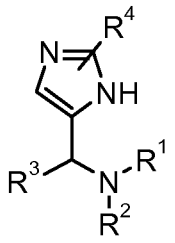
AMINOMETHYL-4-IMIDAZOLES

The present invention relates to compounds of formula I



I

wherein

R^1 is hydrogen, lower alkyl, -$(CR_2)_n$-OH, -$(CH_2)_n$-aryl or -$(CH_2)_n$-heteroaryl, which are optionally substituted by halogen, lower alkoxy or lower alkyl substituted by halogen, or is -$(CR_2)_n$- cycloalkyl, optionally substituted by hydroxy, -$(CH_2)_n$-heterocyclyl, -$(CH_2)_n$-NH-$S(O)_2CH_3$, or is -$(CR_2)_n$O-lower alkyl or lower alkyl substituted by halogen;

R is hydrogen or lower alkyl, and when two R-groups are present, they may or may not be the same;

R^2 is 2,2-dioxo-2,3-dihydro-1*H*-benzo[c]thiophenyl, 6,7-dihydro-5*H*-cyclopentapyrimidin-2-yl, 2,2-difluoro-benzo[1,3]dioxol-5-yl, 2,2,3,3-tetrafluoro-2,3-dihydro-benzo[1,4]dioxin-6-yl, or is aryl or heteroaryl, optionally substituted by one or more substituents, selected from the group consisting of halogen, lower alkyl, cycloalkyl, -$(CH_2)_n$-hydroxy, lower alkyl substituted by halogen, lower alkoxy substituted by halogen, -$S(O)_2$-lower alkyl, -$(CH_2)_n$-$S(O)_2$-NH-lower alkyl, -$(CH_2)_n$-O-lower alkyl, nitro, amino, cyano, -NHC(O)-lower alkyl, -C(O)NH-lower alkyl, or O-tetrahydro-naphthalenyl, or are substituted by -$(CH_2)_n$-aryl, optionally substituted by halogen, or by

-CH=CH-aryl, optionally substituted by halogen, or by
-$(CH_2)_n$-O-aryl, optionally substituted by halogen, lower alkoxy or lower alkyl substituted by halogen, or by
-O-$(CH_2)_n$-aryl, optionally substituted by halogen, or by
-$(CH_2)_n$-heteroaryl, or by
-$(CH_2)_n$-O-heteroaryl or by
-$(CH_2)_n$-heterocyclyl, optionally substituted by =O, or by
-$(CH_2)_n$-O-heterocyclyl, optionally substituted by lower alkyl, or by
-S-aryl,
-CH(OH)-aryl,
-$C(CH_3)_2$-aryl,
-NR-aryl, or by
2-oxo-2H-pyridin-1-yl;

R^3 is hydrogen or lower alkyl;

R^4 is hydrogen or lower alkyl;

n is 0, 1, 2, 3 or 4

and to their pharmaceutically active salts, with the exception of 4-phenylaminomethyl-imidazol (CAS 32563-81-8), benzyl-(*3H*-imidazol-4-ylmethyl)-phenyl-amine (Beilstein BRN 20612), (1H-imidazol-4-ylmethyl)-(4-methoxy-phenyl)-amine (CAS 17049-89-7), (3,4-dichloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine (CAS 87471-76-9), (4-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine (CAS 17049-90-0), (4-bromo-phenyl)-(1H-imidazol-4-ylmethyl)-amine (CAS 87471-95-2), (3,5-dichloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine (CAS 87471-74-7) and (3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine (CAS 87471-78-1).

The excluded compounds of formula I are known compounds, described for example in the below mentioned references or are enclosed in public libraries.

Furthermore, the invention includes all racemic mixtures, all their corresponding enantiomers and/or optical isomers.

In addition, all tautomeric forms of compounds of formula I are also encompassed by the present invention.

It has been found that the compounds of formula I have a good affinity to the trace amine associated receptors (TAARs), especially for TAAR1.
The compounds may be used for the treatment of depression, anxiety disorders, bipolar disorder, attention deficit hyperactivity disorder (ADHD), stress-related disorders, psychotic disorders such as schizophrenia, neurological diseases such as Parkinson's disease, neurodegenerative disorders such as Alzheimer's disease, epilepsy, migraine, hypertension, substance abuse and metabolic disorders such as eating disorders, diabetes, diabetic complications, obesity, dyslipidemia, disorders of energy consumption and assimilation, disorders and malfunction of body temperature homeostasis, disorders of sleep and circadian rhythm, and cardiovascular disorders.

The classical biogenic amines (serotonin, norepinephrine, epinephrine, dopamine, histamine) play important roles as neurotransmitters in the central and peripheral nervous system [1]. Their synthesis and storage, as well as their degradation and reuptake after release are tightly regulated. An imbalance in the levels of biogenic amines is known to be responsible for the altered brain function under many pathological conditions [2-5]. A second class of endogenous amine compounds, the so-called trace amines (TAs) significantly overlap with the classical biogenic amines regarding structure, metabolism and subcellular localization. The TAs include p-tyramine, β-phenylethylamine, tryptamine and octopamine, and they are present in the mammalian nervous system at generally lower levels than classical biogenic amines [6].

Their dysregulation has been linked to various psychiatric diseases like schizophrenia and depression [7] and for other conditions like attention deficit hyperactivity disorder, migraine headache, Parkinson's disease, substance abuse and eating disorders [8,9].

For a long time, TA-specific receptors had only been hypothesized based on anatomically discrete high-affinity TA binding sites in the CNS of humans and other mammals [10,11]. Accordingly, the pharmacological effects of TAs were believed to be mediated through the well known machinery of classical biogenic amines, by either triggering their release, inhibiting their reuptake or by "crossreacting" with their receptor systems [9,12,13]. This view changed significantly with the recent identification of several members of a novel family of GPCRs, the trace amine associated receptors (TAARs) [7,14]. There are 9 TAAR genes in human (including 3 pseudogenes) and 16 genes in mouse (including 1 pseudogene). The TAAR genes do not contain introns (with one

exception, TAAR2 contains 1 intron) and are located next to each other on the same chromosomal segment. The phylogenetic relationship of the receptor genes, in agreement with an in-depth GPCR pharmacophore similarity comparison and pharmacological data suggest that these receptors form three distinct subfamilies [7,14]. TAAR1 is in the first subclass of four genes (TAAR1-4) highly conserved between human and rodents. TAs activate TAAR1 via Gαs. Dysregulation of TAs was shown to contribute to the aetiology of various diseases like depression, psychosis, attention deficit hyperactivity disorder, substance abuse, Parkinson's disease, migraine headache, eating disorders, metabolic disorders and therefore TAAR1 ligands have a high potential for the treatment of these diseases.

Therefore, there is a broad interest to increase the knowledge about trace amine associated receptors.

References used:

1 Deutch, A.Y. and Roth, R.H. (1999) Neurotransmitters. In *Fundamental Neuroscience* (2nd edn) (Zigmond, M.J., Bloom, F.E., Landis, S.C., Roberts, J.L, and Squire, L.R., eds.), pp. 193-234, Academic Press;

2 Wong, M.L. and Licinio, J. (2001) Research and treatment approaches to depression. *Nat. Rev. Neurosci.* 2, 343-351;

3 Carlsson, A. *et al.* (2001) Interactions between monoamines, glutamate, and GABA in schizophrenia: new evidence. *Annu. Rev. Pharmacol. Toxicol.* 41, 237-260;

4 Tuite, P. and Riss, J. (2003) Recent developments in the pharmacological treatment of Parkinson's disease. *Expert Opin. Investig. Drugs* 12, 1335-1352,

5 Castellanos, F.X. and Tannock, R. (2002) Neuroscience of attention-deficit/hyperactivity disorder: the search for endophenotypes. *Nat. Rev. Neurosci.* 3, 617-628;

6 Usdin, Earl; Sandler, Merton; Editors. *Psychopharmacology Series, Vol. 1: Trace Amines and the Brain.* [*Proceedings of a Study Group at the 14th Annual Meeting of the American College of Neuropsychoparmacology*, San Juan, Puerto Rico] (1976);

7 Lindemann, L. and Hoener, M. (2005) A renaissance in trace amines inspired by a novel GPCR family. *Trends in Pharmacol. Sci.* 26, 274-281;

8 Branchek, T.A. and Blackburn, T.P. (2003) Trace amine receptors as targets for novel therapeutics: legend, myth and fact. *Curr. Opin. Pharmacol.* 3, 90-97;

9 Premont, R.T. *et al.* (2001) Following the trace of elusive amines. *Proc. Natl. Acad. Sci. U. S. A.* 98, 9474-9475;

10 Mousseau, D.D. and Butterworth, R.F. (1995) A high-affinity [3H] tryptamine binding site in human brain. *Prog. Brain Res.* 106, 285-291;

11 McCormack, J.K. *et al.* (1986) Autoradiographic localization of tryptamine binding sites in the rat and dog central nervous system. *J. Neurosci.* 6, 94-101;

12 Dyck, L.E. (1989) Release of some endogenous trace amines from rat striatal slices in the presence and absence of a monoamine oxidase inhibitor. *Life Sci.* 44, 1149-1156;

13 Parker, E.M. and Cubeddu, L.X. (1988) Comparative effects of amphetamine, phenylethylamine and related drugs on dopamine efflux, dopamine uptake and mazindol binding. *J. Pharmacol. Exp. Ther.* 245, 199-210;

14 Lindemann, L. *et al.* (2005) Trace amine associated receptors form structurally and functionally distinct subfamilies of novel G protein-coupled receptors. *Genomics* 85, 372-385.

Objects of the present invention are novel compounds of formula I, their manufacture, medicaments based on a compound in accordance with the invention and their production as well as the use of compounds of formula I in the control or prevention of illnesses such as depression, anxiety disorders, bipolar disorder, attention deficit hyperactivity disorder, stress-related disorders, psychotic disorders such as schizophrenia, neurological diseases such as Parkinson's disease, neurodegenerative disorders such as Alzheimer's disease, epilepsy, migraine, hypertension, substance abuse and metabolic disorders such as eating disorders, diabetes, diabetic complications, obesity, dyslipidemia, disorders of energy consumption and assimilation, disorders and malfunction of body temperature homeostasis, disorders of sleep and circadian rhythm, and cardiovascular disorders.

The preferred indications using the compounds of the present invention are depression, psychosis, Parkinson's disease, anxiety and attention deficit hyperactivity disorder (ADHD).

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

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

As used herein, the term "cycloalkyl" denotes a saturated carbon ring containing 3 to 7 carbon atoms, for example cyclopropyl, cyclohexyl and the like.

As used herein, the term "lower alkyl substituted by halogen" denotes a saturated straight- or branched-chain group containing from 1 to 7 carbon atoms wherein one or more hydrogen atoms are replaced by a halogen atom, for example CH_2F, CF_3, CH_2CF_3, CF_2CHF_2, CF_2CF_3, $CH_2CH_2CF_3$, $CH_2CF_2CF_3$ and the like.

As used herein, the term "lower alkoxy substituted by halogen" denotes a lower alkoxy group as defined above wherein one or more hydrogen atoms are replaced by a halogen atom, for example OCH_2F, OCF_3, OCF_2CF_3, $OCH_2CH_2CF_3$, $OCH_2CF_2CF_3$ OCH_2CF_3, OCF_2CHF_2 and the like.

As used herein, the term "aryl" denotes a carbon ring or ring system, wherein at least one ring is aromatic in nature, for example phenyl, naphthyl, or indanyl.

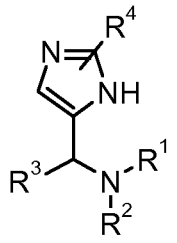
As used herein, the term heteroaryl is an aromatic ring or a ring system, wherein at least one ring is aromatic in nature and containing at least one O, N or S ring atom, selected from the group consisting of quinolinyl, pyrazinyl, thiophenyl, pyrrolyl, imidazolyl, thiazolyl, pyrazolyl, pyridinyl, pyrimidinyl, benzofuranyl, benzo[1.3]dioxolyl or indolyl.

As used herein, the term heterocyclyl is a non-aromatic group, containing at least one O, N or S ring atom, selected from the group consisting of morpholinyl, pyrrolidinyl, [1.3]dioxalanyl, tetrahydrofuranyl, tetrahydropyranyl, piperidinyl, or oxetanyl.

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

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

One embodiment of the present invention are compounds of formula



I A

wherein

R^1 is hydrogen, lower alkyl, -$(CH_2)_n$-aryl, optionally substituted by halogen, lower alkoxy or lower alkyl substituted by halogen, or is -$(CR_2)_n$- cycloalkyl, optionally substituted by hydroxy, or is -$(CR_2)_n$-OH, -$(CH_2)_n$-heterocyclyl, -$(CH_2)_n$-NH-$S(O)_2CH_3$, -$(CR_2)_n$O-lower alkyl or lower alkyl substituted by halogen;

R is hydrogen or lower alkyl, and when two R-groups are present, they may or may not be the same ;

R^2 is aryl or heteroaryl, optionally substituted by one or more substituents, selected from the group consisting of
halogen, lower alkyl, lower alkoxy, -$(CH_2)_n$-hydroxy, lower alkyl substituted by halogen, lower alkoxy substituted by halogen, -$S(O)_2$-lower alkyl, -$(CH_2)_n$-$S(O)_2$-NH-lower alkyl, -$(CH_2)_n$-O-lower alkyl, nitro, amino, -NHC(O)-lower alkyl or -C(O)NH-lower alkyl, or
-$(CH_2)_n$-aryl, optionally substituted by halogen, or by
aryloxy, optionally substituted by halogen, lower alkoxy or lower alkyl substituted by halogen,

or aryl or heteroaryl are optionally substituted by benzyloxy, -S-aryl, -CH(OH)-aryl,
-$C(CH_3)_2$-aryl, -NR-aryl, 2-oxo-2H-pyridin-1-yl, -$(CH_2)_n$-heterocyclyl, optionally substituted by =O, or by -$(CH_2)_n$-heteroaryl or -$(CH_2)_n$-O-heteroaryl;

R^3 is hydrogen or lower alkyl;

R^4 is hydrogen or lower alkyl;

n is 0, 1, 2, 3 or 4

and their pharmaceutically active salts, with the exception of 4-phenylaminomethyl-imidazol-dihydrochloride and benzyl-(*3H*-imidazol-4-ylmethyl)-phenyl-amine.

Preferred compounds of formula I are those, wherein R^1 is lower alkyl. Especially preferred from this group are compounds, wherein R^2 is optionally substituted aryl, for example the following compounds:

ethyl-(3H-imidazol-4-ylmethyl)-phenyl-amine

methyl-(3H-imidazol-4-ylmethyl)-phenyl-amine

(3-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine

ethyl-(3H-imidazol-4-ylmethyl)-m-tolyl-amine

(3H-imidazol-4-ylmethyl)-isopropyl-phenyl-amine

(3-chloro-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine

(4-chloro-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine

(3-chloro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(3,5-dichloro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(3H-imidazol-4-ylmethyl)-isopropyl-(3-methoxy-phenyl)-amine

(3H-imidazol-4-ylmethyl)-isopropyl-m-tolyl-amine

(3H-imidazol-4-ylmethyl)-isopropyl-(3-trifluoromethyl-phenyl)-amine

(4-chloro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(4-chloro-3-trifluoromethyl-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(3,4-dichloro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(3-chloro-4-trifluoromethoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(4-chloro-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine

(3,4-difluoro-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine

(4-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(3H-imidazol-4-ylmethyl)-isopropyl-(4-trifluoromethoxy-phenyl)-amine

(3H-imidazol-4-ylmethyl)-isopropyl-naphthalen-2-yl-amine

(3H-imidazol-4-ylmethyl)-indan-5-yl-isopropyl-amine

(3-chloro-5-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(3,4-difluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(5-chloro-2-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(3-chloro-2-fluoro-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine

ethyl-(3H-imidazol-4-ylmethyl)-naphthalen-2-yl-amine

(3,5-difluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(2,4-difluoro-3-methoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(4-fluoro-3-methyl-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(3H-imidazol-4-ylmethyl)-(3-isopropoxy-phenyl)-isopropyl-amine

(3-benzyloxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(3H-imidazol-4-ylmethyl)-isopropyl-(3-trifluoromethoxy-phenyl)-amine
(3H-imidazol-4-ylmethyl)-isopropyl-(3-phenoxy-phenyl)-amine
((3-difluoromethoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(3H-imidazol-4-ylmethyl)-isopropyl-[3-(1,1,2,2-tetrafluoro-ethoxy)-phenyl]-amine
(3-chloro-4-methyl-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine
(3,4-dimethyl-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(4-benzyloxy-3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine
[3-chloro-4-(4-chloro-phenoxy)-phenyl]-ethyl-(1H-imidazol-4-ylmethyl)-amine
(3-benzyl-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
biphenyl-3-yl-(3H-imidazol-4-ylmethyl)-isopropyl-amine
[3-(4-chloro-phenoxy)-phenyl]-(3H-imidazol-4-ylmethyl)-isopropyl-amine
N-(1H-imidazol-4-ylmethyl)-N'-phenyl-benzene-1,4-diamine
{4-[2-(4-chloro-phenyl)-ethyl]-phenyl}-ethyl-(1H-imidazol-4-ylmethyl)-amine
(3-bromo-4-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(3H-imidazol-4-ylmethyl)-methyl-(3-phenoxy-phenyl)-amine
(3H-imidazol-4-ylmethyl)-(3-methoxy-phenyl)-methyl-amine
ethyl-(3H-imidazol-4-ylmethyl)-(3-phenoxy-phenyl)-amine
(3-difluoromethoxy-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine
(3-benzyloxy-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine
(3-benzyloxy-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine
ethyl-(3H-imidazol-4-ylmethyl)-(3-methoxy-phenyl)-amine
ethyl-(4-fluoro-3-methoxy-phenyl)-(3H-imidazol-4-ylmethyl)-amine
(3-ddifluoromethoxy-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine
(4-chloro-3-methoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
[3-(3-chloro-phenoxy)-phenyl]-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(3H-imidazol-4-ylmethyl)-isopropyl-(3-phenoxymethyl-phenyl)-amine
(4-fluoro-3-phenoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(3-bromo-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(3,4-dichloro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(3-bromo-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine
(3-bromo-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine
(3,4-difluoro-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine
(3,4-dichloro-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine
(3,5-dichloro-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine
(3,5-difluoro-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine

(4-bromo-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine
(3,4-dibromo-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine
(4-bromo-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(3,5-dichloro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(3-chloro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(4-bromo-3-fluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(3,5-difluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(4-chloro-3-fluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(3-chloro-5-fluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(3-bromo-4-fluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(3-chloro-4-fluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(4-chloro-3-methoxy-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(4-bromo-3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine or
(3-chloro-4-trifluoromethoxy-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine.

Preferred compounds of formula I are those, wherein R^1 is hydrogen. Especially preferred from this group are compounds, wherein R^2 is optionally substituted aryl, for example the following compounds:
(3-chloro-5-fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-amine
{3-[ethyl-(3H-imidazol-4-ylmethyl)-amino]-2,6-difluoro-phenyl}-methanol
(3-bromo-4-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-amine
[3-(3-chloro-phenoxy)-phenyl]-(3H-imidazol-4-ylmethyl)-amine
(4-fluoro-3-phenoxy-phenyl)-(3H-imidazol-4-ylmethyl)-amine
(3-bromo-phenyl)-(3H-imidazol-4-ylmethyl)-amine
(3-bromo-5-trifluoromethyl-phenyl)-(3H-imidazol-4-ylmethyl)-amine
(3H-imidazol-4-ylmethyl)-(3-isopropyl-phenyl)-amine
(3, 5-difluoro-phenyl)-(1H-imidazol-4-ylmethyl)-amine
(3,4-dibromo-phenyl)-(1H-imidazol-4-ylmethyl)-amine
(3-chloro-4-fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-amine
(4-bromo-3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine or
(3-chloro-4-trifluoromethoxy-phenyl)-(1H-imidazol-4-ylmethyl)-amine.

Further preferred are compounds of formula I, wherein R^1 is lower alkyl and R^2 is optionally substituted heteroaryl, for example the following compounds
(4,6-dichloro-pyrimidin-2-yl)-ethyl-(1H-imidazol-4-ylmethyl)-amine

(6-bromo-pyridin-2-yl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine or ethyl-(1H-imidazol-4-ylmethyl)-(6-trifluoromethyl-pyridin-2-yl)-amine.

A further embodiment of the invention are compounds or formula 1, wherein R^1 is optionally substituted CH_2-aryl. Especially preferred from this group are compounds, wherein R^2 is optionally substituted aryl, for example the following compounds:

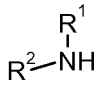
(2-chloro-benzyl)-(3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine
(3-chloro-benzyl)-(3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine
(4-chloro-benzyl)-(3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine or
benzyl-(3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine.

Further preferred compounds are those, wherein R^1 is CRH-cyloalkyl and R^2 is optionally substituted aryl, for example

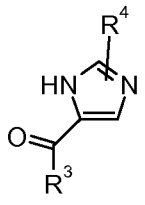
(3-chloro-phenyl)-cyclopropylmethyl-(3H-imidazol-4-ylmethyl)-amine or
(3-chloro-phenyl)-(1-cyclopropylethyl)-(3H-imidazol-4-ylmethyl)-amine.

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

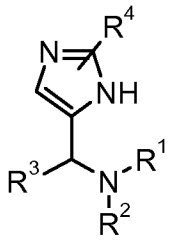
a) reacting an amine of formula


II

with a compound of formula


III

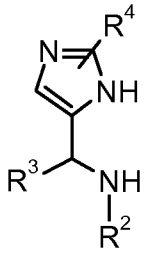
to a compound of formula



I

wherein R^1, R^2, R^3, and R^4 are as defined above, or

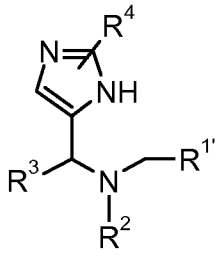
b) reacting a compound of formula



I-1

with a compound of formula $R^{1'}$-CHO

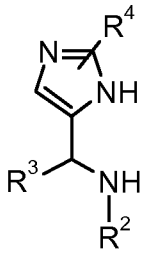
to a compound of formula



I-2

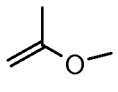
wherein $R^{1'}$ is lower alkyl, -$(CH_2)_{n-1}$-aryl or -$(CH_2)_{n-1}$-heteroaryl, which are optionally substituted by lower alkoxy, lower alkyl substituted by halogen or halogen, or is -$(CR_2)_{n-1}$- cycloalkyl, optionally substituted by hydroxy, or is -$(CR_2)_{n-1}$-OH, -$(CH_2)_{n-1}$-heterocyclyl, -$(CH_2)_{n-1}$-NH-$S(O)_2CH_3$, -$(CR_2)_{n-1}$O-lower alkyl and the other definitions are as described above, or

c) reacting a compound of formula



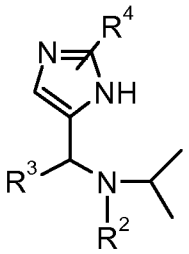
I-1

with



V

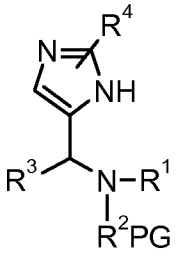
to a compound of formula



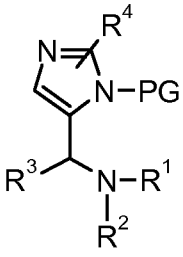
I-3

wherein the substituents are as defined above, or

d) removing a protecting group of compounds of formulas

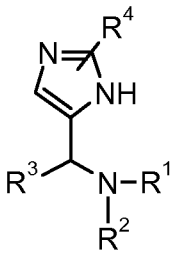


VI or



X

to a compound of formula



I

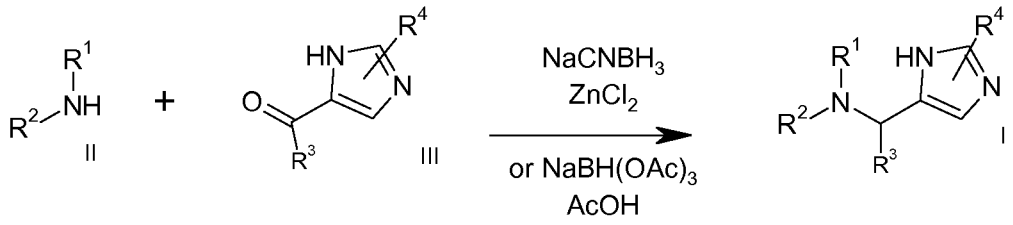
wherein the substituents are as defined above, or

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

The compounds of formula I may be prepared in accordance with the process variants as described above and with the following schemes 1 - 4. The starting materials are either commercially available, are otherwise known in the chemical literature, or may be prepared in accordance with methods well known in the art.

Method 1

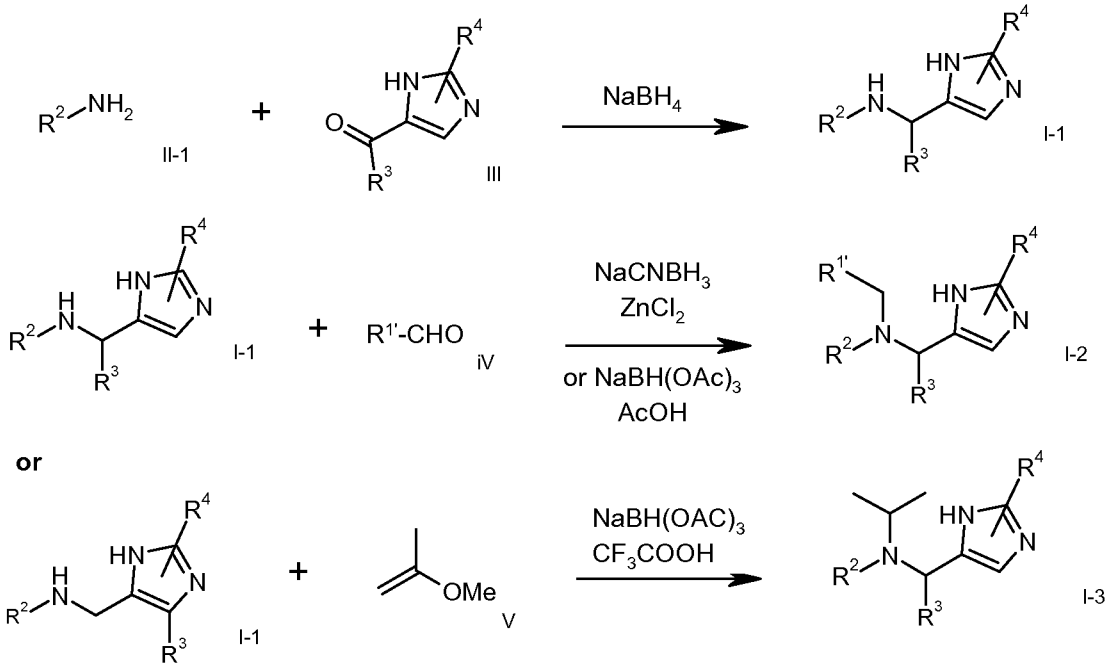
Scheme 1



Compounds of formula I may be prepared by reductive amination using an amine of formula II and a corresponding imidazole-4-carbaldehyde/ketone of formula III.

Method 2

Scheme 2

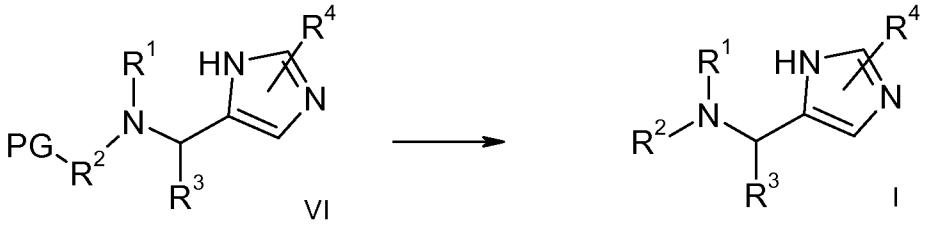


Compounds of formula I-1 may be prepared by reductive amination followed by N-derivatisation to obtain compounds of formulas I-2 or I-3.

$R^{1'}$ is lower alkyl, $-(CH_2)_{n-1}$-aryl or $-(CH_2)_{n-1}$-heteroaryl, which are optionally substituted by lower alkoxy, lower alkyl substituted by halogen or halogen, or is $-(CR_2)_{n-1}$- cycloalkyl, optionally substituted by hydroxy, or is $-(CR_2)_{n-1}$-OH, $-(CH_2)_{n-1}$-heterocyclyl, $-(CH_2)_{n-1}$-NH-$S(O)_2CH_3$, $-(CR_2)_{n-1}$O-lower alkyl and the other definitions are as described above.

