₃ are H; and R₄ and R₅ are each independently H or alkyl.

Preferred compounds of the invention include:

- 1-(2-benzylaminoethyl)-6,7-dihydro-1H-pyrrolo[3,2-f]isoquinolin-6-one;
- 5 1-(2-aminoethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one;
- 1-(2-aminoethyl)-2-bromo-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one;
- 1-(2-aminoethyl)-7-methyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one;
- 1-(2-aminoethyl)-7-benzyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one;
- 1-(2-aminoethyl)-7-cyclohexylmethyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one;
- 10 1-(2-aminoethyl)-7-thien-3-ylmethyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one;
- 1-(2-aminoethyl)-7-(furan-2-ylmethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one;
- 1-(2-methylaminoethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one;
- 9-(2-aminoethyl)-3-benzyl-3H,7H-pyrrolo[2,3-h]quinazolin-4-one;
- 9-(2-aminoethyl)-3-methyl-3H,7H-pyrrolo[2,3-h]quinazolin-4-one;
- 15 9-(2-aminoethyl)-3-benzyl-3H,7H-pyrrolo[2,3-h]quinazolin-4-one;
- 9-(2-aminoethyl)-3H,7H-pyrrolo[2,3-h]quinazolin-4-one;
- 9-(2-aminoethyl)-2-(3-pyridinyl)-3H,7H-pyrrolo[2,3-h]quinazolin-4-one;
- 9-(2-aminoethyl)-2,3-dimethyl-3H,7H-pyrrolo[2,3-h]quinazolin-4-one;
- a stereoisomer thereof; or a pharmaceutically acceptable salt thereof.

- 20 Compounds of formula I may be prepared using conventional synthetic methods and, if required, standard separation or isolation techniques. For example, compounds of formula I wherein R₄ and R₅ are H (Ia) may be prepared by reacting an isoquinolinone of formula II with a dioxolan derivative of formula III via a Fisher indole synthesis to obtain the desired compound of formula Ia. The formula Ia free
- 25 amine may be reacted with an appropriate halide, R₄-Hal, in the presence of a base such as NaH to give a compound of formula I wherein R₅ is H and R₄ is other than H (Ib). Similarly, the formula Ib compound may then be reacted with another halide, R₅-Hal, in the presence of a base, to give the compound of formula I wherein R₄ and R₅ are other than H (Ic). The reactions are shown in flow diagram I wherein Hal is Cl,
- 30 Br or I.

FLOW DIAGRAM I



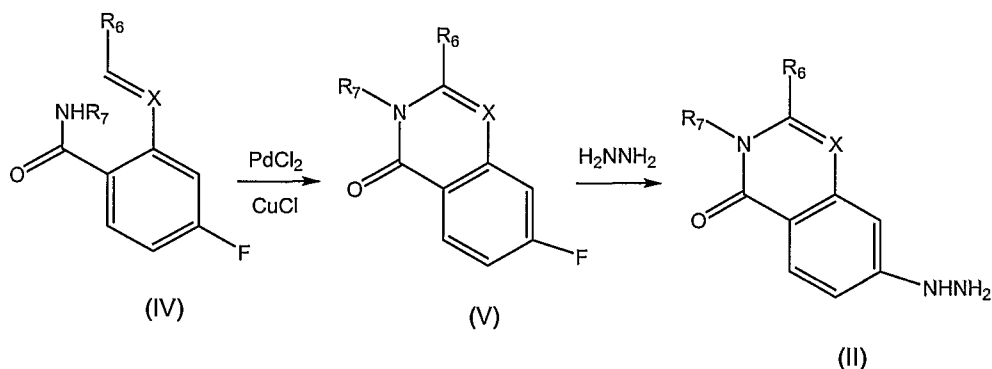
Alternatively, compounds of formula Ib may be obtained using a two-step reaction sequence involving, the reaction of Ia with a carboxylic acid derivative to provide the corresponding amide and subsequent reduction of said amide with a suitable reducing agent, such as LiAlH₄, to give the desired amine of formula Ib. This process may be repeated with an alternative carboxylic acid derivative with subsequent reduction to provide the fully substituted amine derivative of formula Ic.

A method useful for preparing libraries of compounds of formula Ib or Ic is the reaction of formula Ia with a suitable aldehyde derivative to form the corresponding imine and reducing said imine with a suitable reducing agent such as NaBH₄, or for ease of automation, polymer supported borohydride, to give a compound of formula Ib in high yield.

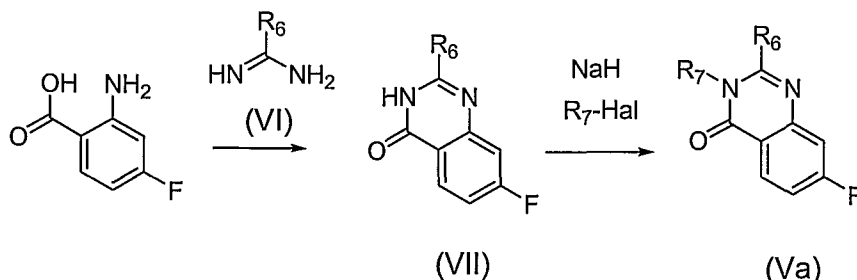
Isoquinolinones or quinazolinones of formula II are known and are commercially available or may be prepared, e.g., by the methods described by Izumi et al., *J. Heterocyclic Chem.* 1990, 27, 1419, and Hegedus et al., *J. Org. Chem.* 1977, 42, 1329. For example, 4-fluoro-2-ethenyl substituted benzamides of formula IV can be intramolecularly cyclized to the corresponding isoquinolinone or quinazolinone by the combined action of palladium(II)chloride and copper(I)chloride

to give the fluoroisoquinolinone or fluoroquinazolinone of formula V and reacting said formula V compound with hydrazine to give the desired compound of formula II. The reaction is shown in flow diagram II.

5

FLOW DIAGRAM II

- 10 Compounds of formula V wherein X is CH may also be prepared by the method described by Heck et al. in *J. Org. Chem.*, 1977, 42, 3903 and *J. Org. Chem.*, 1978, 43, 2454. Compounds of formula V wherein X is N (Va) may be prepared by the cyclocondensation reaction of anthranilic acid derivatives, i.e. Rewcastle et al., *J. Med. Chem.* 1996, 39(4), 918-928, Hudson et al. (WO 96/09294),
- 15 Houghten et al., (WO 98/11438), Fantin et al., *J. Org. Chem.* 1993, 58(3), 741-743, or Bhattacharya et al. (WO 97/28118, WO 97/28132 and WO 97/28134). Compounds of formula Va may also be prepared by the reaction of 2-amino-4-fluorobenzoic acid with a formamidine acetate derivative of formula VI, followed by the reaction of the formula VI compound with an electrophile, R₇-Hal, in the presence
- 20 of a base to give the desired compound of formula Va. The reaction is shown in flow diagram III wherein Hal is Cl, Br or I.

FLOW DIAGRAM III

5 Compounds of formula V are then converted, via reaction with hydrazine as shown in flow diagram II, to compounds of formula II and the formula II compounds are then used to prepare compounds of formula I as shown in flow diagram I hereinabove.

Advantageously, the formula I compounds of the invention are useful for the
 10 treatment of CNS disorders relating to or affected by the 5-HT₆ receptor including mood, personality, behavioral, psychiatric, cognitive, neurodegenerative, or the like disorders, for example, Alzheimer's disease, Parkinson's disease, attention deficit disorder, anxiety, epilepsy, depression, obsessive-compulsive disorder, sleep disorders, neurodegenerative disorders (such as head trauma or stroke), feeding
 15 disorders (such as anorexia or bulimia), schizophrenia, memory loss, disorders associated with withdrawal from drug or nicotine abuse, or the like or certain gastrointestinal disorders such as irritable bowel syndrome. Accordingly, the present invention provides a method for the treatment of a disorder of the central nervous
 20 system related to or affected by the 5-HT₆ receptor in a patient in need thereof which comprises providing said patient a therapeutically effective amount of a compound of formula I as described hereinabove. The compounds may be provided by oral or parenteral administration or in any common manner known to be an effective administration of a therapeutic agent to a patient in need thereof.

The term "providing" as used herein with respect to providing a compound or
 25 substance embraced by the invention, designates either directly administering such a compound or substance, or administering a prodrug, derivative or analog which forms an equivalent amount of the compound or substance within the body. The therapeutically effective amount provided in the treatment of a specific CNS disorder may vary according to the specific condition(s) being treated, the size, age and
 30 response pattern of the patient, the severity of the disorder, the judgment of the

attending physician or the like. In general, effective amounts for daily oral administration may be about 0.01 to 1,000 mg/kg, preferably about 0.5 to 500 mg/kg and effective amounts for parenteral administration may be about 0.1 to 100 mg/kg, preferably about 0.5 to 50 mg/kg.

5 In actual practice, the compounds of the invention are provided by administering the compound or a precursor thereof in a solid or liquid form, either neat or in combination with one or more conventional pharmaceutical carriers or excipients. Accordingly, the present invention provides a pharmaceutical composition which comprises a pharmaceutically acceptable carrier and an effective
10 amount of a compound of formula I as described hereinabove.

 Solid carriers suitable for use in the composition of the invention include one or more substances which may also act as flavoring agents, lubricants, solubilizers, suspending agents, fillers, glidants, compression aides, binders, tablet-disintegrating agents or encapsulating materials. In powders, the carrier may be a finely divided
15 solid which is in admixture with a finely divided compound of formula I. In tablets, the formula I compound may be mixed with a carrier having the necessary compression properties in suitable proportions and compacted in the shape and size desired. Said powders and tablets may contain up to 99% by weight of the formula I compound. Solid carriers suitable for use in the composition of the invention include calcium
20 phosphate, magnesium stearate, talc, sugars, lactose, dextrin, starch, gelatin, cellulose, methyl cellulose, sodium carboxymethyl cellulose, polyvinylpyrrolidone, low melting waxes and ion exchange resins.

 Any pharmaceutically acceptable liquid carrier suitable for preparing solutions, suspensions, emulsions, syrups and elixirs may be employed in the
25 composition of the invention. Compounds of formula I may be dissolved or suspended in a pharmaceutically acceptable liquid carrier such as water, an organic solvent, or a pharmaceutically acceptable oil or fat, or a mixture thereof. Said liquid composition may contain other suitable pharmaceutical additives such as solubilizers, emulsifiers, buffers, preservatives, sweeteners, flavoring agents,
30 suspending agents, thickening agents, coloring agents, viscosity regulators, stabilizers, osmo-regulators, or the like. Examples of liquid carriers suitable for oral and parenteral administration include water (particularly containing additives as above, e.g., cellulose derivatives, preferably sodium carboxymethyl cellulose solution), alcohols (including monohydric alcohols and polyhydric alcohols, e.g.,
35 glycols) or their derivatives, or oils (e.g., fractionated coconut oil and arachis oil). For

parenteral administration the carrier may also be an oily ester such as ethyl oleate or isopropyl myristate.

Compositions of the invention which are sterile solutions or suspensions are suitable for intramuscular, intraperitoneal or subcutaneous injection. Sterile solutions
5 may also be administered intravenously. Inventive compositions suitable for oral administration may be in either liquid or solid composition form.

For a more clear understanding, and in order to illustrate the invention more clearly, specific examples thereof are set forth hereinbelow. The following examples are merely illustrative and are not to be understood as limiting the scope and
10 underlying principles of the invention in any way.

Unless otherwise stated, all parts are parts by weight. The term NMR designates nuclear magnetic resonance. The terms THF, DMF and EtOAc designate tetrahydrofuran, dimethyl formamide and ethyl acetate, respectively.

EXAMPLE 1**4-Fluorocinnamyl azide**

An acetone solution (25 ml) of 4-fluorocinnamic acid (2.0 g, 12.0 mmol) and triethylamine (1.27 g, 12.6 mmol) was cooled to -20°C under nitrogen and the stirred mixture was treated with ethyl chloroformate (1.76 g, 16.2 mmol). After two hours, an aqueous solution of sodium azide (1.09 g, 16.8 mmol in 5 mL) was added, and the reaction mixture was stirred for a further two hours. The mixture was filtered and concentrated to dryness to provide the acylazide as a white crystalline solid (2.2 g, 95% yield).

Elemental Analysis for: $C_9H_6FN_3O$

Calculated: C, 56.55; H, 3.16; N, 21.98

Found: C, 56.65; H, 3.19; N, 22.01

EXAMPLE 2**6-Fluoro-1-isoquinolinone**

A solution of 4-fluorocinnamylazide from Example 1 (10.0 g, 52.6 mmol) in diphenyl ether (90 ml), containing a crystal of iodine, was heated at 320°C for fifteen minutes. The mixture was cooled to ambient temperature, diluted with hexane (900 ml) and the precipitated product (6.1 g, 71% yield) was collected by filtration. The product was crystallized from acetone to afford a white solid.

Elemental Analysis for: C_9H_6FNO

Calculated: C, 66.26; H, 3.71; N, 8.59

Found: C, 66.45; H, 3.92; N, 8.66

EXAMPLE 3**6-Hydrazino-1-isoquinolinone**

A solution of 6-fluoro-1-isoquinolinone (11.5 g, 70.5 mmol) from Example 2 and hydrazine (56.4 g, 1.76 mol) was refluxed in dioxane (175 ml) under nitrogen for 19 hours. The mixture was concentrated under vacuo, 200 ml of water added thereto, and the product collected by filtration. An ethanolic solution (500 ml) of the product was treated with 50 ml of 2N HCl, and the solution was filtered and concentrated in vacuo to afford the required product as a light yellow colored solid (12.8 g, 86% yield, mp 270°C).

Elemental Analysis for: $C_9H_9N_3O \cdot 1.0 \text{ HCl}$

Calculated: C, 51.07; H, 4.76; N, 19.85

Found: C, 50.41; H, 4.91; N, 19.33

EXAMPLE 4

1-(2-Aminoethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one

5 A solution of 6-hydrazino-1-isoquinolinone (1.0 g, 4.73 mmol) from Example 3 and 2-(3-chloropropyl)-1,3 dioxolan (1.32 g, 8.9 mmol) in degassed ethanol (80 ml)/water (15 ml) was refluxed under nitrogen for one hour. The reaction mixture was concentrated in vacuo, and the product was purified by flash silica gel chromatography to afford an amber colored solid (0.45 g, 42% yield). Treatment of
10 the product with ethereal HCl and crystallization from ethanol-ether gave the mono hydrochloride salt as a light amber colored solid (mp > 280°C).

Elemental Analysis for: C₁₃H₁₃N₃O, 1.0 HCl 0.3 H₂O

Calculated: C, 58.02; H, 5.47; N, 15.61

Found: C, 57.92; H, 5.38; N, 15.20

15

EXAMPLE 5

1-(2-Aminoethyl)-2-bromo-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one

Bromine (1.27 mmol) was added to a stirred solution of 1-(2-aminoethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one (0.240 g, 1.06 mmol) from Example 4 in DMF
20 (2 ml). After three hours, the solution was concentrated to dryness, and the product was purified by crystallization from ethereal ethanol. Two further recrystallizations from the same solvent system provided the titled compound as a white solid (0.114 g, 27 % yield, mp 252°C, decomposes).

Elemental Analysis for: C₁₃H₁₂BrN₃O 1.0 HBr

25 Calculated: C, 40.34; H, 3.39; N, 10.89

Found: C, 40.58; H, 3.54; N, 10.46

EXAMPLE 6

1-(2-N-Benzoylaminoethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one

30 A solution of benzoyl chloride (0.928 g, 6.6 mmol) in methylene chloride (10 ml) was added dropwise to a stirred aqueous solution of 1-(2-aminoethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one (0.75 g, 3.3 mmol in 10 ml) from Example 4 containing potassium carbonate (0.684 g, 4.95 mmol). After one hour, the mixture was concentrated under vacuum, and the product was purified by flash silica gel

chromatography (eluting with 5% MeOH/CH₂Cl₂) to afford the required product as a light brown solid.

EXAMPLE 7A

1-(2-Benzylaminoethyl)-6,7-dihydro-1H-pyrrolo[3,2-f]isoquinolin-6-one

A solution of the amide (0.47 g, 1.4 mmol) from Example 6 in THF (5 ml) was treated with an excess of borane THF (1M, 20 mmol) at room temperature under nitrogen, and the mixture was stirred for 30 hours. The reaction was terminated by the addition of HCl, and the product isolated by flash silica gel chromatography (20% MeOH/5% NH₄OH/75% CH₂Cl₂) to afford a clear solid. Treatment with ethanolic HCl afforded the salt of the titled compound as a white solid. (mp 210°C).

Elemental Analysis for: C₂₀H₁₉N₃O 1.0 HCl

Calculated: C, 67.89; H, 5.70; N, 11.87

Found: C, 67.95; H, 5.67; N, 11.98

EXAMPLE 7B

Library Procedure

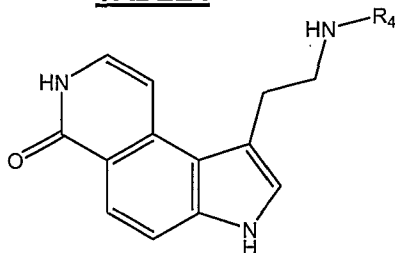
1-(2-Benzylaminoethyl)-6,7-dihydro-1H-pyrrolo[3,2-f]isoquinolin-6-one

Molecular sieves (100 mg), benzaldehyde (100 µL), and 500 µL of a 0.1 M solution of the HCl salt of 1-(2-aminoethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one (from Example 4) in anhydrous methanol (containing two equivalents of triethylamine) was shaken for 24 hours. Borohydride resin (57 mg) was added to the reaction well, and the mixture shaken for 16 hours at room temperature. Methanol (1 ml) was added, the mixture vortexed, and the top solution removed and concentrated. The product was dissolved in DMSO (1.6 ml), and the product purity confirmed by HPLC and MS analysis.

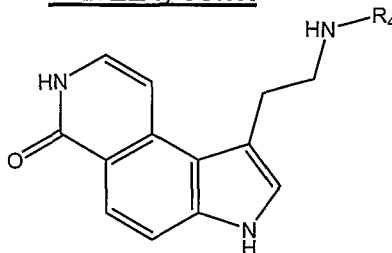
C₂₀H₁₉N₃O (MW 317.39)

EXAMPLES 8-91

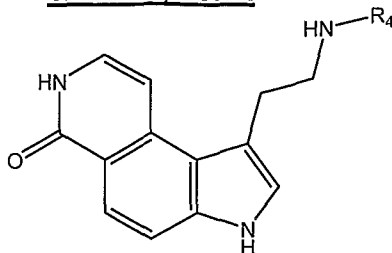
Using essentially the same procedure described in Example 7B and employing 1-(2-aminoethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one as substrate and a suitable aldehyde, the compounds shown in Table I were obtained and identified by HPLC and mass spectral analyses.

TABLE I

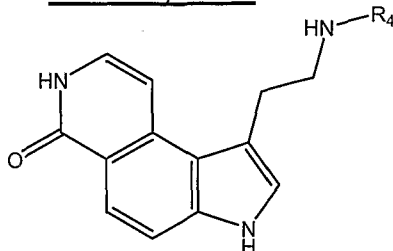
Ex. No.	R4	Mass
8	naphth-2-ylmethyl	367.45
9	4-phenoxybenzyl	409.48
10	ethyl	255.31
11	2-chlorobenzyl	351.83
12	furfur-2-ylmethyl	307.35
13	4-dimethylaminobenzyl	360.45
14	thiophen-2-ylmethyl	323.41
15	4-methylbenzyl	331.41
16	4-chlorobenzyl	351.83
17	4-cyanobenzyl	342.40
18	n-pentyl	297.40
19	3,4-methylenedioxybenzyl	361.40
20	4-isopropylbenzyl	359.47
21	5-methylfurfur-2-ylmethyl	321.37
22	4-hydroxybenzyl	333.38
23	4-methoxybenzyl	347.41
24	2-methoxybenzyl	347.41
25	3-fluoro-4-methoxybenzyl	365.40
26	3,5-bis(trifluoromethyl)benzyl	453.38
27	2,6-difluorobenzyl	353.37
28	2-fluorobenzyl	335.38
29	2-trifluoromethylbenzyl	385.38
30	3-trifluoromethylbenzyl	385.38
31	4-trifluoromethylbenzyl	385.38
32	3-fluorobenzyl	335.38

TABLE I, CONT.

Ex. No.	R4	Mass
33	4-fluorobenzyl	335.38
34	indol-3-ylmethyl	356.42
35	furfur-3-ylmethyl	307.35
36	thiophen-3-ylmethyl	323.41
37	pyridin-3-ylmethyl	318.37
38	2-methylbenzyl	331.41
39	3-chlorobenzyl	351.83
40	3-methylbutyl	297.40
41	3-methoxybenzyl	347.41
42	4-trifluoromethoxybenzyl	401.38
43	pyridin-4-ylmethyl	318.37
44	2,4-dichlorobenzyl	386.28
45	pyridin-2-ylmethyl	318.37
46	6-methyl-pyridin-2-ylmethyl	332.40
47	4-bromobenzyl	396.28
48	1-methylpyrrol-2-ylmethyl	320.39
49	2,4-difluorobenzyl	353.37
50	4-carbomethoxybenzyl	375.42
51	cyclohexylmethyl	323.43
52	4-phenylbenzyl	393.48
53	4-thiomethylbenzyl	363.48
54	4-ethylbenzyl	345.44
55	quinolin-2-ylmethyl	368.43
56	4-n-propyloxybenzyl	375.47
57	(S)-(-)-3,7-dimethyloct-6-enyl	365.51

TABLE I, CONT.

Ex. No.	R4	Mass
58	3,4-dichlorobenzyl	386.28
59	2,4-dimethylbenzyl	345.44
60	1,4-benzodioxan-6-ylmethyl	375.42
61	3,5-difluorobenzyl	353.37
62	3,4-difluorobenzyl	353.37
63	2-chloro-4-hydroxybenzyl	367.83
64	2-fluoro-3-trifluoromethylbenzyl	403.37
65	3-trifluoromethoxybenzyl	401.38
66	3-bromo-4-methoxybenzyl	426.31
67	3-methylbenzyl	331.41
68	3-bromobenzyl	396.28
69	3,5-dimethoxybenzyl	377.44
70	2-chloro-4-fluorobenzyl	369.82
71	5-chloro-thiophen-2-ylmethyl	357.86
72	2-bromobenzyl	396.28
73	benzofuran-2-ylmethyl	357.41
74	5-bromo-furan-2-ylmethyl	386.24
75	4-diethylaminobenzyl	388.51
76	6-chloro-3,4-methylenedioxybenzyl	396.84
77	3-bromo-4-fluorobenzyl	414.27
78	3-chloro-4-fluorobenzyl	369.82
79	3,5-dichlorobenzyl	386.28
80	4-n-hexyloxybenzyl	417.55
81	trans-4-stilbene-2-yl-methyl	419.52
82	(R)-(+)-3,7-dimethyloct-6-enyl	365.51

TABLE I, CONT.

Ex. No.	R4	Mass
83	2-carboethoxy-cycloprop-1-ylmethyl	353.42
84	2,3-dihydrobenzo[b]furan-5-ylmethyl	359.42
85	5-bromothiophen-2-ylmethyl	402.31
86	3-(3,4-dichlorophenoxy)benzyl	478.37
87	3-nitrobenzyl	362.38
88	3,4,5-trihydroxy-n-pentyl	345.39
89	3-cyanobenzyl	342.40
90	4(5)-imidazolylmethyl	307.35
91	3-hydroxybenzyl	333.38

EXAMPLE 92

5

2-N-methyl-6-fluoro-1-isoquinolinone

A stirred solution of 6-fluoro-1-isoquinolinone (3.1 g, 19.0 mmol from Example 2) and sodium hydride (0.684 g, 28.5 mmol) in DMF (40 ml) was treated with methyl iodide (4.05 g, 28.5 mmol) at -30°C. After stirring under nitrogen at ambient temperature for 30 minutes, 50 ml of 1N aqueous HCl was added thereto, and the product was extracted into CH₂Cl₂ (3 x 50 ml). The combined organic layers were washed with 50 ml of water, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to give a solid. This was crystallized from hexane/CH₂Cl₂ to afford the titled product as a white solid (3.0 g, 89% yield).

Elemental Analysis for: C₁₀H₈FNO

15 Calculated: C, 67.79; H, 4.55; N, 7.91

Found: C, 67.95; H, 4.67; N, 7.98

EXAMPLE 93**2-N-methyl-6-hydrazino-1-isoquinolinone**

A stirred solution of 2-N-methyl-6-fluoro-1-isoquinolinone (3.0 g, 16.9 mmol from Example 92) and hydrazine (5 g, 0.156 mmol) was refluxed in 50 ml of dioxane under nitrogen for 19 hours. The mixture was concentrated under vacuo, 50 ml of water was added thereto and the product collected by filtration. An ethanolic solution of the product (100 ml) was treated with 2N HCl (10 ml), filtered and concentrated in vacuo to afford the required product as a light yellow colored solid (3.1 g, 81% yield).

Elemental Analysis for: $C_{10}H_{11}N_3O \cdot 1.0 \text{ HCl}$

Calculated: C, 53.22; H, 5.36; N, 18.62

Found: C, 53.51; H, 5.45; N, 18.69

EXAMPLE 94

1-(2-aminoethyl -7-methyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one

A solution of 2-N-methyl-6-hydrazino-1-isoquinolinone (1.0 g, 4.4 mmol, from Example 93) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan (0.89 g, 5.94 mmol) according to the process outlined in Example 4. After refluxing for 3.5 hours, the product was isolated in the manner described in Example 4 and purified by flash silica gel chromatography (20% MeOH, 5% NH_4OH in CH_2Cl_2) to afford a light brown oil (0.584 g, 55% yield). Treatment with ethanolic HCl gave the required product as its mono hydrochloride salt which was crystallized twice from EtOH/Et₂O to afford the product as a light tan colored solid (mp 295-298°C).

Elemental Analysis for: $C_{14}H_{15}N_3O \cdot 1.0 \text{ HCl} \cdot 0.6H_2O$

Calculated: C, 58.27; H, 6.01; N, 14.56

Found: C, 58.11; H, 5.99; N, 14.43

EXAMPLE 95**7-methyl-1-(2-phenethylaminoethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

A solution of phenacetyl chloride (0.58 g, 3.8 mmol) in methylene chloride (10 ml) was added dropwise to a stirred aqueous solution of 1-(2-aminoethyl)-7-methyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one (0.60 g, 2.5 mmol in 10 ml) from Example 94 containing triethylamine (0.51 g, 5 mmol). After one hour, the mixture was concentrated under vacuum, and the product was purified by flash silica gel chromatography (eluting with 3% MeOH/EtOAc) to afford the required product as a cream colored solid (0.56 g, 63% yield). A solution of the amide (1.53 mmol) in THF (5 ml) was treated with an excess of borane-THF (1M, 9 mmol) at room temperature under nitrogen, and the mixture was stirred for 30 hours. The reaction was terminated by the addition of HCl, and the product was isolated by flash silica gel chromatography (10% MeOH / 5% NH₄OH / 85% CH₂Cl₂) to afford a light brown colored solid (0.24 g, 45% yield). Treatment with ethanolic HCl afforded the salt of the titled compound as an off white colored solid (mp 205-208°C).

Elemental Analysis for: C₂₂H₂₃N₃O 1.0 HCl

Calculated: C, 69.19; H, 6.33; N, 11.00

Found: C, 69.25; H, 6.47; N, 11.08

EXAMPLE 96**7-methyl-1-(2-benzylaminoethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

A solution of benzoic anhydride (1.7 g, 7.9 mmol) in DMF (10 ml) was added dropwise to a stirred solution of 1-(2-aminoethyl)-7-methyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one (1.2 g, 4.97 mmol in 10 ml DMF) from Example 94 containing triethylamine (0.80 g, 7.9 mmol). After one hour, the mixture was concentrated under vacuum and the product purified by flash silica gel chromatography (eluting with 5% MeOH/CH₂Cl₂) to afford the required product as an off white colored solid (0.95 g, 55% yield). A solution of the amide (2.61 mmol) in THF (30 ml) was treated with an excess of borane-THF (1M, 10.4 mmol) at room temperature under nitrogen, and the mixture was refluxed for two hours. The reaction was terminated by the addition of concentrated HCl, and the product isolated by chromatography (10% MeOH / 5% NH₄OH / 85% CH₂Cl₂, on A1203) to afford a tan colored solid (21% yield). Treatment with ethanolic HCl afforded the salt of the titled compound as a white solid (mp 186-192°C).

Elemental Analysis for: C₂₁H₂₁N₃O 1.0 HCl

Calculated: C, 68.56; H, 6.03; N, 11.42

Found: C, 68.75; H, 6.17; N, 11.58

EXAMPLE 97

5 1-(2-dimethylaminoethyl)-7-methyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one

A solution of 1-(2-aminoethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one (0.2 g, 0.88 mmol from Example 4) in DMF (2 mL) was treated with sodium hydroxide (2.5 N, 0.2 mmol) and methyl iodide (2.1 mmol), and the mixture was stirred at room temperature for 3 days. The product was purified by flash silica gel chromatography (50% MeOH, 5% NH₄OH in CH₂Cl₂) to afford the titled compound which was treated with ethereal HCl to afford the required salt as a white solid (0.26 mmol, 30% yield, mp 180°C).

Elemental Analysis for: C₁₆H₁₉N₃O 1.0 HCl

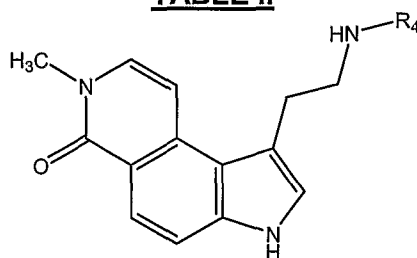
Calculated: C, 62.84; H, 6.59; N, 13.74

15 Found: C, 62.85; H, 6.67; N, 13.87

EXAMPLES 98-181

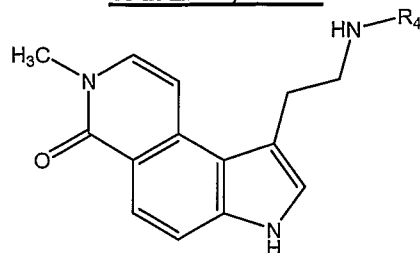
Using essentially the same procedure described in Example 7B and employing 1-(2-aminoethyl)-7-methyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one as substrate and a suitable aldehyde, The compounds shown in Table II were obtained and identified by HPLC and mass spectral analyses.

TABLE II

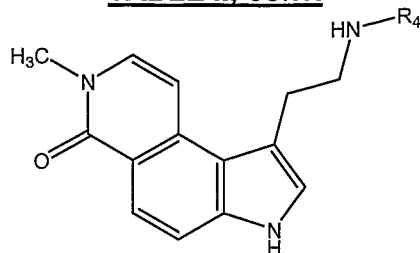


Ex. No.	R4	Mass
98	naphth-2-ylmethyl	381.47
99	4-phenoxybenzyl	423.51
100	ethyl	269.34

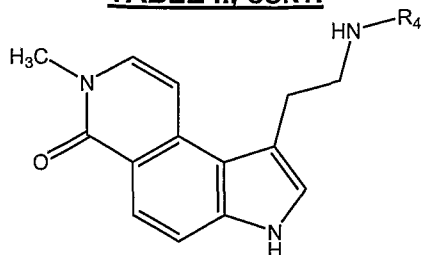
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TABLE II, CONT.

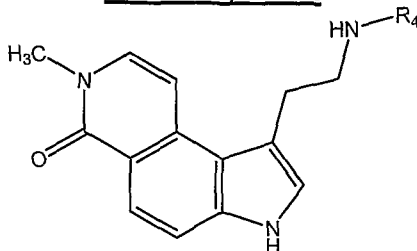
Ex. No.	R4	Mass
101	2-chlorobenzyl	365.86
102	furfur-2-ylmethyl	321.37
103	4-dimethylaminobenzyl	374.48
104	thiophen-2-ylmethyl	337.44
105	4-methylbenzyl	345.44
106	4-chlorobenzyl	365.86
107	4-cyanobenzyl	356.42
108	n-pentyl	311.42
109	3,4-methylenedioxybenzyl	375.42
110	4-isopropylbenzyl	373.49
111	5-methylfurfur-2-ylmethyl	335.40
112	4-hydroxybenzyl	347.41
113	4-methoxybenzyl	361.44
114	2-methoxybenzyl	361.44
115	3-fluoro-4-methoxybenzyl	379.43
116	3,5-bis(trifluoromethyl)benzyl	467.41
117	2,6-difluorobenzyl	367.39
118	2-fluorobenzyl	349.40
119	2-trifluoromethylbenzyl	399.41
120	3-trifluoromethylbenzyl	399.41
121	4-trifluoromethylbenzyl	399.41
122	3-fluorobenzyl	349.40
123	4-fluorobenzyl	349.40
124	indol-3-ylmethyl	370.45
125	furfur-3-ylmethyl	321.37

TABLE II, CONT.

Ex. No.	R4	Mass
126	thiophen-3-ylmethyl	337.44
127	pyridin-3-ylmethyl	332.40
128	2-methylbenzyl	345.44
129	3-chlorobenzyl	365.86
130	3-methylbutyl	311.42
131	3-methoxybenzyl	361.44
132	4-trifluoromethoxybenzyl	415.41
133	pyridin-4-ylmethyl	332.40
134	2,4-dichlorobenzyl	400.30
135	pyridin-2-ylmethyl	332.40
136	6-methyl-pyridin-2-ylmethyl	346.43
137	4-bromobenzyl	410.31
138	1-methylpyrrol-2-ylmethyl	334.42
139	2,4-difluorobenzyl	367.39
140	4-carbomethoxybenzyl	389.45
141	cyclohexylmethyl	337.46
142	4-phenylbenzyl	407.51
143	4-thiomethylbenzyl	377.51
144	4-ethylbenzyl	359.47
145	quinolin-2-ylmethyl	382.46
146	4-n-propyloxybenzyl	389.49
147	(S)-(-)-3,7-dimethyloct-6-enyl	379.54
148	3,4-dichlorobenzyl	400.30
149	2,4-dimethylbenzyl	359.47
150	1,4-benzodioxan-6-ylmethyl	389.45

TABLE II, CONT.

Ex. No.	R4	Mass
151	3,5-difluorobenzyl	367.39
152	3,4-difluorobenzyl	367.39
153	2-chloro-4-hydroxybenzyl	381.86
154	2-fluoro-3-trifluoromethylbenzyl	417.40
155	3-trifluoromethoxybenzyl	415.41
156	3-bromo-4-methoxybenzyl	440.33
157	3-methylbenzyl	345.44
158	3-bromobenzyl	410.31
159	3,5-dimethoxybenzyl	391.46
160	2-chloro-4-fluorobenzyl	383.85
161	5-chloro-thiophen-2-ylmethyl	371.89
162	2-bromobenzyl	410.31
163	benzofuran-2-ylmethyl	371.43
164	5-bromo-furan-2-ylmethyl	400.27
165	4-diethylaminobenzyl	402.53
166	6-chloro-3,4-methylenedioxybenzyl	409.87
167	3-bromo-4-fluorobenzyl	428.30
168	3-chloro-4-fluorobenzyl	383.85
169	3,5-dichlorobenzyl	400.30
170	4-n-hexyloxybenzyl	431.57
171	trans-4-stilbene-2-yl-methyl	433.55
172	(R)-(+)-3,7-dimethyloct-6-enyl	379.54
173	2-carboethoxy-cyclopropyl-1-ylmethyl	367.44
174	2,3-dihydrobenzo[b]furan-5-ylmethyl	373.45
175	5-bromothiophen-2-ylmethyl	416.34

TABLE II, CONT.

Ex. No.	R4	Mass
176	3-(3,4-dichlorophenoxy)benzyl	492.40
177	3-nitrobenzyl	376.41
178	3,4,5-trihydroxy-n-pentyl	359.42
179	3-cyanobenzyl	356.42
180	4(5)-imidazolylmethyl	321.38
181	3-hydroxybenzyl	347.41

EXAMPLE 182**5 1-(2-aminoethyl)-7-benzyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

A solution of 2-N-benzyl-6-hydrazino-1-isoquinolinone (0.5 g, 1.66 mmol, prepared from benzyl bromide in 66% yield according to Examples 92 and 93) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan (0.34 g, 2.24 mmol) according to the process outlined in Example 4. After refluxing for four hours, the product was isolated as reported above and purified by flash silica gel chromatography (20% MeOH, 5% NH₄OH in CH₂Cl₂) to afford a light brown oil. Treatment with ethanolic HCl gave the required product (0.162 g, 27% yield) as its mono hydrochloride salt as an off white colored solid (mp 266-268°C).