Method 3

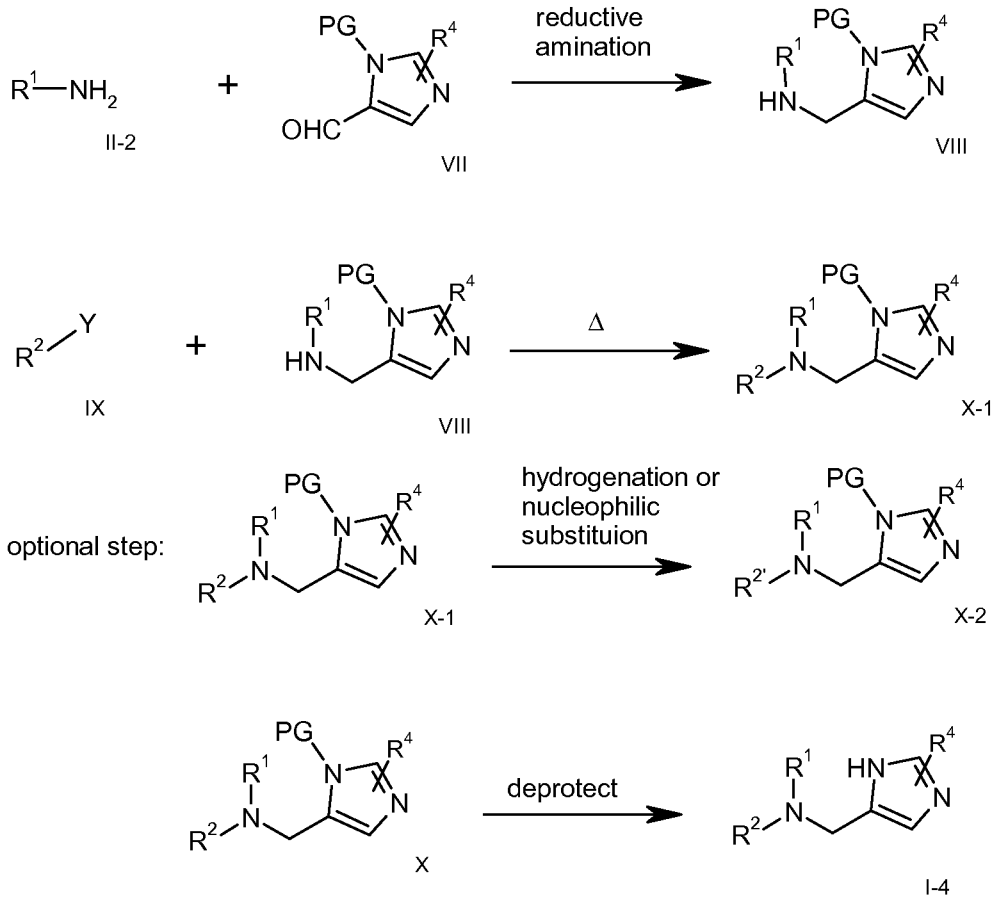
Scheme 3



Compounds of formula I may be prepared from protected compounds of formula VI by removal of the protecting group. The protecting groups are known groups described in the literature.

Method 4

Scheme 4



The processes described in scheme 4 are preferred for compounds, wherein R^2 is substituted or unsubstituted pyridine-4-yl, pyridine-2-yl, pyrimidin-4-yl or pyrimidine-2-yl. The corresponding heteroaryl compounds of formula I-4 may then be prepared by reaction of halogen substituted compounds of formula IX (Y = F preferred for pyridinyl; Y = Cl or Br preferred for pyrimidinyl) with protected aminomethylimidazoles of formula VIII to afford protected compounds of formula X followed by deprotection to afford compounds of formula I-4. Optionally the substituent R^2 in compound X (if R^2 is for instance a bromo- or chlorosubstituted pyridine or pyrimidine) can be transformed into a different substituent $R^{2'}$ (for instance an unsubstituted or alkoxysubstituted pyridine or pyrimidine) before deprotection by a suitable reaction such as hydrogenation or nucleophilic substitution (replacement of the bromo- or chlorosubstituent in R^2 by hydrogen or alkoxy).

Isolation and purification of the compounds

Isolation and purification of the compounds and intermediates described herein can be effected, if desired, by any suitable separation or purification procedure such as, for example, filtration, extraction, crystallization, column chromatography, thin-layer chromatography, thick-layer chromatography, preparative low or high-pressure liquid chromatography or a combination of these procedures. Specific illustrations of suitable separation and isolation procedures can be had by reference to the preparations and examples herein below. However, other equivalent separation or isolation procedures could, of course, also be used. Racemic mixtures of chiral compounds of formula I can be separated using chiral HPLC.

Salts of compounds of formula I

The compounds of formula I are basic and may be converted to a corresponding acid addition salt. The conversion is accomplished by treatment with at least a stoichiometric amount of an appropriate acid, such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, and organic acids such as acetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, malic acid, malonic acid, succinic acid, maleic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid and the like. Typically, the free base is dissolved in an inert organic solvent such as diethyl ether, ethyl acetate, chloroform, ethanol or methanol and the like, and the acid added in a similar solvent. The temperature is maintained between 0 °C and 50 °C. The resulting salt precipitates spontaneously or may be brought out of solution with a less polar solvent.

The acid addition salts of the basic compounds of formula I may be converted to the corresponding free bases by treatment with at least a stoichiometric equivalent of a suitable base such as sodium or potassium hydroxide, potassium carbonate, sodium bicarbonate, ammonia, and the like.

The compounds of formula I and their pharmaceutically usable addition salts possess valuable pharmacological properties. Specifically, it has been found that the compounds of the present invention have a good affinity to the trace amine associated receptors (TAARs), especially TAAR1.

The compounds were investigated in accordance with the test given hereinafter.

Materials and Methods

Construction of TAAR expression plasmids and stably transfected cell lines

For the construction of expression plasmids the coding sequences of human, rat and mouse TAAR 1 were amplified from genomic DNA essentially as described by Lindemann et al. [14]. The Expand High Fidelity PCR System (Roche Diagnostics) was used with 1.5 mM Mg^{2+} and purified PCR products were cloned into pCR2.1-TOPO cloning vector (Invitrogen) following the instructions of the manufacturer. PCR products were subcloned into the pIRESneo2 vector (BD Clontech, Palo Alto, California), and expression vectors were sequence verified before introduction in cell lines.

HEK293 cells (ATCC # CRL-1573) were cultured essentially as described Lindemann et al. (2005). For the generation of stably transfected cell lines HEK293 cells were transfected with the pIRESneo2 expression plasmids containing the TAAR coding sequences (described above) with Lipofectamine 2000 (Invitrogen) according to the instructions of the manufacturer, and 24 hrs post transfection the culture medium was supplemented with 1 mg/ml G418 (Sigma, Buchs, Switzerland). After a culture period of about 10 d clones were isolated, expanded and tested for responsiveness to trace amines (all compounds purchased from Sigma) with the cAMP Biotrak Enzyme immunoassay (EIA) System (Amersham) following the non-acetylation EIA procedure provided by the manufacturer. Monoclonal cell lines which displayed a stable EC_{50} for a culture period of 15 passages were used for all subsequent studies.

Membrane preparation and radioligand binding

Cells at confluence were rinsed with ice-cold phosphate buffered saline without Ca^{2+} and Mg^{2+} containing 10 mM EDTA and pelleted by centrifugation at 1000 rpm for 5 min at 4 °C. The pellet was then washed twice with ice-cold phosphate buffered saline and cell pellet was frozen immediately by immersion in liquid nitrogen and stored until use at -80 °C. Cell pellet was then suspended in 20 ml HEPES-NaOH (20 mM), pH 7.4 containing 10 mM EDTA, and homogenized with a Polytron (PT 3000, Kinematica) at 10,000 rpm for 10 s. The homogenate was centrifuged at 48,000×*g* for 30 min at 4 °C and the pellet

resuspended in 20 ml HEPES-NaOH (20 mM), pH 7.4 containing 0.1 mM EDTA (buffer A), and homogenized with a Polytron at 10,000 rpm for 10 s. The homogenate was then centrifuged at 48,000×*g* for 30 min at 4 °C and the pellet resuspended in 20 ml buffer A, and homogenized with a Polytron at 10,000 rpm for 10 s. Protein concentration was determined by the method of Pierce (Rockford, IL). The homogenate was then centrifuged at 48,000×*g* for 10 min at 4 °C, resuspended in HEPES-NaOH (20 mM), pH 7.0 including $MgCl_2$ (10 mM) and $CaCl_2$ g protein per ml and (2 mM) (buffer B) at 200 homogenized with a Polytron at 10,000 rpm for 10 s.

Binding assay was performed at 4 °C in a final volume of 1 ml, and with an incubation time of 30 min. The radioligand [^{3}H]-rac-2-(1,2,3,4-tetrahydro-1-naphthyl)-2-imidazoline was used at a concentration equal to the calculated K_d value of 60 nM to give a bound at around 0.1 % of the total added radioligand concentration, and a specific binding which represented approximately 70 – 80 % of the total binding. Non-specific binding was defined as the amount of [^{3}H]-rac-2-(1,2,3,4-tetrahydro-1-naphthyl)-2-imidazoline bound in the presence of the appropriate unlabelled ligand (10μM). Competing ligands were tested in a wide range of concentrations (10 pM – 30 μM). The final dimethylsulphoxide concentration in the assay was 2%, and it did not affect radioligand binding. Each experiment was performed in duplicate. All incubations were terminated by rapid filtration through UniFilter-96 plates (Packard Instrument Company) and glass filter GF/C, pre-soaked for at least 2 h in polyethylenimine 0.3%, and using a Filtermate 96 Cell Harvester (Packard Instrument Company). The tubes and filters were then washed 3 times with 1 ml aliquots of cold buffer B. Filters were not dried and soaked in Ultima gold (45 μl/well, Packard Instrument Company) and bound radioactivity was counted by a TopCount Microplate Scintillation Counter (Packard Instrument Company).

The preferred compounds show a Ki value (μM) in mouse on TAAR1 in the range of 0.0009 – 0.01 as shown in the table below.

Example	Ki (μM) mouse	Example	Ki (μM) mouse	Example	Ki (μM) mouse	Example	Ki (μM) mouse
1	0.0061	67	0.0067	170	0.0025	251	0.009
2	0.0081	70	0.0082	175	0.0036	275	0.001

4	0.0029	73	0.0055	179	0.0026	277	0.006
6	0.0018	76	0.0011	181	0.0098	279	0.004
7	0.0046	77	0.0053	183	0.0051	281	0.004
9	0.0013	78	0.0052	186	0.0089	284	0.002
10	0.0045	81	0.0036	188	0.0024	287	0.007
18	0.0039	82	0.0012	189	0.0068	288	0.002
19	0.0077	101	0.003	190	0.0014	291	0.001
20	0.0059	102	0.006	192	0.001	292	0.007
21	0.0078	109	0.0041	193	0.008	296	0.004
23	0.0012	110	0.0067	194	0.0048	297	0.001
24	0.001	113	0.0024	195	0.0042	302	0.003
25	0.0055	114	0.0041	200	0.0028	303	0.001
26	0.0034	115	0.009	202	0.0084	304	0.001
27	0.0023	123	0.0021	204	0.005	305	0.002
28	0.0031	125	0.0044	206	0.005	306	0.002
31	0.0045	128	0.0023	207	0.002	307	0.002
32	0.0012	130	0.0039	208	0.003	308	0.001
33	0.0028	133	0.0077	225	0.001	309	0.003
51	0.0009	139	0.0039	226	0.001	312	0.001
52	0.004	141	0.0015	228	0.002	324	0.002
53	0.0015	142	0.0079	237	0.004	325	0.002
57	0.0014	149	0.0082	242	0.001	327	0.002

58	0.0014	155	0.0094	244	0.004	331	0.001
62	0.0081	161	0.0072	247	0.001	333	0.001

The compounds of formula I and the pharmaceutically acceptable salts of the compounds of formula I can be used as medicaments, e.g. in the form of pharmaceutical preparations. The pharmaceutical preparations can be administered orally, e.g. in the form of tablets, coated tablets, dragées, hard and soft gelatine capsules, solutions, emulsions or suspensions. The administration can, however, also be effected rectally, e.g. in the form of suppositories, parenterally, e.g. in the form of injection solutions.

The compounds of formula I can be processed with pharmaceutically inert, inorganic or organic carriers for the production of pharmaceutical preparations. Lactose, corn starch or derivatives thereof, talc, stearic acids or its salts and the like can be used, for example, as such carriers for tablets, coated tablets, dragées and hard gelatine capsules. Suitable carriers for soft gelatine capsules are, for example, vegetable oils, waxes, fats, semi-solid and liquid polyols and the like. Depending on the nature of the active substance no carriers are however usually required in the case of soft gelatine capsules. Suitable carriers for the production of solutions and syrups are, for example, water, polyols, glycerol, vegetable oil and the like. Suitable carriers for suppositories are, for example, natural or hardened oils, waxes, fats, semi-liquid or liquid polyols and the like.

The pharmaceutical preparations can, moreover, contain preservatives, solubilizers, stabilizers, wetting agents, emulsifiers, sweeteners, colorants, flavorants, salts for varying the osmotic pressure, buffers, masking agents or antioxidants. They can also contain still other therapeutically valuable substances.

Medicaments containing a compound of formula I or a pharmaceutically acceptable salt thereof and a therapeutically inert carrier are also an object of the present invention, as is a process for their production, which comprises bringing one or more compounds of formula I and/or pharmaceutically acceptable acid addition salts and, if desired, one or more other therapeutically valuable substances into a galenical administration form together with one or more therapeutically inert carriers.

The most preferred indications in accordance with the present invention are those, which include disorders of the central nervous system, for example the treatment or prevention of schizophrenia, depression, cognitive impairment and Alzheimer's disease.

The dosage can vary within wide limits and will, of course, have to be adjusted to the individual requirements in each particular case. In the case of oral administration the dosage for adults can vary from about 0.01 mg to about 1000 mg per day of a compound of general formula I or of the corresponding amount of a pharmaceutically acceptable salt thereof. The daily dosage may be administered as single dose or in divided doses and, in addition, the upper limit can also be exceeded when this is found to be indicated.

Tablet Formulation (Wet Granulation)

Item	Ingredients	mg/tablet			
		5 mg	25 mg	100 mg	500 mg
1.	Compound of formula I	5	25	100	500
2.	Lactose Anhydrous DTG	125	105	30	150
3.	Sta-Rx 1500	6	6	6	30
4.	Microcrystalline Cellulose	30	30	30	150
5.	Magnesium Stearate	1	1	1	1
	Total	167	167	167	831

Manufacturing Procedure

1. Mix items 1, 2, 3 and 4 and granulate with purified water.
2. Dry the granules at 50°C.
3. Pass the granules through suitable milling equipment.
4. Add item 5 and mix for three minutes; compress on a suitable press.

Capsule Formulation

Item	Ingredients	mg/capsule			
		5 mg	25 mg	100 mg	500 mg
1.	Compound of formula I	5	25	100	500
2.	Hydrous Lactose	159	123	148	---
3.	Corn Starch	25	35	40	70

4.	Talc	10	15	10	25
5.	Magnesium Stearate	1	2	2	5
	Total	200	200	300	600

Manufacturing Procedure

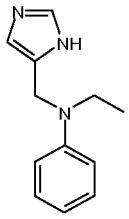
1. Mix items 1, 2 and 3 in a suitable mixer for 30 minutes.
2. Add items 4 and 5 and mix for 3 minutes.
3. Fill into a suitable capsule.

Experimental

The following examples illustrate the invention but are not intended to limit its scope.

Example 1

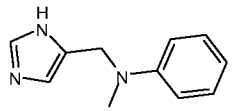
Ethyl-(3H-imidazol-4-ylmethyl)-phenyl-amine



To a solution of N-ethylaniline (0.145 g, 1.2 mmol) in 1,2-dichloroethane (5 ml) were added molecular sieves (2g, size 0.4 nM) and 4-formylimidazole (0.3 g, 3.12 mmol). After stirring the mixture for 5 min at room temperature sodium triacetoxyborohydride (1.02 g, 4.8 mmol) and acetic acid (5 drops) were added. The reaction mixture was stirred at room temperature overnight. For workup ethyl acetate (50 ml) and 1M sodium bicarbonate solution (30 ml) were added and the mixture was shaken. The organic layer was separated, dried over magnesium sulfate and evaporated. The residue was purified using flash chromatography (column: Isolute® Flash-NH_2 (Separtis); eluent: ethyl acetate/methanol = 95:5) to yield a white solid (122 mg, 51%); MS (ISP): 202.0 ($(M+H)^{+\cdot}$).

Example 2

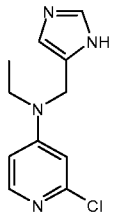
Methyl-(3H-imidazol-4-ylmethyl)-phenyl-amine



The title compound, MS (ISP): 188.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using N-methylaniline instead of N-ethylaniline.

Example 3

(2-Chloro-pyridin-4-yl)-ethyl-(3H-imidazol-4-ylmethyl)-amine



a) 5-Ethylaminomethyl-imidazole-1-sulfonic acid dimethylamide

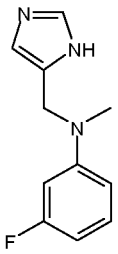
To a saturated solution of ethylamine in methanol (40 ml) was added 4-formyl-imidazole-1-sulfonic acid dimethylamide (2.5 g, 12.3 mmol) and the mixture was stirred overnight. Sodium borohydride (0.70 g, 18.5 mmol) was added and the mixture was stirred at room temperature for 3 h. Water was added and the solution was extracted three times with ethyl acetate. The combined organic layers were dried over magnesium sulfate and evaporated. The residue was purified by flash chromatography (SiO2: dichloromethane/methanol = 9:1) to yield a light yellow oil (0.785 g, 27%); MS (ISP): 233.1 $((M+H)^{+\cdot})$.

b) (2-Chloro-pyridin-4-yl)-ethyl-(3H-imidazol-4-ylmethyl)-amine

A mixture of 5-ethylaminomethyl-imidazole-1-sulfonic acid dimethylamide (0.2 g, 0.86 mmol) and 2-chloro-4-fluoropyridine (0.12 g; 0.91 mmol) was heated in a sealed vessel in a microwave oven for 30 min at 140°C. Then after cooling a solution of hydrochloric acid in ethanol (5N, 1 ml) was added and the mixture was stirred at 90°C overnight. For workup aqueous ammonia solution was added to basic pH and the mixture was extracted three times with ethyl acetate. The combined organic layers were dried over magnesium sulfate and evaporated. The residue was purified by flash chromatography (SiO_2; ethyl acetate/methanol = 8:2) to yield a white solid, (0.13 g, 64 %); MS (ISP): 239.0 $((M+H)^{+\cdot})$.

Example 4

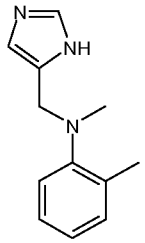
(3-Fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (EI): 205.1 ($M^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using N-methyl-3-fluoroaniline instead of N-ethylaniline.

Example 5

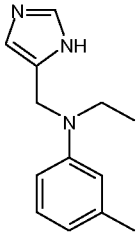
(3H-Imidazol-4-ylmethyl)-methyl-o-tolyl-amine



The title compound, MS (ISP): 202.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using N-methyl-o-tolylamine instead of N-ethylaniline.

Example 6

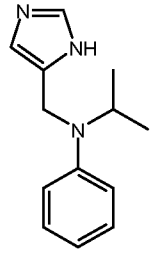
Ethyl-(3H-imidazol-4-ylmethyl)-m-tolyl-amine



The title compound, MS (ISP): 216.2 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using N-ethyl-m-tolylamine instead of N-ethylaniline.

Example 7

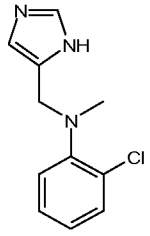
(3H-Imidazol-4-ylmethyl)-isopropyl-phenyl-amine



The title compound, MS (ISP): 216.2 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using isoporopyl-phenyl-amine instead of N-ethylaniline.

Example 8

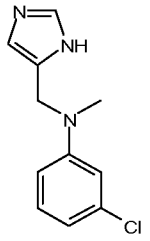
(2-Chloro-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 221.9 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using 2-(chlorophenyl)-methyl-amine instead of N-ethylaniline.

Example 9

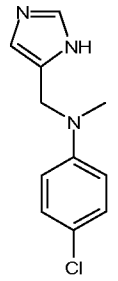
(3-Chloro-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 221.9 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using 3-(chlorophenyl)-methyl-amine instead of N-ethylaniline.

Example 10

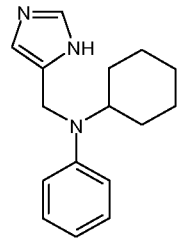
(4-Chloro-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 221.9 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using 4-(chlorophenyl)-methyl-amine instead of N-ethylaniline.

Example 11

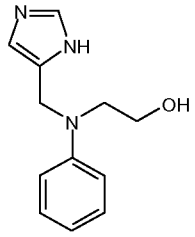
Cyclohexyl-(3H-imidazol-4-ylmethyl)-phenyl-amine



The title compound, MS (ISP): 256.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using cyclohexyl-phenyl-amine instead of N-ethylaniline.

Example 12

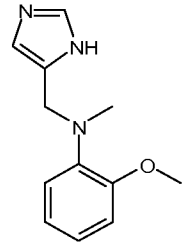
2-[(3H-Imidazol-4-ylmethyl)-phenyl-amino]-ethanol



The title compound, MS (ISP): 218.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using 2-phenylamino-ethanol instead of N-ethylaniline.

Example 13

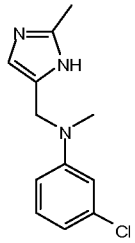
(3H-Imidazol-4-ylmethyl)-(2-methoxy-phenyl)-methyl-amine



The title compound, MS (ISP): 218.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (2-methoxy-phenyl)-methyl-amine instead of N-ethylaniline.

Example 14

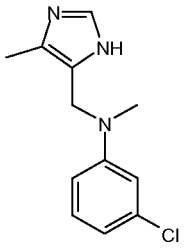
(3-Chloro-phenyl)-methyl-(2-methyl-3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 236.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using 3-(chlorophenyl)-methyl-amine instead of N-ethylaniline and 4-formyl-2-methylimidazole instead of 4-formylimidazole.

Example 15

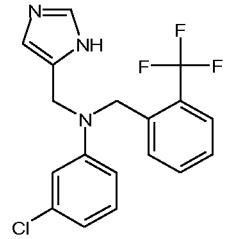
(3-Chloro-phenyl)-methyl-(5-methyl-3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 235.8 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using 3-(chlorophenyl)-methyl-amine instead of N-ethylaniline and 4-formyl-5-methylimidazole instead of 4-formylimidazole.

Example 16

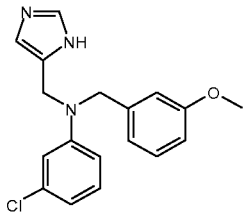
(3-Chloro-phenyl)-(1H-imidazol-4-ylmethyl)-(2-trifluoromethyl-benzyl)-amine



The title compound, MS (ISP): 366.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (3-chloro-phenyl)-(3-trifluoromethyl-benzyl)-amine instead of N-ethylaniline.

Example 17

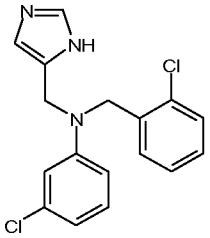
(3-Chloro-phenyl)-(1H-imidazol-4-ylmethyl)-(3-methoxy-benzyl)-amine



The title compound, MS (ISP): 327.9 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (3-chloro-phenyl)-(3-methoxy-benzyl)-amine instead of N-ethylaniline.

Example 18

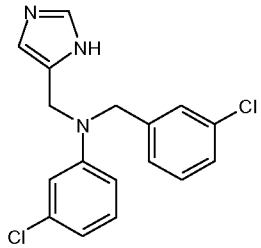
(2-Chloro-benzyl)-(3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 332.0; 334.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (2-chloro-benzyl)-(3-chloro-phenyl)-amine instead of N-ethylaniline.

Example 19

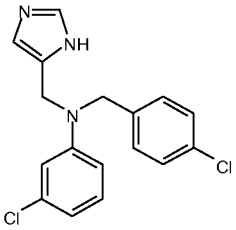
(3-Chloro-benzyl)-(3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 331.9; 334.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (3-chloro-benzyl)-(3-chloro-phenyl)-amine instead of N-ethylaniline.

Example 20

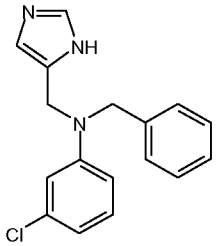
(4-Chloro-benzyl)-(3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 332.0; 334.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (4-chloro-benzyl)-(3-chloro-phenyl)-amine instead of N-ethylaniline.

Example 21

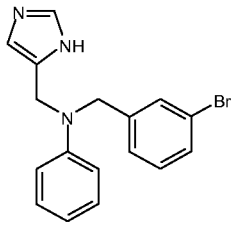
Benzyl-(3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 298.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using benzyl-(3-chloro-phenyl)-amine instead of N-ethylaniline.

Example 22

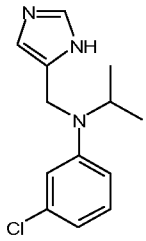
(3-Bromo-benzyl)-(1H-imidazol-4-ylmethyl)-phenyl-amine



The title compound, MS (ISP): 341.9; 343.9 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (3-bromo-benzyl)-phenyl-amine instead of N-ethylaniline.

Example 23

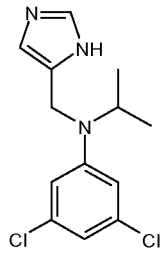
(3-Chloro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 250.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (3-chloro-phenyl)-isopropyl-amine instead of N-ethylaniline.

Example 24

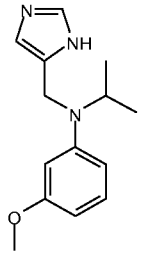
(3,5-Dichloro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 283.9; 285.9 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (3,5-dichloro-phenyl)-isopropyl-amine instead of N-ethylaniline.

Example 25

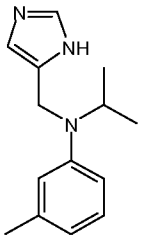
(3H-Imidazol-4-ylmethyl)-isopropyl-(3-methoxy-phenyl)-amine



The title compound, MS (ISP): 246.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using isopropyl-(3-methoxy-phenyl)-amine instead of N-ethylaniline.

Example 26

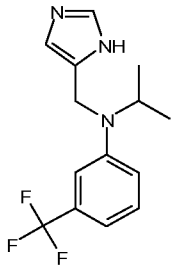
(3H-Imidazol-4-ylmethyl)-isopropyl-m-tolyl-amine



The title compound, MS (ISP): 230.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using N-isopropyl-m-tolylamine instead of N-ethylaniline.

Example 27

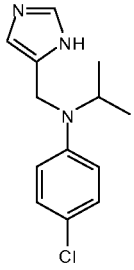
(3H-Imidazol-4-ylmethyl)-isopropyl-(3-trifluoromethyl-phenyl)-amine



The title compound, MS (ISP): 284.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using N-isopropyl-3-(trifluoromethyl)aniline instead of N-ethylaniline.

Example 28

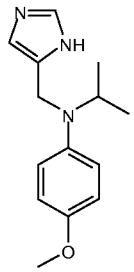
(4-Chloro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 250.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (4-chloro-phenyl)-isopropyl-amine instead of N-ethylaniline.

Example 29

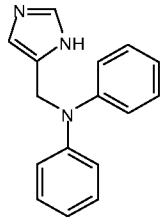
(3H-Imidazol-4-ylmethyl)-isopropyl-(4-methoxy-phenyl)-amine



The title compound, MS (ISP): 246.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using isopropyl-(4-methoxy-phenyl)-amine instead of N-ethylaniline.

Example 30

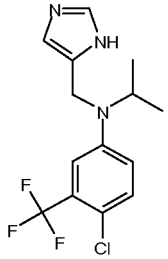
(1H-Imidazol-4-ylmethyl)-diphenyl-amine



The title compound, MS (ISP): 250.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using diphenyl-amine instead of N-ethylaniline.

Example 31

(4-Chloro-3-trifluoromethyl-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



a) (4-Chloro-3-trifluoromethyl-phenyl)-isopropyl-amine

5-Amino-2-chlorobenzotrifluoride (0.587 g, 3.0 mmol) was dissolved in methanol (30 ml). Then acetone (1.58 ml, 30 mmol) and zinc chloride (1.635 g, 12 mmol) were added and the reaction mixture was cooled with an ice bath. After adding sodium cyanoborohydride (0.566 g, 9.0 mmol) the mixture was allowed to stir at 40°C overnight. After cooling, the reaction mixture was poured onto ammonium chloride/ice and extracted with ethyl acetate (2 times 50 ml). The organic layer was dried over magnesium sulfate and evaporated. The residue was purified using flash chromatography (SiO_2;

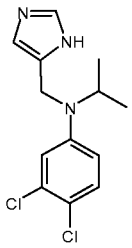
eluent: heptane/ethyl acetate = 95:5) to yield a light yellow oil (0.530g, 74 %) that was directly used for the next step; MS (EI): 222.1 ($(M-CH_3)^{+\cdot}$); 237.1 ($M^{+\cdot}$).

b) (4-Chloro-3-trifluoromethyl-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(4-Chloro-3-trifluoromethyl-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine, MS (ISP): 318.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (4-chloro-3-trifluoromethyl-phenyl)-isopropyl-amine instead of N-ethylaniline.

Example 32

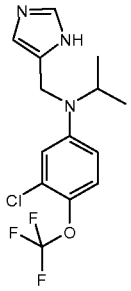
(3,4-Dichloro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 284.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (3,4-dichloro-phenyl)-isopropyl-amine instead of N-ethylaniline.

Example 33

(3-Chloro-4-trifluoromethoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



a) (3-Chloro-4-trifluoromethoxy-phenyl)-isopropyl-amine

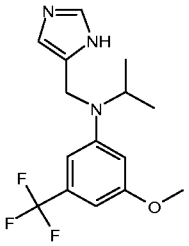
(3-Chloro-4-trifluoromethoxy-phenyl)-isopropyl-amine was obtained in comparable yield analogous to the procedure described for Example 31 step a) using 3-chloro-4-trifluoromethoxy-phenylamine instead of 5-amino-2-chlorobenzotrifluoride and was used directly in the next step.

b) (3-Chloro-4-trifluoromethoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

The title compound, MS (ISP): 334.2 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (3-chloro-4-trifluoromethoxy-phenyl)-isopropyl-amine instead of N-ethylaniline.

Example 34

(3H-Imidazol-4-ylmethyl)-isopropyl-(3-methoxy-5-trifluoromethyl-phenyl)-amine



a) Isopropyl-(3-methoxy-5-trifluoromethyl-phenyl)-amine

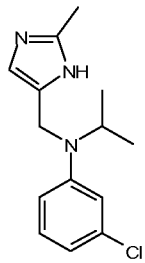
Isopropyl-(3-methoxy-5-trifluoromethyl-phenyl)-amine was obtained in comparable yield analogous to the procedure described for Example 31 step a) using 3-methoxy-5-(trifluoromethyl)-aniline instead of 5-amino-2-chlorobenzotrifluoride and was used directly in the next step.

b) (3H-Imidazol-4-ylmethyl)-isopropyl-(3-methoxy-5-trifluoromethyl-phenyl)-amine

The title compound, MS (ISP): 314.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using isopropyl-(3-methoxy-5-trifluoromethyl-phenyl)-amine instead of N-ethylaniline.

Example 35

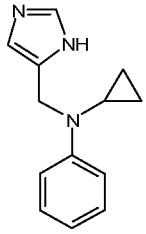
(3-Chloro-phenyl)-isopropyl-(2-methyl-3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 264.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using 3-(chlorophenyl)-isopropyl-amine instead of N-ethylaniline and 4-formyl-2-methylimidazole instead of 4-formylimidazole.

Example 36

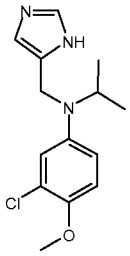
Cyclopropyl-(3H-imidazol-4-ylmethyl)-phenyl-amine



The title compound, MS (ISP): 214.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using N-cyclopropyl-aniline instead of N-ethylaniline.

Example 37

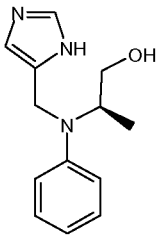
(3-Chloro-4-methoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



N-Isopropyl-3-chloro-4-methoxy-aniline (0.20 g, 1.0 mmol) was dissolved in methanol (10 ml). Then 4-formylimidazole (0.288 g, 3.0 mmol) and zinc chloride (0.545 g, 4.0 mmol) were added and the reaction mixture was cooled with an ice bath. After adding sodium cyanoborohydride (0.189 g, 3.0 mmol) the mixture was allowed to stir at 40°C overnight. After cooling, the reaction mixture was poured onto ammoniumchloride/ice and extracted with ethyl acetate (3 times 20 ml). The organic layer was dried over magnesium sulfate and evaporated. The residue was purified using flash chromatography (column: Isolute® Flash-NH_2 (Separtis); eluent: ethyl acetate/methanol = 95:5) to yield a white solid (136 mg, 49%); MS (ISP): 280.0 ($(M+H)^{+\cdot}$).

Example 38

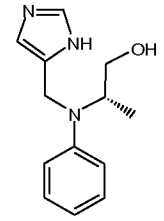
(R)-2-[(3H-Imidazol-4-ylmethyl)-phenyl-amino]-propan-1-ol



The title compound, MS (ISP): 231.9 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 37 using (R)-2-phenylamino-propan-1-ol instead of N-isopropyl-3-chloro-4-methoxy-aniline.

Example 39

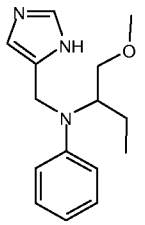
(S)-2-[(3H-Imidazol-4-ylmethyl)-phenyl-amino]-propan-1-ol



The title compound, MS (ISP): 231.9 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 37 using (S)-2-phenylamino-propan-1-ol instead of N-isopropyl-3-chloro-4-methoxy-aniline.

Example 40

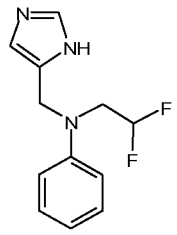
(3H-Imidazol-4-ylmethyl)-(1-methoxymethyl-propyl)-phenyl-amine



The title compound, MS (ISP): 260.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 37 using (1-methoxymethyl-propyl)-phenyl-amine instead of N-isopropyl-3-chloro-4-methoxy-aniline.

Example 41

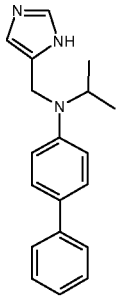
(2,2-Difluoro-ethyl)-(3H-imidazol-4-ylmethyl)-phenyl-amine



The title compound, MS (ISP): 237.9 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 37 using (2,2-difluoroethyl)-phenyl-amine instead of N-isopropyl-3-chloro-4-methoxy-aniline.

Example 42

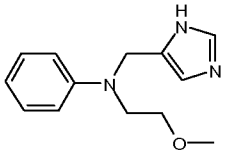
Biphenyl-4-yl-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 292.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 37 using biphenyl-4-yl-isopropylamine instead of N-isopropyl-3-chloro-4-methoxy-aniline.

Example 43

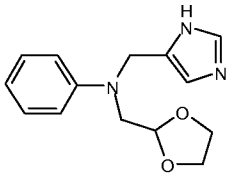
(1H-Imidazol-4-ylmethyl)-(2-methoxy-ethyl)-phenyl-amine



The title compound, MS (ISP): 232.2 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 37 using (2-methoxyethyl)-phenyl-amine instead of N-isopropyl-3-chloro-4-methoxy-aniline.

Example 44

[1,3]Dioxolan-2-ylmethyl-(1H-imidazol-4-ylmethyl)-phenyl-amine



a) [1,3]Dioxolan-2-ylmethyl-phenyl-amine

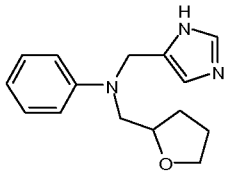
A suspension of phenylboronic acid (0.5 g, 4.1 mmol), copper(II)-acetate-1-hydrate (0.041 g, 0.21 mmol) and molecular sieves (1.5g, size 0.4 nm, powdered) in dichloromethane (12 ml) was stirred for 5 min. Then 2-(aminomethyl)-1,3-dioxolane (0.211g, 2.05 mmol) was added and oxygen was bubbled through the mixture for 5 min. The vessel was closed and shaken overnight at room temperature. For workup ethyl acetate (50 ml) and 1M sodium bicarbonate solution (30 ml) were added and the mixture was shaken. The organic layer was separated, dried over magnesium sulfate and evaporated. The residue was purified using flash chromatography (SiO_2; eluent: heptane/ethyl acetate = 90:10) to yield a light yellow oil (105 mg, 14%); MS (EI): 179.1 ($M^{+\cdot}$).

b) [1,3]Dioxolan-2-ylmethyl-(1H-imidazol-4-ylmethyl)-phenyl-amine

The title compound, MS (ISP): 260.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 37 using [1,3]dioxolan-2-ylmethyl-phenyl-amine instead of N-isopropyl-3-chloro-4-methoxy-aniline.

Example 45

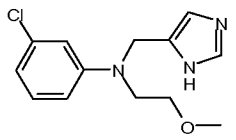
(1H-Imidazol-4-ylmethyl)-phenyl-(tetrahydro-furan-2-ylmethyl)-amine



The title compound, MS (ISP): 258.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 37 using phenyl-(tetrahydro-furan-2-ylmethyl)-amine instead of N-isopropyl-3-chloro-4-methoxy-aniline.

Example 46

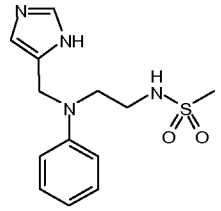
(3-Chloro-phenyl)-(1H-imidazol-4-ylmethyl)-(2-methoxy-ethyl)-amine



The title compound, MS (ISP): 266.2 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 37 using (3-chloro-phenyl)-(2-methoxy-ethyl)-amine instead of N-isopropyl-3-chloro-4-methoxy-aniline.

Example 47

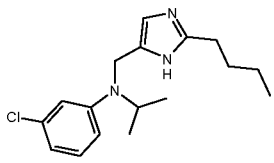
N-{2-[(3H-Imidazol-4-ylmethyl)-phenyl-amino]-ethyl}-methanesulfonamide



The title compound, MS (ISP): 295.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using N-(2-anilinoethyl)-methansulfonamide instead of N-ethylaniline.

Example 48

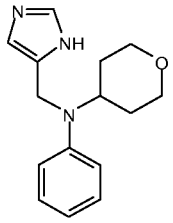
(2-Butyl-3H-imidazol-4-ylmethyl)-(3-chloro-phenyl)-isopropyl-amine



The title compound, MS (ISP): 306.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 37 using N-isopropyl-3-chloro-aniline instead of N-isopropyl-3-chloro-4-methoxy-aniline and 2-butyl-4-formyl-imidazole instead of 4-formylimidazole.

Example 49

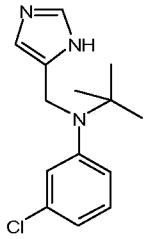
(3H-Imidazol-4-ylmethyl)-phenyl-(tetrahydro-pyran-4-yl)-amine



The title compound, MS (ISP): 257.9 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using phenyl-(tetrahydro-pyran-4-yl)-amine instead of N-ethylaniline.

Example 50

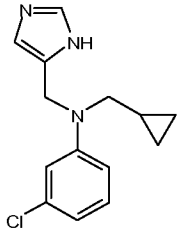
tert-Butyl-(3-chloro-phenyl)-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 263.9; 266.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using tert-butyl-(3-chloro-phenyl)-amine instead of N-ethylaniline.

Example 51

(3-Chloro-phenyl)-cyclopropylmethyl-(3H-imidazol-4-ylmethyl)-amine



a) (3-chloro-phenyl)-cyclopropylmethyl-amine

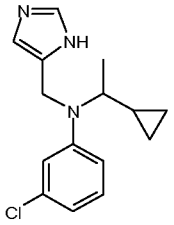
To a solution of 3-chloroaniline (1.27 g, 10 mmol) in 1,2-dichloroethane (20 ml) were added molecular sieves (4g, size 0.4 nM) and cyclopropanecarboxyaldehyde (0.7 g, 10 mmol). After stirring the mixture for 5 min at room temperature sodium triacetoxyborohydride (3.18 g, 15 mmol) and acetic acid (0.6 g, 10 mmol) were added. The reaction mixture was stirred at room temperature overnight. For workup dichloromethane (100 ml) and 1M sodium bicarbonate solution (40 ml) were added and the mixture was shaken. The organic layer was separated, dried over magnesium sulfate and evaporated. The residue was purified using flash chromatography (heptane/ethyl acetate = 9:1) to yield a colourless liquid (1.09 g, 60%); MS (EI): 181.1 ($M^{+\cdot}$).

b) (3-Chloro-phenyl)-cyclopropylmethyl-(3H-imidazol-4-ylmethyl)-amine

The title compound, MS (ISP): 261.9; 263.9 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (3-chloro-phenyl)-cyclopropylmethyl-amine instead of N-ethylaniline.

Example 52

(3-Chloro-phenyl)-(1-cyclopropylethyl)-(3H-imidazol-4-ylmethyl)-amine



a) (3-chloro-phenyl)-(1-cyclopropylethyl)-amine

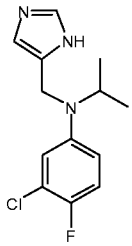
To a solution of 3-chloroaniline (1.27 g, 10 mmol) in 1,2-dichloroethane (20 ml) were added molecular sieves (4g, size 0.4 nM) and cyclopropyl methyl ketone (0.84 g, 10 mmol). After stirring the mixture for 5 min at room temperature sodium triacetoxyborohydride (3.18 g, 15 mmol) and acetic acid (0.6 g, 10 mmol) were added. The reaction mixture was stirred at room temperature overnight. For workup dichloromethane (100 ml) and 1M sodium bicarbonate solution (40 ml) were added and the mixture was shaken. The organic layer was separated, dried over magnesium sulfate and evaporated. The residue was purified using flash chromatography (heptane/ethyl acetate = 9:1) to yield a colourless liquid (0.083 g, 4.5%); MS (ISP): 196.3 ($(M+H)^{+\cdot}$).

b) (3-Chloro-phenyl)-(1-cyclopropylethyl)-(3H-imidazol-4-ylmethyl)-amine

The title compound, MS (ISP): 276.0; 277.9 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (3-chloro-phenyl)-(1-cyclopropylethyl)-amine instead of N-ethylaniline.

Example 53

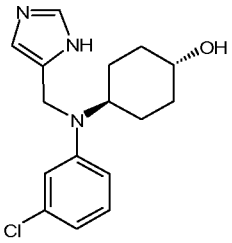
(3-Chloro-4-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 268.1 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 1 using (3-chloro-4-fluoro-phenyl)-isopropyl-amine instead of N-ethylaniline.

Example 54

trans-4-[(3-Chloro-phenyl)-(3H-imidazol-4-ylmethyl)-amino]-cyclohexanol



a) trans-[4-(tert-Butyl-dimethyl-silanyloxy)-cyclohexyl]-(3-chloro-phenyl)-amine

To a solution of 3-chloroaniline (1.27 g, 10 mmol) in 1,2-dichloroethane (20 ml) were added molecular sieves (4g, size 0.4 nM) and 4-(tert-butyldimethylsilyloxy)-cyclohexanone (4.57 g, 20 mmol). After stirring the mixture for 30 min at room temperature sodium triacetoxyborohydride (8.48 g, 40 mmol) and acetic acid (1.2 g, 20 mmol) were added. The reaction mixture was stirred at room temperature overnight. For workup dichloromethane (100 ml) and 1M sodium bicarbonate solution (40 ml) were added and the mixture was shaken. The organic layer was separated, dried over magnesium sulfate and evaporated. The residue was purified using flash chromatography (heptane/ethyl acetate = 1:1) to yield a colourless liquid (0.80 mg, 23.5%); MS (EI): 339.2; 341.3 ($M^{+\cdot}$).

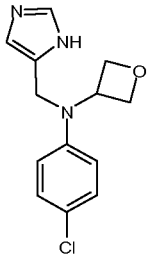
b) trans-4-[(3-Chloro-phenyl)-(3H-imidazol-4-ylmethyl)-amino]-cyclohexanol

To a solution of [4-(tert-butyl-dimethyl-silanyloxy)-cyclohexyl]-(3-chloro-phenyl)-amine (0.68 g, 20 mmol) in 1,2-dichloroethane (10 ml) were added molecular sieves (2 g, size 0.4 nM) and 4-formyl-imidazole (0.50 g, 5.2 mmol). After stirring the mixture for 30 min at room temperature sodium triacetoxyborohydride (1.70 g, 8 mmol) and acetic acid (0.24 g, 4 mmol) were added. The reaction mixture was stirred at room temperature overnight. For workup dichloromethane (50 ml) and 1M sodium bicarbonate solution (30 ml) were added and the mixture was shaken. The organic layer was separated, dried

over magnesium sulfate and evaporated. The residue was purified using flash chromatography (heptane/ethyl acetate = 1:1) to yield a 0.3 g of a white solid. This compound was dissolved in tetrahydrofuran (5 ml), tetrabutylammonium fluoride solution (1M in tetrahydrofuran, 2 ml) was added at 0°C, and the mixture was stirred at room temperature overnight. The solvent was evaporated and the residue was mixed with water and ethyl acetate. The organic layer was separated, dried over magnesium sulfate and evaporated. The residue was purified using flash chromatography (ethyl acetate /methanol = 9:1) to yield a white foam (0.14 mg, 65%); MS (ISP): 306.2 $(M+H)^{+\cdot}$).

Example 55

(4-Chloro-phenyl)-(3H-imidazol-4-ylmethyl)-oxetan-3-yl-amine



a) (4-Chloro-phenyl)-oxetan-3-yl-amine

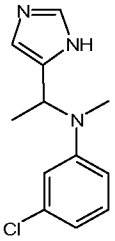
4-Chloroaniline (0.26 g, 2.0 mmol) was dissolved in methanol (25 ml). Then 3-oxetanone (0.22 g, 3 mmol) and zinc chloride (1.09 g, 8.0 mmol) were added and the reaction mixture was cooled with an ice bath. After adding sodium cyanoborohydride (0.377 g, 6.0 mmol) the mixture was allowed to stir at 40°C for 5 hours. After cooling, the reaction mixture was poured onto ammonium chloride/ice and extracted with ethyl acetate (3 times 20 ml). The organic layer was dried over magnesium sulfate and evaporated. The residue was purified using flash chromatography (heptane/ethyl acetate = 95:5) to yield a light yellow liquid (108 mg, 29%); ^{1}H-NMR ($CDCl_3$): 4.14 b, 1H (NH); 4.55 m, 3H (CHO, CHN); 5.00 t, 2H (CHO), 6.43 d, 2H (aryl-H) and 7.15 d, 2H (aryl-H).

b) (4-Chloro-phenyl)-(3H-imidazol-4-ylmethyl)-oxetan-3-yl-amine

The title compound, MS (ISP): 264.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (4-chloro-phenyl)-oxetan-3-yl-amine instead of N-ethylaniline.

Example 56

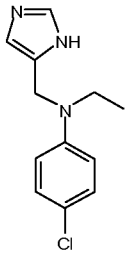
(3-Chloro-phenyl)-[1-(3H-imidazol-4-yl)-ethyl]-methyl-amine



The title compound, MS (ISP): 236.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (3-chlorophenyl)-methyl-amine instead of N-ethylaniline and 4-acetylimidazole instead of 4-formylimidazole.

Example 57

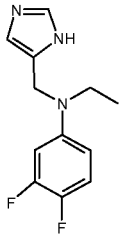
(4-Chloro-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 236.1; 238.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (4-chlorophenyl)-ethyl-amine instead of N-ethylaniline.

Example 58

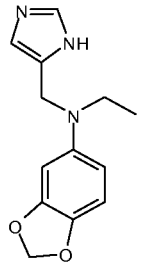
(3,4-Difluoro-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 238.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (3,4-difluorophenyl)-ethyl-amine instead of N-ethylaniline.

Example 59

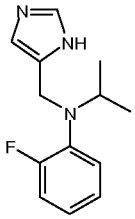
Benzo[1,3]dioxol-5-yl-ethyl-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 246.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (benzo[1,3]dioxol-5-yl)-ethyl-amine instead of N-ethylaniline.

Example 60

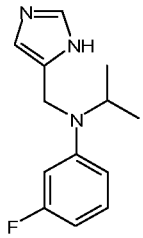
(2-Fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 234.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (2-fluorophenyl)-isopropyl-amine instead of N-ethylaniline.

Example 61

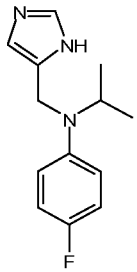
(3-Fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 234.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (3-fluorophenyl)-isopropyl-amine instead of N-ethylaniline.

Example 62

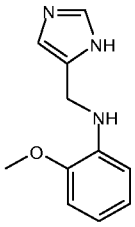
(4-Fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 234.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using (4-fluorophenyl)-isopropyl-amine instead of N-ethylaniline.

Example 63

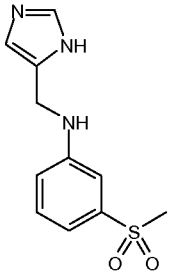
(3H-Imidazol-4-ylmethyl)-(2-methoxy-phenyl)-amine



To a solution of 2-methoxyaniline (0.62 g, 5 mmol) in methanol (5 ml) was added 4-formylimidazole (0.48 g, 5 mmol). After stirring the mixture overnight at 60°C the solution was cooled and sodium borohydride (0.28 g, 7.5 mmol) were added. The reaction mixture was stirred at room temperature for 4 hours. Then water was added and the mixture was extracted with ethyl acetate. The organic layer was separated, washed with water, dried over magnesium sulfate and evaporated. The residue was purified by recrystallisation from heptane/ethyl acetate to yield off-white crystals (0.85 mg, 84%); MS (ISP): 204.3 ($(M+H)^{+\cdot}$).

Example 64

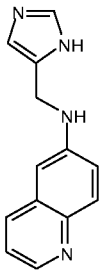
(3H-Imidazol-4-ylmethyl)-(3-methanesulfonyl-phenyl)-amine



The title compound, MS (ISP): 252.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 3-methylsulfonyl-aniline instead of 2-methoxyaniline.

Example 65

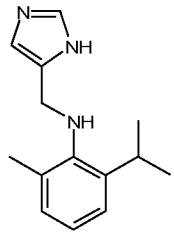
(3H-Imidazol-4-ylmethyl)-quinolin-6-yl-amine



The title compound, MS (ISP): 225.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 6-aminoquinoline instead of 2-methoxyaniline.

Example 66

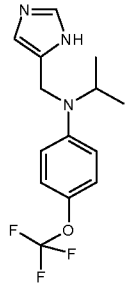
(3H-Imidazol-4-ylmethyl)-(2-isopropyl-6-methyl-phenyl)-amine



The title compound, MS (ISP): 230.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 2-isopropyl-6-methylaniline instead of 2-methoxyaniline.

Example 67

(3H-Imidazol-4-ylmethyl)-isopropyl-(4-trifluoromethoxy-phenyl)-amine



a) (3H-Imidazol-4-ylmethyl)-(4-trifluoromethoxy-phenyl)-amine

To a solution of 4-trifluoromethoxyaniline (0.89 g, 5 mmol) in methanol (5 ml) was added 4-formylimidazole (0.48 g, 5 mmol). After stirring the mixture overnight at 60°C the solution was cooled and sodium borohydride (0.28 g, 7.5 mmol) were added. The reaction mixture was stirred at room temperature for 4 hours. Then water was added and the mixture was extracted with ethyl acetate. The organic layer was separated, washed with water, dried over magnesium sulfate and evaporated. The residue was purified by

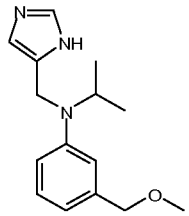
column filtration (heptane/ethyl acetate=1:1) to yield a light yellow liquid (1.0 g, 78%); MS (ISP): 258.1 ($(M+H)^{+\cdot}$).

b) (3H-Imidazol-4-ylmethyl)-isopropyl-(4-trifluoromethoxy-phenyl)-amine

To a solution of (3H-imidazol-4-ylmethyl)-(4-trifluoromethoxy-phenyl)-amine (0.39 g, 1.5 mmol) in 1,2-dichloroethane (5 ml) were added successively 2-methoxypropene (0.16g, 2.25 mmol), trifluoroacetic acid (0.26 g, 2.25 mmol) and sodium triacetoxyborohydride (0.48 g, 2.25 mmol). After stirring the mixture overnight at 60°C 1 M sodium hydroxide solution (5 ml) was added and the mixture was extracted with dichloromethane. The organic layer was washed with brine, dried over magnesium sulfate and evaporated. The residue was purified by column chromatography (heptane/ethyl acetate=1:1) to yield a white solid (0.24 g, 53%); MS (ISP): 300.1 ($(M+H)^{+\cdot}$).

Example 68

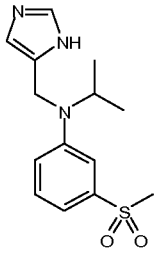
(3H-Imidazol-4-ylmethyl)-isopropyl-(3-methoxymethyl-phenyl)-amine



The title compound, MS (ISP): 260.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-methoxymethyl-aniline instead of 4-trifluoromethoxyaniline in step a).

Example 69

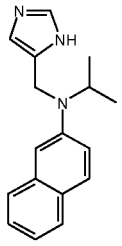
(3H-Imidazol-4-ylmethyl)-isopropyl-(3-methanesulfonyl-phenyl)-amine



The title compound, MS (ISP): 280.3 ($(M-CH_3)^{+\cdot}$); 294.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-methanesulfonyl-aniline instead of 4-trifluoromethoxyaniline in step a).

Example 70

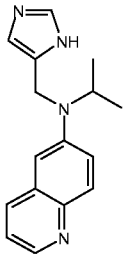
(3H-Imidazol-4-ylmethyl)-isopropyl-naphthalen-2-yl-amine



The title compound, MS (ISP): 266.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 2-aminonaphthaline instead of 4-trifluoromethoxyaniline in step a).

Example 71

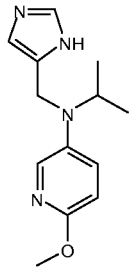
(3H-Imidazol-4-ylmethyl)-isopropyl-quinolin-6-yl-amine



The title compound, MS (ISP): 267.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 6-aminoquinoline instead of 4-trifluoromethoxyaniline in step a).

Example 72

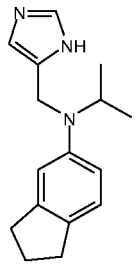
(3H-Imidazol-4-ylmethyl)-isopropyl-(6-methoxy-pyridin-3-yl)-amine



The title compound, MS (ISP): 247.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 5-amino-2-methoxypyridine instead of 4-trifluoromethoxyaniline in step a).

Example 73

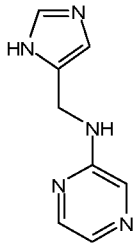
(3H-Imidazol-4-ylmethyl)-indan-5-yl-isopropyl-amine



The title compound, MS (ISP): 256.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using indan-5-ylamine instead of 4-trifluoromethoxyaniline in step a).

Example 74

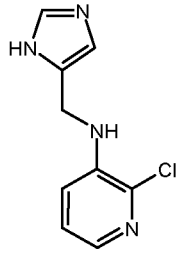
(3H-Imidazol-4-ylmethyl)-pyrazin-2-yl-amine



The title compound, MS (ISP): 176.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using pyrazin-2-ylamine instead of 2-methoxyaniline.

Example 75

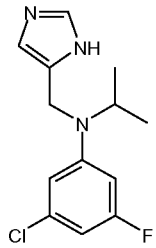
(2-Chloro-pyridin-3-yl)-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 208.8; 210.9 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 3-amino-2-chloro-pyridine instead of 2-methoxyaniline.

Example 76

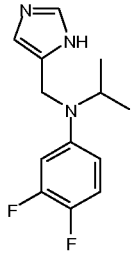
(3-Chloro-5-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 268.3, 270.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-chloro-5-fluoroaniline instead of 4-trifluoromethoxyaniline in step a).

Example 77

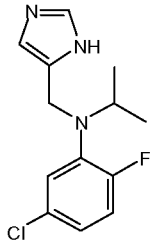
(3,4-Difluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 252.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3,4-difluoroaniline instead of 4-trifluoromethoxyaniline in step a).

Example 78

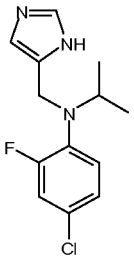
(5-Chloro-2-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 268.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 5-chloro-2-fluoroaniline instead of 4-trifluoromethoxyaniline in step a).

Example 79

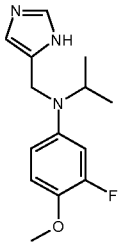
(4-Chloro-2-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 268.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 4-chloro-2-fluoroaniline instead of 4-trifluoromethoxyaniline in step a).

Example 80

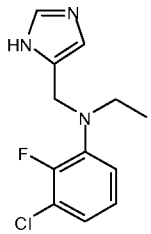
(3-Fluoro-4-methoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 264.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-fluoro-4-methoxyaniline instead of 4-trifluoromethoxyaniline in step a).