Elemental Analysis for: C₂₀H₁₉N₃O 1.0 HCl 1.3H₂O

15 Calculated: C, 63.67; H, 6.04; N, 11.14

Found: C, 63.59; H, 6.04; N, 11.01

EXAMPLE 183**20 1-(2-aminoethyl)-7-benzyl-3-methyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

A solution of 1-(2-aminoethyl)-7-benzyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one (0.25 g, 0.79 mmol) from Example 182 and methyl iodide (0.135 g, 0.95 mmol) in DMF (2 ml) was treated with sodium hydride (0.022 g, 0.91 mmol), and the resulting

mixture was stirred at 0°C under nitrogen for one hour. Water (10 ml) was added and the product extracted with ethyl acetate (2 x 15 ml). The combined organics were washed with 15 ml of brine, separated and dried over anhydrous sodium sulfate. Filtration and concentration in vacuo gave a light brown colored solid (0.21 g). The product was purified by flash silica gel chromatography (10% MeOH / 5% NH₄OH in CH₂Cl₂) to afford a white solid. Treatment with ethanolic HCl gave the titled compound as its mono hydrochloride salt as a white solid (0.138 g, 48% yield, mp 172-176°C).

Elemental Analysis for: C₂₁H₂₁N₃O 1.0 HCl 1H₂O

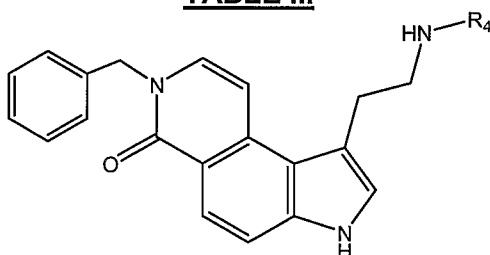
Calculated: C, 65.36; H, 6.27; N, 10.89

Found: C, 65.16; H, 6.04; N, 10.52

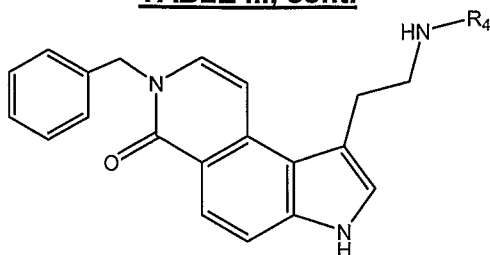
EXAMPLES 184-267

Using essentially the same procedure described in Example 7B and employing 1-(2-aminoethyl)-7-benzyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one as substrate and a suitable aldehyde, the compounds shown in Table III were obtained and identified by HPLC and mass spectral analyses.

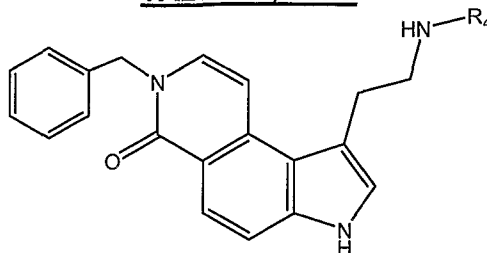
TABLE III



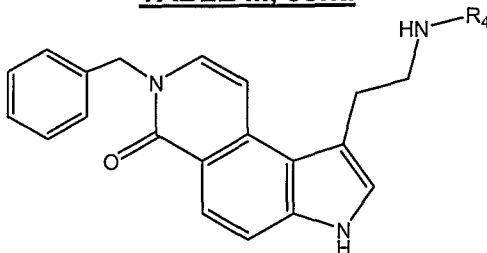
Ex. No.	R4	Mass
184	naphth-2-ylmethyl	457.57
185	4-phenoxybenzyl	499.61
186	ethyl	345.44
187	2-chlorobenzyl	441.95
188	furfur-2-ylmethyl	397.47
189	4-dimethylaminobenzyl	450.58
190	thiophen-2-ylmethyl	413.54

TABLE III, cont.

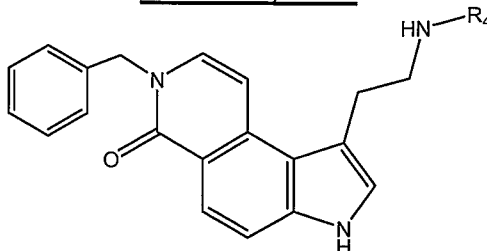
Ex. No.	R4	Mass
191	4-methylbenzyl	421.54
192	4-chlorobenzyl	441.95
193	4-cyanobenzyl	432.59
194	n-pentyl	387.52
195	3,4-methylenedioxybenzyl	451.52
196	4-isopropylbenzyl	449.59
197	5-methylfurfur-2-ylmethyl	441.5
198	4-hydroxybenzyl	423.51
199	4-methoxybenzyl	437.54
200	2-methoxybenzyl	437.54
201	3-fluoro-4-methoxybenzyl	455.53
202	3,5-bis(trifluoromethyl)benzyl	543.51
203	2,6-difluorobenzyl	443.49
204	2-fluorobenzyl	425.50
205	2-trifluoromethylbenzyl	475.51
206	3-trifluoromethylbenzyl	475.51
207	4-trifluoromethylbenzyl	475.51
208	3-fluorobenzyl	425.50
209	4-fluorobenzyl	425.50
210	indol-3-ylmethyl	446.55
211	furfur-3-ylmethyl	397.47
212	thiophen-3-ylmethyl	413.54
213	pyridin-3-ylmethyl	408.50
214	2-methylbenzyl	421.54
215	3-chlorobenzyl	441.95

TABLE III, cont.

Ex. No.	R4	Mass
216	3-methylbutyl	387.52
217	3-methoxybenzyl	437.54
218	4-trifluoromethoxybenzyl	491.51
219	pyridin-4-ylmethyl	408.50
220	2,4-dichlorobenzyl	476.40
221	pyridin-2-ylmethyl	408.50
222	6-methyl-pyridin-2-ylmethyl	422.52
223	4-bromobenzyl	486.41
224	1-methylpyrrol-2-ylmethyl	410.51
225	2,4-difluorobenzyl	443.49
226	4-carbomethoxybenzyl	465.55
227	cyclohexylmethyl	413.56
228	4-phenylbenzyl	483.61
229	4-thiomethylbenzyl	453.60
230	4-ethylbenzyl	435.56
231	quinolin-2-ylmethyl	458.56
232	4-n-propyloxybenzyl	465.59
233	(S)-(-)-3,7-dimethyloct-6-enyl	455.64
234	3,4-dichlorobenzyl	476.40
235	2,4-dimethylbenzyl	435.56
236	1,4-benzodioxan-6-ylmethyl	465.55
237	3,5-difluorobenzyl	443.49
238	3,4-difluorobenzyl	443.49
239	2-chloro-4-hydroxybenzyl	457.95
240	2-fluoro-3-trifluoromethylbenzyl	493.50

TABLE III, cont.

Ex. No.	R4	Mass
241	3-trifluoromethoxybenzyl	491.51
242	3-bromo-4-methoxybenzyl	516.43
243	3-methylbenzyl	421.54
244	3-bromobenzyl	486.41
245	3,5-dimethoxybenzyl	467.56
246	2-chloro-4-fluorobenzyl	459.95
247	5-chloro-thiophen-2-ylmethyl	447.98
248	2-bromobenzyl	486.41
249	benzofuran-2-ylmethyl	447.53
250	5-bromo-furan-2-ylmethyl	476.37
251	4-diethylaminobenzyl	478.63
252	6-chloro-3,4-methylenedioxybenzyl	485.96
253	3-bromo-4-fluorobenzyl	504.40
254	3-chloro-4-fluorobenzyl	459.95
255	3,5-dichlorobenzyl	476.40
256	4-n-hexyloxybenzyl	507.67
257	trans-4-stilbene-2-yl-methyl	509.65
258	(R)-(+)-3,7-dimethyloct-6-enyl	455.64
259	2-carboethoxy-cycloprop-1-ylmethyl	443.54
260	2,3-dihydrobenzo[b]furan-5-ylmethyl	449.55
261	5-bromothiophen-2-ylmethyl	492.43
262	3-(3,4-dichlorophenoxy)benzyl	568.50
263	3-nitrobenzyl	452.51
264	3,4,5-trihydroxy-n-pentyl	435.52
265	3-cyanobenzyl	432.52

TABLE III, cont.

Ex. No.	R4	Mass
266	4(5)-imidazolylmethyl	397.47
267	3-hydroxybenzyl	423.51

EXAMPLE 268**5 1-(3-aminopropyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

A solution of 6-hydrazino-1-isoquinolinone (1.0 g, 4.73 mmol) from Example 3 and 2-(4-chlorobutyl)-1,3-dioxolan (1.05 g, 6.39 mmol) in degassed ethanol (80 ml)/water (16 ml) was refluxed under nitrogen for five hours. The reaction mixture was concentrated in vacuo and the product purified by flash silica gel chromatography (20% MeOH / 5% NH₄OH in CH₂Cl₂) to afford a light amber colored solid (0.08 g, 7% yield). Treatment of the product with ethereal HCl and crystallization from ethanol ether gave the mono hydrochloride salt of the titled compound as a light tan colored solid (mp 225-230°C).

Elemental Analysis for: C₁₄H₁₅N₃O 1.0 HCl

15 Calculated: C, 60.54; H, 5.81; N, 15.13

Found: C, 60.65; H, 5.87; N, 15.19

EXAMPLE 269**1-(2-aminoethyl)-7-cyclohexylmethyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

20 A solution of 2-N-cyclohexylmethyl-6-hydrazino-1-isoquinolinone (1.0 g, 3.2 mmol, prepared from cyclohexylmethylbromide in 69% yield according to Example 92 and Example 93) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan (0.651 g, 4.32 mmol) in a mixture of degassed ethanol (80 ml) and water (20 ml) according to the process outlined in Example 4. After refluxing for three hours,

25 the product was isolated as reported above and purified by flash silica gel chromatography (20% MeOH / 5% NH₄OH in CH₂Cl₂) to afford a viscous brown oil

(0.8 g). Treatment with ethanolic HCl gave the required product as its mono hydrochloride salt which was crystallized twice from EtOH/Et₂O to afford the product as a light brown colored solid (0.33 g, 28% yield, mp 220-224°C).

Elemental Analysis for: C₂₀H₂₅N₃O 1.0 HCl 1.5H₂O

5 Calculated: C, 62.09; H, 7.55; N, 10.86

Found: C, 62.32; H, 7.27; N, 10.56

EXAMPLE 270

1-(2-aminoethyl)-7-phenylethyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one

10 A solution of 2-N-phenylethyl-6-hydrazino-1-isoquinolinone (1.0 g, 3.2 mmol, prepared from 2-phenylethylbromide in 72% yield in the manner described in Example 92 and Example 93) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan (0.65 g, 4.3 mmol) in a mixture of degassed ethanol (80 ml) and water (20 ml) according to the process outlined in Example 4. After refluxing

15 for three hours, the product was isolated as reported above and purified by flash silica gel chromatography (20% MeOH / 5% NH₄OH in CH₂Cl₂) to afford a light brown colored solid (0.37 g). Treatment with ethanolic HCl gave the required product as its mono hydrochloride salt which was crystallized twice from EtOH/Et₂O to afford the product as a white solid (0.36 g, 31% yield, mp 162-166°C).

20 Elemental Analysis for: C₂₁H₂₁N₃O 1.0 HCl 1.75H₂O

Calculated: C, 63.15; H, 6.43; N, 10.52

Found: C, 63.47; H, 6.14; N, 10.52

EXAMPLE 271

1-(2-aminoethyl)-7-naphthalen-2-ylmethyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one

25 A solution of 2-N-naphthalen-2-ylmethyl-6-hydrazino-1-isoquinolinone (2.25 g, 6.40 mmol, prepared from naphthalen-2-ylmethylbromide in 59% yield according to Example 92 and Example 93) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan (1.3 g, 8.64 mmol) in degassed ethanol (130 ml)/water (90 ml) according to the process outlined in Example 4. After refluxing for three hours,

30 the product was isolated as reported above and purified by flash silica gel chromatography (20% MeOH / 5% NH₄OH in CH₂Cl₂) to afford an off white colored solid (0.43 g, 18% yield). Treatment with ethanolic HCl gave the titled product as its mono hydrochloride salt which was crystallized from EtOH/Et₂O to afford an off white

35 colored solid (0.43 g, mp 288-292°C).

Elemental Analysis for: $C_{24}H_{21}N_{30}$ 1.0 HCl 0.25 H_2O

Calculated: C, 70.58; H, 5.55; N, 10.29

Found: C, 70.64; H, 5.62; N, 10.17

5

EXAMPLE 272

1-(2-aminoethyl)-7-heptyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one

A solution of 2-N-heptyl-6-hydrazino-1-isoquinolinone (0.95 g, 3.07 mmol, prepared from heptylbromide in 72% yield according to Example 92 and Example 93) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan (0.623 g, 4.14 mmol) in degassed ethanol (80 ml)/water (20 ml) according to the process outlined in Example 4. After refluxing for 3.5 hours, the product was isolated as reported above and purified by flash silica gel chromatography (20% MeOH / 5% NH_4OH in CH_2Cl_2) to afford an off white colored solid (0.33 g, 33% yield). Treatment with ethanolic HCl gave the titled product as its mono hydrochloride salt which was crystallized from EtOH/Et₂O to afford a white solid (0.33 g, mp 239-241°C).

10

15

Elemental Analysis for: $C_{20}H_{27}N_{30}$ 1.0 HCl

Calculated: C, 66.37; H, 7.80; N, 11.61

Found: C, 65.95; H, 7.51; N, 11.64

20

EXAMPLE 273

1-(2-aminoethyl)-7-(3,4-dichlorobenzyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one

A solution of 2-N-(3,4-dichlorobenzyl)-6-hydrazino-1-isoquinolinone (1.30 g, 3.51 mmol, prepared from 3,4-dichlorobenzyl bromide in 79% yield according to Example 92 and Example 93) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan (0.80 g, 5.31 mmol) in a mixture of degassed ethanol (100ml) and water (25 ml) according to the process outlined in Example 4. After refluxing for three hours, the product was isolated as reported above and purified by flash silica gel chromatography (20% MeOH / 5% NH_4OH in CH_2Cl_2) to afford a light yellow colored solid (0.395 g). Treatment with ethanolic HCl gave the titled product as its mono hydrochloride salt which was crystallized from EtOH/Et₂O to afford a white solid (0.37 g, 27% yield, mp 188-190°C).

25

30

Elemental Analysis for: $C_{20}H_{17}N_3OCl_2$ 1.0 HCl 1 H_2O

Calculated: C, 54.50; H, 4.57; N, 9.53

Found: C, 54.76; H, 4.36; N, 9.31

35

EXAMPLE 274**1-(2-aminoethyl)-7-thiophen-3-ylmethyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

A solution of 2-N-(thiophen-3-ylmethyl)-6-hydrazino-1-isoquinolinone (0.5 g, 1.62 mmol, prepared from thiophen-3-ylmethyl bromide in 64% yield according to Example 92 and Example 93) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan (0.33 g, 2.19 mmol) in a mixture of degassed ethanol (40 ml) and water (8 ml) according to the process outlined in Example 4. After refluxing for four hours, the product was isolated as reported above and purified by flash silica gel chromatography (20% MeOH / 5% NH₄OH in CH₂Cl₂) to afford a yellow colored solid (0.17 g, 32% yield). Treatment with ethanolic HCl gave the titled product as its mono hydrochloride salt which was crystallized from EtOH/Et₂O to afford a light yellow colored solid (0.17 g, mp 260-264°C).

Elemental Analysis for: C₁₈H₁₇N₃OS 1.0 HCl 1.1 H₂O

Calculated: C, 56.94; H, 5.36; N, 11.07

Found: C, 56.63; H, 5.30; N, 10.66

EXAMPLE 275**3-methyl-6-fluoro-1-isoquinolinone**

A suspension of 4-fluoro-2-isopropenylbenzamide (2.50 g, 14 mmol), palladium (II) chloride (0.248 g, 1.4 mmol) and copper (I) chloride (1.386 g, 14 mmol) in DME (25 ml) was stirred under nitrogen at 60°C for 24 hours. The mixture was cooled, filtered and concentrated in vacuo. The product was purified by crystallization twice from acetone to afford a white solid (1.3 g, 52% yield).

Elemental Analysis for: C₁₀H₈FNO

Calculated: C, 67.79; H, 4.55; N, 7.91

Found: C, 68.01; H, 4.67; N, 8.10

EXAMPLE 276**3-methyl-6-hydrazino-1-isoquinolinone**

The titled compound was obtained as a light yellow colored solid in 84% yield from 3-methyl-6-fluoro-1-isoquinolinone using the procedure described in Example 3.

Elemental Analysis for: C₁₀H₁₁N₃O 1.0 HCl

Calculated: C, 53.22; H, 5.36; N, 18.62

Found: C, 53.54; H, 5.46; N, 18.80

EXAMPLE 277**1-(2-aminoethyl)-8-methyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

- A solution of 3-methyl-6-hydrazino-1-isoquinolinone (1.0 g, 5.2 mmol) and 2-(3-chloropropyl)-1,3-dioxolan (1.32 g, 8.9 mmol) in a mixture of degassed ethanol (80 ml) and water (15 ml) was refluxed under nitrogen for four hours. The reaction mixture was concentrated in vacuo and the product purified by flash silica gel chromatography to afford an amber colored solid (0.71 g, 56% yield). Treatment of the product with ethereal HCl and crystallization from ethanol ether gave the mono hydrochloride salt as a light amber colored solid (m.p. > 200°C).
- Elemental Analysis for: C₁₄H₁₅N₃O 1.0 HCl
Calculated: C, 60.54; H, 5.81; N, 15.13
Found: C, 60.45; H, 5.88; N, 15.20

EXAMPLE 278**1-(2-aminoethyl)-2-(4-chlorophenyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

- A solution of 6-hydrazino-1-isoquinolinone (1.0 g, 4.73 mmol) from Example 3 and 4,4'-dichlorobutyrophenone (1.39 g, 6.4 mmol, 1.35 equivalents) in degassed ethanol (50 ml)/water (50 ml) was refluxed under nitrogen for six hours. The reaction mixture was concentrated in vacuo, and the product was purified by flash silica gel chromatography to afford a yellow colored solid (0.21 g, 13% yield). Treatment of the product with methanolic HCl and crystallization from ethanol ether gave the hydrochloride salt as a light tan colored solid (mp > 300°C).
- Elemental Analysis for: C₁₉H₁₆ClN₃O 2.0 HCl
Calculated: C, 55.56; H, 4.42; N, 10.23
Found: C, 55.63; H, 4.56; N, 10.20

EXAMPLE 279**1-(2-aminoethyl)-9-chloro-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

- A solution of 4-chloro-6-hydrazino-1-isoquinolinone (0.51 g, 2.07 mmol) and 2-(3-chloropropyl)-1,3-dioxolan (0.39 g, 2.59 mmol, 1.25 equivalents) in degassed ethanol (40 ml)/water (8 ml) was refluxed under nitrogen for four hours. The reaction mixture was concentrated in vacuo and the product purified by flash silica gel chromatography to afford a light brown colored solid (0.16 g, 29% yield). Treatment of the product with methanolic HCl and crystallization from ethanol ether gave the mono hydrochloride salt as a light tan colored solid (mp 239-243°C).