Example 81

(3-Chloro-2-fluoro-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine



a) (3-Chloro-2-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-amine

To a solution of 3-chloro-2-fluoroaniline (0.44 g, 3 mmol) in methanol (5 ml) was added 4-formylimidazole (0.29 g, 3 mmol). After stirring the mixture overnight at 60°C the solution was cooled and sodium borohydride (0.57 g, 15 mmol) was added. The reaction mixture was stirred at room temperature for 4 hours. Then water was added and the mixture was extracted with ethyl acetate. The organic layer was separated, washed with water, dried over magnesium sulfate and evaporated. The residue was purified by column

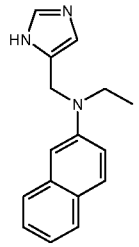
filtration (heptane/ethyl acetate=1:1) to yield a light yellow liquid (0.55 mg, 81%); MS (ISP): 226.3 ($(M+H)^{+\cdot}$).

b) (3-Chloro-2-fluoro-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine

(3-Chloro-2-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-amine (0.24 g, 1 mmol) was dissolved in methanol (15 ml). Then acetaldehyde (0.28 ml, 5 mmol), zinc chloride (0.55 g, 4 mmol) and sodium cyanoborohydride (0.19 g, 3 mmol) were added and the reaction mixture was allowed to stir at 40°C overnight. After cooling, the reaction mixture was poured onto ammoniumchloride/ice and extracted with ethyl acetate (2 times 50 ml). The organic layer was dried over magnesium sulfate and evaporated. The residue was purified using flash chromatography (SiO_2; eluent: heptane/ethyl acetate = 90:10) to yield a light yellow oil (0.16g, 63 %); MS (ISP): 254.1 ($(M+H)^{+\cdot}$).

Example 82

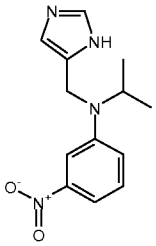
Ethyl-(3H-imidazol-4-ylmethyl)-naphthalen-2-yl-amine



The title compound, MS (ISP): 252.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 2-naphthylamine instead of 3-chloro-2-fluoroaniline in step a).

Example 83

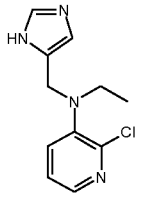
(3H-Imidazol-4-ylmethyl)-isopropyl-(3-nitro-phenyl)-amine



The title compound, MS (ISP): 261 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-nitronaniline instead of 4-trifluoromethoxyaniline in step a).

Example 84

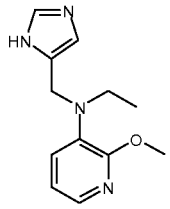
(2-Chloro-pyridin-3-yl)-ethyl-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 237.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 3-amino-2-chloropyridine instead of 3-chloro-2-fluoroaniline in step a).

Example 85

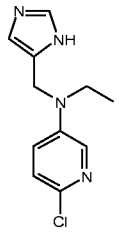
Ethyl-(3H-imidazol-4-ylmethyl)-(2-methoxy-pyridin-3-yl)-amine



The title compound, MS (ISP): 233.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 3-amino-2-methoxypyridine instead of 3-chloro-2-fluoroaniline in step a).

Example 86

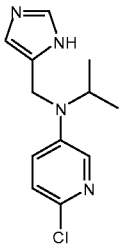
(6-Chloro-pyridin-3-yl)-ethyl-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 236.8; 238.9 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 5-amino-2-chloropyridine instead of 3-chloro-2-fluoroaniline in step a).

Example 87

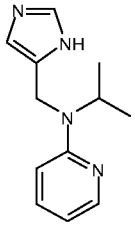
(6-Chloro-pyridin-3-yl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 250.9; 252.9 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 5-amino-2-chloropyridine instead of 4-trifluoromethoxyaniline in step a).

Example 88

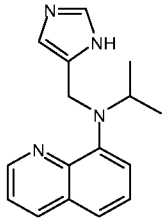
(3H-Imidazol-4-ylmethyl)-isopropyl-pyridin-2-yl-amine



The title compound, MS (ISP): 217.4 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 2-aminopyridine instead of 4-trifluoromethoxyaniline in step a).

Example 89

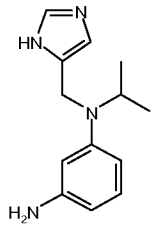
(3H-Imidazol-4-ylmethyl)-isopropyl-quinolin-8-yl-amine



The title compound, MS (ISP): 267.3 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 8-aminoquinoline instead of 4-trifluoromethoxyaniline in step a).

Example 90

N-(3H-Imidazol-4-ylmethyl)-N-isopropyl-benzene-1,3-diamine



a) Isopropyl-(3-nitro-phenyl)-[3-(2-trimethylsilanyl-ethoxymethyl)-3H-imidazol-4-ylmethyl]-amine

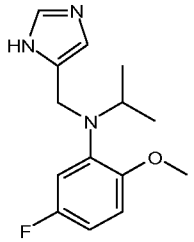
To sodium hydride (149 mg, 55% in mineral oil, 3.42 mmol) in tetrahydrofuran (240 ml) was added a solution of (3H-imidazol-4-ylmethyl)-isopropyl-(3-nitro-phenyl)-amine (685 mg, 2.63 mmol) in tetahydrofuran (100ml) and stirring was continued for 45 min at room temperature. The reaction mixture was cooled with an ice bath and 2-(trimethylsilyl)ethoxymethylchloride (439 mg, 2.63 mmol) was added. After stirring the suspension overnight the reaction was quenched with saturated sodium bicarbonate solution. Tetrahydrofuran was evaporated and the residue was extracted with ethyl acetate twice. The combined organic layers were washed with water, dried over magnesium sulphate and evaporated. The residue was purified using flash chromatography (SiO_2; eluent: heptane/ethyl acetate = 80:20) to yield a light yellow oil, (0.20 g, 20 %); MS (ISP): 391.3 ($(M+H)^{+\cdot}$).

b) N-(3H-Imidazol-4-ylmethyl)-N-isopropyl-benzene-1,3-diamine

Isopropyl-(3-nitro-phenyl)-[3-(2-trimethylsilanyl-ethoxymethyl)-3H-imidazol-4-ylmethyl]-amine (0.2 g, 0.51 mmol) was dissolved in ethanol, palladium on charcoal (20 mg, 10% Pd) was added and the mixture was hydrogenated overnight. The catalyst was filtered off and the solvent was evaporated. The residue was dissolved in ethyl acetate and filtered over silica gel. After evaporation the residue was dissolved in hydrochloric acid in ethanol (5M, 1 ml) and stirred at 60°C for 2 hours. The solvent was evaporated and the residue was partitioned between sodium hydroxide solution (10%) and dichloromethane. After separation the aqueous layer was extracted again with dichloromethane. The combined organic layers were dried over magnesium sulphate and evaporated. The residue was purified using flash chromatography (column: Isolute® Flash-NH_2 from Separtis; eluent: ethyl acetate/methanol = 90:10) to yield a light yellow gum, (0.054 g, 51 %); MS (ISP): 231.4 ($(M+H)^{+\cdot}$).

Example 91

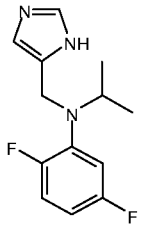
(5-Fluoro-2-methoxy-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 263.9 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 5-fluoro-2-methoxy-aniline instead of 4-trifluoromethoxyaniline in step a).

Example 92

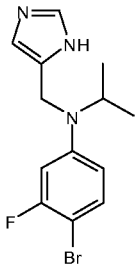
(2,5-Difluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 251.9 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 2,5-difluoroaniline instead of 4-trifluoromethoxyaniline in step a).

Example 93

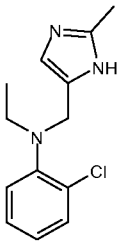
(4-Bromo-3-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 251.9 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 4-bromo-3-fluoroaniline instead of 4-trifluoromethoxyaniline in step a).

Example 94

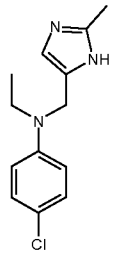
(2-Chloro-phenyl)-ethyl-(2-methyl-3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 250.3; 252.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 2-chloroaniline instead of 3-chloro-2-fluoroaniline and 4-formyl-2-methyl-imidazole instead of 4-formylimidazole in step a).

Example 95

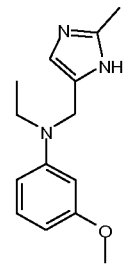
(4-Chloro-phenyl)-ethyl-(2-methyl-3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 250.1; 252.2 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 4-chloroaniline instead of 3-chloro-2-fluoroaniline and 4-formyl-2-methyl-imidazole instead of 4-formylimidazole in step a).

Example 96

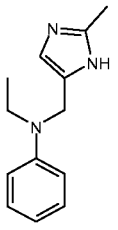
Ethyl-(3-methoxy-phenyl)-(2-methyl-3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 246.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 3-methoxyaniline instead of 3-chloro-2-fluoroaniline and 4-formyl-2-methyl-imidazole instead of 4-formylimidazole in step a).

Example 97

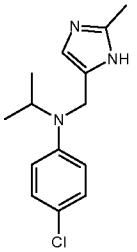
Ethyl-(2-methyl-3H-imidazol-4-ylmethyl)-phenyl-amine



The title compound, MS (ISP): 216.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using aniline instead of 3-chloro-2-fluoroaniline and 4-formyl-2-methyl-imidazole instead of 4-formylimidazole in step a).

Example 98

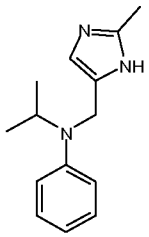
(4-Chloro-phenyl)-isopropyl-(2-methyl-3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 264.0 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 4-chloroaniline instead of 4-trifluoromethoxyaniline and 4-formyl-2-methyl-imidazole instead of 4-formylimidazole in step a).

Example 99

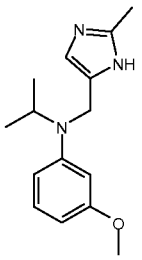
Isopropyl-(2-methyl-3H-imidazol-4-ylmethyl)-phenyl-amine



The title compound, MS (ISP): 230.3 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using aniline instead of 4-trifluoromethoxyaniline and 4-formyl-2-methyl-imidazole instead of 4-formylimidazole in step a).

Example 100

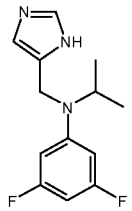
Isopropyl-(3-methoxy-phenyl)-(2-methyl-3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 260.3 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-methoxyaniline instead of 4-trifluoromethoxyaniline and 4-formyl-2-methyl-imidazole instead of 4-formylimidazole in step a).

Example 101

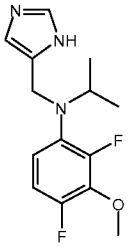
(3,5-Difluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 252.3 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3,5-difluoroaniline instead of 4-trifluoromethoxyaniline in step a).

Example 102

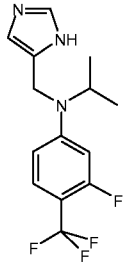
(2,4-Difluoro-3-methoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 282.4 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 2,4-difluoro-3-methoxyaniline instead of 4-trifluoromethoxyaniline in step a).

Example 103

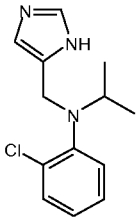
(3-Fluoro-4-trifluoromethyl-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 302.4 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-fluoro-4-trifluoromethyl-aniline instead of 4-trifluoromethoxyaniline in step a).

Example 104

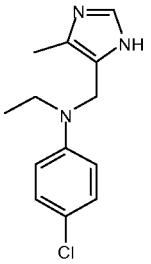
(2-Chloro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 250.1 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 2-chloroaniline instead of 4-trifluoromethoxyaniline in step a).

Example 105

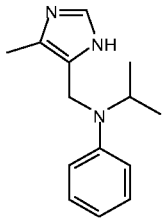
(4-Chloro-phenyl)-ethyl-(5-methyl-3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 249.9 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 81 using 4-chloroaniline instead of 3-chloro-2-fluoroaniline and 4-formyl-5-methyl-imidazole instead of 4-formylimidazole in step a).

Example 106

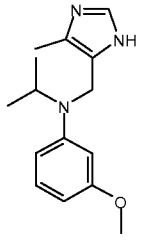
Isopropyl-(5-methyl-3H-imidazol-4-ylmethyl)-phenyl-amine



The title compound, MS (ISP): 230.0 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using aniline instead of 4-trifluoromethoxyaniline and 4-formyl-5-methyl-imidazole instead of 4-formylimidazole in step a).

Example 107

Isopropyl-(3-methoxy-phenyl)-(5-methyl-3H-imidazol-4-ylmethyl)-amine

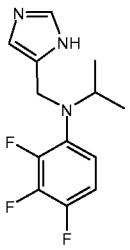


The title compound, MS (ISP): 260.0 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-methoxyaniline instead of 4-

trifluoromethoxyaniline and 4-formyl-5-methyl-imidazole instead of 4-formylimidazole in step a).

Example 108

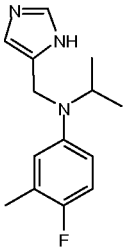
(3H-Imidazol-4-ylmethyl)-isopropyl-(2,3,4-trifluoro-phenyl)-amine



The title compound, MS (ISP): 270.4 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 2,3,4-trifluoroaniline instead of 4-trifluoromethoxyaniline in step a).

Example 109

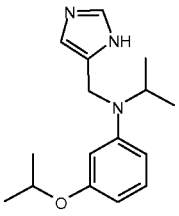
(4-Fluoro-3-methyl-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 248.2 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 4-trifluoro-3-methylaniline instead of 4-trifluoromethoxyaniline in step a).

Example 110

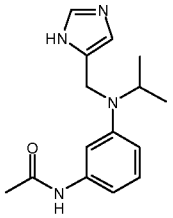
(3H-Imidazol-4-ylmethyl)-(3-isopropoxy-phenyl)-isopropyl-amine



The title compound, MS (ISP): 274.4 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-isopropoxyaniline instead of 4-trifluoromethoxyaniline in step a).

Example 111

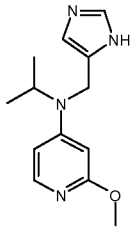
N-{3-[(3H-Imidazol-4-ylmethyl)-isopropyl-amino]-phenyl}-acetamide



Isopropyl-(3-nitro-phenyl)-[3-(2-trimethylsilanyl-ethoxymethyl)-3H-imidazol-4-ylmethyl]-amine (0.055 g, 0.14 mmol) was dissolved in ethanol, palladium on charcoal (20 mg, 10% Pd) was added and the mixture was hydrogenated overnight. The catalyst was filtered off and the solvent was evaporated. The residue was dissolved in ethyl acetate and filtered over silica gel. After evaporation the residue was dissolved in toluene (1.5 ml) and tetrahydrofuran (3 ml), acetic anhydride (0.015 mg, 0.14 mmol) was added and the mixture was stirred overnight. The solvents were evaporated and the residue was partitioned between sodium bicarbonate solution and ethyl acetate. The organic layer was dried over magnesium sulphate and evaporated. The residue was dissolved in tetrahydrofuran (5 ml) and tetrabutylammonium fluoride solution (0.3 ml, 1M) in tetrahydrofuran was added. After stirring the mixture at 65°C overnight the solvent was evaporated and the residue was purified by flash chromatography (column: Isolute® Flash-NH_2 from Separtis; eluent: ethyl acetate/methanol = 95:5) to yield a white gum, (0.005 g, 34 %); MS (ISP): 273.2 ($(M+H)^{+\cdot}$).

Example 112

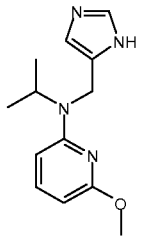
(3H-Imidazol-4-ylmethyl)-isopropyl-(2-methoxy-pyridin-4-yl)-amine



The title compound, MS (ISP): 247.3 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 4-amino-2-methoxypyridine instead of 4-trifluoromethoxyaniline in step a).

Example 113

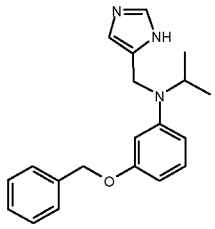
(3H-Imidazol-4-ylmethyl)-isopropyl-(6-methoxy-pyridin-2-yl)-amine



The title compound, MS (ISP): 247.3 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 2-amino-6-methoxypyridine instead of 4-trifluoromethoxyaniline in step a).

Example 114

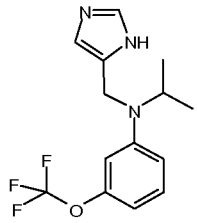
(3-Benzyloxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 322.3 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-benzyloxy-aniline instead of 4-trifluoromethoxyaniline in step a).

Example 115

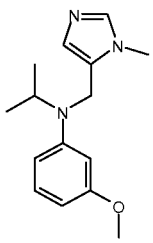
(3H-Imidazol-4-ylmethyl)-isopropyl-(3-trifluoromethoxy-phenyl)-amine



The title compound, MS (ISP): 300.1 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-trifluoromethoxyaniline instead of 4-trifluoromethoxyaniline in step a).

Example 116

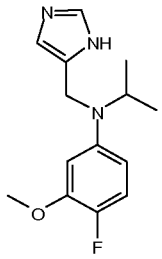
Isopropyl-(3-methoxy-phenyl)-(3-methyl-3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 260.0 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-methoxyaniline instead of 4-trifluoromethoxyaniline and 4-formyl-1-methyl-imidazole instead of 4-formylimidazole in step a).

Example 117

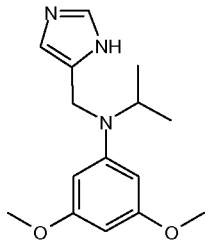
(4-Fluoro-3-methoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 264.0 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 4-fluoro-3-methoxyaniline instead of 4-trifluoromethoxyaniline in step a).

Example 118

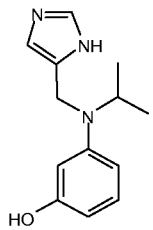
(3,5-Dimethoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 276.4 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3,5-dimethoxyaniline instead of 4-trifluoromethoxyaniline in step a).

Example 119

3-[(3H-Imidazol-4-ylmethyl)-isopropyl-amino]-phenol

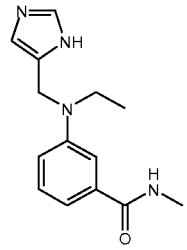


(3-Benzyloxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine (0.109 g, 0.34 mmol) was dissolved in ethanol (10 ml), palladium on charcoal (10 mg, 10% Pd) was added and the mixture was hydrogenated overnight at room temperature. The catalyst was filtered

off and the solvent was evaporated. The residue was purified by flash chromatography (column: Isolute® Flash-NH_2 from Separtis; eluent: ethyl acetate/methanol = 95:5) to yield a white foam, (0.042 g, 53 %); MS (ISP): 232.1 ($(M+H)^{+\cdot}$).

Example 120

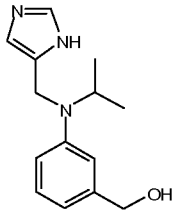
3-[Ethyl-(3H-imidazol-4-ylmethyl)-amino]-N-methyl-benzamide



The title compound, MS (ISP): 259.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 3-amino-benzoylmethylamide instead of 3-chloro-2-fluoroaniline in step a).

Example 121

{3-[(3H-Imidazol-4-ylmethyl)-isopropyl-amino]-phenyl}-methanol



a) [3-tert-Butyl-dimethyl-silanyloxymethyl]phenyl]-(3H-imidazol-4-ylmethyl)-isopropyl-amine

[3-tert-Butyl-dimethyl-silanyloxymethyl]phenyl]-(3H-imidazol-4-ylmethyl)-isopropyl-amine, MS (ISP): 228.4 ($(M-TBDMSO)^{+\cdot}$) , 360.5 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-(tert-butyl-dimethylsilanyloxymethyl)-phenylamine instead of 4-trifluoromethoxyaniline in step a).

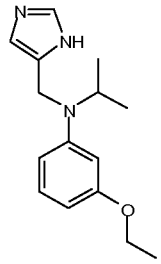
b) {3-[(3H-Imidazol-4-ylmethyl)-isopropyl-amino]-phenyl}-methanol

[3-tert-Butyl-dimethyl-silanyloxymethyl]phenyl]-(3H-imidazol-4-ylmethyl)-isopropyl-amine (0.724 g, 2 mmol) was dissolved in tetrahydrofuran (20 ml) and tetrabutylammonium fluoride solution (4 ml, 1M) in tetrahydrofuran was added. After stirring the mixture at room temperature overnight the solvent was evaporated and the

residue was purified by flash chromatography (SiO2, eluent: ethyl acetate) to yield a colourless gum, (0.252 g, 51 %); MS (ISP): 246.4 ($(M+H)^{+\cdot}$).

Example 122

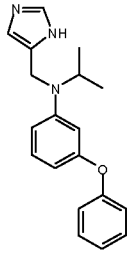
(3-Ethoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 260.1 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-ethoxyaniline instead of 4-trifluoromethoxyaniline in step a).

Example 123

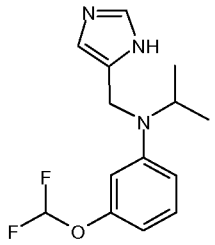
(3H-Imidazol-4-ylmethyl)-isopropyl-(3-phenoxy-phenyl)-amine



The title compound, MS (ISP): 308.4 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-phenoxyaniline instead of 4-trifluoromethoxyaniline in step a).

Example 124

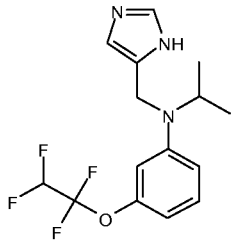
((3-Difluoromethoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 282.4 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-difluoromethoxyaniline instead of 4-trifluoromethoxyaniline in step a).

Example 125

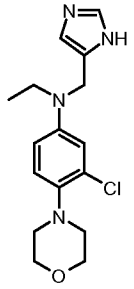
(3H-Imidazol-4-ylmethyl)-isopropyl-[3-(1,1,2,2-tetrafluoro-ethoxy)-phenyl]-amine



The title compound, MS (ISP): 332.3 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 1,1,2,2-tetrafluoro-ethoxy-aniline instead of 4-trifluoromethoxyaniline in step a).

Example 126

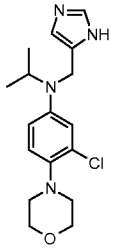
(3-Chloro-4-morpholin-4-yl-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 321.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 3-chloro-4-morpholin-4-yl-phenylamine instead of 3-chloro-2-fluoroaniline in step a).

Example 127

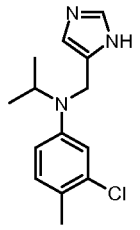
(3-Chloro-4-morpholin-4-yl-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 335.4 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-chloro-4-morpholin-4-yl-phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 128

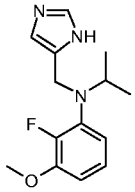
(3-Chloro-4-methyl-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 264.0 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-chloro-4-methylaniline instead of 4-trifluoromethoxyaniline in step a).

Example 129

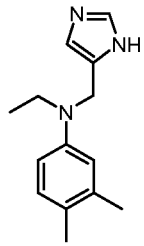
(2-Fluoro-3-methoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 264.0 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 2-fluoro-3-methoxy-aniline instead of 4-trifluoromethoxyaniline in step a).

Example 130

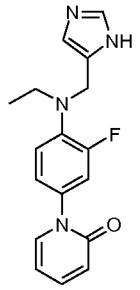
(3,4-Dimethyl-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 230.3 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 81 using 3,4-dimethylaniline instead of 3-chloro-2-fluoroaniline in step a).

Example 131

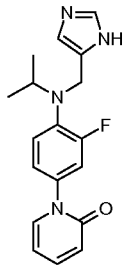
1-{4-[Ethyl-(1H-imidazol-4-ylmethyl)-amino]-3-fluoro-phenyl}-1H-pyridin-2-one



The title compound, MS (ISP): 313.3 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 81 using 1-(4-amino-3-fluoro-phenyl)-1H-pyridin-2-one instead of 3-chloro-2-fluoroaniline in step a).

Example 132

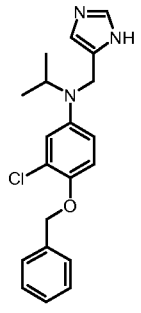
1-{3-Fluoro-4-[(1H-imidazol-4-ylmethyl)-isopropyl-amino]-phenyl}-1H-pyridin-2-one



The title compound, MS (ISP): 327.3 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 1-(4-amino-3-fluoro-phenyl)-1H-pyridin-2-one instead of 4-trifluoromethoxyaniline in step a).

Example 133

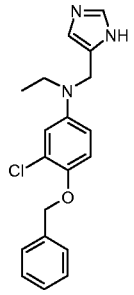
(4-Benzyloxy-3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 356.5 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 4-benzyloxy-3-chloroaniline instead of 4-trifluoromethoxyaniline in step a).

Example 134

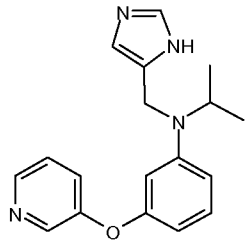
(4-Benzyloxy-3-chloro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 342.1 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 81 using 4-benzyloxy-3-chloroaniline instead of 3-chloro-2-fluoroaniline in step a).

Example 135

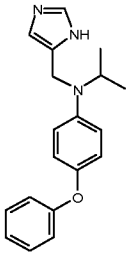
(3H-Imidazol-4-ylmethyl)-isopropyl-[3-(pyridin-3-yloxy)-phenyl]-amine



The title compound, MS (ISP): 309.6 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-(pyridine-3-yloxy)-phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 136

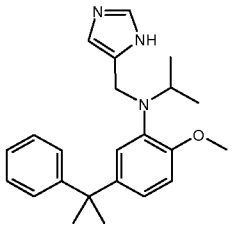
(3H-Imidazol-4-ylmethyl)-isopropyl-(4-phenoxy-phenyl)-amine



The title compound, MS (ISP): 308.3 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 4-phenoxyaniline instead of 4-trifluoromethoxyaniline in step a).

Example 137

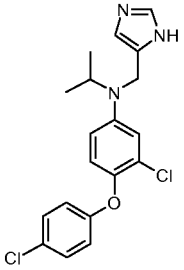
(3H-Imidazol-4-ylmethyl)-isopropyl-[2-methoxy-5-(1-methyl-1-phenyl-ethyl)-phenyl]-amine



The title compound, MS (ISP): 364.2 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 2-methoxy-5-(1-methyl-1-phenyl-ethyl)-phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 138

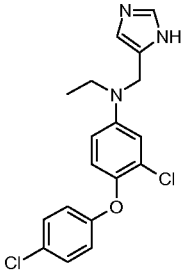
[3-Chloro-4-(4-chloro-phenoxy)-phenyl]-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 376.1 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-chloro-4-(4-chloro-phenoxy)-phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 139

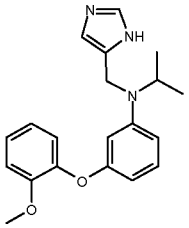
[3-Chloro-4-(4-chloro-phenoxy)-phenyl]-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 362.3 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 81 using 3-chloro-4-(4-chloro-phenoxy)-phenylamine instead of 3-chloro-2-fluoroaniline in step a).

Example 140

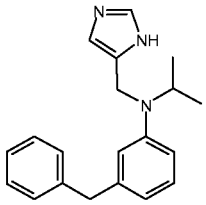
(3H-Imidazol-4-ylmethyl)-isopropyl-[3-(2-methoxy-phenoxy)-phenyl]-amine



The title compound, MS (ISP): 338.4 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-(2-methoxy-phenoxy)-phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 141

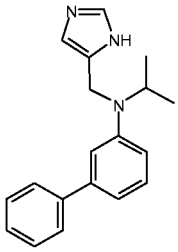
(3-Benzyl-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 306.4 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-benzylaniline instead of 4-trifluoromethoxyaniline in step a).

Example 142

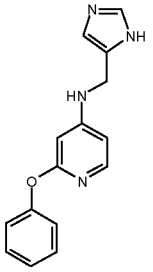
Biphenyl-3-yl-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 292.4 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-aminobiphenyl instead of 4-trifluoromethoxyaniline in step a).

Example 143

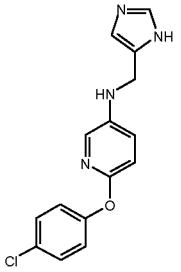
(3H-Imidazol-4-ylmethyl)-(2-phenoxy-pyridin-4-yl)-amine



The title compound, MS (ISP): 267.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using 2-phenoxy-pyridin-4-yl-amine instead of N-ethylaniline.

Example 144

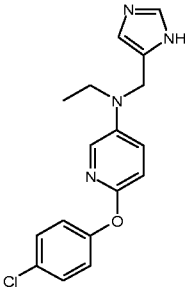
[6-(4-Chloro-phenoxy)-pyridin-3-yl]-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 301.1; 303.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using 6-(4-chloro-phenoxy-pyridin-3-yl-amine instead of N-ethylaniline.

Example 145

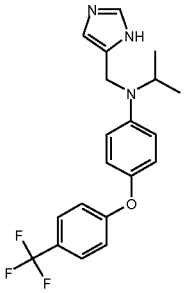
[6-(4-Chloro-phenoxy)-pyridin-3-yl]-ethyl-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 329.1; 331.1 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 81 using 6-(4-chloro-phenoxy-pyridin-3-yl-amine instead of 3-chloro-2-fluoroaniline in step a).

Example 146

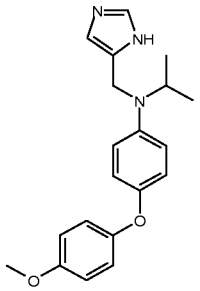
(3H-Imidazol-4-ylmethyl)-isopropyl-[4-(4-trifluoromethyl-phenoxy)-phenyl]-amine



The title compound, MS (ISP): 376.3 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 4-(4-trifluoromethoxy-phenoxy)-aniline instead of 4-trifluoromethoxyaniline in step a).

Example 147

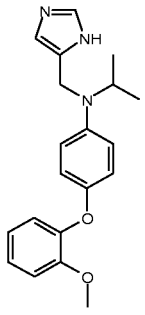
(3H-Imidazol-4-ylmethyl)-isopropyl-[4-(4-methoxy-phenoxy)-phenyl]-amine



The title compound, MS (ISP): 338.5 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 4-(4-methoxy-phenoxy)-aniline instead of 4-trifluoromethoxyaniline in step a).

Example 148

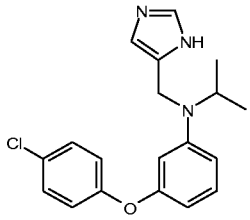
(3H-Imidazol-4-ylmethyl)-isopropyl-[4-(2-methoxy-phenoxy)-phenyl]-amine



The title compound, MS (ISP): 338.4 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 4-(2-methoxy-phenoxy)-aniline instead of 4-trifluoromethoxyaniline in step a).

Example 149

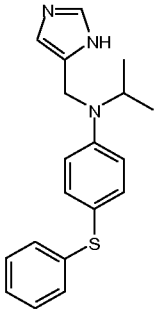
[3-(4-Chloro-phenoxy)-phenyl]-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 342.1 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-(4-chloro-phenoxy)-aniline instead of 4-trifluoromethoxyaniline in step a).

Example 150

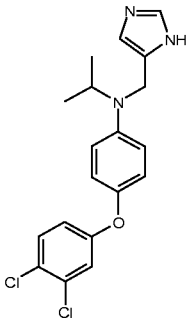
(3H-Imidazol-4-ylmethyl)-isopropyl-(4-phenylsulfanyl-phenyl)-amine



The title compound, MS (ISP): 324.5 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 4-phenylsulfanyl-phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 151

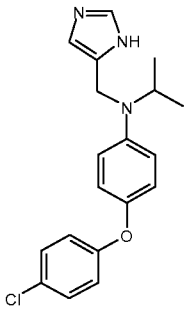
[4-(3,4-Dichloro-phenoxy)-phenyl]-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 376.2; 378.1 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 4-(3,4-dichloro-phenoxy)-phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 152

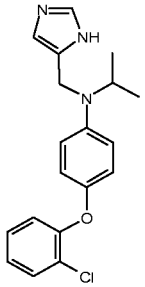
[4-(4-Chloro-phenoxy)-phenyl]-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 342.0 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 4-(4-chloro-phenoxy)-phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 153

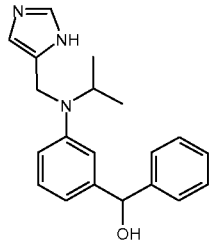
[4-(2-Chloro-phenoxy)-phenyl]-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 342.1 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 4-(2-chloro-phenoxy)-phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 154

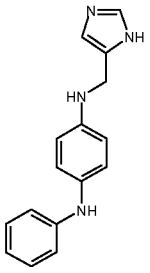
{3-[(3H-Imidazol-4-ylmethyl)-isopropyl-amino]-phenyl}-phenyl-methanol



The title compound, MS (ISP): 322.4 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-amino-benzophenone instead of 4-trifluoromethoxyaniline in step a).

Example 155

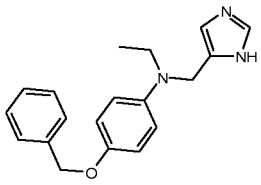
N-(1H-Imidazol-4-ylmethyl)-N'-phenyl-benzene-1,4-diamine



The title compound, MS (ISP): 265.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81.a) using 4-aminodiphenylamine instead of 3-chloro-2-fluoroaniline.

Example 156

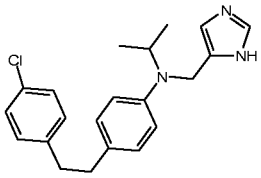
(4-Benzyloxy-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 308.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 4-benzyloxyaniline instead of 3-chloro-2-fluoroaniline in step a).

Example 157

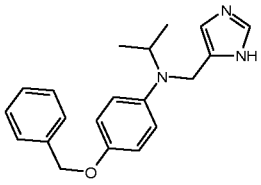
{4-[2-(4-Chloro-phenyl)-ethyl]-phenyl}-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 354.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 4-[2-(4-chloro-phenyl)-ethyl]-phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 158

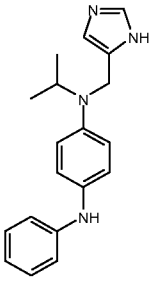
(4-Benzyloxy-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 322.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 4-benzyloxyaniline instead of 4-trifluoromethoxyaniline in step a).

Example 159

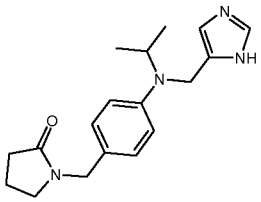
N-(1H-Imidazol-4-ylmethyl)-N-isopropyl-N-phenyl-benzene-1,4-diamine



The title compound, MS (ISP): 307.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 4-aminodiphenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 160

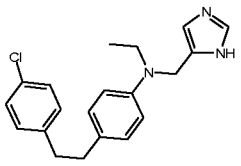
1-{4-[(1H-Imidazol-4-ylmethyl)-isopropyl-amino]-benzyl}-pyrrolidin-2-one



The title compound, MS (ISP): 313.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 1-(4-amino-benzyl)-pyrrolidin-2-one instead of 4-trifluoromethoxyaniline in step a).

Example 161

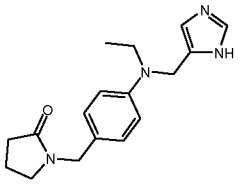
{4-[2-(4-Chloro-phenyl)-ethyl]-phenyl}-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 304.5 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 4-[2-(4-chloro-phenyl)-ethyl]-phenylamine instead of 3-chloro-2-fluoroaniline in step a).

Example 162

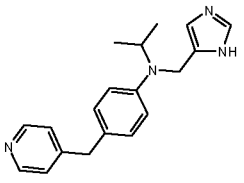
1-{4-[Ethyl-(1H-imidazol-4-ylmethyl)-amino]-benzyl}-pyrrolidin-2-one



The title compound, MS (ISP): 299.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 1-(4-amino-benzyl)-pyrrolidin-2-one instead of 3-chloro-2-fluoroaniline in step a).

Example 163

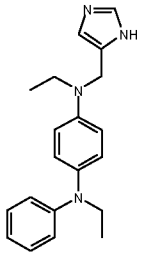
(1H-Imidazol-4-ylmethyl)-isopropyl-(4-pyridin-4-ylmethyl-phenyl)-amine



The title compound, MS (ISP): 307.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 4-pyridin-4-ylmethyl-phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 164

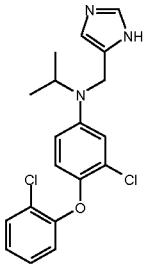
N,N'-Diethyl-N-(1H-imidazol-4-ylmethyl)-N'-phenyl-benzene-1,4-diamine



The title compound, MS (ISP): 321.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 4-aminodiphenylamine instead of 3-chloro-2-fluoroaniline in step a).

Example 165

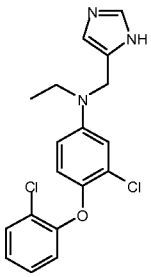
[3-Chloro-4-(2-chloro-phenoxy)-phenyl]-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 376.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-chloro-4-(2-chloro-phenoxy)-phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 166

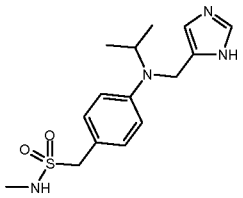
[3-Chloro-4-(2-chloro-phenoxy)-phenyl]-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 362.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 3-chloro-4-(2-chloro-phenoxy)-phenylamine instead of 3-chloro-2-fluoroaniline in step a).

Example 167

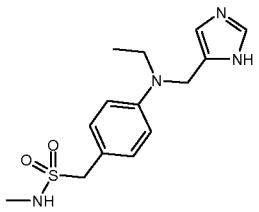
C-{4-[(1H-Imidazol-4-ylmethyl)-isopropyl-amino]-phenyl}-N-methyl-methanesulfonamide



The title compound, MS (ISP): 323.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using C-(4-amino-phenyl)-N-methyl-methanesulfonamide instead of 4-trifluoromethoxyaniline in step a).

Example 168

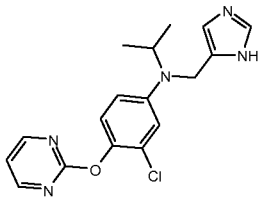
C-{4-[Ethyl-(1H-imidazol-4-ylmethyl)-amino]-phenyl}-N-methyl-methanesulfonamide



The title compound, MS (ISP): 309.5 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using C-(4-amino-phenyl)-N-methyl-methanesulfonamide instead of 3-chloro-2-fluoroaniline in step a).

Example 169

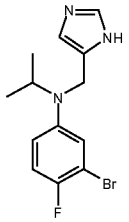
[3-Chloro-4-(pyrimidin-2-yloxy)-phenyl]-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 344.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-chloro-4-(2-pyrimidinyloxy)phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 170

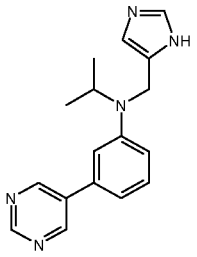
(3-Bromo-4-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 311.9; 314.0 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-bromo-4-fluoroaniline instead of 4-trifluoromethoxyaniline in step a).

Example 171

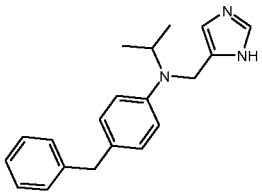
(3H-Imidazol-4-ylmethyl)-isopropyl-(3-pyrimidin-5-yl-phenyl)-amine



The title compound, MS (ISP): 294.2 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 67 using 3-pyrimidin-5-yl-phenyl-amine instead of 4-trifluoromethoxyaniline in step a).

Example 172

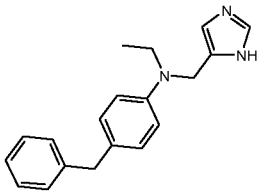
(4-Benzyl-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 306.5 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 4-benzylaniline instead of 4-trifluoromethoxyaniline in step a).

Example 173

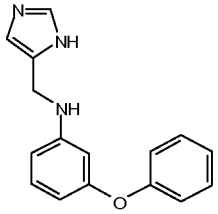
(4-Benzyl-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 292.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 4-benzylaniline instead of 3-chloro-2-fluoroaniline in step a).

Example 174

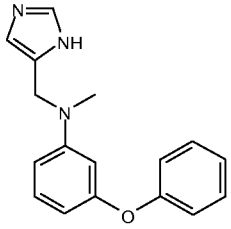
(3H-Imidazol-4-ylmethyl)-(3-phenoxy-phenyl)-amine



The title compound, MS (ISP): 266.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 3-phenoxy-aniline instead of 2-methoxyaniline.

Example 175

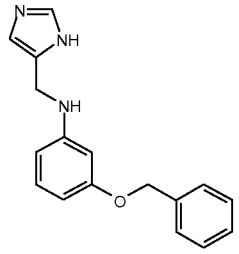
(3H-Imidazol-4-ylmethyl)-methyl-(3-phenoxy-phenyl)-amine



The title compound, MS (ISP): 280.5 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 81 using 3-phenoxyaniline instead of 3-chloro-2-fluoroaniline in step a) and formaldehyde instead of acetaldehyde in step b).

Example 176

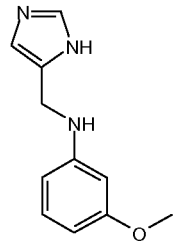
(3-Benzyloxy-phenyl)-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 280.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 3-benzyloxy-aniline instead of 2-methoxyaniline.

Example 177

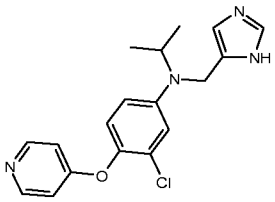
(3H-Imidazol-4-ylmethyl)-(3-methoxy-phenyl)-amine



The title compound, MS (ISP): 204.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 3-methoxy-aniline instead of 2-methoxyaniline.

Example 178

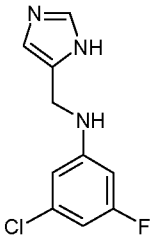
[3-Chloro-4-(pyridin-4-yloxy)-phenyl]-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 343.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-chloro-4-(pyridin-4-yloxy)-phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 179

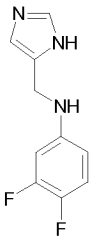
(3-Chloro-5-fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 228.1 ($[^{37}Cl\ M+H]^{+\cdot}$), 226.1 ($[^{35}Cl\ M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 63 using 3-chloro-5-fluoro-aniline instead of 2-methoxyaniline.

Example 180

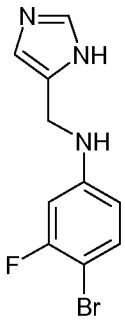
(3,4-Difluoro-phenyl)-(1H-imidazol-4-ylmethyl)-amine



To a solution of 3,4-difluoroaniline (0.60 g, 4.65 mmol) in 1,2-dichloroethane (5 ml) were added 4-formylimidazole (0.67 g, 6.97 mmol), sodium triacetoxyborohydride (1.97 g, 9.29 mmol) and acetic acid (0.05 ml). The reaction mixture was stirred at 50 °C for 4 h. The reaction mixture was then concentrated *in vacuo* and the residue was purified using flash chromatography (column: Isolute® Flash-NH_2 (Separtis); eluent: methanol/dichloromethane gradient) to yield an off-white solid (284 mg, 29%); MS (ISP): 210.1 ($(M+H)^{+\cdot}$).

Example 181

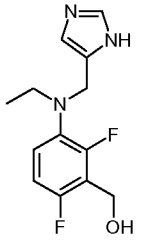
(4-Bromo-3-fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 272.1 ([^{81}Br M+H]$^+$), 270.1 ([^{79}Br M+H]$^+$), was obtained in comparable yield analogous to the procedure described for Example 180 using 4-bromo-3-fluoro-aniline instead of 3,4-difluoro-aniline.

Example 182

{3-[Ethyl-(3H-imidazol-4-ylmethyl)-amino]-2,6-difluoro-phenyl}-methanol



a) 5-[(3-[1,3]Dioxolan-2-yl-2,4-difluoro-phenylamino)-methyl]-imidazole-1-sulfonic acid dimethylamide.

To a stirred solution of 3-[1,3]dioxolan-2-yl-2,4-difluoro-phenylamine (0.41 g, 1.94 mmol) in methanol (10 ml) was added 4-formyl-imidazole-1-sulfonic acid dimethylamide (0.46 g, 2.24 mmol) and the mixture was heatde at 60 °C for 18 h. After cooling to room temperature sodium borohydride (0.39 g, 10.3 mmol) was added and the mixture stirred at room temperature for 2 h. The mixture was concentrated *in vacuo* and the residue was purified by flash chromatography (column: Isolute® Flash-NH_2 (Separtis); eluent: ethyl acetate/cyclohexane gradient) to yield a light brown gum (604 mg, 76%); MS (ISP): 389.1 ($(M+H)^{+\cdot}$).

b) 5-[(3-[1,3]Dioxolan-2-yl-2,4-difluoro-phenylamino)-methyl]-imidazole-1-sulfonic acid dimethylamide.

To a stirred solution of 5-[(3-[1,3]dioxolan-2-yl-2,4-difluoro-phenylamino)-methyl]-imidazole-1-sulfonic acid dimethylamide (0.60 g, 1.53 mmol) in methanol (20 ml) were added acetaldehyde (0.43 ml, 7.61 mmol), zinc chloride (6.13 mmol) and sodium cyanoborohydride (0.29 g, 4.60 mmol) and the mixture was heated at 40 °C for 18 h. The mixture was then concentrated *in vacuo* and the residue taken up in ethyl acetate and washed with saturated aq. ammonium chloride solution. The layers were separated and the aqueous phase was back extracted twice with ethyl acetate. The combined organic phases were washed sequentially with water and with saturated brine, then dried over magensium sulfate and concentrated *in vacuo*. The residue was purified by flash chromatography (column: Isolute® Flash-NH_2 (Separtis); eluent: ethyl

acetate/cyclohexane gradient) to yield a colourless viscous oil (538 mg, 84%); MS (ISP): 417.3 ($(M+H)^{+\cdot}$).

c) (3-[1,3]Dioxolan-2-yl-2,4-difluoro-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine.

To a stirred solution of 5-[(3-[1,3]dioxolan-2-yl-2,4-difluoro-phenylamino)-methyl]-imidazole-1-sulfonic acid dimethylamide (0.53 g, 1.27 mmol) in tetrahydrofuran (10 ml) was added a 4 N solution of hydrogen chloride in dioxane (3.87 ml, 15.5 mmol) and the mixture was stirred at room temperature for 24 h. The mixture was then concentrated *in vacuo* and the residue taken up in dichloromethane/methanol (95:5) and washed with 1 N aq. sodium hydroxide solution. The layers were separated and the aqueous phase was back extracted twice with dichloromethane/methanol (95:5). The combined organic phases were washed with saturated brine, then dried over magensium sulfate and concentrated *in vacuo*. The residue was purified by flash chromatography (column: Isolute® Flash-NH_2 (Separtis); eluent: methanol/dichloromethane gradient) to yield a colourless gum (225 mg, 57%); MS (ISP): 310.3 ($(M+H)^{+\cdot}$).

d) 3-[Ethyl-(3H-imidazol-4-ylmethyl)-amino]-2,6-difluoro-benzaldehyde.

To a stirred solution of (3-[1,3]dioxolan-2-yl-2,4-difluoro-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine (0.22 g, 0.70 mmol) in tetrahydrofuran (5 ml) was added a 3 N aqueous solution of hydrochloric acid (0.93 ml, 2.79 mmol) and the mixture was stirred at room temperature for 48 h. The mixture was then concentrated *in vacuo* and the residue taken up in ethyl acetate and washed with 1 N aq. sodium hydroxide solution. The layers were separated and the aqueous phase was back extracted twice with ethyl acetate. The combined organic phases were washed with saturated brine, then dried over magensium sulfate and concentrated *in vacuo*. The residue was purified by flash chromatography (column: Isolute® Flash-NH_2 (Separtis); eluent: methanol/dichloromethane gradient) to yield a yellow gum (111 mg, 48%); MS (ISP): 266.0 ($(M+H)^{+\cdot}$).

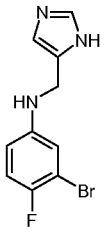
e) {3-[Ethyl-(3H-imidazol-4-ylmethyl)-amino]-2,6-difluoro-phenyl}-methanol.

To a stirred solution of 3-[ethyl-(3H-imidazol-4-ylmethyl)-amino]-2,6-difluoro-benzaldehyde (0.10 g, 0.39 mmol) in methanol (3 ml) was added sodium borohydride (0.06 g, 1.56 mmol) and the mixture was stirred at room temperature for 5 h. The mixture was concentrated *in vacuo* and the residue was purified by flash chromatography

(column: Isolute® Flash-NH_2 (Separtis); eluent: methanol/dichloromethane gradient) to yield a colourless gum (604 mg, 76%); MS (ISP): 268.3 ($(M+H)^{+\cdot}$).

Example 183

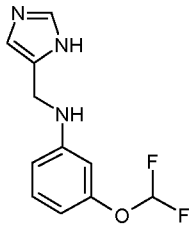
(3-Bromo-4-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 272.1 ($[^{81}Br\ M+H]^+$), 270.1 ($[^{79}Br\ M+H]^+$), was obtained in comparable yield analogous to the procedure described for Example 180 using 3-bromo-4-fluoro-aniline instead of 3,4-difluoro-aniline.

Example 184

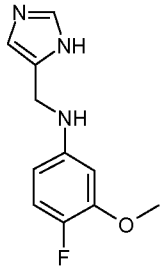
(3-Difluoromethoxy-phenyl)-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 240.1 ($[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 63 using 3-(difluoromethoxy)-aniline instead of 2-methoxyaniline.

Example 185

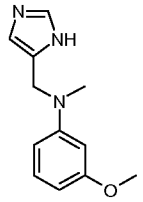
(4-Fluoro-3-methoxy-phenyl)-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 222.1 ($[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 63 using 4-fluoro-3-methoxy-aniline instead of 2-methoxyaniline.

Example 186

(3H-Imidazol-4-ylmethyl)-(3-methoxy-phenyl)-methyl-amine



a) (3H-Imidazol-4-ylmethyl)-(3-methoxy-phenyl)-amine

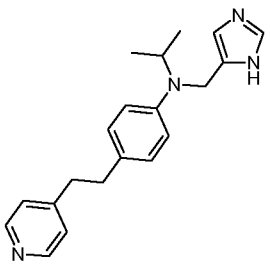
To a solution of m-anisidine (0.91 ml, 8.12 mmol) in methanol (25 ml) was added 4-formylimidazole (0.86 g, 8.93 mmol). After stirring the mixture overnight at room temperature sodium borohydride (0.46 g, 12.2 mmol) was added. The reaction mixture was then concentrated *in vacuo*. The residue was purified using flash chromatography (column: Isolute® Flash-NH_2 from Separtis; eluent: methanol/dichloromethane 9:1) to yield a white solid (1.34 g, 18 %); MS (ISP): 204.1 ($[M+H]^+$).

b) (3H-Imidazol-4-ylmethyl)-(3-methoxy-phenyl)-methyl-amine

(3H-Imidazol-4-ylmethyl)-(3-methoxy-phenyl)-amine (0.070 g, 0.34 mmol) was dissolved in acetonitrile (10 ml). Then formaldehyde (0.0.06 ml, 0.86 mmol, 37% aqueous solution) and sodium cyanoborohydride (0.065 g, 1.03 mmol) were added and the reaction mixture was allowed to stir at room temperature for 10 minutes. The reaction mixture was then acidified to pH 2-3 by dropwise addition of concentrated hydrochloric acid whereupon precipitation occurred. The mixture was stirred for a further 1 h at room temperature before being concentrated *in vacuo*. The residue was taken up in ethyl acetate, washed with 1 M aqueous sodium hydroxide solution and the organic layer was dried over magnesium sulfate and concentrated *in vacuo*. The residue was purified using flash chromatography (column: Isolute® Flash-NH_2 from Separtis; eluent: methanol/dichloromethane gradient) to yield a white solid (0.056 g, 75 %); MS (ISP): 218.3 ($[M+H]^+$).

Example 187

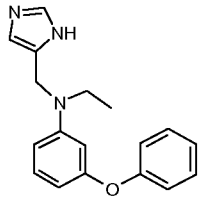
(1H-Imidazol-4-ylmethyl)-isopropyl-[4-(2-pyridin-4-yl-ethyl)-phenyl]-amine



The title compound, MS (ISP): 321.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 4-(2-pyridin-4-yl-ethyl)-phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 188

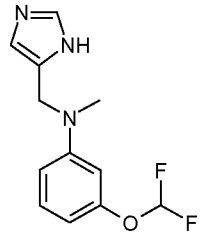
Ethyl-(3H-imidazol-4-ylmethyl)-(3-phenoxy-phenyl)-amine



The title compound, MS (ISP): 294.1 ($[M+H]^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 3-phenoxyaniline instead of 3-chloro-2-fluoroaniline in step a).

Example 189

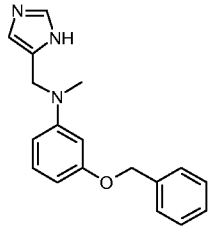
(3-Difluoromethoxy-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 254.3 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 186 using 3-(difluoromethoxy)aniline instead of m-anisidine in step a).

Example 190

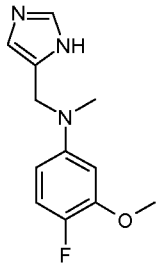
(3-Benzyloxy-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 294.1 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 186 using 3-benzyloxyaniline instead of m-anisidine in step a).

Example 191

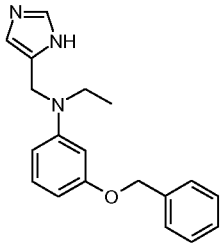
(4-Fluoro-3-methoxy-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 236.1 ($(M+H)^{+\cdot}$) was obtained analogous to the procedure described for Example 186 using 4-fluoro-3-methoxyaniline instead of m-anisidine in step a).

Example 192

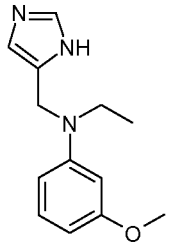
(3-Benzyloxy-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 308.4 ($[M+H]^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 3-benzyloxyaniline instead of 3-chloro-2-fluoroaniline in step a).

Example 193

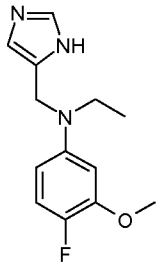
Ethyl-(3H-imidazol-4-ylmethyl)-(3-methoxy-phenyl)-amine



The title compound, MS (ISP): 232.1 ($[M+H]^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 3-methoxyaniline instead of 3-chloro-2-fluoroaniline in step a).

Example 194

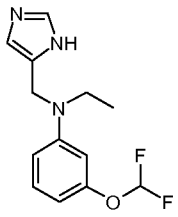
Ethyl-(4-fluoro-3-methoxy-phenyl)-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 250.1 ($[M+H]^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 4-fluoro-3-methoxyaniline instead of 3-chloro-2-fluoroaniline in step a).

Example 195

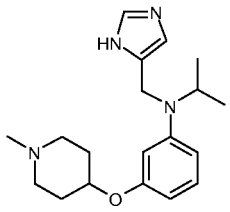
(3-Difluoromethoxy-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 268.3 ($[M+H]^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 3-(difluoromethoxy)aniline instead of 3-chloro-2-fluoroaniline in step a).

Example 196

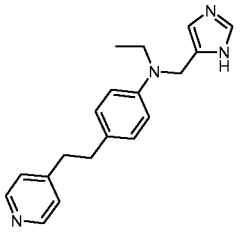
(3H-Imidazol-4-ylmethyl)-isopropyl-[3-(1-methyl-piperidin-4-yloxy)-phenyl]-amine



The title compound, MS (ISP): 459.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-[(1-methyl-4-(piperidinyl)oxy)]-phenylamine instead of 4-trifluormethoxyaniline in step a).

Example 197

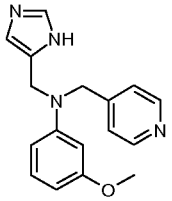
Ethyl-(1H-imidazol-4-ylmethyl)-[4-(2-pyridin-4-yl-ethyl)-phenyl]-amine



The title compound, MS (ISP): 307.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using using 4-(2-pyridin-4-yl-ethyl)-phenylamine instead of 3-chloro-2-fluoroaniline in step a).

Example 198

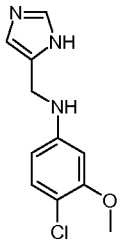
(3H-Imidazol-4-ylmethyl)-(3-methoxy-phenyl)-pyridin-4-ylmethyl-amine



To a solution of (3H-imidazol-4-ylmethyl)-(3-methoxy-phenyl)-amine (0.05 g, 0.25 mmol, Example 186 step a) in 1,2-dichloroethane (2 ml) were added pyridine-4-carbaldehyde (0.06 ml, 0.64 mmol) and sodium triacetoxyborohydride (0.21 g, 0.98 mmol). The reaction mixture was stirred at 40 °C for 72 h. The reaction mixture was then concentrated *in vacuo* and the residue was purified using flash chromatography (column: Isolute® Flash-NH_2 (Separtis); eluent: methanol/dichloromethane gradient) to yield a yellow oil (7 mg, 10%); MS (ISP): 295.3 ($(M+H)^{+\cdot}$).

Example 199

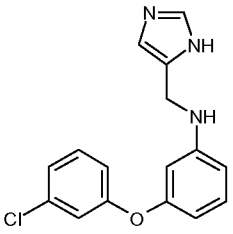
(4-Chloro-3-methoxy-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 240.1 ($[^{37}Cl\ M+H]^+$), 238.1 ($[^{35}Cl\ M+H]^+$), was obtained in comparable yield analogous to the procedure described for Example 180 using 4-chloro-3-methoxy-aniline instead of 3,4-difluoro-aniline.

Example 200

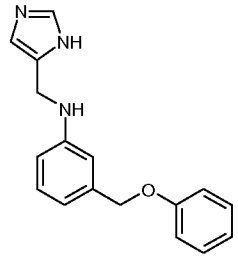
[3-(3-Chloro-phenoxy)-phenyl]-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 300.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 3-chloro-phenoxy-aniline instead of 2-methoxyaniline.

Example 201

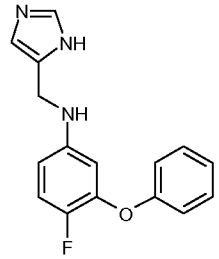
(3H-Imidazol-4-ylmethyl)-(3-phenoxymethyl-phenyl)-amine



The title compound, MS (ISP): 280.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 3-phenoxymethyl-aniline instead of 2-methoxyaniline.