Elemental Analysis for: C₁₃H₁₂ClN₃O 1.0 HCl

Calculated: C, 52.37; H, 4.39; N, 14.39

Found: C, 52.48; H, 4.56; N, 14.55

5

EXAMPLE 280

1-(2-aminoethyl)-7-ethyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one

A solution of 2-N-ethyl-6-hydrazino-1-isoquinolinone (0.45 g, 1.88 mmol, prepared from iodoethane by the method described in Example 92 and Example 93) in degassed ethanol (40 ml)/water (8 ml) was reacted in a Fisher indole reaction with
10 2-(3-chloropropyl)-1,3-dioxolan (0.354g, 2.35 mmol, 1.25 equivalents) according to the process outlined in Example 4. After refluxing for 4 hours, the product was isolated in the manner described in Example 4 and purified by chromatography (neutral alumina, type III, eluting with 4% MeOH in CH₂Cl₂) to afford a light yellow oil (0.105 g, 22% yield). Treatment with ethanolic HCl gave the required product as its
15 mono hydrochloride salt which was crystallized from EtOH/Et₂O to afford the product as a white solid (mp 224-227°C).

Elemental Analysis for: C₁₅H₁₇N₃O 1.0 HCl

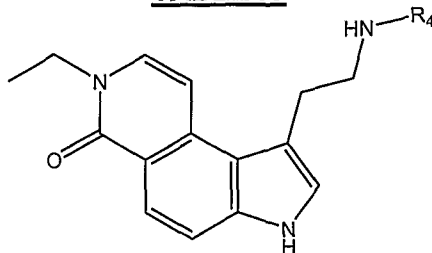
Calculated: C, 61.75; H, 6.22; N, 14.40

Found: C, 61.95; H, 6.49; N, 14.43

20

EXAMPLES 281-288

Using essentially the same procedure described in Example 7B and employing 1-(2-aminoethyl)-7-ethyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one as substrate and a suitable aldehyde, the compounds shown in Table IV were obtained
25 and identified by HPLC and mass spectral analyses.

TABLE IV

Ex. No.	R4	Mass
281	3-nitrobenzyl	390.44
282	3,4,5-trihydroxy-n-pentyl	373.45
283	3-chlorobenzyl	379.88
284	3-methoxybenzyl	375.47
285	pyridin-4-ylmethyl	346.43
286	3-cyanobenzyl	370.45
287	4(5)-imidazolylmethyl	335.40
288	3-hydroxybenzyl	361.44

5

EXAMPLE 289**1-(2-aminoethyl)-7-(tetrahydropyran-2-ylmethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

A solution of 2-N-(tetrahydropyran-2-ylmethyl)-6-hydrazinoisoquinolinone (0.70 g, 2.26 mmol, prepared from tetrahydropyran-2-ylmethylbromide by the method described in Example 92 and Example 93) in degassed ethanol (55 ml)/water (10 ml) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan (0.426 g, 2.83 mmol, 1.25 equivalents) according to the process outlined in Example 4. After refluxing for 4 hours, the product was isolated in the manner described in Example 4, and purified by chromatography (neutral alumina, type III, eluting with 5% MeOH in CH₂Cl₂) to afford a yellow colored solid (0.251 g, 34% yield). Treatment with ethanolic HCl gave the required product as its mono hydrochloride salt which was crystallized from EtOH/Et₂O to afford the product as a white solid (mp 260-262°C). Elemental Analysis for: C₁₉H₂₃N₃O₂ 1.0 HCl
 Calculated: C, 63.06; H, 6.68; N, 11.61
 Found: C, 63.25; H, 6.69; N, 11.63

EXAMPLE 290**1-(2-aminoethyl)-7-(2-methoxyethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

A solution of 2-N-(2-methoxyethyl)-6-hydrazinoisoquinolinone (1.37 g, 5.87 mmol, prepared from 1-bromo-2-methoxyethane by the method described in Example 92 and Example 93) in degassed ethanol (100 ml)/water (16 ml) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan (1.11 g, 7.34 mmol, 1.25 equivalents) according to the process outlined in Example 4. After refluxing for 4 hours, the product was isolated in the manner described in Example 4 and purified by chromatography (silica gel, eluting with 8% MeOH in CH₂Cl₂) to afford a yellow colored solid (0.200 g, 12% yield). Treatment with ethanolic HCl gave the required product as its mono hydrochloride salt which was crystallized from EtOH/Et₂O to afford the product as a white solid (mp 246-249°C).
Elemental Analysis for: C₁₆H₁₉N₃O₂ 1.0 HCl
Calculated: C, 59.72; H, 6.26; N, 13.06
Found: C, 59.92; H, 6.39; N, 13.23

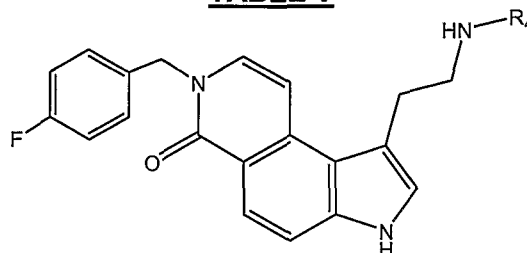
EXAMPLE 291**1-(2-aminoethyl)-7-(4-fluorobenzyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

A solution of 2-N-(4-fluorobenzyl)-6-hydrazinoisoquinolinone (0.88 g, 3.10 mmol, prepared from 4-fluorobenzylbromide by the method described in Example 92 and Example 93) in degassed ethanol (100 ml)/water (16 ml) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan (0.46 g, 3.1 mmol) according to the process outlined in Example 4. After refluxing for 16 hours, the product was isolated in the manner described in Example 4 and purified by chromatography (silica gel, eluting with 10% MeOH in CH₂Cl₂) to afford a yellow colored solid (0.45 g). Treatment with ethanolic HCl gave the required product as its mono hydrochloride salt as a pale yellow colored solid (mp 247-249°C).
Elemental Analysis for: C₂₀H₁₈FN₃O 1.0 HCl
Calculated: C, 64.60; H, 5.15; N, 11.30
Found: C, 64.72; H, 5.39; N, 11.33

EXAMPLES 292-376

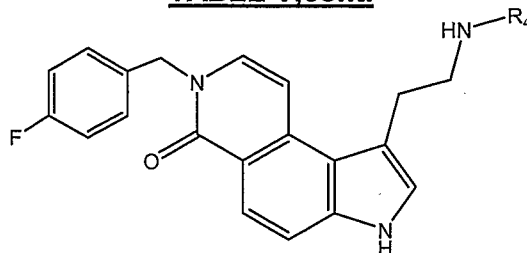
Using essentially the same procedure described in Example 7B and employing 1-(2-aminoethyl)-7-(4-fluorobenzyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one

as substrate and a suitable aldehyde, the compounds shown in Table V were obtained and identified by HPLC and mass spectral analyses.

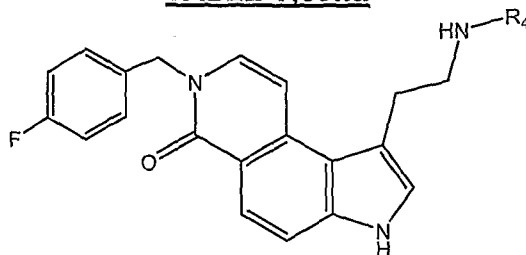
TABLE V

5

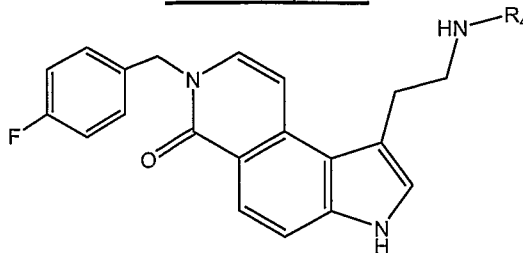
Ex. No.	R4	Mass
292	naphth-2-ylmethyl	475.56
293	4-phenoxybenzyl	517.60
294	ethyl	363.43
295	2-chlorobenzyl	459.95
296	furfur-2-ylmethyl	415.46
297	4-dimethylaminobenzyl	468.57
298	benzyl	425.50
299	thiophen-2-ylmethyl	431.53
300	4-methylbenzyl	439.53
301	4-chlorobenzyl	459.95
302	4-cyanobenzyl	450.51
303	n-pentyl	405.51
304	3,4-methylenedioxybenzyl	469.51
305	4-isopropylbenzyl	467.58
306	5-methylfurfur-2-ylmethyl	429.49
307	4-hydroxybenzyl	441.50
308	4-methoxybenzyl	455.53
309	2-methoxybenzyl	455.53
310	3-fluoro-4-methoxybenzyl	473.52
311	3,5-bis(trifluoromethyl)benzyl	561.50
312	2,6-difluorobenzyl	461.48

TABLE V,cont.

Ex. No.	R4	Mass
313	2-fluorobenzyl	443.49
314	2-trifluoromethylbenzyl	493.50
315	3-trifluoromethylbenzyl	493.50
316	4-trifluoromethylbenzyl	493.50
317	3-fluorobenzyl	443.49
318	4-fluorobenzyl	443.49
319	indol-3-ylmethyl	464.54
320	furfur-3-ylmethyl	415.46
321	thiophen-3-ylmethyl	431.53
322	pyridin-3-ylmethyl	426.49
323	2-methylbenzyl	439.53
324	3-chlorobenzyl	459.95
325	3-methylbutyl	405.51
326	3-methoxybenzyl	455.53
327	4-trifluoromethoxybenzyl	509.50
328	pyridin-4-ylmethyl	426.49
329	2,4-dichlorobenzyl	494.39
330	pyridin-2-ylmethyl	426.49
331	6-methyl-pyridin-2-ylmethyl	440.52
332	4-bromobenzyl	504.40
333	1-methylpyrrol-2-ylmethyl	428.50
334	2,4-difluorobenzyl	461.48
335	4-carbomethoxybenzyl	483.54
336	cyclohexylmethyl	431.55

TABLE V,cont.

Ex. No.	R ₄	Mass
337	4-phenylbenzyl	401.60
338	4-thiomethylbenzyl	471.59
339	4-ethylbenzyl	453.55
340	quinolin-2-ylmethyl	476.55
341	4-n-propyloxybenzyl	483.58
342	(S)-(-)-3,7-dimethyloct-6-enyl	473.63
343	3,4-dichlorobenzyl	494.39
344	2,4-dimethylbenzyl	453.55
345	1,4-benzodioxan-6-ylmethyl	483.54
346	3,5-difluorobenzyl	461.48
347	3,4-difluorobenzyl	461.48
348	2-chloro-4-hydroxybenzyl	475.94
349	2-fluoro-3-trifluoromethylbenzyl	511.49
350	3-trifluoromethoxybenzyl	509.50
351	3-bromo-4-methoxybenzyl	534.42
352	3-methylbenzyl	539.55
353	3-bromobenzyl	504.40
354	3,5-dimethoxybenzyl	485.55
355	2-chloro-4-fluorobenzyl	477.94
356	5-chloro-thiophen-2-ylmethyl	465.97
357	2-bromobenzyl	504.40
358	benzofuran-2-ylmethyl	465.52
359	5-bromo-furan-2-ylmethyl	494.36
360	4-diethylaminobenzyl	496.62

TABLE V,cont.

Ex. No.	R4	Mass
361	6-chloro-3,4-methylenedioxybenzyl	503.96
362	3-bromo-4-fluorobenzyl	522.39
363	3-chloro-4-fluorobenzyl	477.94
364	3,5-dichlorobenzyl	494.39
365	4-n-hexyloxybenzyl	525.66
366	trans-4-stilbene-2-yl-methyl	527.64
367	(R)-(+)-3,7-dimethyloct-6-enyl	473.63
368	2-carboethoxy-cycloprop-1-ylmethyl	461.53
369	2,3-dihydrobenzo[b]furan-5-ylmethyl	467.54
370	5-bromothiophen-2-ylmethyl	510.42
371	3-(3,4-dichlorophenoxy)benzyl	586.49
372	3-nitrobenzyl	470.50
373	3,4,5-trihydroxy-n-pentyl	453.51
374	3-cyanobenzyl	450.51
375	4(5)-imidazolylmethyl	415.47
376	3-hydroxybenzyl	441.50

EXAMPLE 377**5 1-(2-aminoethyl)-7-(2-fluorobenzyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

A solution of 2-N-(2-fluorobenzyl)-6-hydrazinoisoquinolinone (0.95 g, 3.35 mmol, prepared from 2-fluorobenzylbromide by the method described in Example 92 and Example 93) in degassed ethanol (100 ml)/water (16 ml) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan (0.5 g, 3.35 mmol) according to

10 the process outlined in Example 4. After refluxing for 16 hours, the product was isolated in the manner described in Example 4 and purified by chromatography (silica gel, eluting with 10% MeOH in CH₂Cl₂) to afford a yellow colored solid (0.47 g).

Treatment with ethanolic HCl gave the required product as its mono hydrochloride salt as a pale yellow colored solid (mp > 250°C).

Elemental Analysis for: C₂₀H₁₈FN₃O 1.0 HCl

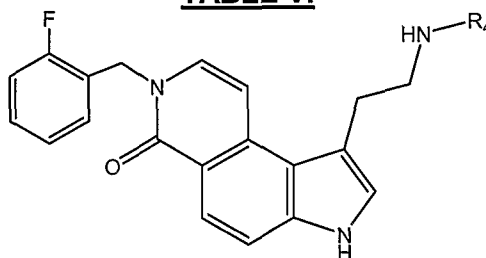
Calculated: C, 64.60; H, 5.15; N, 11.30

5 Found: C, 64.79; H, 5.27; N, 11.42

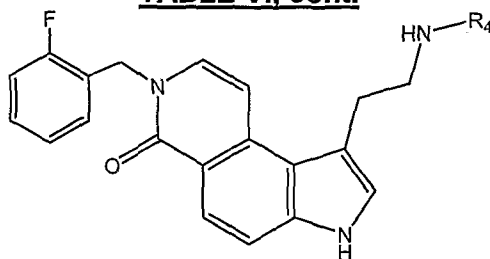
EXAMPLES 378-462

Using essentially the same procedure described in Example 7B and employing 1-(2-aminoethyl)-7-(2-fluorobenzyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one as substrate and a suitable aldehyde, the compounds shown in Table VI were
10 obtained and identified by HPLC and mass spectral analyses.

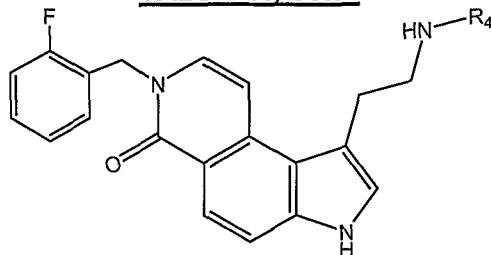
TABLE VI



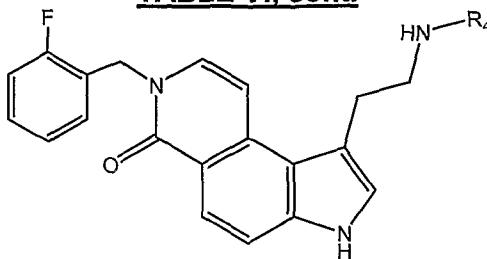
Ex. No.	R4	Mass
378	naphth-2-ylmethyl	475.56
379	4-phenoxybenzyl	517.60
380	ethyl	363.43
381	2-chlorobenzyl	459.95
382	furfur-2-ylmethyl	415.46
383	4-dimethylaminobenzyl	468.57
384	benzyl	425.50
385	thiophen-2-ylmethyl	431.53
386	4-methylbenzyl	439.53
387	4-chlorobenzyl	459.95
388	4-cyanobenzyl	450.51
389	n-pentyl	405.51
390	3,4-methylenedioxybenzyl	469.51

TABLE VI, cont.

Ex. No.	R4	Mass
391	4-isopropylbenzyl	467.58
392	5-methylfurfur-2-ylmethyl	429.49
393	4-hydroxybenzyl	441.50
394	4-methoxybenzyl	455.53
395	2-methoxybenzyl	455.53
396	3-fluoro-4-methoxybenzyl	473.52
397	3,5-bis(trifluoromethyl)benzyl	561.50
398	2,6-difluorobenzyl	461.48
399	2-fluorobenzyl	443.49
400	2-trifluoromethylbenzyl	493.50
401	3-trifluoromethylbenzyl	493.50
402	4-trifluoromethylbenzyl	493.50
403	3-fluorobenzyl	443.49
404	4-fluorobenzyl	443.49
405	indol-3-ylmethyl	464.54
406	furfur-3-ylmethyl	415.46
407	thiophen-3-ylmethyl	431.53
408	pyridin-3-ylmethyl	426.49
409	2-methylbenzyl	439.53
410	3-chlorobenzyl	459.95
411	3-methylbutyl	405.51
412	3-methoxybenzyl	455.53
413	4-trifluoromethoxybenzyl	509.50
414	pyridin-4-ylmethyl	426.49
415	2,4-dichlorobenzyl	494.39

TABLE VI, cont.

Ex. No.	R ₄	Mass
416	pyridin-2-ylmethyl	426.49
417	6-methyl-pyridin-2-ylmethyl	440.52
418	4-bromobenzyl	504.40
419	1-methylpyrrol-2-ylmethyl	428.50
420	2,4-difluorobenzyl	461.48
421	4-carbomethoxybenzyl	483.54
422	cyclohexylmethyl	431.55
423	4-phenylbenzyl	401.60
424	4-thiomethylbenzyl	471.59
425	4-ethylbenzyl	453.55
426	quinolin-2-ylmethyl	476.55
427	4-n-propyloxybenzyl	483.58
428	(S)-(-)-3,7-dimethyloct-6-enyl	473.63
429	3,4-dichlorobenzyl	494.39
430	2,4-dimethylbenzyl	453.55
431	1,4-benzodioxan-6-ylmethyl	483.54
432	3,5-difluorobenzyl	461.48
433	3,4-difluorobenzyl	461.48
434	2-chloro-4-hydroxybenzyl	475.94
435	2-fluoro-3-trifluoromethylbenzyl	511.49
436	3-trifluoromethoxybenzyl	509.50
437	3-bromo-4-methoxybenzyl	534.42
438	3-methylbenzyl	539.55
439	3-bromobenzyl	504.40
440	3,5-dimethoxybenzyl	485.55

TABLE VI, cont.