Example 202

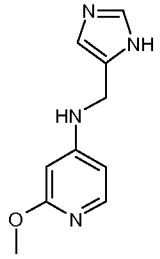
(4-Fluoro-3-phenoxy-phenyl)-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 284.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 4-fluoro-3-phenoxy-aniline instead of 2-methoxyaniline.

Example 203

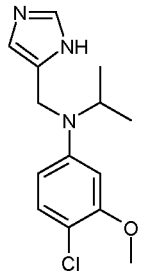
(3H-Imidazol-4-ylmethyl)-(2-methoxy-pyridin-4-yl)-amine



The title compound, MS (ISP): 205.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 4-amino-2-methoxypyridine instead of 2-methoxyaniline.

Example 204

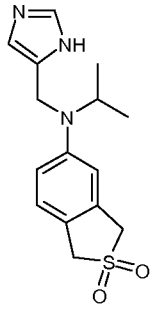
(4-Chloro-3-methoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 280.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 4-chloro-3-methoxy-phenylamine instead of 4-trifluormethoxyaniline in step a).

Example 205

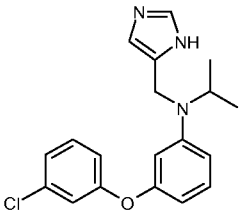
(2,2-Dioxo-2,3-dihydro-1H-benzo[c]thiophen-5-yl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 306.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 5-amino-1,3-dihydrobenzo[c]thiophene 2,2-dioxide instead of 4-trifluormethoxyaniline in step a).

Example 206

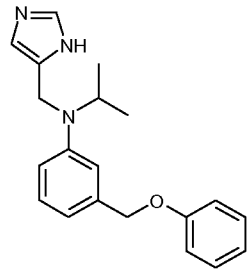
[3-(3-Chloro-phenoxy)-phenyl]-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 342.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-(3-chloro-phenoxy)-phenylamine instead of 4-trifluormethoxyaniline in step a).

Example 207

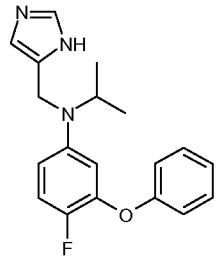
(3H-Imidazol-4-ylmethyl)-isopropyl-(3-phenoxymethyl-phenyl)-amine



The title compound, MS (ISP): 322.5 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-phenoxymethyl-phenylamine instead of 4-trifluormethoxyaniline in step a).

Example 208

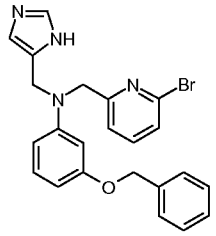
(4-Fluoro-3-phenoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 326.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 4-fluoro-3-phenoxy-phenylamine instead of 4-trifluormethoxyaniline in step a).

Example 209

(3-Benzyloxy-phenyl)-(6-bromo-pyridin-2-ylmethyl)-(3H-imidazol-4-ylmethyl)-amine



a) (3-Benzyloxy-phenyl)-(6-bromo-pyridin-2-ylmethyl)-amine

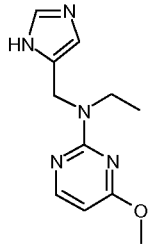
To a solution of 3-benzyloxyaniline (0.70 g, 3.51 mmol) in 1,2-dichloroethane (10 ml) were added 6-bromo-pyridine-2-carboxaldehyde (0.65 g, 3.51 mmol), sodium triacetoxyborohydride (1.49 g, 7.03 mmol) and acetic acid (0.80 ml, 14.1 mmol). The reaction mixture was shaken at 40 °C overnight. For work-up dichloromethane (100 ml) and 1M sodium bicarbonate solution (40 ml) were added and the mixture was shaken. The organic layer was separated, dried over magnesium sulfate and evaporated. The residue was purified using flash chromatography (heptane/ethyl acetate = 3:1) to yield an orange oil (1.03 g, 80%); MS (ISP): 371.1 ($[^{81}Br\ M+H]^+$), 369.1 ($[^{79}Br\ M+H]^+$).

b) (3-Benzyloxy-phenyl)-(6-bromo-pyridin-2-ylmethyl)-(3H-imidazol-4-ylmethyl)-amine

(3-Benzyloxy-phenyl)-(6-bromo-pyridin-2-ylmethyl)-amine (0.10 g, 0.27 mmol) was dissolved in methanol (2 ml). Then 4-formylimidazole (0.13 g, 1.35 mmol), zinc chloride (0.15 g, 1.08 mmol) and sodium cyanoborohydride (0.05 g, 0.81 mmol) were added and the reaction mixture was allowed to stir at 40 °C overnight. After cooling, the reaction mixture was poured onto ammoniumchloride/ice and extracted with ethyl acetate (2 times 50 ml). The organic layer was dried over magnesium sulfate and evaporated. The residue was purified using flash chromatography (SiO_2; eluent: methanol/dichloromethane= 1:9) to yield an off-white gum (0.11 g, 94 %); MS (ISP): 451.1 ($[^{81}Br\ M+H]^+$), 449.1 ($[^{79}Br\ M+H]^+$).

Example 210

Ethyl-(3H-imidazol-4-ylmethyl)-(4-methoxy-pyrimidin-2-yl)-amine



a) 5-Ethylaminomethyl-imidazole-1-sulfonic acid dimethylamide

To a saturated solution of ethylamine in methanol (40 ml) was added 4-formyl-imidazole-1-sulfonic acid dimethylamide (2.5 g, 12.3 mmol) and the mixture was stirred overnight. Sodium borohydride (0.70 g, 18.5 mmol) was added and the mixture was stirred at room temperature for 3 h. Water was added and the solution was extracted three times with ethyl acetate. The combined organic layers were dried over magnesium sulfate and evaporated. The residue was purified by flash chromatography (SiO2: dichloromethane/methanol = 9:1) to yield a light yellow oil (0.785 g, 27%); MS (ISP): 233.1 $((M+H)^{+\cdot})$.

b) 4-{[Ethyl-(4-methoxy-pyrimidin-2-yl)-amino]-methyl}-imidazole-1-sulfonic acid dimethylamide

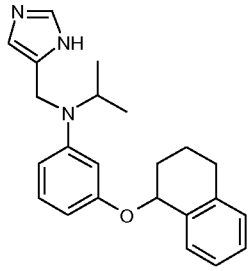
A solution of 5-ethylaminomethyl-imidazole-1-sulfonic acid dimethylamide (0.527 g, 2.25 mmol), 2-chloro-4-methoxy-pyrimidine (0.217 g; 1.5 mmol) and N,N-diisopropyl ethyl amine (0.51 ml, 3.0 mmol) in isopropanol (2 ml) was heated in a sealed vessel in a microwave oven for 20 min at 160°C. Ethyl acetate (20 ml) and silicagel (1 g) was added and the mixture was evaporated. The residue was purified by flash chromatography, column: Isolute® Flash-NH_2 (Separtis); eluent: heptane / ethyl acetate = 8:2) to yield a white solid, (0.265 g, 52 %); MS (ISP): 341.0 $((M+H)^{+\cdot})$.

c) Ethyl-(3H-imidazol-4-ylmethyl)-(4-methoxy-pyrimidin-2-yl)-amine

4-{[Ethyl-(4-methoxy-pyrimidin-2-yl)-amino]-methyl}-imidazole-1-sulfonic acid dimethylamide (0.265 g, 0.78 mmol) was dissolved in aqueous hydrochloric acid (4N, 2 ml) and the mixture was stirred at 100°C for 2 hours. After cooling concentrated sodium hydroxide solution was added slowly until basic pH. The mixture was extracted three times with ethyl acetate. The combined organic layers were dried over magnesium sulfate and evaporated. The residue was purified by flash chromatography, column: Isolute® Flash-NH_2 (Separtis); eluent: heptane / ethyl acetate = 1:1) to yield a colorless liquid, (0.10 g, 55 %); MS (ISP): 234.3 $((M+H)^{+\cdot})$.

Example 211

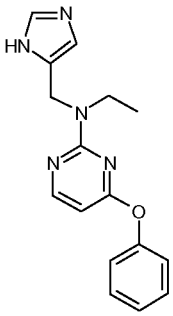
(3H-Imidazol-4-ylmethyl)-isopropyl-[3-(1,2,3,4-tetrahydro-naphthalen-1-yloxy)-phenyl]-amine



The title compound, MS (ISP): 362.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-(1,2,3,4-tetrahydro-naphthalen-1-yloxy)-phenylamine (synthesized in analogy to its 2-chloro derivative as published in WO2007046392) instead of 4-trifluormethoxyaniline in step a).

Example 212

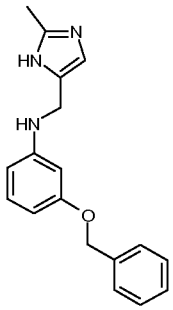
Ethyl-(3H-imidazol-4-ylmethyl)-(4-phenoxy-pyrimidin-2-yl)-amine



The title compound, MS (ISP): 296.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using 2-chloro-4-phenoxy-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 213

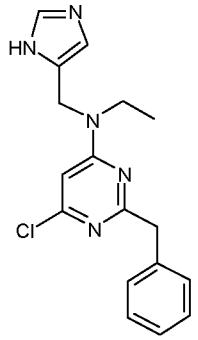
(3-Benzyloxy-phenyl)-(2-methyl-1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 294.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 4-formyl-2-methylimidazole instead of 4-formyl-imidazole and 3-benzyloxyaniline instead of 2-methoxyaniline.

Example 214

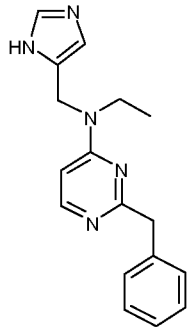
(2-Benzyl-6-chloro-pyrimidin-4-yl)-ethyl-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 328.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using 2-benzyl-4,6-dichloro-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 215

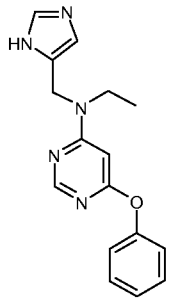
(2-Benzyl-pyrimidin-4-yl)-ethyl-(3H-imidazol-4-ylmethyl)-amine



(2-Benzyl-6-chloro-pyrimidin-4-yl)-ethyl-(3H-imidazol-4-ylmethyl)-amine (0.164 g, 0.5 mmol) was dissolved in methanol (3 ml), ammonium formate (0.315 g, 0.5 mmol) and palladium on charcoal (0.164 g, 10% Pd) was added and the mixture was refluxed for one hour. After cooling the catalyst was filtered off and the solvent was evaporated. The residue was purified by flash chromatography (column: Isolute® Flash-NH_2 from Separtis; eluent: ethyl acetate / methanol = 95:5) to yield a white solid, (0.03 g, 21 %); MS (ISP): 294.4 ($(M+H)^{+\cdot}$).

Example 216

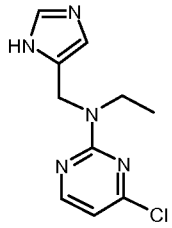
Ethyl-(3H-imidazol-4-ylmethyl)-(6-phenoxy-pyrimidin-4-yl)-amine



The title compound, MS (ISP): 296.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using 2-chloro-6-phenoxy-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 217

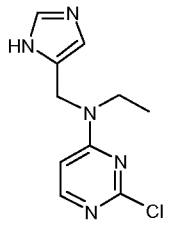
(4-Chloro-pyrimidin-2-yl)-ethyl-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 238.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using 2,4-dichloro-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b) and chromatographic separation from the 2-chloro-pyrimidin-4-yl isomer before step c).

Example 218

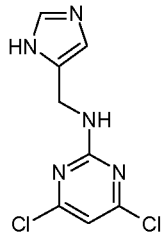
(2-Chloro-pyrimidin-4-yl)-ethyl-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 238.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using 2,4-dichloro-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b) and chromatographic separation from the 4-chloro-pyrimidin-2-yl isomer before step c).

Example 219

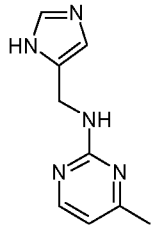
(4,6-Dichloro-pyrimidin-2-yl)-(1H-imidazol-4-ylmethyl)-amine



To a solution of 2-amino-4,6-dichloropyrimidine (1.00 g, 7.72 mmol) in dichloromethane (8 ml) were added 4-formylimidazole (0.74 g, 7.72 mmol) and tetraisopropyl orthotitanate (2.86 ml, 9.65 mmol). After stirring the mixture at 40 °C overnight ethanol (8 ml) and sodium borohydride (0.38 g, 10.0 mmol) were added. The reaction mixture was stirred 40 °C for 7 hours. Then mixture was concentrated *in vacuo* and the residue was purified by flash chromatography (methanol/dichloromethane gradient) to yield white crystals (43 mg, 26%); MS (EI): 247.1 (^{37}Cl M$^{+\cdot}$), 245.1 (^{37}Cl^{35}Cl M$^{+\cdot}$), 243.1 (^{35}Cl M$^{+\cdot}$).

Example 220

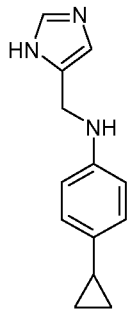
(1H-Imidazol-4-ylmethyl)-(4-methyl-pyrimidin-2-yl)-amine



The title compound, MS (ISP): 190.4 ([M+H]$^+$), was obtained in comparable yield analogous to the procedure described for Example 219 using 2-amino-4-methylpyrimidine instead of 2-amino-4,6-dichloropyrimidine.

Example 221

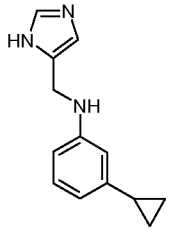
(4-Cyclopropyl-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 214.1 ([M+H]$^+$), was obtained in comparable yield analogous to the procedure described for Example 180 using 4-cyclopropyl-aniline instead of 3,4-difluoro-aniline.

Example 222

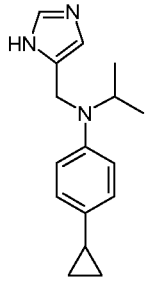
(3-Cyclopropyl-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 214.1 ([M+H]$^+$), was obtained in comparable yield analogous to the procedure described for Example 180 using 3-cyclopropyl-aniline instead of 3,4-difluoro-aniline.

Example 223

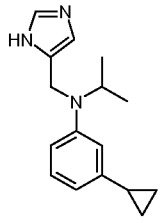
(4-Cyclopropyl-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 256.3 ([M+H]$^{+\cdot}$) was obtained analogous to the procedure described for Example 67 step b) using (4-cyclopropyl-phenyl)-(1H-imidazol-4-ylmethyl)-amine (Example 221) instead of (3H-imidazol-4-ylmethyl)-(4-trifluoromethoxy-phenyl)-amine.

Example 224

(3-Cyclopropyl-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine

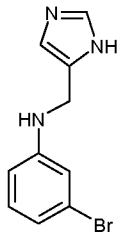


The title compound, MS (ISP): 256.3 ([M+H]$^{+\cdot}$) was obtained analogous to the procedure described for Example 67 step b) using (3-cyclopropyl-phenyl)-(1H-imidazol-

4-ylmethyl)-amine (Example 222) instead of (3H-imidazol-4-ylmethyl)-(4-trifluoromethoxy-phenyl)-amine.

Example 225

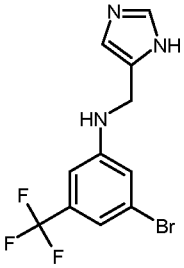
(3-Bromo-phenyl)-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 252.2, 254.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 3-bromoaniline instead of 2-methoxyaniline.

Example 226

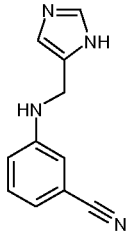
(3-Bromo-5-trifluoromethyl-phenyl)-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 320.1; 322.2 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 3-bromo-5-trifluoromethyl-aniline instead of 2-methoxyaniline.

Example 227

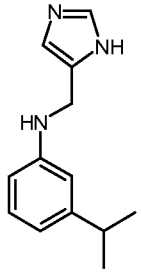
3-[(3H-Imidazol-4-ylmethyl)-amino]-benzonitrile



The title compound, MS (ISP): 199.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 3-amino-benzonitrile instead of 2-methoxyaniline.

Example 228

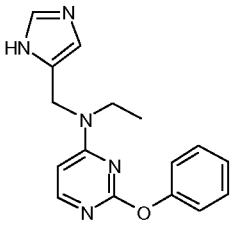
(3H-Imidazol-4-ylmethyl)-(3-isopropyl-phenyl)-amine



The title compound, MS (ISP): 216.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 3-isopropylaniline instead of 2-methoxyaniline.

Example 229

Ethyl-(1H-imidazol-4-ylmethyl)-(2-phenoxy-pyrimidin-4-yl)-amine



a) 4-{[(2-Chloro-pyrimidin-4-yl)-ethyl-amino]-methyl}-imidazole-1-sulfonic acid dimethylamide

The title compound, MS (ISP): 345.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using 2,4-dichloro-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b) and chromatographic separation from the 4-chloro-pyrimidin-2-yl isomer without performing step c) at the end.

b) 4-{[Ethyl-(2-phenoxy-pyrimidin-4-yl)-amino]-methyl}-imidazole-1-sulfonic acid dimethylamide

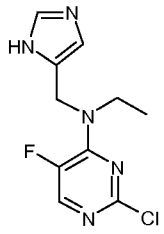
To sodium hydride (0.194 g, 55% in mineral oil, 4.4 mmol) in dimethylformamide (1.5 ml) was added phenol (0.418 g, 4.4 mmol) and stirring was continued for 15 min at room temperature. To this reaction mixture 4-{[(2-chloro-pyrimidin-4-yl)-ethyl-amino]-methyl}-imidazole-1-sulfonic acid dimethylamide (0.153 g, 0.44 mmol) was added. After stirring and heating to 80°C overnight the solvent was evaporated. Water was added (5 ml) and the mixture was extracted with ethyl acetate (20 ml) twice. The combined organic layers were washed with water, dried over magnesium sulphate and evaporated. The residue was purified using flash chromatography (SiO_2; eluent: heptane/ethyl acetate = 95:5) to yield the title compound as a colourless gum, MS (ISP): 403.4 ($(M+H)^{+\cdot}$) .

c) Ethyl-(1H-imidazol-4-ylmethyl)-(2-phenoxy-pyrimidin-4-yl)-amine

To remove the dimethylaminosulfonyl protecting group 4-{[ethyl-(2-phenoxy-pyrimidin-4-yl)-amino]-methyl}-imidazole-1-sulfonic acid dimethylamide (65 mg, 0.16 mmol) was dissolved in hydrochloric acid in ethanol (5N, 1 ml) and the mixture was stirred at 100°C for 2 hours. For workup aqueous sodium hydroxide solution (0,5 ml, 1N) was added to basic pH and the mixture was extracted three times with dichloromethane. The combined organic layers were dried over magnesium sulfate and evaporated. The residue was purified by flash chromatography (SiO_2; ethyl acetate/methanol = 95:5) to yield a white solid, (0.022 g, 46 %); MS (ISP): 296.3 ($(M+H)^{+\cdot}$).

Example 230

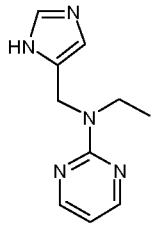
(2-Chloro-5-fluoro-pyrimidin-4-yl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 256.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using 2,4-dichloro-5-fluoro-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 231

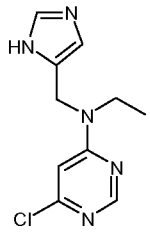
Ethyl-(1H-imidazol-4-ylmethyl)-pyrimidin-2-yl-amine



The title compound, MS (ISP): 204.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using 2-chloro-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 232

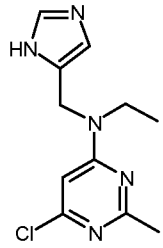
(6-Chloro-pyrimidin-4-yl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 238.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using 4,6-dichloro-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 233

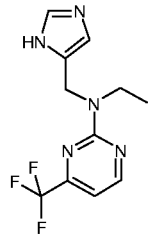
(6-Chloro-2-methyl-pyrimidin-4-yl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 252.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using 4,6-dichloro-2-methyl-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 234

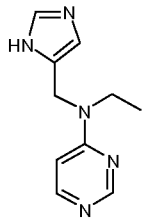
Ethyl-(1H-imidazol-4-ylmethyl)-(4-trifluoromethyl-pyrimidin-2-yl)-amine



The title compound, MS (ISP): 272.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using 2-chloro-4-(trifluoromethyl)-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 235

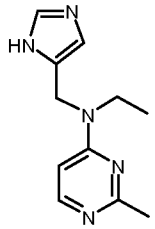
Ethyl-(1H-imidazol-4-ylmethyl)-pyrimidin-4-yl-amine



The title compound, MS (ISP): 204.2 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 215 using (6-chloro-pyrimidin-4-yl)-ethyl-(1H-imidazol-4-ylmethyl)-amine instead of (2-benzyl-6-chloro-pyrimidin-4-yl)-ethyl-(3H-imidazol-4-ylmethyl)-amine.

Example 236

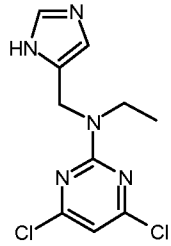
Ethyl-(1H-imidazol-4-ylmethyl)-(2-methyl-pyrimidin-4-yl)-amine



The title compound, MS (ISP): 218.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 215 using (6-chloro-2-methyl-pyrimidin-4-yl)-ethyl-(1H-imidazol-4-ylmethyl)-amine instead of (2-benzyl-6-chloro-pyrimidin-4-yl)-ethyl-(3H-imidazol-4-ylmethyl)-amine.

Example 237

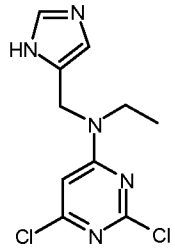
(4,6-Dichloro-pyrimidin-2-yl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 272.5 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using 2,4,6-trichloro-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b) and chromatographic separation from the 2,6-dichloro-pyrimidin-2-yl isomer before step c).

Example 238

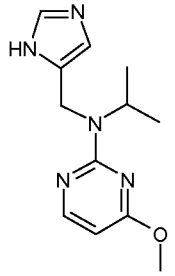
(2,6-Dichloro-pyrimidin-4-yl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 272.8 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using 2,4,6-trichloro-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b) and chromatographic separation from the 4,6-dichloro-pyrimidin-2-yl isomer before step c).

Example 239

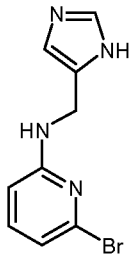
(1H-Imidazol-4-ylmethyl)-isopropyl-(4-methoxy-pyrimidin-2-yl)-amine



The title compound, MS (ISP): 248.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using isopropylamine instead of ethylamine in step a).

Example 240

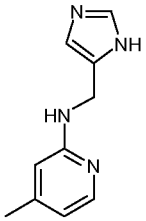
(6-Bromo-pyridin-2-yl)-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 253.0; 255.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 2-amino-6-bromopyridine instead of 2-methoxyaniline.

Example 241

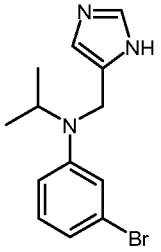
(3H-Imidazol-4-ylmethyl)-(4-methyl-pyridin-2-yl)-amine



The title compound, MS (ISP): 189.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 2-amino-4-methylpyridine instead of 2-methoxyaniline.

Example 242

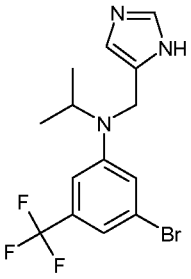
(3-Bromo-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 294.1; 296.2 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-bromoaniline instead of 4-trifluormethoxyaniline in step a).

Example 243

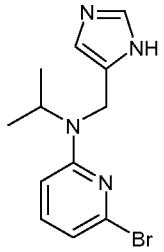
(3-Bromo-5-trifluoromethyl-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 362.1; 364.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-bromo-5-trifluoromethyl-aniline instead of 4-trifluormethoxyaniline in step a).

Example 244

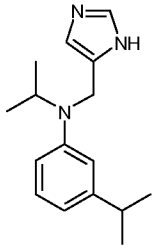
(6-Bromo-pyridin-2-yl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 295.1; 297.2 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 2-amino-6-bromopyridine instead of 4-trifluormethoxyaniline in step a).

Example 245

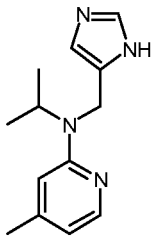
(3H-Imidazol-4-ylmethyl)-isopropyl-(3-isopropyl-phenyl)-amine



The title compound, MS (ISP): 258.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-isopropylaniline instead of 4-trifluormethoxyaniline in step a).

Example 246

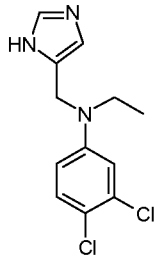
(3H-Imidazol-4-ylmethyl)-isopropyl-(4-methyl-pyridin-2-yl)-amine



The title compound, MS (ISP): 231.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 2-amino-4-methylpyridine instead of 4-trifluormethoxyaniline in step a).

Example 247

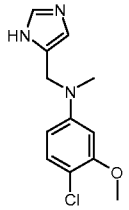
(3,4-Dichloro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 274.1 ([^{37}Cl M+H]$^{+\cdot}$), 272.1 ([^{37}Cl^{35}Cl M+H]$^{+\cdot}$), 270.2 ([^{35}Cl M+H]$^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 81 using 3,4-dichloroaniline instead of 3-chloro-2-fluoroaniline in step a).

Example 248

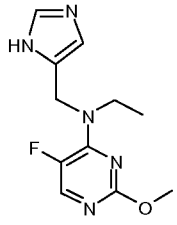
(4-Chloro-3-methoxy-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 254.1 ([^{37}Cl M+H]$^{+\cdot}$), 252.1 ([^{35}Cl M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 186 using 4-chloro-3-methoxyaniline instead of m-anisidine in step a).

Example 249

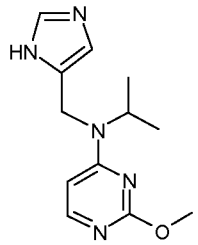
Ethyl-(5-fluoro-2-methoxy-pyrimidin-4-yl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 252.1 ((M+H)$^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 229 using 2,4-dichloro-5-fluoro-pyrimidine instead of 2,4-dichloro-pyrimidine in step a) and sodium methoxide in 1,2-dimethoxyethane instead of sodium hydride / phenol in dimethylformamide in step b).

Example 250

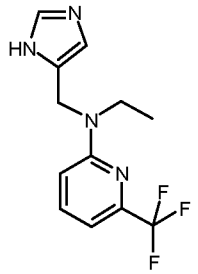
(1H-Imidazol-4-ylmethyl)-isopropyl-(2-methoxy-pyrimidin-4-yl)-amine



The title compound, MS (ISP): 247.9 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 229 using sodium methoxide in 1,2-dimethoxyethane instead of sodium hydride / phenol in dimethylformamide in step b).

Example 251

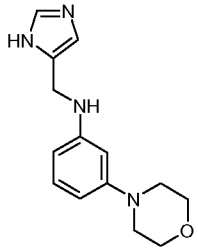
Ethyl-(1H-imidazol-4-ylmethyl)-(6-trifluoromethyl-pyridin-2-yl)-amine



The title compound, MS (ISP): 271.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using 2-bromo-6-(trifluoromethyl)-pyridine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 252

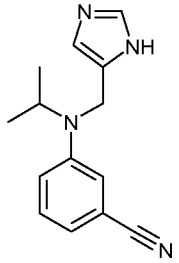
(1H-Imidazol-4-ylmethyl)-(3-morpholin-4-yl-phenyl)-amine



The title compound, MS (ISP): 259.3 ($[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 63 using 3-morpholin-4-yl-phenylamine instead of 2-methoxyaniline.

Example 253

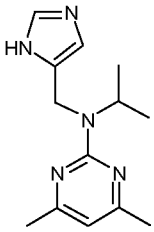
3-[(3H-Imidazol-4-ylmethyl)-isopropyl-amino]-benzonitrile



The title compound, MS (ISP): 241.2 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-aminobenzonitrile instead of 4-trifluormethoxyaniline in step a).