Ex. No.	R4	Mass
441	2-chloro-4-fluorobenzyl	477.94
442	5-chloro-thiophen-2-ylmethyl	465.97
443	2-bromobenzyl	504.40
444	benzofuran-2-ylmethyl	465.52
445	5-bromo-furan-2-ylmethyl	494.36
446	4-diethylaminobenzyl	496.62
447	6-chloro-3,4-methylenedioxybenzyl	503.96
448	3-bromo-4-fluorobenzyl	522.39
449	3-chloro-4-fluorobenzyl	477.94
450	3,5-dichlorobenzyl	494.39
451	4-n-hexyloxybenzyl	525.66
452	trans-4-stilbene-2-yl-methyl	527.64
453	(R)-(+)-3,7-dimethyloct-6-enyl	473.63
454	2-carboethoxy-cycloprop-1-ylmethyl	461.53
455	2,3-dihydrobenzo[b]furan-5-ylmethyl	467.54
456	5-bromothiophen-2-ylmethyl	510.42
457	3-(3,4-dichlorophenoxy)benzyl	586.49
458	3-nitrobenzyl	470.50
459	3,4,5-trihydroxy-n-pentyl	453.51
460	3-cyanobenzyl	450.51
461	4(5)-imidazolylmethyl	415.47
462	3-hydroxybenzyl	441.50

EXAMPLE 463**1-(2-aminoethyl)-7-(thiophen-2-ylmethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

A solution of 2-N-(thiophen-2-ylmethyl)-6-hydrazino-1-isoquinolinone (prepared from 2-thienyl bromide according to Example 92 and Example 93) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan according to the process outlined in Example 4. After refluxing for four hours, the product was isolated as reported above and purified by flash silica gel chromatography (20% MeOH, 5% NH₄OH in CH₂Cl₂) to afford a light brown oil. Treatment with ethanolic HCl gave the required product as its mono hydrochloride salt as an off white colored solid, MW = 359.87; HPLC single component; identified by HNMR.

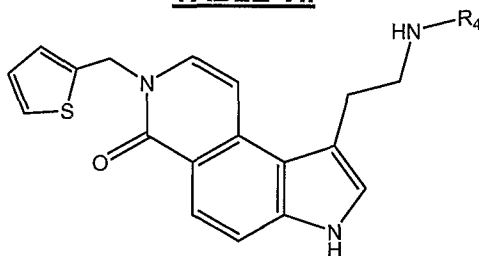
Elemental Analysis for: C₁₈H₁₇N₃OS 1.0 HCl

Calculated: C, 64.07; H, 5.04; N, 11.68

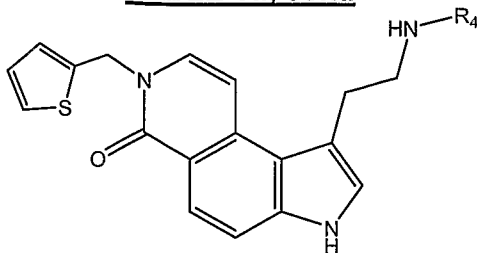
Found: C, 64.09; H, 5.07; N, 11.72

EXAMPLES 464-548

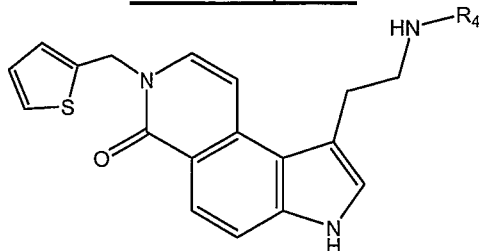
Using essentially the same procedure described in Example 7B and employing 1-(2-aminoethyl)-7-(thiophen-2-ylmethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one as substrate and a suitable aldehyde, the compounds shown in Table VII were obtained and identified by HPLC and mass spectral analyses.

TABLE VII

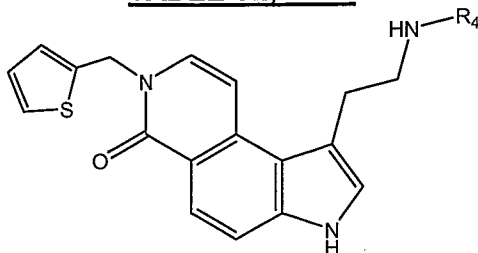
Ex. No.	R4	Mass
464	naphthyl-2-ylmethyl	463.60
465	4-phenoxybenzyl	505.64
466	ethyl	351.47
467	2-chlorobenzyl	447.98
468	furfur-2-ylmethyl	403.50

TABLE VII, cont.

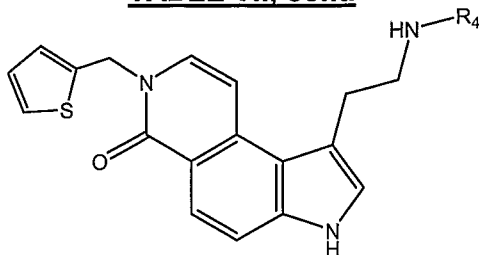
Ex. No.	R4	Mass
469	4-dimethylaminobenzyl	456.61
470	benzyl	413.54
471	thiophen-2-ylmethyl	419.57
472	4-methylbenzyl	427.57
473	4-chlorobenzyl	447.98
474	4-cyanobenzyl	438.55
475	n-pentyl	393.55
476	3,4-methylenedioxybenzyl	457.55
477	4-isopropylbenzyl	455.62
478	5-methylfurfur-2-ylmethyl	417.53
479	4-hydroxybenzyl	429.54
480	4-methoxybenzyl	443.56
481	2-methoxybenzyl	443.56
482	3-fluoro-4-methoxybenzyl	461.56
483	3,5-bis(trifluoromethyl)benzyl	549.53
484	2,6-difluorobenzyl	449.52
485	2-fluorobenzyl	431.53
486	2-trifluoromethylbenzyl	481.54
487	3-trifluoromethylbenzyl	481.54
488	4-trifluoromethylbenzyl	481.54
489	3-fluorobenzyl	431.53
490	4-fluorobenzyl	431.53
491	indol-3-ylmethyl	452.57
492	furfur-3-ylmethyl	403.50
493	thiophen-3-ylmethyl	419.57

TABLE VII, cont.

Ex. No.	R4	Mass
494	pyridin-3-ylmethyl	414.53
495	2-methylbenzyl	427.57
496	3-chlorobenzyl	447.98
497	3-methylbutyl	393.55
498	3-methoxybenzyl	443.56
499	4-trifluoromethoxybenzyl	497.54
500	pyridin-4-ylmethyl	414.53
501	2,4-dichlorobenzyl	482.43
502	pyridin-2-ylmethyl	414.53
503	6-methyl-pyridin-2-ylmethyl	428.55
504	4-bromobenzyl	492.43
505	1-methylpyrrol-2-ylmethyl	416.54
506	2,4-difluorobenzyl	449.52
507	4-carbomethoxybenzyl	471.57
508	cyclohexylmethyl	419.59
509	4-phenylbenzyl	489.64
510	4-thiomethylbenzyl	459.63
511	4-ethylbenzyl	441.59
512	quinolin-2-ylmethyl	464.59
513	4-n-propyloxybenzyl	471.62
514	(S)-(-)-3,7-dimethyloct-6-enyl	461.67
515	3,4-dichlorobenzyl	482.43
516	2,4-dimethylbenzyl	441.59
517	1,4-benzodioxan-6-ylmethyl	471.57
518	3,5-difluorobenzyl	449.52

TABLE VII, cont.

Ex. No.	R4	Mass
519	3,4-difluorobenzyl	449.52
520	2-chloro-4-hydroxybenzyl	463.98
521	2-fluoro-3-trifluoromethylbenzyl	499.53
522	3-trifluoromethoxybenzyl	497.54
523	3-bromo-4-methoxybenzyl	522.46
524	3-methylbenzyl	427.57
525	3-bromobenzyl	492.43
526	3,5-dimethoxybenzyl	473.59
527	2-chloro-4-fluorobenzyl	465.97
528	5-chloro-thiophen-2-ylmethyl	454.01
529	2-bromobenzyl	492.43
530	benzofuran-2-ylmethyl	453.56
531	5-bromo-furan-2-ylmethyl .	482.40
532	4-diethylaminobenzyl	484.66
533	6-chloro-3,4-methylenedioxybenzyl	491.99
534	3-bromo-4-fluorobenzyl	510.42
535	3-chloro-4-fluorobenzyl	565.97
536	3,5-dichlorobenzyl	482.43
537	4-n-hexyloxybenzyl	513.70
538	trans-4-stilbene-2-yl-methyl	515.67
539	(R)-(+)-3,7-dimethyloct-6-enyl	461.67
540	2-carboethoxy-cycloprop-1-ylmethyl	449.57
541	2,3-dihydrobenzo[b]furan-5-ylmethyl	455.58
542	5-bromothiophen-2-ylmethyl	498.46
543	3-(3,4-dichlorophenoxy)benzyl	574.52

TABLE VII, cont.

Ex. No.	R4	Mass
544	3-nitrobenzyl	458.54
545	3,4,5-trihydroxy-n-pentyl	441.55
546	3-cyanobenzyl	438.55
547	4(5)-imidazolymethyl	403.50
548	3-hydroxybenzyl	429.54

EXAMPLE 549**5 1-(2-aminoethyl)-7-cyclopropylmethyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

A solution of 2-N-cyclopropylmethyl-6-hydrazino-1-isoquinolinone (prepared from bromomethylcyclopropane according to Example 92 and Example 93) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan according to the process outlined in Example 4. After refluxing for four hours, the product was isolated as reported above and purified by flash silica gel chromatography (20% MeOH, 5% NH₄OH in CH₂Cl₂) to afford a light brown oil. Treatment with ethanolic HCl gave the required product as its mono hydrochloride salt as an off white colored solid (MW = 317.81; HPLC single component; ¹H-NMR, 3.9 δ, 2H, d).

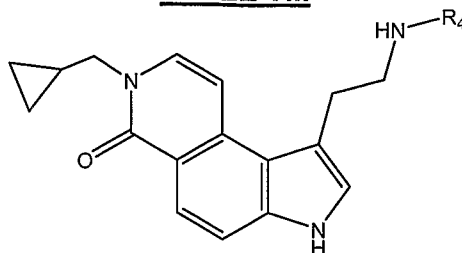
Elemental Analysis for: C₁₇H₁₉N₃O 1.0 HCl

15 Calculated: C, 64.25; H, 6.34; N, 13.22

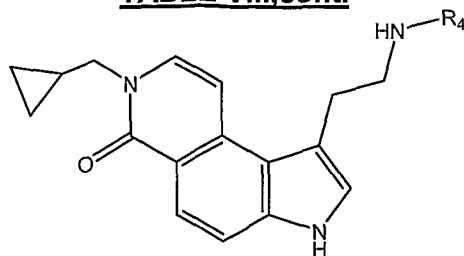
Found: C, 64.49; H, 6.47; N, 13.42

EXAMPLES 550-634

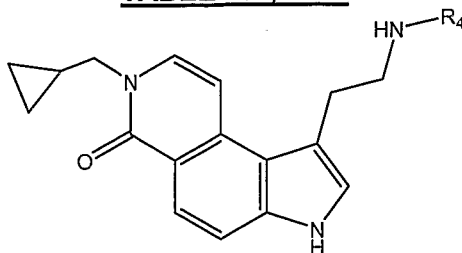
Using essentially the same procedure described in Example 7B and employing 1-(2-aminoethyl)-7-cyclopropylmethyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one as substrate and a suitable aldehyde, the compounds shown in Table VIII were obtained and identified by HPLC and mass spectral analyses.

TABLE VIII

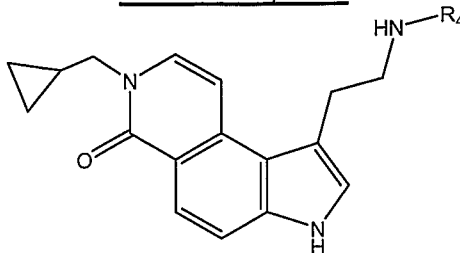
Ex. No.	R4	Mass
550	naphth-2-ylmethyl	421.54
551	4-phenoxybenzyl	463.57
552	ethyl	309.41
553	2-chlorobenzyl	405.92
554	furfur-2-ylmethyl	361.44
555	4-dimethylaminobenzyl	414.55
556	benzyl	371.48
557	thiophen-2-ylmethyl	377.51
558	4-methylbenzyl	385.50
559	4-chlorobenzyl	405.92
560	4-cyanobenzyl	396.49
561	n-pentyl	351.49
562	3,4-methylenedioxybenzyl	415.49
563	4-isopropylbenzyl	413.56
564	5-methylfurfur-2-ylmethyl	375.47
565	4-hydroxybenzyl	387.48
566	4-methoxybenzyl	401.50
567	2-methoxybenzyl	401.50
568	3-fluoro-4-methoxybenzyl	419.49
569	3,5-bis(trifluoromethyl)benzyl	507.47
570	2,6-difluorobenzyl	407.46
571	2-fluorobenzyl	389.47
572	2-trifluoromethylbenzyl	439.48
573	3-trifluoromethylbenzyl	439.48
574	4-trifluoromethylbenzyl	439.48

TABLE VIII.cont.

Ex. No.	R4	Mass
575	3-fluorobenzyl	389.47
576	4-fluorobenzyl	389.47
577	indol-3-ylmethyl	410.51
578	furfur-3-ylmethyl	361.44
579	thiophen-3-ylmethyl	377.51
580	pyridin-3-ylmethyl	372.46
581	2-methylbenzyl	385.50
582	3-chlorobenzyl	405.92
583	3-methylbutyl	351.49
584	3-methoxybenzyl	401.50
585	4-trifluoromethoxybenzyl	455.47
586	pyridin-4-ylmethyl	372.46
587	2,4-dichlorobenzyl	440.37
588	pyridine-2-ylmethyl	372.46
589	6-methyl-pyridin-2-ylmethyl	386.49
590	4-bromobenzyl	450.37
591	1-methylpyrrol-2-ylmethyl	374.48
592	2,4-difluorobenzyl	407.46
593	4-carbomethoxybenzyl	429.51
594	cyclohexylmethyl	377.52
595	4-phenylbenzyl	447.57
596	4-thiomethylbenzyl	417.57
597	4-ethylbenzyl	399.53
598	quinolin-2-ylmethyl	422.52
599	4-n-propyloxybenzyl	429.56

TABLE VIII,cont.

Ex. No.	R4	Mass
600	(S)-(-)-3,7-dimethyloct-6-enyl	419.61
601	3,4-dichlorobenzyl	440.37
602	2,4-dimethylbenzyl	399.53
603	1,4-benzodioxan-6-ylmethyl	429.51
604	3,5-difluorobenzyl	407.46
605	3,4-difluorobenzyl	407.46
606	2-chloro-4-hydroxybenzyl	421.92
607	2-fluoro-3-trifluoromethylbenzyl	457.47
608	3-trifluoromethoxybenzyl	455.47
609	3-bromo-4-methoxybenzyl	480.40
610	3-methylbenzyl	385.50
611	3-bromobenzyl	450.37
612	3,5-dimethoxybenzyl	431.53
613	2-chloro-4-fluorobenzyl	423.91
614	5-chloro-thiophen-2-ylmethyl	411.95
615	2-bromobenzyl	450.37
616	benzofuran-2-ylmethyl	411.50
617	5-bromo-furan-2-ylmethyl	440.33
618	4-diethylaminobenzyl	442.60
619	6-chloro-3,4-methylenedioxybenzyl	449.93
620	3-bromo-4-fluorobenzyl	468.37
621	3-chloro-4-fluorobenzyl	423.91
622	3,5-dichlorobenzyl	440.37
623	4-n-hexyloxybenzyl	471.64
624	trans-4-stilbene-2-yl-methyl	473.61

TABLE VIII,cont.

Ex. No.	R4	Mass
625	(R)-(+)-3,7-dimethyloct-6-enyl	419.61
626	2-carboethoxy-cycloprop-1-ylmethyl	407.51
627	2,3-dihydrobenzo[b]furan-5-ylmethyl	413.51
628	5-bromothiophen-2-ylmethyl	456.40
629	3-(3,4-dichlorophenoxy)benzyl	432.46
630	3-nitrobenzyl	458.54
631	3,4,5-trihydroxy-n-pentyl	399.49
632	3-cyanobenzyl	396.49
633	4(5)-imidazolylmethyl	361.44
634	3-hydroxybenzyl	387.48

EXAMPLE 635**5 1-(2-aminoethyl)-7-propyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

A solution of 2-N-propyl-6-hydrazino-1-isoquinolinone (prepared from n-propyl bromide according to Example 92 and Example 93) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan according to the process outlined in Example 4. After refluxing for four hours, the product was isolated as reported above and purified by flash silica gel chromatography (20% MeOH, 5% NH₄OH in CH₂Cl₂) to afford a light brown oil. Treatment with ethanolic HCl gave the required product as its mono hydrochloride salt as an off white colored solid (MW = 305.13; HPLC single component; ¹H-NMR, 0.9 δ, t 3H; 3.9 δ, 2H, m).

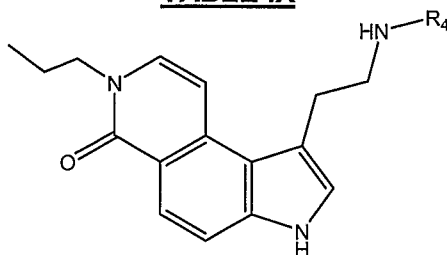
Elemental Analysis for: C₁₆H₁₉N₃O 1.0 HCl

15 Calculated: C, 62.84; H, 6.59; N, 13.74

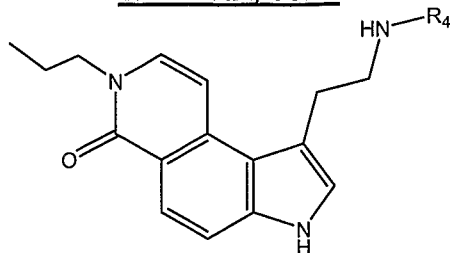
Found: C, 62.96; H, 6.66; N, 13.82

EXAMPLES 636-720

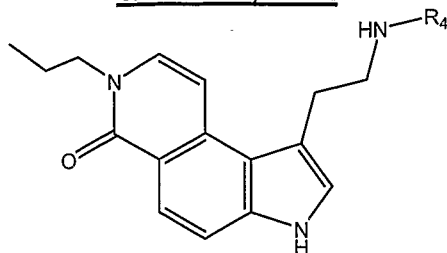
Using essentially the same procedure described in Example 7B and employing 1-(2-aminoethyl)-7-propyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one as substrate and a suitable aldehyde, the compounds shown in Table IX were obtained and identified by HPLC and mass spectral analyses.