Example 254

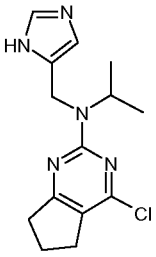
(4,6-Dimethyl-pyrimidin-2-yl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 246.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using isopropylamine instead of ethylamine in step a) and 4,6-dimethyl-2-chloro-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 255

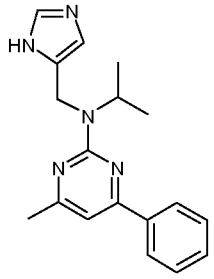
(4-Chloro-6,7-dihydro-5H-cyclopentapyrimidin-2-yl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 292.2 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using isopropylamine instead of ethylamine in step a) and 2,4-dichloro-6,7-dihydro-5H-cyclopentapyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 256

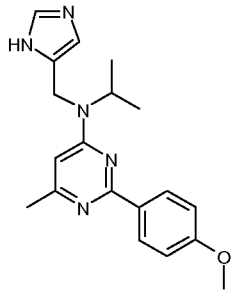
(1H-Imidazol-4-ylmethyl)-isopropyl-(4-methyl-6-phenyl-pyrimidin-2-yl)-amine



The title compound, MS (ISP): 308.4 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using isopropylamine instead of ethylamine in step a) and 2-chloro-4-methyl-6-phenyl-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 257

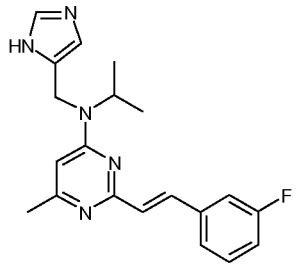
(1H-Imidazol-4-ylmethyl)-isopropyl-[2-(4-methoxy-phenyl)-6-methyl-pyrimidin-4-yl]-amine



The title compound, MS (ISP): 338.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using isopropylamine instead of ethylamine in step a) and 4-chloro-2-(4-methoxy-phenyl)-6-methyl-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 258

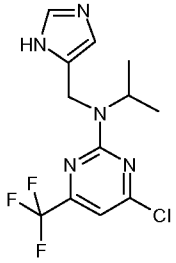
{2-[(E)-2-(3-Fluoro-phenyl)-vinyl]-6-methyl-pyrimidin-4-yl}-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 352.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using isopropylamine instead of ethylamine in step a) and 4-chloro-2-[(1E)-2-(3-fluoro-phenyl)-vinyl]-6-methyl-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 259

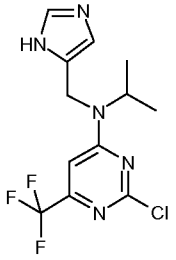
(4-Chloro-6-trifluoromethyl-pyrimidin-2-yl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 320.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using isopropylamine instead of ethylamine in step a) and 2,4-dichloro-6-trifluoromethyl-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b) and chromatographic separation from the 2-chloro-6-trifluoromethyl-pyrimidin-4-yl isomer before step c).

Example 260

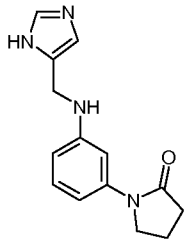
(2-Chloro-6-trifluoromethyl-pyrimidin-4-yl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 320.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using isopropylamine instead of ethylamine in step a) and 2,4-dichloro-6-trifluoromethyl-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b) and chromatographic separation from the 4-chloro-6-trifluoromethyl-pyrimidin-2-yl isomer before step c).

Example 261

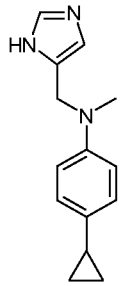
1-{3-[(1H-Imidazol-4-ylmethyl)-amino]-phenyl}-pyrrolidin-2-one



The title compound, MS (ISP): 257.1 ($[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 63 using 1-(3-amino-phenyl)-pyrrolidin-2-one instead of 2-methoxyaniline.

Example 262

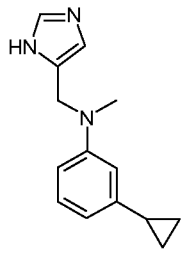
(4-Cyclopropyl-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 228.1 ($[M+H]^{+\cdot}$), was obtained analogous to the procedure described for Example 186 using 4-cyclopropyl-aniline instead of m-anisidine in step a).

Example 263

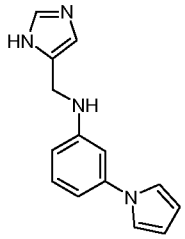
(3-Cyclopropyl-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 228.1 ($[M+H]^{+\cdot}$), was obtained analogous to the procedure described for Example 186 using 3-cyclopropyl-aniline instead of m-anisidine in step a).

Example 264

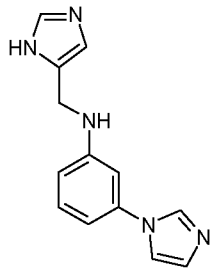
(1H-Imidazol-4-ylmethyl)-(3-pyrrol-1-yl-phenyl)-amine



The title compound, MS (ISP): 239.3 ($[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 63 using 3-pyrrol-1-yl-phenylamine instead of 2-methoxyaniline.

Example 265

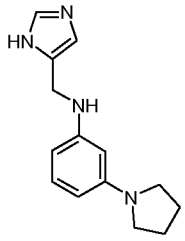
(1H-Imidazol-4-ylmethyl)-(3-imidazol-1-yl-phenyl)-amine



The title compound, MS (ISP): 240.1 ($[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 63 using 3-(1H-imidazol-1-yl)benzenamine instead of 2-methoxyaniline.

Example 266

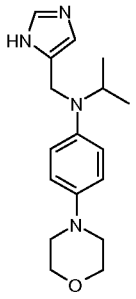
(1H-Imidazol-4-ylmethyl)-(3-pyrrolidin-1-yl-phenyl)-amine



The title compound, MS (ISP): 243.3 ($[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 63 using 3-pyrrolidin-1-yl-phenylamine instead of 2-methoxyaniline.

Example 267

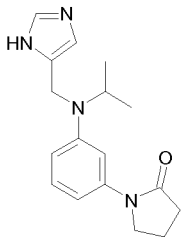
(1H-Imidazol-4-ylmethyl)-isopropyl-(4-morpholin-4-yl-phenyl)-amine



The title compound, MS (ISP): 301.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 4-morpholinoaniline instead of 4-trifluoromethoxyaniline in step a).

Example 268

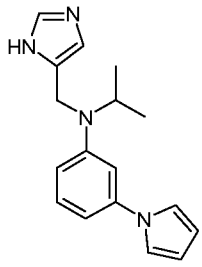
1-{3-[(1H-Imidazol-4-ylmethyl)-isopropyl-amino]-phenyl}-pyrrolidin-2-one



The title compound, MS (ISP): 299.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 1-(3-amino-phenyl)-pyrrolidin-2-one instead of 4-trifluoromethoxyaniline in step a).

Example 269

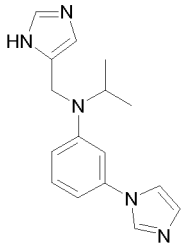
(1H-Imidazol-4-ylmethyl)-isopropyl-(3-pyrrol-1-yl-phenyl)-amine



The title compound, MS (ISP): 281.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-pyrrol-1-yl-phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 270

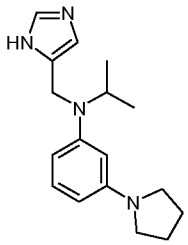
(1H-Imidazol-4-ylmethyl)-(3-imidazol-1-yl-phenyl)-isopropyl-amine



The title compound, MS (ISP): 282.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-(1H-imidazol-1-yl)benzenamine instead of 4-trifluoromethoxyaniline in step a).

Example 271

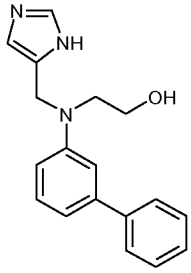
(1H-Imidazol-4-ylmethyl)-isopropyl-(3-pyrrolidin-1-yl-phenyl)-amine



The title compound, MS (ISP): 285.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 3-pyrrolidin-1-yl-phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 272

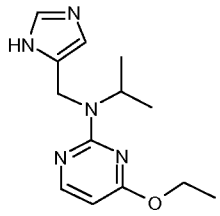
2-[Biphenyl-3-yl-(3H-imidazol-4-ylmethyl)-amino]-ethanol



The title compound, MS (ISP): 294.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 1 using 2-(biphenyl-3-ylamino)-ethanol instead of N-ethylaniline.

Example 273

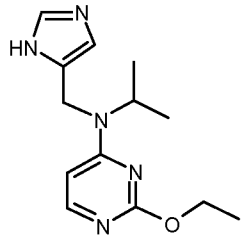
(4-Ethoxy-pyrimidin-2-yl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 262.1 ((M+H)$^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 229 using the 4-chloro-pyrimidin-2-yl isomer and sodium ethoxide in 1,2-dimethoxyethane instead of sodium hydride / phenol in dimethylformamide in step b).

Example 274

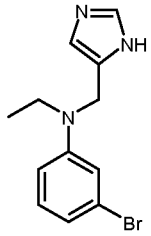
(2-Ethoxy-pyrimidin-4-yl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 262.1 ((M+H)$^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 229 using the 2-chloro-pyrimidin-4-yl isomer and sodium ethoxide in 1,2-dimethoxyethane instead of sodium hydride / phenol in dimethylformamide in step b).

Example 275

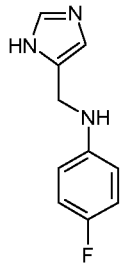
(3-Bromo-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 280.1; 282.2 ((M+H)$^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 3-bromoaniline instead of 3-chloro-2-fluoroaniline in step a).

Example 276

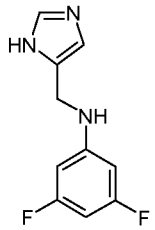
(4-Fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 192.3 ($[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 180 using 4-fluoro-aniline instead of 3,4-difluoro-aniline.

Example 277

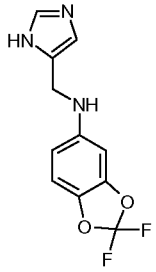
(3, 5-Difluoro-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 210.3 ($[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 180 using 3,5-difluoro-aniline instead of 3,4-difluoro-aniline.

Example 278

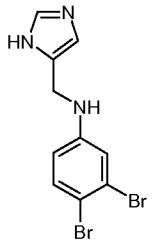
(2,2-Difluoro-benzo[1,3]dioxol-5-yl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 254.3 ($[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 180 using 2,2-difluoro-5-aminobenzodioxole instead of 3,4-difluoro-aniline.

Example 279

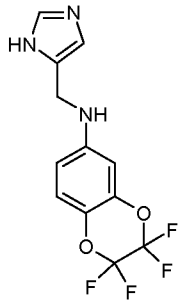
(3,4-Dibromo-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 334.3 ($^{81}Br^{81}Br$ $[M+H]^{+\cdot}$), 332.3 ($^{81}Br^{79}Br$ $[M+H]^{+\cdot}$), 330.3 ($^{79}Br^{79}Br$ $[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 180 using 3,4-dibromoaniline instead of 3,4-difluoro-aniline.

Example 280

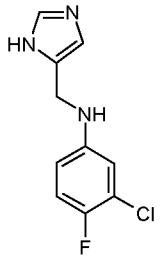
(1H-Imidazol-4-ylmethyl)-(2,2,3,3-tetrafluoro-2,3-dihydro-benzo[1,4]dioxin-6-yl)-amine



The title compound, MS (ISP): 304.0 ($[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 180 using 2,2,3,3-tetrafluoro-6-aminobenzodioxene instead of 3,4-difluoro-aniline.

Example 281

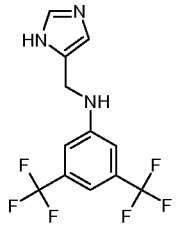
(3-Chloro-4-fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 228.1 (^{37}Cl $[M+H]^{+\cdot}$), 226.1 (^{35}Cl $[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 180 using 3-chloro-4-fluoro-aniline instead of 3,4-difluoro-aniline.

Example 282

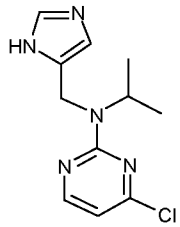
(3,5-Bis-trifluoromethyl-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 310.3 ($[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 180 using 3,5-bis(trifluoromethyl)-aniline instead of 3,4-difluoro-aniline.

Example 283

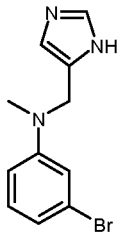
(4-Chloro-pyrimidin-2-yl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 252.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using isopropylamine instead of ethylamine in step a) and 2,4-dichloro-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b) and chromatographic separation from the 2-chloro-pyrimidin-4-yl isomer before step c).

Example 284

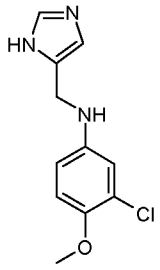
(3-Bromo-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 266.0; 268.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 81 using 3-bromoaniline instead of 3-chloro-2-fluoroaniline in step a) and formaldehyde solution (40% in water) instead of acetaldehyde in step b).

Example 285

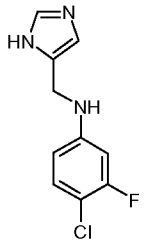
(3-Chloro-4-methoxy-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 240.1 (^{37}Cl [M+H]$^{+\cdot}$), 238.0 (^{35}Cl [M+H]$^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 63 using 3-chloro-4-methoxy-aniline instead of 2-methoxyaniline.

Example 286

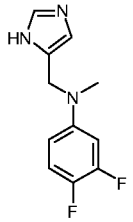
(4-Chloro-3-fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 228.1 (^{37}Cl [M+H]$^{+\cdot}$), 226.1 (^{35}Cl [M+H]$^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 63 using 3-chloro-4-fluoro-aniline instead of 2-methoxyaniline.

Example 287

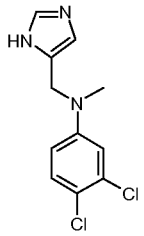
(3,4-Difluoro-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 224.4 ([M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 186 using 3,4-difluoro-aniline instead of m-anisidine in step a).

Example 288

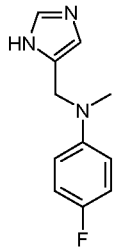
(3,4-Dichloro-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 260.0 (^{37}Cl [M+H]$^{+\cdot}$), 257.9 (^{37}Cl ^{35}Cl [M+H]$^{+\cdot}$), 256.1 (^{35}Cl [M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 186 using 3,4-dichloro-aniline instead of m-anisidine in step a).

Example 289

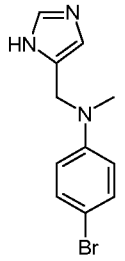
(4-Fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 206.1 ([M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 186 using 4-fluoro-aniline instead of m-anisidine in step a).

Example 290

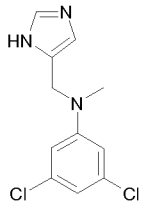
(4-Bromo-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 268.0 (^{81}Br [M+H]$^{+\cdot}$), 266.1 (^{79}Br [M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 186 using 4-bromo-aniline instead of m-anisidine in step a).

Example 291

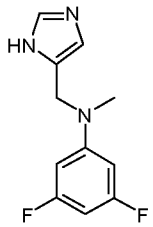
(3,5-Dichloro-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 259.8 (^{37}Cl [M+H]$^{+\cdot}$), 258.0 (^{37}Cl ^{35}Cl [M+H]$^{+\cdot}$), 256.1 (^{35}Cl [M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 186 using 3,5-dichloro-aniline instead of m-anisidine in step a).

Example 292

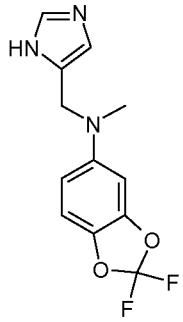
(3,5-Difluoro-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 224.4 ([M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 186 using 3,5-difluoro-aniline instead of m-anisidine in step a).

Example 293

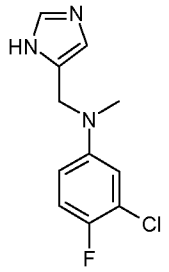
(2,2-Difluoro-benzo[1,3]dioxol-5-yl)-(1H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 268.1 ([M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 186 using 2,2-difluoro-5-amino-benzodioxole instead of m-anisidine in step a).

Example 294

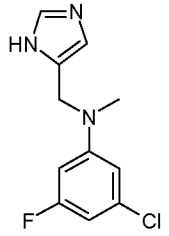
(3-Chloro-4-fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): MS (ISP): 242.2 ([^{37}Cl M+H]$^{+\cdot}$), 240.1 ([^{35}Cl M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 186 using 3-chloro-4-fluoro-aniline instead of m-anisidine in step a).

Example 295

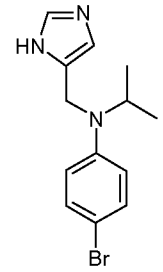
(3-Chloro-5-fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): MS (ISP): 242.2 ([^{37}Cl M+H]$^{+\cdot}$), 240.1 ([^{35}Cl M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 186 using 3-chloro-5-fluoro-aniline instead of m-anisidine in step a).

Example 296

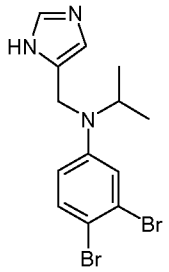
(4-Bromo-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 296.1 ([^{81}Br M+H]$^{+\cdot}$), 294.0 ([^{79}Br M+H]$^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 67 using 4-bromo-aniline instead of 4-trifluoromethoxyaniline in step a).

Example 297

(3,4-Dibromo-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine



a) (4-Bromo-phenyl)-(1H-imidazol-4-ylmethyl)-amine

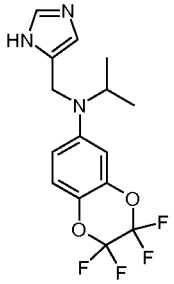
The title compound, MS (ISP): 334.1 ([^{81}Br M+H]$^{+\cdot}$), 331.9 ([^{81}Br^{79}Br M+H]$^{+\cdot}$), 329.9 ([^{79}Br M+H]$^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 180 using 3,4-dibromoaniline instead of 3,4-difluoroaniline.

b) (3,4-Dibromo-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine

The title compound, MS (ISP): 376.1 ([^{81}Br M+H]$^{+\cdot}$), 374.1 ([^{81}Br^{79}Br M+H]$^{+\cdot}$), 372.0 ([^{79}Br M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 67 step b).

Example 298

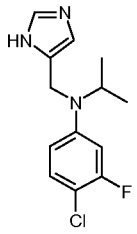
(1H-Imidazol-4-ylmethyl)-isopropyl-(2,2,3,3-tetrafluoro-2,3-dihydro-benzo[1,4]dioxin-6-yl)-amine



The title compound, MS (ISP): 346.3 ([M+H]$^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 297 using 2,2,3,3-tetrafluoro-6-aminobenzodioxene instead of 3,4-dibromoaniline in step a).

Example 299

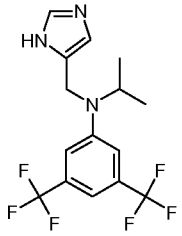
(4-Chloro-3-fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 270.2 ([^{37}Cl M+H]$^{+\cdot}$), 268.2 ([^{35}Cl M+H]$^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 67 using 4-chloro-3-fluoro-aniline instead of 4-trifluoromethoxyaniline in step a).

Example 300

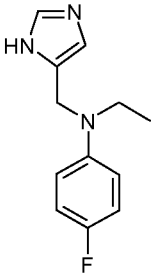
(3,5-Bis-trifluoromethyl-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 352.5 ([M+H]$^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 297 using 3,5-bis(trifluoromethyl)aniline instead of 3,4-dibromoaniline in step a).

Example 301

Ethyl-(4-fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-amine



a) (4-Fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-amine

To a solution of 4-fluoroaniline (0.60 g, 5.40 mmol) in 1,2-dichloroethane (5 ml) were added 4-formylimidazole (0.78 g, 8.10 mmol), sodium triacetoxyborohydride (2.29 g, 10.8 mmol) and acetic acid (0.06 ml). The reaction mixture was stirred at 50 °C for 4 h. The reaction mixture was then concentrated *in vacuo* and the residue was purified using flash chromatography (column: Isolute® Flash-NH_2 (Separtis); eluent: methanol/dichloromethane gradient) to yield a white solid (160 mg, 16%); MS (ISP): 192.2 ((M+H)$^{+\cdot}$).

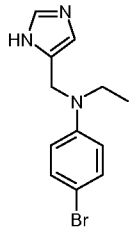
b) Ethyl-(4-fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-amine

To a solution of (4-fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-amine (0.20 g, 1.05 mmol) in 1,2-dichloroethane (6 ml) were added acetaldehyde (0.30 ml, 5.23 mmol), sodium

triacetoxyborohydride (0.67 g, 3.14 mmol) and acetic acid (0.06 ml). The reaction mixture was stirred at 40 °C for 16 h. The reaction mixture was then concentrated *in vacuo* and the residue was purified using flash chromatography (column: Isolute® Flash-NH_2 (Separtis); eluent: methanol/ethyl acetate/heptane gradient) to yield a white solid (131 mg, 57%); MS (ISP): 220.4 ($(M+H)^{+\cdot}$).

Example 302

(4-Bromo-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



a) (4-Bromo-phenyl)-(1H-imidazol-4-ylmethyl)-amine

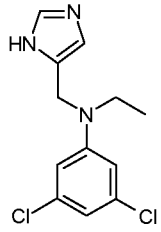
The title compound, MS (ISP): 254.0 ($[^{81}Br\ M+H]^{+\cdot}$), 252.1 ($[^{79}Br\ M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 63 using 4-bromoaniline instead of 2-methoxyaniline.

b) (4-Bromo-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine

The title compound, MS (ISP): 282.1 ($[^{81}Br\ M+H]^{+\cdot}$), 280.0 ($[^{79}Br\ M+H]^{+\cdot}$), was obtained analogous to the procedure described for Example 301 step b).

Example 303

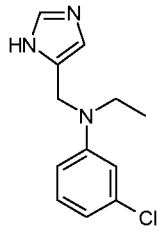
(3,5-Dichloro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 274.0 ($[^{37}Cl\ M+H]^{+\cdot}$), 272.1 ($[^{37}Cl^{35}Cl\ M+H]^{+\cdot}$), 270.2 ($[^{35}Cl\ M+H]^{+\cdot}$), was obtained analogous to the procedure described for Example 301 using 3,5-dichloro-aniline instead of 4-fluoroaniline in step a).

Example 304

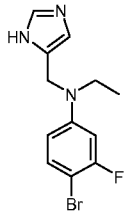
(3-Chloro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 238.0 ([^{37}Cl M+H]$^{+\cdot}$), 236.1 ([^{35}Cl M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 301 using 3,5-dichloro-aniline instead of 4-fluoroaniline in step a).

Example 305

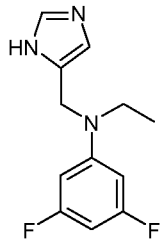
(4-Bromo-3-fluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 300.0 ([^{81}Br M+H]$^{+\cdot}$), 298.1 ([^{79}Br M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 301 using 4-bromo-3-fluoro-aniline instead of 4-fluoroaniline in step a).

Example 306

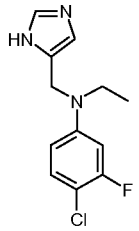
(3,5-Difluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 238.1 ([M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 301 using 3,5-difluoro-aniline instead of 4-fluoroaniline in step a).

Example 307

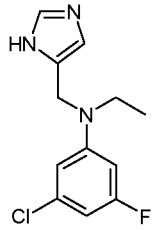
(4-Chloro-3-fluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 256.0 ([^{37}Cl M+H]$^{+\cdot}$), 254.1 ([^{35}Cl M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 302 using 4-chloro-3-fluoro-aniline instead of 4-bromoaniline in step a).

Example 308

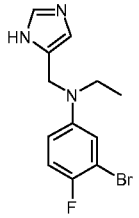
(3-Chloro-5-fluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 256.0 ([^{37}Cl M+H]$^{+\cdot}$), 253.9 ([^{35}Cl M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 302 using 3-chloro-5-fluoro-aniline instead of 4-bromoaniline in step a).

Example 309

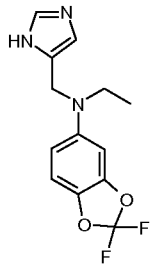
(3-Bromo-4-fluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 300.0 ([^{81}Br M+H]$^{+\cdot}$), 298.1 ([^{79}Br M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 301 using 3-bromo-4-fluoro-aniline instead of 4-fluoroaniline in step a).

Example 310

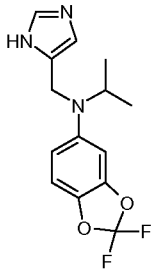
(2,2-Difluoro-benzo[1,3]dioxol-5-yl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 282.0 ([M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 302 using 2,2-difluoro-5-amino-benzodioxole instead of 4-bromoaniline in step a).

Example 311

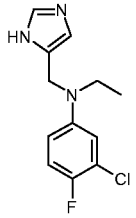
(2,2-Difluoro-benzo[1,3]dioxol-5-yl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 296.4 ([M+H]$^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 67 using 2,2-difluoro-5-aminobenzodioxole instead of 4-trifluoromethoxyaniline in step a).

Example 312

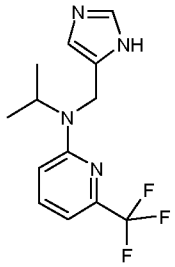
(3-Chloro-4-fluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 256.1 ([^{37}Cl M+H]$^{+\cdot}$), 253.9 ([^{35}Cl M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 302 using 3-chloro-4-fluoro-aniline instead of 4-bromoaniline in step a).

Example 313

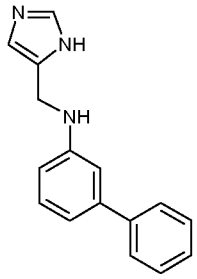
(3H-Imidazol-4-ylmethyl)-isopropyl-(6-trifluoromethyl-pyridin-2-yl)-amine



The title compound, MS (ISP): 285.0 ((M+H)$^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 2-amino-6-trifluoromethyl-pyridine instead of 4-trifluormethoxyaniline in step a).

Example 314

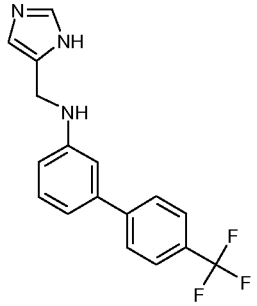
Biphenyl-3-yl-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 250.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 3-aminobiphenyl instead of 2-methoxyaniline.

Example 315

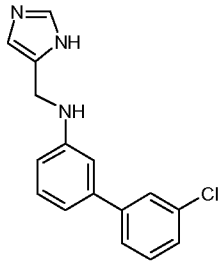
(3H-Imidazol-4-ylmethyl)-(4'-trifluoromethyl-biphenyl-3-yl)-amine



The title compound, MS (ISP): 318.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 4'-trifluoromethyl-biphenyl-3-ylamine instead of 2-methoxyaniline.

Example 316

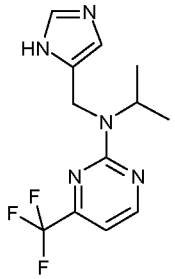
(3'-Chloro-biphenyl-3-yl)-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 284.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 3'-chloro-biphenyl-3-ylamine instead of 2-methoxyaniline.

Example 317

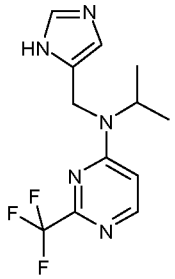
(1H-Imidazol-4-ylmethyl)-isopropyl-(4-trifluoromethyl-pyrimidin-2-yl)-amine



The title compound, MS (ISP): 286.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using isopropylamine instead of ethylamine in step a) and 2-chloro-4-(trifluoromethyl)-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 318

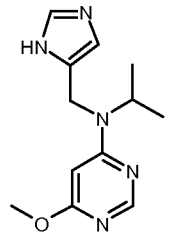
(1H-Imidazol-4-ylmethyl)-isopropyl-(2-trifluoromethyl-pyrimidin-4-yl)-amine



The title compound, MS (ISP): 286.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using isopropylamine instead of ethylamine in step a) and 4-chloro-2-(trifluoromethyl)-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 319

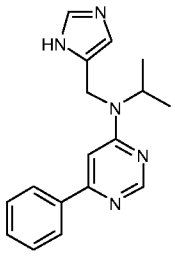
(1H-Imidazol-4-ylmethyl)-isopropyl-(6-methoxy-pyrimidin-4-yl)-amine



The title compound, MS (ISP): 248.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using isopropylamine instead of ethylamine in step a) and 4-chloro-6-methoxy-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 320

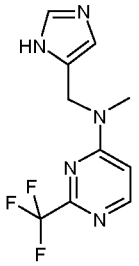
(1H-Imidazol-4-ylmethyl)-isopropyl-(6-phenyl-pyrimidin-4-yl)-amine



The title compound, MS (ISP): 294.2 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using isopropylamine instead of ethylamine in step a) and 4-chloro-6-phenyl-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 321

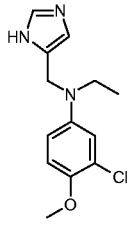
(1H-Imidazol-4-ylmethyl)-methyl-(2-trifluoromethyl-pyrimidin-4-yl)-amine



The title compound, MS (ISP): 258.0 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using methylamine instead of ethylamine in step a) and 4-chloro-2-(trifluoromethyl)-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 322

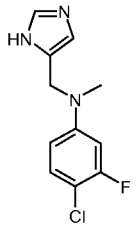
(3-Chloro-4-methoxy-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 268.2 ($[^{37}Cl\ M+H]^{+\cdot}$), 266.1 ($[^{35}Cl\ M+H]^{+\cdot}$), was obtained analogous to the procedure described for Example 302 using 3-chloro-4-methoxy-aniline instead of 4-bromoaniline in step a).

Example 323

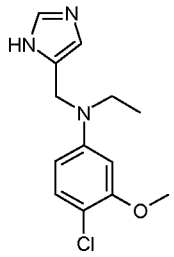
(4-Chloro-3-fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): 242.1 ([^{37}Cl M+H]$^{+\cdot}$), 240.1 ([^{35}Cl M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 186 using 4-chloro-3-fluoro-aniline instead of m-anisidine in step a).