TABLE IX

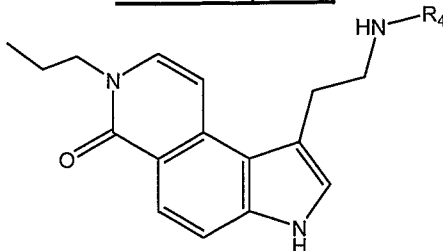
Ex. No.	R4	Mass
636	naphth-2-ylmethyl	409.53
637	4-phenoxybenzyl	451.56
638	ethyl	297.40
639	2-chlorobenzyl	393.91
640	furfur-2-ylmethyl	349.43
641	4-dimethylaminobenzyl	402.53
642	benzyl	359.47
643	thiophen-2-ylmethyl	365.49
644	4-methylbenzyl	373.49
645	4-chlorobenzyl	393.91
646	4-cyanobenzyl	384.48
647	n-pentyl	339.48
648	3,4-methylenedioxybenzyl	403.48
649	4-isopropylbenzyl	401.55
650	5-methylfurfur-2-ylmethyl	363.45
651	4-hydroxybenzyl	375.47
652	4-methoxybenzyl	389.49
653	2-methoxybenzyl	389.49
654	3-fluoro-4-methoxybenzyl	407.48

TABLE IX, cont.

Ex. No.	R4	Mass
655	3,5-bis(trifluoromethyl)benzyl	495.46
656	2,6-difluorobenzyl	395.42
657	2-fluorobenzyl	377.46
658	2-trifluoromethylbenzyl	427.46
659	3-trifluoromethylbenzyl	427.46
660	4-trifluoromethylbenzyl	427.46
661	3-fluorobenzyl	377.46
662	4-fluorobenzyl	377.46
663	indol-3-ylmethyl	398.50
664	furfur-3-ylmethyl	349.43
665	thiophen-3-ylmethyl	365.49
666	pyridin-3-ylmethyl	360.45
667	2-methylbenzyl	373.49
668	3-chlorobenzyl	393.91
669	3-methylbutyl	339.48
670	3-methoxybenzyl	389.49
671	4-trifluoromethoxybenzyl	443.46
672	pyridin-4-ylmethyl	360.45
673	2,4-dichlorobenzyl	428.36
674	pyridin-2-ylmethyl	360.45
675	6-methyl-pyridin-2-ylmethyl	374.48
676	4-bromobenzyl	438.36
677	1-methylpyrrol-2-ylmethyl	362.47
678	2,4-difluorobenzyl	395.45
679	4-carbomethoxybenzyl	417.50

TABLE IX, cont.

Ex. No.	R4	Mass
680	cyclohexylmethyl	365.51
681	4-phenylbenzyl	435.56
682	4-thiomethylbenzyl	405.56
683	4-ethylbenzyl	387.52
684	quinolin-2-ylmethyl	410.51
685	4-n-propyloxybenzyl	417.55
686	(S)-(-)-3,7-dimethyloct-6-enyl	407.59
687	3,4-dichlorobenzyl	428.36
688	2,4-dimethylbenzyl	387.52
689	1,4-benzodioxan-6-ylmethyl	417.50
690	3,5-difluorobenzyl	395.45
691	3,4-difluorobenzyl	395.45
692	2-chloro-4-hydroxybenzyl	409.91
693	2-fluoro-3-trifluoromethylbenzyl	445.45
694	3-trifluoromethoxybenzyl	443.46
695	3-bromo-4-methoxybenzyl	468.39
696	3-methylbenzyl	373.49
697	3-bromobenzyl	438.36
698	3,5-dimethoxybenzyl	419.52
699	2-chloro-4-fluorobenzyl	411.90
700	5-chloro-thiophen-2-ylmethyl	499.94
701	2-bromobenzyl	438.36
702	benzofuran-2-ylmethyl	399.49
703	5-bromo-furan-2-ylmethyl	428.32
704	4-diethylaminobenzyl	430.59

TABLE IX, cont.

Ex. No.	R4	Mass
705	6-chloro-3,4-methylenedioxybenzyl	437.92
706	3-bromo-4-fluorobenzyl	456.35
707	3-chloro-4-fluorobenzyl	411.90
708	3,5-dichlorobenzyl	428.36
709	4-n-hexyloxybenzyl	459.63
710	trans-4-stilbene-2-yl-methyl	461.60
711	(R)-(+)-3,7-dimethyloct-6-enyl	407.59
712	2-carboethoxy-cycloprop-1-ylmethyl	395.50
713	2,3-dihydrobenzo[b]furan-5-ylmethyl	401.50
714	5-bromothiophen-2-ylmethyl	444.39
715	3-(3,4-dichlorophenoxy)benzyl	520.45
716	3-nitrobenzyl	404.46
717	3,4,5-trihydroxy-n-pentyl	387.47
718	3-cyanobenzyl	384.48
719	4(5)-imidazolylmethyl	349.43
720	3-hydroxybenzyl	375.47

EXAMPLE 721**5 1-(2-aminoethyl)-7-(pyridin-4-ylmethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

A solution of 2-N-(pyridin-4-ylmethyl)-6-hydrazino-1-isoquinolinone (prepared from 4-bromomethylpyridine according to Example 92 and Example 93) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan according to the process outlined in Example 4. After refluxing for four hours, the product was

10 isolated as reported above and purified by flash silica gel chromatography (20% MeOH, 5% NH₄OH in CH₂Cl₂) to afford a light brown oil. Treatment with ethanolic

HCl gave the required product as its mono hydrochloride salt as an off white colored solid (MW = 354.83; HPLC single component; $^1\text{H-NMR}$, 5.5 δ , 2H, s).

Elemental Analysis for: $\text{C}_{19}\text{H}_{18}\text{N}_4\text{O}$ 1.0 HCl

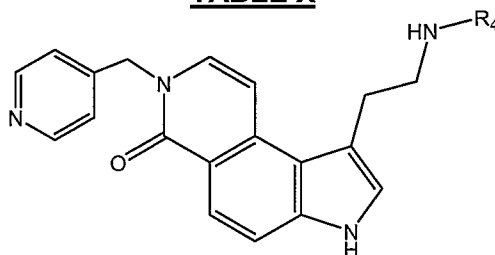
Calculated: C, 64.31; H, 5.40; N, 15.79

5 Found: C, 64.47; H, 5.47; N, 15.86

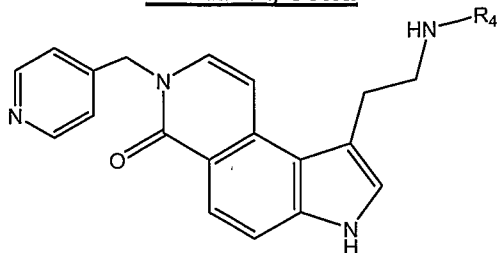
EXAMPLES 722-806

Using essentially the same procedure described in Example 7B and employing 1-(2-aminoethyl)-7-(pyridin-4-ylmethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one as substrate and a suitable aldehyde, the compounds shown in Table X were
10 obtained and identified by HPLC and mass spectral analyses.

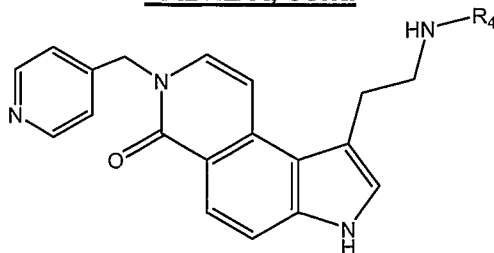
TABLE X



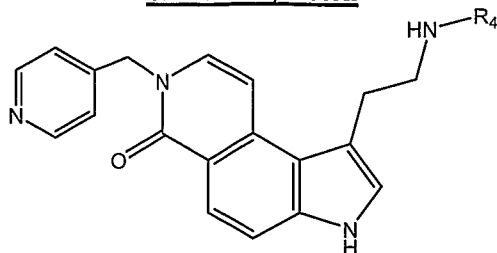
Ex. No.	R4	Mass
722	naphth-2-ylmethyl	458.56
723	4-phenoxybenzyl	500.60
724	ethyl	346.43
725	2-chlorobenzyl	442.94
726	furfur-2-ylmethyl	398.46
727	4-dimethylaminobenzyl	451.57
728	benzyl	408.50
729	thiophen-2-ylmethyl	414.53
730	4-methylbenzyl	422.52
731	4-chlorobenzyl	442.94
732	4-cyanobenzyl	433.51
733	n-pentyl	388.51
734	3,4-methylenedioxybenzyl	452.51

TABLE X, cont.

Ex. No.	R4	Mass
735	4-isopropylbenzyl	450.58
736	5-methylfurfur-2-ylmethyl	512.49
737	4-hydroxybenzyl	424.50
738	4-methoxybenzyl	438.52
739	2-methoxybenzyl	438.52
740	3-fluoro-4-methoxybenzyl	456.51
741	3,5-bis(trifluoromethyl)benzyl	544.49
742	2,6-difluorobenzyl	444.48
743	2-fluorobenzyl	426.49
744	2-trifluoromethylbenzyl	476.50
745	3-trifluoromethylbenzyl	476.50
746	4-trifluoromethylbenzyl	476.50
747	3-fluorobenzyl	426.49
748	4-fluorobenzyl	426.49
749	indol-3-ylmethyl	447.53
750	furfur-3-ylmethyl	398.46
751	thiophen-3-ylmethyl	414.53
752	pyridin-3-ylmethyl	409.49
753	2-methylbenzyl	422.52
754	3-chlorobenzyl	442.94
755	3-methylbutyl	388.51
756	3-methoxybenzyl	438.52
757	4-trifluoromethoxybenzyl	492.50
758	pyridin-4-ylmethyl	409.49
759	2,4-dichlorobenzyl	477.39

TABLE X, cont.

Ex. No.	R4	Mass
760	pyridin-2-ylmethyl	409.49
761	6-methyl-pyridin-2-ylmethyl	423.51
762	4-bromobenzyl	487.39
763	1-methylpyrrol-2-ylmethyl	411.50
764	2,4-difluorobenzyl	444.48
765	4-carbomethoxybenzyl	466.53
766	cyclohexylmethyl	414.55
767	4-phenylbenzyl	484.60
768	4-thiomethylbenzyl	454.59
769	4-ethylbenzyl	436.55
770	quinolin-2-ylmethyl	459.55
771	4-n-propyloxybenzyl	466.58
772	(S)-(-)-3,7-dimethyloct-6-enyl	456.63
773	3,4-dichlorobenzyl	477.39
774	2,4-dimethylbenzyl	436.55
775	1,4-benzodioxan-6-ylmethyl	466.53
776	3,5-difluorobenzyl	444.48
777	3,4-difluorobenzyl	444.48
778	2-chloro-4-hydroxybenzyl	458.94
779	2-fluoro-3-trifluoromethylbenzyl	494.49
780	3-trifluoromethoxybenzyl	492.50
781	3-bromo-4-methoxybenzyl	517.42
782	3-methylbenzyl	422.52
783	3-bromobenzyl	487.39
784	3,5-dimethoxybenzyl	468.55

TABLE X, cont.

Ex. No.	R4	Mass
785	2-chloro-4-fluorobenzyl	460.93
786	5-chloro-thiophen-2-ylmethyl	448.97
787	2-bromobenzyl	487.39
788	benzofuran-2-ylmethyl	448.52
789	5-bromo-furan-2-ylmethyl	477.36
790	4-diethylaminobenzyl	479.62
791	6-chloro-3,4-methylenedioxybenzyl	486.95
792	3-bromo-4-fluorobenzyl	505.38
793	3-chloro-4-fluorobenzyl	460.93
794	3,5-dichlorobenzyl	477.39
795	4-n-hexyloxybenzyl	508.66
796	trans-4-stilbene-2-yl-methyl	510.63
797	(R)-(+)-3,7-dimethyloct-6-enyl	456.63
798	2-carboethoxy-cycloprop-1-ylmethyl	444.53
799	2,3-dihydrobenzo[b]furan-5-ylmethyl	450.54
800	5-bromothiophen-2-ylmethyl	493.42
801	3-(3,4-dichlorophenoxy)benzyl	569.48
802	3-nitrobenzyl	453.50
803	3,4,5-trihydroxy-n-pentyl	436.51
804	3-cyanobenzyl	433.51
805	4(5)-imidazolylmethyl	398.46
806	3-hydroxybenzyl	424.50

EXAMPLE 807**1-(2-aminoethyl)-7-(pyridin-2-ylmethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

A solution of 2-N-(pyridin-2-ylmethyl)-6-hydrazino-1-isoquinolinone (prepared from 2-bromomethylpyridine according to Example 92 and Example 93) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan according to the process outlined in Example 4. After refluxing for four hours, the product was isolated as reported above and purified by flash silica gel chromatography (20% MeOH, 5% NH₄OH in CH₂Cl₂) to afford a light brown oil. Treatment with ethanolic HCl gave the required product as its mono hydrochloride salt as an off white colored solid (MW = 354.83; HPLC single component; ¹H-NMR, 5.5 δ, 2H, s).

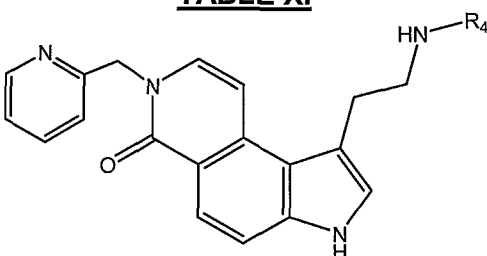
Elemental Analysis for: C₁₉H₁₈N₄O 1.0 HCl

Calculated: C, 64.31; H, 5.40; N, 15.79

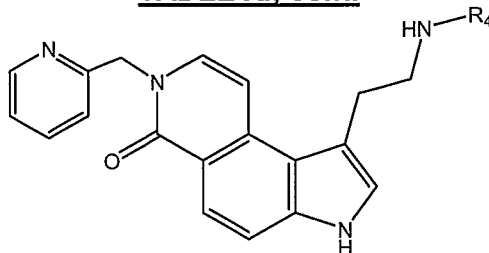
Found: C, 64.41; H, 5.44; N, 15.80

EXAMPLES 808-892

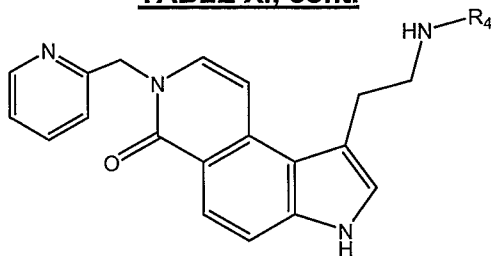
Using essentially the same procedure described in Example 7B and employing 1-(2-aminoethyl)-7-(pyridin-2-ylmethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one as substrate and a suitable aldehyde, the compounds shown in Table XI were obtained and identified by HPLC and mass spectral analyses.

TABLE XI


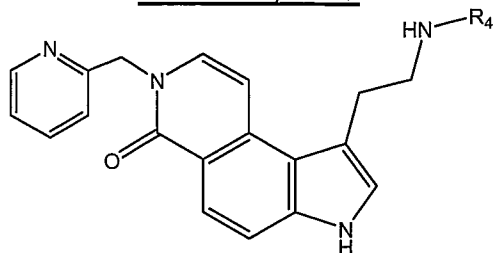
Ex. No.	R4	Mass
808	naphth-2-ylmethyl	458.56
809	4-phenoxybenzyl	500.60
810	ethyl	346.43
811	2-chlorobenzyl	442.94
812	furfur-2-ylmethyl	398.46

TABLE XI, cont.

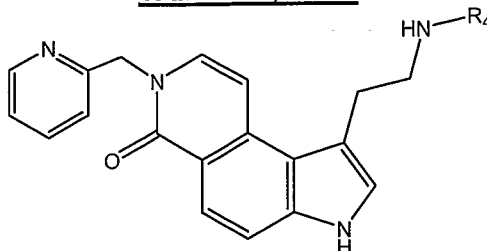
Ex. No.	R4	Mass
813	4-dimethylaminobenzyl	451.57
814	benzyl	408.50
815	thiophen-2-ylmethyl	414.53
816	4-methylbenzyl	422.52
817	4-chlorobenzyl	442.94
818	4-cyanobenzyl	433.51
819	n-pentyl	388.51
820	3,4-methylenedioxybenzyl	452.51
821	4-isopropylbenzyl	450.58
822	5-methylfurfur-2-ylmethyl	512.49
823	4-hydroxybenzyl	424.50
824	4-methoxybenzyl	438.52
825	2-methoxybenzyl	438.52
826	3-fluoro-4-methoxybenzyl	456.51
827	3,5-bis(trifluoromethyl)benzyl	544.49
828	2,6-difluorobenzyl	444.48
829	2-fluorobenzyl	426.49
830	2-trifluoromethylbenzyl	476.50
831	3-trifluoromethylbenzyl	476.50
832	4-trifluoromethylbenzyl	476.50
833	3-fluorobenzyl	426.49
834	4-fluorobenzyl	426.49
835	indol-3-ylmethyl	447.53
836	furfur-3-ylmethyl	398.46
837	thiophen-3-ylmethyl	414.53

TABLE XI, cont.

Ex. No.	R4	Mass
838	pyridin-3-ylmethyl	409.49
839	2-methylbenzyl	422.52
840	3-chlorobenzyl	442.94
841	3-methylbutyl	388.51
842	3-methoxybenzyl	438.52
843	4-trifluoromethoxybenzyl	492.50
844	pyridin-4-ylmethyl	409.49
845	2,4-dichlorobenzyl	477.39
846	pyridin-2-ylmethyl	409.49
847	6-methyl-pyridin-2-ylmethyl	423.51
848	4-bromobenzyl	487.39
849	1-methylpyrrol-2-ylmethyl	411.50
850	2,4-difluorobenzyl	444.48
851	4-carbomethoxybenzyl	466.53
852	cyclohexylmethyl	414.55
853	4-phenylbenzyl	484.60
854	4-thiomethylbenzyl	454.59
855	4-ethylbenzyl	436.55
856	quinolin-2-ylmethyl	459.55
857	4-n-propyloxybenzyl	466.58
858	(S)-(-)-3,7-dimethyloct-6-enyl	456.63
859	3,4-dichlorobenzyl	477.39
860	2,4-dimethylbenzyl	436.55
861	1,4-benzodioxan-6-ylmethyl	466.53
862	3,5-difluorobenzyl	444.48

TABLE XI, cont.

Ex. No.	R4	Mass
863	3,4-difluorobenzyl	444.48
864	2-chloro-4-hydroxybenzyl	458.94
865	2-fluoro-3-trifluoromethylbenzyl	494.49
866	3-trifluoromethoxybenzyl	492.50
867	3-bromo-4-methoxybenzyl	517.42
868	3-methylbenzyl	422.52
869	3-bromobenzyl	487.39
870	3,5-dimethoxybenzyl	468.55
871	2-chloro-4-fluorobenzyl	460.93
872	5-chloro-thiophen-2-ylmethyl	448.97
873	2-bromobenzyl	487.39
874	benzofuran-2-ylmethyl	448.52
875	5-bromo-furan-2-ylmethyl	477.36
876	4-diethylaminobenzyl	479.62
877	6-chloro-3,4-methylenedioxybenzyl	486.95
878	3-bromo-4-fluorobenzyl	505.38
879	3-chloro-4-fluorobenzyl	460.93
880	3,5-dichlorobenzyl	477.39
881	4-n-hexyloxybenzyl	508.66
882	trans-4-stilbene-2-yl-methyl	510.63
883	(R)-(+)-3,7-dimethyloct-6-enyl	456.63
884	2-carboethoxy-cycloprop-1-ylmethyl	444.53
885	2,3-dihydrobenzo[b]furan-5-ylmethyl	450.54
886	5-bromothiophen-2-ylmethyl	493.42
887	3-(3,4-dichlorophenoxy)benzyl	569.48

TABLE XI, cont.

Ex. No.	R4	Mass
888	3-nitrobenzyl	453.50
889	3,4,5-trihydroxy-n-pentyl	436.51
890	3-cyanobenzyl	433.51
891	4(5)-imidazolymethyl	398.46
892	3-hydroxybenzyl	424.50

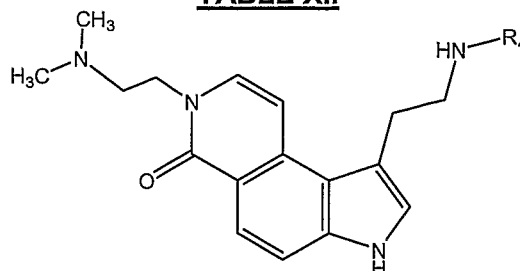
EXAMPLE 893

5 **1-(2-aminoethyl)-7-(2-dimethylaminoethyl)-3H,7H-Pyrrolo[3,2-f]isoquinolin-6-one**

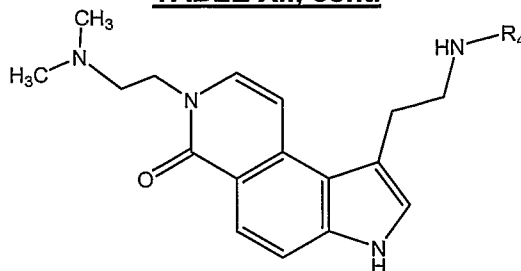
- A solution of 2-N-(2-dimethylaminoethyl)-6-hydrazino-1-isoquinolinone (prepared from 2-bromo-N,N-dimethylamine according to Example 92 and Example 93) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan
- 10 according to the process outlined in Example 4. After refluxing for four hours the product was isolated as reported above and purified by flash silica gel chromatography (20% MeOH, 5% NH₄OH in CH₂Cl₂) to afford a light brown oil. Treatment with ethanolic HCl gave the required product as an off white colored solid (MW = 370.30; HPLC single component; ¹H-NMR, 4.4 δ, 2H, t; 3.35 δ, 6H, s).
- 15 Elemental Analysis for: C₁₇H₂₂N₄O 2.0 HCl
 Calculated: C, 54.99; H, 6.52; N, 15.09
 Found: C, 55.17; H, 6.67; N, 15.16

EXAMPLES 894-978

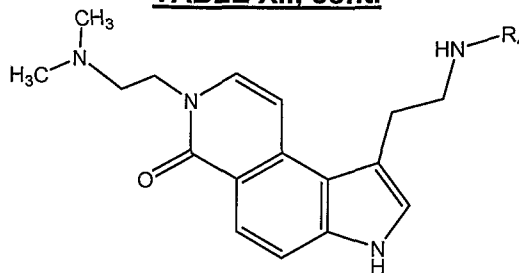
- 20 Using essentially the same procedure described in Example 7B and employing 1-(2-aminoethyl)-7-(2-dimethylaminoethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one as substrate and a suitable aldehyde, the compounds shown in Table XII were obtained and identified by HPLC and mass spectral analyses.

TABLE XII

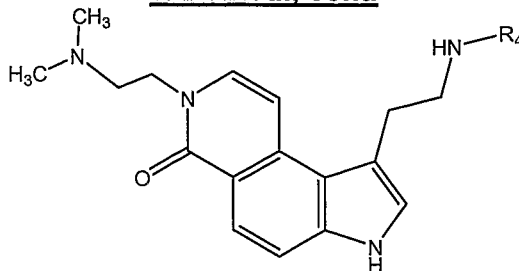
Ex. No.	R4	Mass
894	naphth-2-ylmethyl	438.57
895	4-phenoxybenzyl	480.60
896	ethyl	326.44
897	2-chlorobenzyl	422.95
898	furfur-2-ylmethyl	378.47
899	4-dimethylaminobenzyl	431.58
900	benzyl	388.51
901	thiophen-2-ylmethyl	394.54
902	4-methylbenzyl	402.53
903	4-chlorobenzyl	422.95
904	4-cyanobenzyl	413.52
905	n-pentyl	368.52
906	3,4-methylenedioxybenzyl	432.52
907	4-isopropylbenzyl	430.59
908	5-methylfurfur 2-ylmethyl	392.50
909	4-hydroxybenzyl	404.51
910	4-methoxybenzyl	418.53
911	2-methoxybenzyl	418.53
912	3-fluoro-4-methoxybenzyl	436.52
913	3,5-bis(trifluoromethyl)benzyl	524.50
914	2,6-difluorobenzyl	424.49
915	2-fluorobenzyl	406.50
916	2-trifluoromethylbenzyl	456.51
917	3-trifluoromethylbenzyl	456.51

TABLE XII, cont.

Ex. No.	R4	Mass
918	4-trifluoromethylbenzyl	456.51
919	3-fluorobenzyl	406.50
920	4-fluorobenzyl	406.50
921	indol-3-ylmethyl	527.54
922	furfur-3-ylmethyl	378.47
923	thiophen-3-ylmethyl	394.54
924	pyridin-3-ylmethyl	389.50
925	2-methylbenzyl	402.53
926	3-chlorobenzyl	422.95
927	3-methylbutyl	368.52
928	3-methoxybenzyl	418.53
929	4-trifluoromethoxybenzyl	472.51
930	pyridin-4-ylmethyl	389.50
931	2,4-dichlorobenzyl	457.40
932	pyridin-2-ylmethyl	389.50
933	6-methyl-pyridin-2-ylmethyl	403.52
934	4-bromobenzyl	467.40
935	1-methylpyrrol-2-ylmethyl	319.51
936	2,4-difluorobenzyl	424.49
937	4-carbomethoxybenzyl	446.54
938	cyclohexylmethyl	394.56
939	4-phenylbenzyl	464.61
940	4-thiomethylbenzyl	434.60
941	4-ethylbenzyl	416.56
942	quinolin-2-ylmethyl	439.56

TABLE XII, cont.

Ex. No.	R ₄	Mass
943	4-n-propyloxybenzyl	446.59
944	(S)-(-)-3,7-dimethyloct-6-enyl	436.64
945	3,4-dichlorobenzyl	457.40
946	2,4-dimethylbenzyl	416.56
947	1,4-benzodioxan-6-ylmethyl	446.54
948	3,5-difluorobenzyl	424.49
949	3,4-difluorobenzyl	424.49
950	2-chloro-4-hydroxybenzyl	438.95
951	2-fluoro-3-trifluoromethylbenzyl	474.50
952	3-trifluoromethoxybenzyl	472.51
953	3-bromo-4-methoxybenzyl	497.43
954	3-methylbenzyl	402.53
955	3-bromobenzyl	467.40
956	3,5-dimethoxybenzyl	448.56
957	2-chloro-4-fluorobenzyl	440.94
958	5-chloro-thiophen-2-ylmethyl	428.98
959	2-bromobenzyl	467.40
960	benzofuran-2-ylmethyl	528.53
961	5-bromo-furan-2-ylmethyl	457.37
962	4-diethylaminobenzyl	459.63
963	6-chloro-3,4-methylenedioxybenzyl	466.96
964	3-bromo-4-fluorobenzyl	485.39
965	3-chloro-4-fluorobenzyl	440.94
966	3,5-dichlorobenzyl	457.40

TABLE XII, cont.

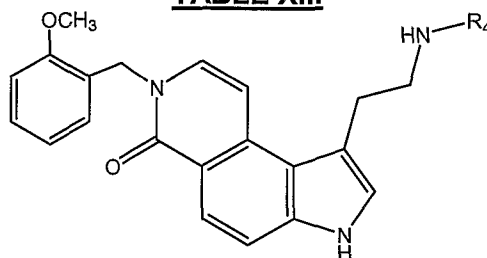
Ex. No.	R4	Mass
967	4-n-hexyloxybenzyl	488.67
968	trans-4-stilbene-2-yl-methyl	490.64
969	(R)-(+)-3,7-dimethyloct-6-enyl	436.64
970	2-carboethoxy-cycloprop-1-ylmethyl	424.54
971	2,3-dihydrobenzo[b]furan-5-ylmethyl	430.55
972	5-bromothiophen-2-ylmethyl	473.43
973	3-(3,4-dichlorophenoxy)benzyl	549.49
974	3-nitrobenzyl	433.51
975	3,4,5-trihydroxy-n-pentyl	416.52
976	3-cyanobenzyl	413.52
977	4(5)-imidazolylmethyl	378.47
978	3-hydroxybenzyl	404.51

EXAMPLE 979**5 1-(2-aminoethyl)-7-(2-methoxybenzyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

- A solution of 2-N-(2-methoxybenzyl)-6-hydrazino-1-isoquinolinone (prepared from 2-methoxybenzylchloride according to Example 92 and Example 93) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan according to the process outlined in Example 4. After refluxing for four hours, the product was
- 10 isolated as reported above and purified by flash silica gel chromatography (20% MeOH, 5% NH₄OH in CH₂Cl₂) to afford a light brown oil. Treatment with ethanolic HCl gave the required product as its mono hydrochloride salt as an off white colored solid (MW = 383.87; HPLC single component; ¹H-NMR, 3.8 δ, 3H, s; 5.2 δ, 2H, s). Elemental Analysis for: C₂₁H₂₁N₃O₂ 1.0 HCl
- 15 Calculated: C, 65.71; H, 5.78; N, 10.95
Found: C, 65.77; H, 5.87; N, 11.16

EXAMPLES 980-987

Using essentially the same procedure described in Example 7B and employing 1-(2-aminoethyl)-7-(2-methoxybenzyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one as substrate and a suitable aldehyde, the compounds shown in Table XIII were obtained and identified by HPLC and mass spectral analyses.

TABLE XIII

Ex. No.	R4	Mass
980	3-nitrobenzyl	482.53
981	3,4,5-trihydroxy-n-pentyl	465.54
982	3-chlorobenzyl	471.98
983	3-methoxybenzyl	467.56
984	pyridin-4-ylmethyl	438.52
985	3-cyanobenzyl	462.55
986	4(5)-imidazolylmethyl	427.50
987	3-hydroxybenzyl	453.54

10

EXAMPLE 988**1-(2-aminoethyl)-7-(4-methoxybenzyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

A solution of 2-N-(4-methoxybenzyl)-6-hydrazino-1-isoquinolinone (prepared from 4-methoxybenzylchloride according to Example 92 and Example 93) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan according to the process outlined in Example 4. After refluxing for four hours, the product was isolated as reported above and purified by flash silica gel chromatography (20% MeOH, 5% NH₄OH in CH₂Cl₂) to afford a light brown oil. Treatment with ethanolic HCl gave the required product as its mono hydrochloride salt as an off white colored solid (MW = 383.87; HPLC single component; ¹H-NMR, 3.7 δ, 3H, s; 5.2 δ, 2H, s).

20

Elemental Analysis for: C₂₁H₂₁N₃O 2 1.0 HCl

Calculated: C, 65.71; H, 5.78; N, 10.95

Found: C, 65.79; H, 5.86; N, 11.05

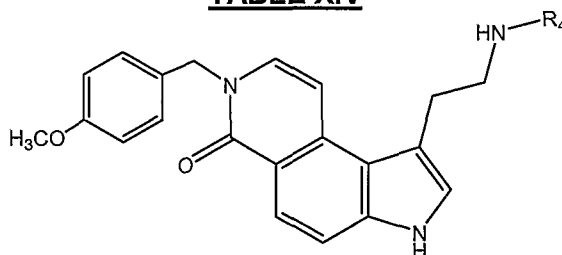
5

EXAMPLES 989-996

Using essentially the same procedure described in Example 7B and employing 1-(2-aminoethyl)-7-(4-methoxybenzyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one as substrate and a suitable aldehyde, the compounds shown in Table XIV were obtained and identified by HPLC and mass spectral analyses.

10

TABLE XIV



Ex. No.	R4	Mass
989	3-nitrobenzyl	482.53
990	3,4,5-trihydroxy-n-pentyl	465.54
991	3-chlorobenzyl	471.98
992	3-methoxybenzyl	467.56
993	pyridin-4-ylmethyl	438.52
994	3-cyanobenzyl	462.55
995	4(5)-imidazolylmethyl	427.50
996	3-hydroxybenzyl	453.54

EXAMPLE 997

15 1-(2-aminoethyl)-7-(furanyl-2-ylmethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one [furanyl-2-yl or furan-2-yl?]

A solution of 2-N-(furanyl-2-ylmethyl)-6-hydrazino-1-isoquinolinone (prepared from furfuryl bromide according to Example 92 and Example 93) was reacted in a Fisher indole reaction with 2-(3-chloropropyl)-1,3-dioxolan according to the process outlined in Example 4. After refluxing for four hours, the product was isolated as

20

reported above and purified by flash silica gel chromatography (20% MeOH, 5% NH₄OH in CH₂Cl₂) to afford a light brown oil. Treatment with ethanolic HCl gave the required product as its mono hydrochloride salt as an off white colored solid (MW = 343.81; HPLC single component; ¹H-NMR, 6.3 δ, 2H, s; 5.2 δ, 2H, s).

5 Elemental Analysis for: C₁₈H₁₈N₃O₂ 1.0 HCl

Calculated: C, 62.88; H, 5.28; N, 12.22

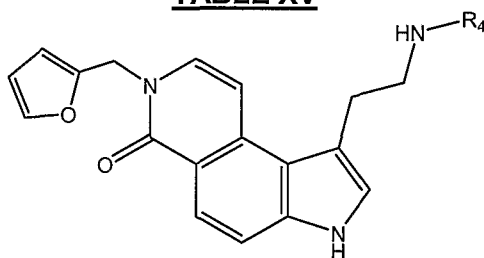
Found: C, 62.89; H, 5.36; N, 12.35

EXAMPLES 998-1005

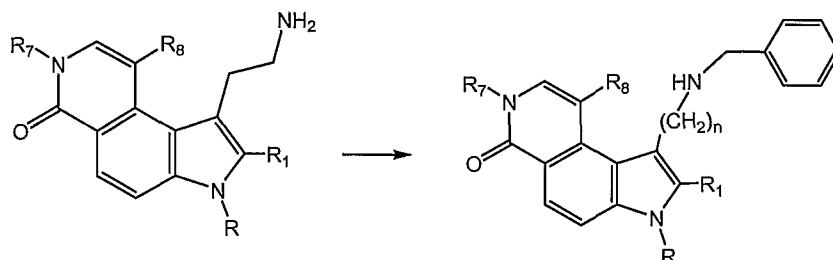
10 Using essentially the same procedure described in Example 7B and employing 1-(2-aminoethyl)-7-(furan-2-ylmethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one as substrate and a suitable aldehyde, the compounds shown in Table XV were obtained and identified by HPLC and mass spectral analyses.

15

TABLE XV



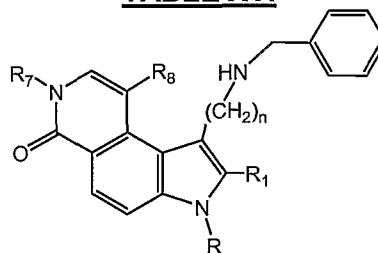
Ex. No.	R4	Mass
998	3-nitrobenzyl	442.47
999	3,4,5-trihydroxy-n-pentyl	425.48
1000	3-chlorobenzyl	431.92
1001	3-methoxybenzyl	427.50
1002	pyridin-4-ylmethyl	398.46
1003	3-cyanobenzyl	422.48
1004	4(5)-imidazolylmethyl	387.44
1005	3-hydroxybenzyl	413.47

EXAMPLES 1006-1017**1-(2-benzylaminoethyl)-substituted-pyrrolo[3,2-f]isoquinolin-6-one Compounds**

5

Using the essentially the same procedure described in Example 7B and employing the appropriate 1-(2-aminoethyl)-pyrrolo[3,2-f]isoquinolin-6-one substrate and benzaldehyde, the compounds shown in Table XVI were prepared and identified by HPLC and mass spectral analyses.

10

TABLE XVI

Ex. No.	n	R	R1	R7	R8	Mass
1006	2	H	Br	H	H	432.74
1007	2	CH ₃	H	benzyl	H	457.99
1008	2	H	H	phenethyl	H	457.99
1009	2	H	H	naphth-2-ylmethyl	H	508.05
1010	2	H	H	heptyl	H	452.03
1011	2	H	H	3,4-dichlorobenzyl	H	512.86
1012	2	H	H	thiophen-3-yl	H	450.00
1013	3	H	H	H	H	367.87
1014	2	H	4-Cl-C ₆ H ₅	H	H	478.41
1015	2	H	H	H	Cl	388.29
1016	2	H	H	tetrahydropyran-2-ylmethyl	H	451.99
1017	2	H	H	2-methoxyethyl	H	411.92

EXAMPLE 1018**3,7-dibenzyl-1-(2-dibenzylaminoethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

5 Tetrabutylammonium bromide (0.03 g) and benzyl bromide (0.3 g, 1.6 mmol) were added to a solution of the amine from Example 4 (0.1 g, 0.44 mmol) in toluene (2 mL) and 50% aqueous sodium hydroxide (1.8 mmol, 4 equivalents). The mixture was stirred for three hours at room temperature, and the product was purified by flash silica gel chromatography (1% methanolic ammonia in CH₂Cl₂) to afford a brown colored solid. Treatment with ethanolic HCl afforded the salt of the titled compound as an off white colored solid (mp 234-236°C; MW = 624.21; HPLC single component).

Elemental Analysis for: C₄₁H₃₇N₃O 1.0 HCl

Calculated: C, 78.89; H, 6.14; N, 6.73

Found: C, 78.91; H, 6.23; N, 6.84

EXAMPLE 1019**1-(2-dibenzylaminoethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

Benzyl bromide (0.226 g, 1.32 mmol) was added to a solution of the amine from Example 4 (0.2 g, 0.88 mmol) in DMF (2 mL) and 50% aqueous sodium hydroxide (1.75 mmol, 2 equivalents). The mixture was stirred for two hours at room temperature, and the product was purified by flash silica gel chromatography (4% methanolic ammonia in CH₂Cl₂). Treatment with ethanolic HCl afforded the salt of the titled compound as a white solid (mp 250-253°C; MW = 624.21; HPLC single component).