Example 324

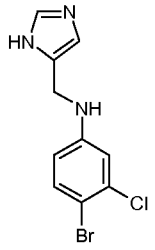
(4-Chloro-3-methoxy-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 268.2 ([^{37}Cl M+H]$^{+\cdot}$), 266.2 ([^{35}Cl M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 302 using 4-chloro-3-methoxy-aniline instead of 4-bromoaniline in step a).

Example 325

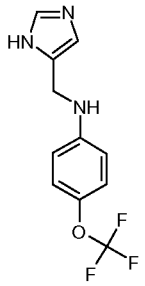
(4-Bromo-3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 290.1 ([^{81}Br^{37}Cl [M+H]$^{+\cdot}$), 288.1 ([^{81}Br^{35}Cl / ^{79}Br^{37}Cl [M+H]$^{+\cdot}$), 286.1 ([^{79}Br^{35}Cl [M+H]$^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 63 using 4-bromo-3-chloro-aniline instead of 2-methoxyaniline.

Example 326

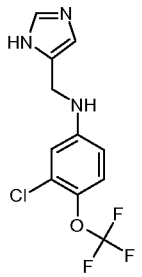
(1H-Imidazol-4-ylmethyl)-(4-trifluoromethoxy-phenyl)-amine



The title compound, MS (ISP): 258.3 ($[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 63 using 4-(trifluoromethoxy)-aniline instead of 2-methoxyaniline.

Example 327

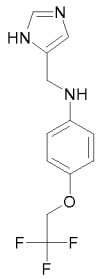
(3-Chloro-4-trifluoromethoxy-phenyl)-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 294.0 (^{37}Cl $[M+H]^{+\cdot}$), 292.1 (^{35}Cl $[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 63 using 3-chloro-4-(trifluoromethyoxy)aniline instead of 2-methoxyaniline.

Example 328

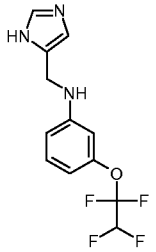
(1H-Imidazol-4-ylmethyl)-[4-(2,2,2-trifluoro-ethoxy)-phenyl]-amine



The title compound, MS (ISP): 272.1 ($[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 63 using 4-(2,2,2-trifluoro-ethoxy)-phenylamine instead of 2-methoxyaniline.

Example 329

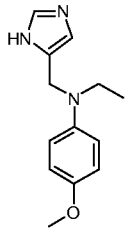
(1H-Imidazol-4-ylmethyl)-[3-(1,1,2,2-tetrafluoro-ethoxy)-phenyl]-amine



The title compound, MS (ISP): 290.0 ([M+H]$^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 63 using 3-(1,1,2,2-tetrafluoroethoxy)aniline instead of 2-methoxyaniline.

Example 330

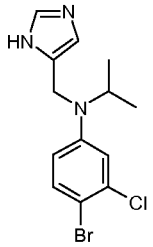
Ethyl-(1H-imidazol-4-ylmethyl)-(4-methoxy-phenyl)-amine



The title compound, MS (ISP): 232.1 ([M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 302 using 4-methoxy-aniline instead of 4-bromoaniline in step a).

Example 331

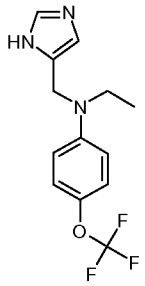
(4-Bromo-3-chloro-phenyl)-(1#H!-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 332.1 (^{81}Br^{37}Cl [M+H]$^{+\cdot}$), 330.0 (^{81}Br^{35}Cl / ^{79}Br^{37}Cl [M+H]$^{+\cdot}$), 328.1 (^{79}Br^{35}Cl [M+H]$^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 67 using 4-bromo-3-chloro-aniline instead of 4-trifluoromethoxyaniline in step a).

Example 332

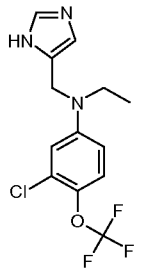
Ethyl-(1H-imidazol-4-ylmethyl)-(4-trifluoromethoxy-phenyl)-amine



The title compound, MS (ISP): 286.1 ([M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 302 using 4-trifluoromethoxy-aniline instead of 4-bromoaniline in step a).

Example 333

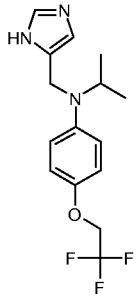
(3-Chloro-4-trifluoromethoxy-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 322.2 ([^{37}Cl M+H]$^{+\cdot}$), 320.1 ([^{35}Cl M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 302 using 3-chloro-4-trifluoromethoxy-aniline instead of 4-bromoaniline in step a).

Example 334

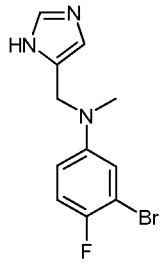
(1H-Imidazol-4-ylmethyl)-isopropyl-[4-(2,2,2-trifluoro-ethoxy)-phenyl]-amine



The title compound, MS (ISP): 314.0 ([M+H]$^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 67 using 4-(2,2,2-trifluoro-ethoxy)-phenylamine instead of 4-trifluoromethoxyaniline in step a).

Example 335

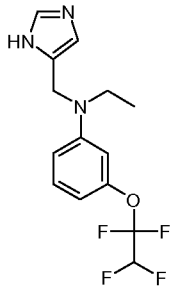
(3-Bromo-4-fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine



The title compound, MS (ISP): MS (ISP): 285.9 ([^{81}Br M+H]$^{+\cdot}$), 283.9 ([^{79}Br M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 186 using 3-bromo-4-fluoro-aniline instead of m-anisidine in step a).

Example 336

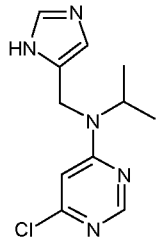
Ethyl-(1H-imidazol-4-ylmethyl)-[3-(1,1,2,2-tetrafluoro-ethoxy)-phenyl]-amine



The title compound, MS (ISP): 318.0 ([M+H]$^{+\cdot}$), was obtained analogous to the procedure described for Example 302 using 3-(1,1,2,2-tetrafluoroethoxy)aniline instead of 4-bromoaniline in step a).

Example 337

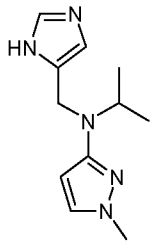
(6-Chloro-pyrimidin-4-yl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 252.1((M+H)$^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using isopropylamine instead of ethylamine in step a) and 4,6-dichloropyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 338

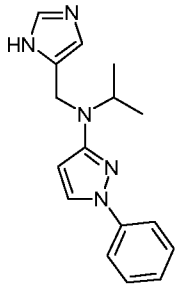
(1H-Imidazol-4-ylmethyl)-isopropyl-(1-methyl-1H-pyrazol-3-yl)-amine



The title compound, MS (ISP): 220.4 ($[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 67 using 3-amino-1-methylpyrazole instead of 4-trifluoromethoxyaniline in step a).

Example 339

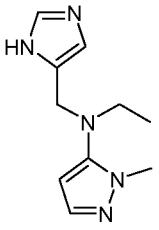
(1H-Imidazol-4-ylmethyl)-isopropyl-(1-phenyl-1H-pyrazol-3-yl)-amine



The title compound, MS (ISP): 282.1 ($[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 67 using 1-phenyl-1H-pyrazol-3-ylamine instead of 4-trifluoromethoxyaniline in step a).

Example 340

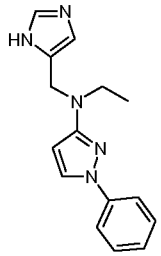
Ethyl-(1H-imidazol-4-ylmethyl)-(2-methyl-2H-pyrazol-3-yl)-amine



The title compound, MS (ISP): 206.1 ($[M+H]^{+\cdot}$), was obtained analogous to the procedure described for Example 302 using 5-amino-1-methylpyrazole instead of 4-bromoaniline in step a).

Example 341

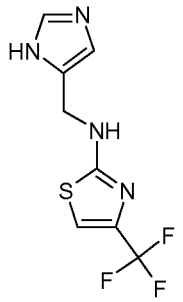
Ethyl-(1H-imidazol-4-ylmethyl)-(1-phenyl-1H-pyrazol-3-yl)-amine



The title compound, MS (ISP): 268.3 ($[M+H]^{+\cdot}$), was obtained analogous to the procedure described for Example 302 using 1-phenyl-1H-pyrazol-3-ylamine instead of 4-bromoaniline in step a).

Example 342

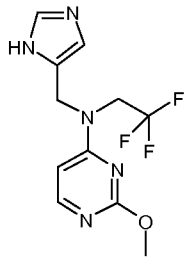
(1H-Imidazol-4-ylmethyl)-(4-trifluoromethyl-thiazol-2-yl)-amine



The title compound, MS (ISP): 249.1 ($[M+H]^{+\cdot}$), was obtained in comparable yield analogous to the procedure described for Example 63 using 4-(trifluoromethyl)-1,3-thiazol-2-amine instead of 2-methoxyaniline.

Example 343

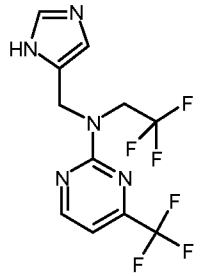
(1H-Imidazol-4-ylmethyl)-(2-methoxy-pyrimidin-4-yl)-(2,2,2-trifluoro-ethyl)-amine



The title compound, MS (ISP): 288.1 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 229 using 2,2,2-trifluoroethylamine instead of ethylamine in step a) and sodium methoxide in 1,2-dimethoxyethane instead of sodium hydride / phenol in dimethylformamide in step b).

Example 344

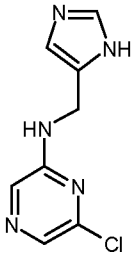
(1H-Imidazol-4-ylmethyl)-(2,2,2-trifluoro-ethyl)-(4-trifluoromethyl-pyrimidin-2-yl)-amine



The title compound, MS (ISP): 326.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 210 using 2,2,2-trifluoroethylamine instead of ethylamine in step a) and 2-chloro-4-(trifluoromethyl)-pyrimidine instead of 2-chloro-4-methoxy-pyrimidine in step b).

Example 345

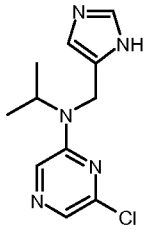
(6-Chloro-pyrazin-2-yl)-(3H-imidazol-4-ylmethyl)-amine



The title compound, MS (ISP): 209.8; 211.8 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 63 using 2-amino-6-chloropyrazine instead of 2-methoxyaniline.

Example 346

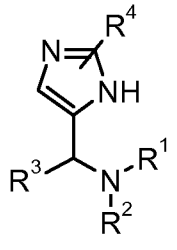
(6-Chloro-pyrazin-2-yl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine



The title compound, MS (ISP): 252.3; 254.3 ($(M+H)^{+\cdot}$) was obtained in comparable yield analogous to the procedure described for Example 67 using 2-amino-6-chloropyrazine instead of 4-trifluormethoxyaniline in step a).

Claims

1. A compound of formula



I

wherein

R^1 is hydrogen, lower alkyl, -$(CR_2)_n$-OH, -$(CH_2)_n$-aryl or -$(CH_2)_n$-heteroaryl, which are optionally substituted by halogen, lower alkoxy or lower alkyl substituted by halogen, or is -$(CR_2)_n$- cycloalkyl, optionally substituted by hydroxy, -$(CH_2)_n$-heterocyclyl, -$(CH_2)_n$-NH-$S(O)_2CH_3$, or is -$(CR_2)_n$O-lower alkyl or lower alkyl substituted by halogen;

R is hydrogen or lower alkyl, and when two R-groups are present, they may or may not be the same;

R^2 is 2,2-dioxo-2,3-dihydro-1*H*-benzo[c]thiophenyl, 6,7-dihydro-5*H*-cyclopentapyrimidin-2-yl, 2,2-difluoro-benzo[1,3]dioxol-5-yl, 2,2,3,3-tetrafluoro-2,3-dihydro-benzo[1,4]dioxin-6-yl, or is aryl or heteroaryl, optionally substituted by one or more substituents, selected from the group consisting of halogen, lower alkyl, cycloalkyl, -$(CH_2)_n$-hydroxy, lower alkyl substituted by halogen, lower alkoxy substituted by halogen, -$S(O)_2$-lower alkyl, -$(CH_2)_n$-$S(O)_2$-NH-lower alkyl, -$(CH_2)_n$-O-lower alkyl, nitro, amino, cyano, -NHC(O)-lower alkyl, -C(O)NH-lower alkyl, or O-tetrahydro-naphthalenyl, or are substituted by -$(CH_2)_n$-aryl, optionally substituted by halogen, or by -CH=CH-aryl, optionally substituted by halogen, or by -$(CH_2)_n$-O-aryl, optionally substituted by halogen, lower alkoxy or lower alkyl

substituted by halogen, or by
-O-$(CH_2)_n$-aryl, optionally substituted by halogen, or by
-$(CH_2)_n$-heteroaryl, or by
-$(CH_2)_n$-O-heteroaryl or by
-$(CH_2)_n$-heterocyclyl, optionally substituted by =O, or by
-$(CH_2)_n$-O-heterocyclyl, optionally substituted by lower alkyl, or by
-S-aryl,
-CH(OH)-aryl,
-$C(CH_3)_2$-aryl,
-NR-aryl, or by
2-oxo-2H-pyridin-1-yl;

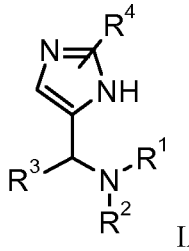
R^3 is hydrogen or lower alkyl;

R^4 is hydrogen or lower alkyl;

n is 0, 1, 2, 3 or 4

and their pharmaceutically active salts, racemic mixtures, enantiomers, optical isomers and tautomeric forms thereof, with the exception of
4-phenylaminomethyl-imidazol-dihydrochloride
benzyl-(*3H*-imidazol-4-ylmethyl)-phenyl-amine
(1H-imidazol-4-ylmethyl)-(4-methoxy-phenyl)-amine
(3,4-dichloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine
(4-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine
(4-bromo-phenyl)-(1H-imidazol-4-ylmethyl)-amine
(3,5-dichloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine and
(3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine.

2. A compound of formula according to claim 1



IA

wherein

R^1 is hydrogen, lower alkyl, -$(CH_2)_n$-aryl, optionally substituted by halogen, lower alkoxy or lower alkyl substituted by halogen, or is -$(CR_2)_n$- cycloalkyl, optionally substituted by hydroxy, or is -$(CR_2)_n$-OH, -$(CH_2)_n$-heterocyclyl, -$(CH_2)_n$-NH-$S(O)_2CH_3$, -$(CR_2)_n$O-lower alkyl or lower alkyl substituted by halogen;

R is hydrogen or lower alkyl, and when two R-groups are present, they may or may not be the same ;

R^2 is aryl or heteroaryl, optionally substituted by one or more substituents, selected from the group consisting of halogen, lower alkyl, lower alkoxy, -$(CH_2)_n$-hydroxy, lower alkyl substituted by halogen, lower alkoxy substituted by halogen, -$S(O)_2$-lower alkyl, -$(CH_2)_n$-$S(O)_2$-NH-lower alkyl, -$(CH_2)_n$-O-lower alkyl, nitro, amino, -NHC(O)-lower alkyl or -C(O)NH-lower alkyl, or -$(CH_2)_n$-aryl, optionally substituted by halogen, or by aryloxy, optionally substituted by halogen, lower alkoxy or lower alkyl substituted by halogen, or aryl or heteroaryl are optionally substituted by benzyloxy, -S-aryl, -CH(OH)-aryl, -$C(CH_3)_2$-aryl, -NR-aryl, 2-oxo-2H-pyridin-1-yl, -$(CH_2)_n$-heterocyclyl, optionally substituted by =O, or by -$(CH_2)_n$-heteroaryl or -$(CH_2)_n$-O-heteroaryl;

R^3 is hydrogen or lower alkyl;

R^4 is hydrogen or lower alkyl;

n is 0, 1, 2, 3 or 4

and their pharmaceutically active salts, racemic mixtures, enantiomers, optical isomers and tautomeric forms thereof

with the exception of
4-phenylaminomethyl-imidazol-dihydrochloride and
benzyl-(*3H*-imidazol-4-ylmethyl)-phenyl-amine.

3. A compound of formula I according to claim 1, wherein R^1 is lower alkyl.

4. A compound of formula I according to claim 3, wherein R^2 is optionally substituted aryl.

5. A compound of formula I according to claim 4, which compounds are

ethyl-(3H-imidazol-4-ylmethyl)-phenyl-amine
methyl-(3H-imidazol-4-ylmethyl)-phenyl-amine
(3-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine
ethyl-(3H-imidazol-4-ylmethyl)-m-tolyl-amine
(3H-imidazol-4-ylmethyl)-isopropyl-phenyl-amine
(3-chloro-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine
(4-chloro-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine
(3-chloro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(3,5-dichloro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(3H-imidazol-4-ylmethyl)-isopropyl-(3-methoxy-phenyl)-amine
(3H-imidazol-4-ylmethyl)-isopropyl-m-tolyl-amine
(3H-imidazol-4-ylmethyl)-isopropyl-(3-trifluoromethyl-phenyl)-amine
(4-chloro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(4-chloro-3-trifluoromethyl-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(3,4-dichloro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(3-chloro-4-trifluoromethoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(4-chloro-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine
(3,4-difluoro-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine
(4-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(3H-imidazol-4-ylmethyl)-isopropyl-(4-trifluoromethoxy-phenyl)-amine
(3H-imidazol-4-ylmethyl)-isopropyl-naphthalen-2-yl-amine
(3H-imidazol-4-ylmethyl)-indan-5-yl-isopropyl-amine
(3-chloro-5-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(3,4-difluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(5-chloro-2-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(3-chloro-2-fluoro-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine
ethyl-(3H-imidazol-4-ylmethyl)-naphthalen-2-yl-amine
(3,5-difluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(2,4-difluoro-3-methoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(4-fluoro-3-methyl-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine
(3H-imidazol-4-ylmethyl)-(3-isopropoxy-phenyl)-isopropyl-amine

(3-benzyloxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(3H-imidazol-4-ylmethyl)-isopropyl-(3-trifluoromethoxy-phenyl)-amine

(3H-imidazol-4-ylmethyl)-isopropyl-(3-phenoxy-phenyl)-amine

((3-difluoromethoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(3H-imidazol-4-ylmethyl)-isopropyl-[3-(1,1,2,2-tetrafluoro-ethoxy)-phenyl]-amine

(3-chloro-4-methyl-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine

(3,4-dimethyl-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine

(4-benzyloxy-3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine

[3-chloro-4-(4-chloro-phenoxy)-phenyl]-ethyl-(1H-imidazol-4-ylmethyl)-amine

(3-benzyl-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

biphenyl-3-yl-(3H-imidazol-4-ylmethyl)-isopropyl-amine

[3-(4-chloro-phenoxy)-phenyl]-(3H-imidazol-4-ylmethyl)-isopropyl-amine

N-(1H-imidazol-4-ylmethyl)-N'-phenyl-benzene-1,4-diamine

{4-[2-(4-chloro-phenyl)-ethyl]-phenyl}-ethyl-(1H-imidazol-4-ylmethyl)-amine

(3-bromo-4-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(3H-imidazol-4-ylmethyl)-methyl-(3-phenoxy-phenyl)-amine

(3H-imidazol-4-ylmethyl)-(3-methoxy-phenyl)-methyl-amine

ethyl-(3H-imidazol-4-ylmethyl)-(3-phenoxy-phenyl)-amine

(3-difluoromethoxy-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine

(3-benzyloxy-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine

(3-benzyloxy-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine

ethyl-(3H-imidazol-4-ylmethyl)-(3-methoxy-phenyl)-amine

ethyl-(4-fluoro-3-methoxy-phenyl)-(3H-imidazol-4-ylmethyl)-amine

(3-ddifluoromethoxy-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine

(4-chloro-3-methoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

[3-(3-chloro-phenoxy)-phenyl]-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(3H-imidazol-4-ylmethyl)-isopropyl-(3-phenoxymethyl-phenyl)-amine

(4-fluoro-3-phenoxy-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(3-bromo-phenyl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine

(3,4-dichloro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine

(3-bromo-phenyl)-ethyl-(3H-imidazol-4-ylmethyl)-amine

(3-bromo-phenyl)-(3H-imidazol-4-ylmethyl)-methyl-amine

(3,4-difluoro-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine

(3,4-dichloro-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine

(3,5-dichloro-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine

(3,5-difluoro-phenyl)-(1H-imidazol-4-ylmethyl)-methyl-amine
(4-bromo-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine
(3,4-dibromo-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine
(4-bromo-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(3,5-dichloro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(3-chloro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(4-bromo-3-fluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(3,5-difluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(4-chloro-3-fluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(3-chloro-5-fluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(3-bromo-4-fluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(3-chloro-4-fluoro-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(4-chloro-3-methoxy-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine
(4-bromo-3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-isopropyl-amine or
(3-chloro-4-trifluoromethoxy-phenyl)-ethyl-(1H-imidazol-4-ylmethyl)-amine.

6. A compound of formula I according to claim 1, wherein R^1 is hydrogen.

7. A compound of formula I according to claim 6, wherein R^2 is optionally substituted aryl.

8. A compound of formula I according to claim 7, which compounds are
(3-chloro-5-fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-amine
{3-[ethyl-(3H-imidazol-4-ylmethyl)-amino]-2,6-difluoro-phenyl}-methanol
(3-bromo-4-fluoro-phenyl)-(3H-imidazol-4-ylmethyl)-amine
[3-(3-chloro-phenoxy)-phenyl]-(3H-imidazol-4-ylmethyl)-amine
(4-fluoro-3-phenoxy-phenyl)-(3H-imidazol-4-ylmethyl)-amine
(3-bromo-phenyl)-(3H-imidazol-4-ylmethyl)-amine
(3-bromo-5-trifluoromethyl-phenyl)-(3H-imidazol-4-ylmethyl)-amine
(3H-imidazol-4-ylmethyl)-(3-isopropyl-phenyl)-amine
(3, 5-difluoro-phenyl)-(1H-imidazol-4-ylmethyl)-amine
(3,4-dibromo-phenyl)-(1H-imidazol-4-ylmethyl)-amine
(3-chloro-4-fluoro-phenyl)-(1H-imidazol-4-ylmethyl)-amine
(4-bromo-3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine or
(3-chloro-4-trifluoromethoxy-phenyl)-(1H-imidazol-4-ylmethyl)-amine.

9. A compound of formula I according to claim 3, wherein R^2 is optionally substituted heteroaryl.

10. A compound of formula I according to claim 9, which compounds are (4,6-dichloro-pyrimidin-2-yl)-ethyl-(1H-imidazol-4-ylmethyl)-amine (6-bromo-pyridin-2-yl)-(3H-imidazol-4-ylmethyl)-isopropyl-amine or ethyl-(1H-imidazol-4-ylmethyl)-(6-trifluoromethyl-pyridin-2-yl)-amine.

11. A compound of formula I according to claim 1, wherein R^1 is optionally substituted CH_2-aryl and R^2 is optionally substituted aryl.

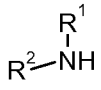
12. A compound of formula I according to claim 11, which compounds are (2-chloro-benzyl)-(3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine (3-chloro-benzyl)-(3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine (4-chloro-benzyl)-(3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine or benzyl-(3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine.

13. A compound of formula I according to claim 1, wherein R^1 is CRH-cycloalkyl and R^2 is optionally substituted aryl.

14. A compound of formula I according to claim 13, which compounds are (3-chloro-phenyl)-cyclopropylmethyl-(3H-imidazol-4-ylmethyl)-amine or (3-chloro-phenyl)-(1-cyclopropylethyl)-(3H-imidazol-4-ylmethyl)-amine.

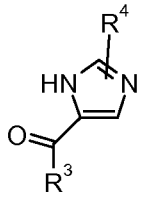
15 . A process for preparation of compounds of formula I, which process comprises

a) reacting an amine of formula



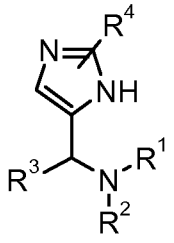
II

with a compound of formula



III

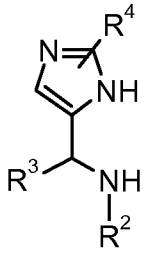
to a compound of formula



I

wherein R^1, R^2, R^3, and R^4 are as defined in claim 1, or

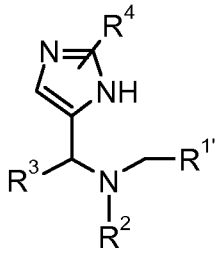
b) reacting a compound of formula



I-1

with a compound of formula $R^{1'}$-CHO

to a compound of formula

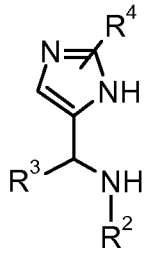


I-2

wherein $R^{1'}$ is lower alkyl, -$(CH_2)_{n-1}$-aryl or –$(CH_2)_{n-1}$-heteroaryl, which are optionally substituted by lower alkoxy, lower alkyl substituted by halogen or halogen, or is -$(CR_2)_{n-1}$- cycloalkyl, optionally substituted by hydroxy, or is –$(CR_2)_{n-1}$-OH,

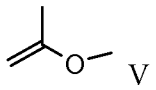
-$(CH_2)_{n-1}$-heterocyclyl, -$(CH_2)_{n-1}$-NH-$S(O)_2CH_3$, -$(CR_2)_{n-1}$O-lower alkyl and the other definitions are as described in claim 1, or

c) reacting a compound of formula



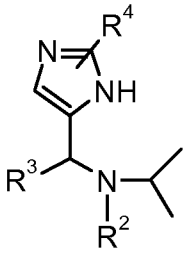
I-1

with



V

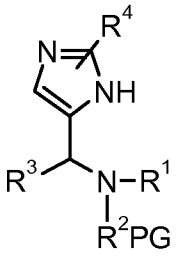
to a compound of formula



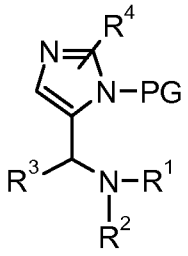
I-3

wherein the substituents are as defined in claim 1, or

d) removing a protecting group of compounds of formulas

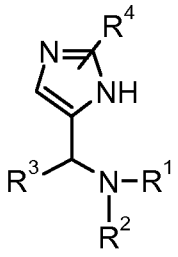


VI or



X

to a compound of formula



I

wherein the substituents are as defined in claim 1, or

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

16. A compound according to claim 1, whenever prepared by a process as claimed in claim 15 or by an equivalent method.

17. A medicament containing one or more compounds of formula I and of
4-phenylaminomethyl-imidazol-dihydrochloride
benzyl-(*3H*-imidazol-4-ylmethyl)-phenyl-amine
(1H-imidazol-4-ylmethyl)-(4-methoxy-phenyl)-amine
(3,4-dichloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine
(4-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine
(4-bromo-phenyl)-(1H-imidazol-4-ylmethyl)-amine
(3,5-dichloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine and
(3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine.

in accordance with claim 1 and pharmaceutically acceptable excipients.

18. A medicament as claimed in claim 17 for the treatment of depression, anxiety disorders, bipolar disorder, attention deficit hyperactivity disorder, stress-related disorders, psychotic disorders, schizophrenia, neurological diseases, Parkinson's disease, neurodegenerative disorders, Alzheimer's disease, epilepsy, migraine, hypertension, substance abuse and metabolic disorders, eating disorders, diabetes, diabetic complications, obesity, dyslipidemia, disorders of energy consumption and assimilation, disorders and malfunction of body temperature homeostasis, disorders of sleep and circadian rhythm, and cardiovascular disorders.

19. A medicament according to claim 18 containing one or more compounds as claimed in claim 1 for the treatment of depression, psychosis, Parkinson's disease, anxiety and attention deficit hyperactivity disorder (ADHD).

20. The use of a compound of formula I and of
4-phenylaminomethyl-imidazol-dihydrochloride
benzyl-(*3H*-imidazol-4-ylmethyl)-phenyl-amine
(1H-imidazol-4-ylmethyl)-(4-methoxy-phenyl)-amine
(3,4-dichloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine
(4-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine
(4-bromo-phenyl)-(1H-imidazol-4-ylmethyl)-amine
(3,5-dichloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine and
(3-chloro-phenyl)-(1H-imidazol-4-ylmethyl)-amine.

according to claim 1 for the preparation of a medicament for the treatment of depression, anxiety disorders, bipolar disorder, attention deficit hyperactivity disorder, stress-related disorders, psychotic disorders, schizophrenia, neurological diseases, Parkinson's disease, neurodegenerative disorders, Alzheimer's disease, epilepsy, migraine, hypertension, substance abuse and metabolic disorders, eating disorders, diabetes, diabetic complications, obesity, dyslipidemia, disorders of energy consumption and assimilation, disorders and malfunction of body temperature homeostasis, disorders of sleep and circadian rhythm, and cardiovascular disorders.

21. The invention as herein before described.

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