25 Elemental Analysis for: C₂₇H₂₅N₃O 1.0 HCl

Calculated: C, 73.04; H, 5.90; N, 9.46

Found: C, 73.20; H, 5.99; N, 9.56

EXAMPLE 1020**1-[2-(benzyl-methylamino)ethyl]-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one**

30 A solution of 6-hydrazino-1-isoquinolinone (0.4 g, 1.89 mmol) from Example 3 and 2-(3-(N-methyl-benzylamine)propyl)-1,3-dioxolan (0.668 g, 2.84 mmol) in degassed ethanol (120 ml)/4% aqueous sulfuric acid (12 ml) was refluxed under nitrogen for six hours. The reaction mixture was concentrated in vacuo and the product purified by flash silica gel chromatography to afford an orange colored solid

(0.155 g, 25% yield). Treatment of the product with ethereal [v. ethanolic?] HCl and crystallization from ethanol ether gave the mono hydrochloride salt as a light amber colored solid (mp = 152-155°C; MW = 367.87; HPLC single component).

Elemental Analysis for: C₂₁H₂₁N₃O 1.0 HCl

5 Calculated: C, 68.56; H, 6.03; N, 11.42

Found: C, 88.62; H, 6.12; N, 11.54

EXAMPLE 1021

1-(2-methylaminoethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one

10 1-[2-(Benzylmethylamino)ethyl]-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one (1.07 g, 3.22 mmol) from Example 1020 was hydrogenated over 10% Pd/C at 50 psi H₂ for 24 hours. The catalyst was removed by filtration, and the product was converted to its HCl salt by the action of ethanolic HCl. Recrystallization from EtOH/Et₂O afforded the titled compound as a light brown colored solid (mp = 160°C; MW = 377.75; HPLC
15 single component).

Elemental Analysis for: C₁₄H₁₅N₃O 1.0 HCl

Calculated: C, 60.54; H, 5.81; N, 15.13

Found: C, 60.64; H, 5.98; N, 15.24

20

EXAMPLE 1022

N-[2-(7-benzyl-6-oxo-6,7-dihydro-3H-pyrrolo[3,2-f]isoquinolin-1-yl)-ethyl]-benzenesulfonamide

A solution of 1-(2-aminoethyl)-7-benzyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one (0.25 g, 0.788 mmol) from Example 182 in DMF (4 mL) was treated with sodium
25 hydride (1.2 equivalents) at 0°C followed after 15 minutes with the addition of benzene sulfonylchloride (0.18 g, 1.02 mmol, 1.3 equivalents). The mixture was stirred for 16 hours and the titled compound isolated as a white solid (m.p. 205-206°C; MW = 457.55; HPLC single component) by flash silica gel chromatography (5% MeOH in CH₂Cl₂).

30 Elemental Analysis for: C₂₆H₂₃N₃O₃S

Calculated: C, 68.25; H, 5.07; N, 9.18

Found: C, 68.33; H, 5.18; N, 9.27

EXAMPLE 1023

35

7-fluoro-3H-quinazolin-4-one

A solution of 2-amino-4-fluorobenzoic acid (8.8 g, 56.7 mmol) and formamidine acetate (23.63 g, 227 mmol, 4 equivalents) in ethoxyethanol (400 ml) was refluxed for 16 hours. The solvent was removed in vacuo and the residue crystallized from methanol-water to provide the titled compound as a light brown solid (8.35 g, 90% yield, M+1 = 165).
Elemental Analysis for: C₈H₅FN₂O
Calculated: C, 58.54; H, 3.07; N, 17.07
Found: C, 58.60; H, 3.19; N, 17.27

10

EXAMPLE 1024**7-fluoro-3-methyl-3H-quinazolin-4-one**

Sodium hydride (19.0 mmol, 1.2 eq) was added to a solution of 7-fluoro-3H-quinazolin-4-one (2.6 g, 15.8 mmol, Example 1023) in DMF (30 ml) under an atmosphere of nitrogen at -20°C. After stirring for one hour, methyl iodide (19.8 mmol, 1.25 equivalents) was added, and the resulting solution was stirred at room temperature for two hours. Water (100 ml) was added and the product extracted into CH₂Cl₂ (3 x 100 ml). The organics were concentrated in vacuo and the product crystallized from hexane/CH₂Cl₂ to afford the titled compound as a light amber colored solid (m.p. 133-135°C, M+1 = 179).
Elemental Analysis for: C₉H₇FN₂O
Calculated: C, 60.67; H, 3.96; N, 15.72
Found: C, 60.72; H, 3.99; N, 15.79

20

EXAMPLE 1025**7-hydrazino-3-methyl-3H-quinazolin-4-one**

A solution containing 7-fluoro-3-methyl-3H-quinazolin-4-one (2.2 g, 12.3 mmol, Example 1026) and hydrazine (7.88 g, 20 equivalents) in dioxane (50 ml) was refluxed for 16 hours under an atmosphere of nitrogen. The mixture was concentrated in vacuo, triturated with dioxane and the resulting solid washed with water (50 ml) and dried under vacuum to provide the titled compound as a white solid (1.63 g, 70% yield, m.p. 208-211°C, M+1 = 191).
Elemental Analysis for: C₉H₁₀N₄O
Calculated: C, 56.83; H, 5.30; N, 29.46
Found: C, 56.98; H, 5.39; N, 29.59

35

EXAMPLE 1026**3-benzyl-7-fluoro-3H-quinazolin-4-one**

Sodium hydride (22.0 mmol, 1.2 equivalents) was added to a solution of 7-fluoro-3H-quinazolin-4-one (3.0 g, 18.3 mmol, Example 1023) in DMF (40 ml) under an atmosphere of nitrogen at -20°C. After stirring for one hour, benzyl bromide (3.7 g, 22 mmol, 1.2 equivalents) was added, and the resulting solution was stirred at room temperature for two hours. Water (100 ml) was added and the product extracted into CH₂Cl₂ (3 x 100 ml). The organics were concentrated in vacuo and the product crystallized from hexane/CH₂Cl₂ to afford the titled compound as a light brown/beige colored solid (m.p. 110-111°C, M+1 = 255).

Elemental Analysis for: C₉H₇FN₂O

Calculated: C, 70.86; H, 4.36; N, 11.02

Found: C, 70.94; H, 4.39; N, 11.19

EXAMPLE 1027**3-benzyl-7-hydrazino-3H-quinazolin-4-one**

A solution containing 3-benzyl-7-fluoro-3H-quinazolin-4-one (3.0 g, 11.8 mmol) and hydrazine (7.56 g, 20 equivalents) in dioxane (60 ml) was refluxed for 16 hours under an atmosphere of nitrogen. The mixture was concentrated in vacuo, and the resulting solid crystallized from methanol/water to provide the titled compound as a cream colored solid (2.4 g, 76% yield, m.p. 165-169°C, M+1 = 267).

Elemental Analysis for: C₁₅H₁₄N₄O

Calculated: C, 67.65; H, 5.30; N, 21.04

Found: C, 67.78; H, 5.41; N, 21.19

EXAMPLE 1028**9-(2-aminoethyl)-3-methyl-3H,7H-pyrrolo[2,3-h]quinazolin-4-one**

A solution of 7-hydrazino-3-methyl-3H-quinazolin-4-one (1.48 g, 7.78 mmol), sulfuric acid (1N, 16 ml) and 2-(3-chloropropyl)-1,3-dioxolan (1.41 g, 9.34 mmol) in degassed ethanol (50 ml)/water (50 ml) was refluxed under nitrogen for three hours. The reaction mixture was concentrated in vacuo and the product purified by flash silica gel chromatography, eluting with Et₃N (2%): MeOH (20%): CH₂Cl₂ (78%), affording an amber colored solid (1.245 g). The product was crystallized from

ethanol to afford the titled compound as a light amber colored solid (m.p. 279-285°C, M+1 = 243).

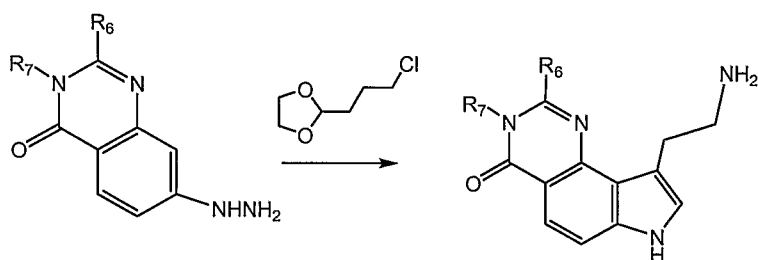
Elemental Analysis for: C₁₃H₁₄N₄O

Calculated: C, 64.45; H, 5.82; N, 23.12

5 Found: C, 64.58; H, 5.89; N, 23.19

EXAMPLES 1029-1032

9-(2-Aminoethyl)-substituted-pyrrolo[2,3-h]quinazolin-4-one Compounds

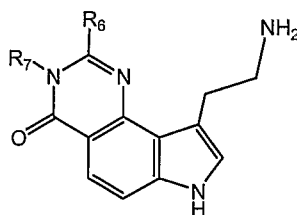


10

Using the essentially the same procedure described in Example 1028 and employing the appropriate 7-hydrazino-3H-quinazolin-4-one substrate and 2-(3-chloropropyl)-1,3-dioxolane, the compounds shown in Table XVII were prepared and identified by HPLC and mass spectral analyses.

15

TABLE XVII



Ex. No.	R6	R7	mp °C	[M+H]
1029	H	benzyl	302-305	319
1030	CH ₃	CH ₃	--	--
1031	3-pyridinyl	H	--	--
1032	H	H	--	--

20

EXAMPLE 1033**Comparative Evaluation of 5-HT₆ Binding Affinity of Test Compounds**

The affinity of test compounds for the 5-HT₆ receptor is evaluated in the following manner. Cultured Hela cells expressing human cloned 5-HT₆ receptors are harvested and centrifuged at low speed (1,000 x g) for 10.0 min to remove the culture media. The harvested cells are suspended in half volume of fresh physiological phosphate buffered saline (PBS) solution and recentrifuged at the same speed. This operation is repeated. The collected cells are then homogenized in ten volumes of 50 mM Tris.HCl (pH 7.4) and 0.5 mM EDTA. The homogenate is centrifuged at 40,000 x g for 30.0 min, and the precipitate is collected. The obtained pellet is resuspended in 10 volumes of Tris.HCl buffer and recentrifuged at the same speed. The final pellet is suspended in a small volume of Tris.HCl buffer, and the tissue protein content is determined in aliquots of 10-25 microliter volumes. Bovine Serum Albumin is used as the standard in the protein determination according to the method described in Lowry et al., *J. Biol. Chem.* **1951**, 193, 265. The volume of the suspended cell membranes is adjusted to give a tissue protein concentration of 1.0 mg/ml of suspension. The prepared membrane suspension (10 times concentrated) is aliquoted in 1.0 ml volumes and stored at -70°C until used in subsequent binding experiments.

Binding experiments are performed in a 96-well microtiter plate format, in a total volume of 200 microliters. To each well is added the following mixture: 80.0 microliter of incubation buffer made in 50 mM Tris.HCl buffer (pH 7.4) containing 10.0 mM MgCl₂ and 0.5 mM EDTA and 20 microliters of [³H]-LSD (S.A., 86.0 Ci/mmol, available from Amersham Life Science), 3.0 nM. The dissociation constant, K_D of the [³H]-LSD at the human 5-HT₆ receptor is 2.9 nM, as determined by saturation binding with increasing concentrations of [³H]-LSD. The reaction is initiated by the final addition of 100.0 microliters of tissue suspension. Nonspecific binding is measured in the presence of 10.0 micromoles methiothepin. The test compounds are added in 20.0 microliter volume.

The reaction is allowed to proceed in the dark for 120 min at room temperature, at which time, the bound ligand-receptor complex is filtered off on a 96-well unfilter with a Packard Filtermate® 196 Harvester. The bound complex caught on the filter disk is allowed to air dry, and the radioactivity is measured in a Packard TopCount® equipped with six photomultiplier detectors, after the addition of 40.0

microliters Microscint®-20 scintillant to each shallow well. The unifilter plate is heat-sealed and counted in a Packard TopCount® with a tritium efficiency of 31%.

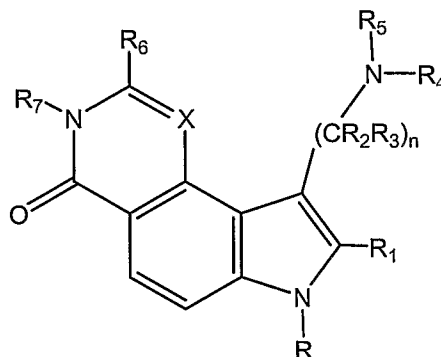
- Specific binding to the 5-HT₆ receptor is defined as the total radioactivity bound less the amount bound in the presence of 10.0 microliter unlabelled methiothepin. Binding in the presence of varying concentrations of test compound is expressed as a percentage of specific binding in the absence of test compound. The results are plotted as log % bound versus log concentration of the test compound. Nonlinear regression analysis of data points with a computer assisted program Prism® yielded both the IC₅₀ and the K_i values of the test compounds with 95% confidence limits. A linear regression is plotted, from which the IC₅₀ value is determined, and the K_i value is determined based upon the following equation:
- $$K_i = IC_{50} / (1 + L/K_D)$$
- where L is the concentration of the radioactive ligand used and K_D is the dissociation constant of the ligand for the receptor, both expressed in nM.
- Using this assay, the K_i values were determined and are shown in Table XVIII below.

TABLE XVIII

Test Compound (Ex. No.)	5-HT ₆ binding K _i (nM)
7	15
94	18
182	11
269	13
274	11
1021	21
1029	32.0
Comparative Examples	5-HT₆ Binding K_i (nM)
loxapine	41.4
bromocriptine	23.0
methiothepin	8.3
mianserin	44.2
olanzepine	19.5

WHAT IS CLAIMED IS:

1. A compound of formula I



(I)

5

wherein

X is N or CR₈;

n is an integer 1, 2, 3, 4, 5 or 6;

R is H, SO₂R₉ or an alkyl, cycloalkyl, alkenyl or alkynyl group each optionally substituted;

10

R₁ is H, halogen or an alkyl, aryl or heteroaryl group each optionally substituted;R₂ and R₃ are each independently H or an optionally substituted alkyl group;R₄ and R₅ are each independently H or an alkyl, alkenyl, cycloalkyl, cycloheteroalkyl, aryl or heteroaryl group each optionally substituted, or R₄ and R₅ may be taken together with the atom to which they are attached to form an optionally substituted 5- to 8-membered ring optionally containing an additional heteroatom selected from O, S or NR₇;

15

R₆ and R₈ are each independently H, halogen or an alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, cycloheteroalkyl, aryl or heteroaryl group each optionally substituted;

20

R₇ is H or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloheteroalkyl, aryl, or heteroaryl group each optionally substituted; and

25

R₉ is an alkyl, aryl or heteroaryl group each optionally substituted; or a stereoisomer thereof or a pharmaceutically acceptable salt thereof.

2. The compound according to claim 1 wherein n is 2.
3. The compound according to claim 1 or claim 2 wherein R is H.
- 5 4. The compound according to any one of claims 1 to 3 wherein R₇ is
Hor an optionally substituted alkyl group.
- 10 5. The compound according to claim 4 in which the alkyl group is
optionally substituted by phenyl, thienyl, furanyl or cycloalkyl.
6. The compound according to any one of claims 1 to 5 wherein X is N or
CH.
- 15 7. The compound according to any one of claims 1 to 6 wherein R₁ is H
or bromo.
8. The compound according to any one of claims 1 to 7 wherein R₂ and
R₃ are H.
- 20 9. The compound according to any one of claims 1 to 8 wherein R₆ is H,
alkyl or heteroaryl.
- 25 10. The compound according to claims 1 to 9 wherein R₆ is H, methyl or
pyridyl.
11. The compound according to any one of claims 1 to 10 wherein R₄ is H,
alkyl or benzyl.
- 30 12. The compound according to any one of claims 1 to 11 wherein R₅ is H.
13. The compound according to claim 1 selected from the group
consisting essentially of:
1-(2-benzylaminoethyl)-3H,7H -pyrrolo[3,2-f]isoquinolin-6-one;
35 1-(2-aminoethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one;

- 1-(2-aminoethyl)-2-bromo-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one;
 1-(2-aminoethyl)-7-methyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one;
 1-(2-aminoethyl)-7-benzyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one;
 1-(2-aminoethyl)-7-cyclohexylmethyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one;
 5 1-(2-aminoethyl)-7-thien-3-ylmethyl-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one;
 1-(2-aminoethyl)-7-(furan-2-ylmethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one;
 1-(2-methylaminoethyl)-3H,7H-pyrrolo[3,2-f]isoquinolin-6-one;
 9-(2-aminoethyl)-3-benzyl-3H,7H-pyrrolo[2,3-h]quinazolin-4-one;
 9-(2-aminoethyl)-3-methyl-3H,7H-pyrrolo[2,3-h]quinazolin-4-one;
 10 9-(2-aminoethyl)-3-benzyl-3H,7H-pyrrolo[2,3-h]quinazolin-4-one;
 9-(2-aminoethyl)-3H,7H-pyrrolo[2,3-h]quinazolin-4-one;
 9-(2-aminoethyl)-2-(3-pyridinyl)-3H,7H-pyrrolo[2,3-h]quinazolin-4-one;
 9-(2-aminoethyl)-2,3-dimethyl-3H,7H-pyrrolo[2,3-h]quinazolin-4-one;
 a stereoisomer thereof; and
 15 a pharmaceutically acceptable salt thereof.

14. A method for the treatment of a central nervous system disorder related to or affected by the 5-HT₆ receptor in a patient in need thereof which comprises providing to said patient a therapeutically effective amount of a compound
 20 of formula I or a pharmaceutically acceptable salt thereof as claimed in any one of claims 1 to 13.

15. The method according to claim 14 wherein said disorder is an anxiety disorder or a cognitive disorder.

25 16. The method according to claim 14 wherein said disorder is a neurodegenerative disorder.

17. The method according to claim 14 wherein said disorder is selected from the group consisting essentially of: schizophrenia; attention deficit disorder;
 30 obsessive compulsive disorder; withdrawal from drug, alcohol or nicotine addiction; depression; and Alzheimer's disease.

18. The method according to claim 16 wherein said disorder is stroke, head trauma or neuropathic pain.

19. A pharmaceutical composition which comprises a pharmaceutically acceptable carrier and a compound of formula I or a pharmaceutically acceptable salt thereof as claimed in any one of claims 1 to 13.

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