Summary of the Invention

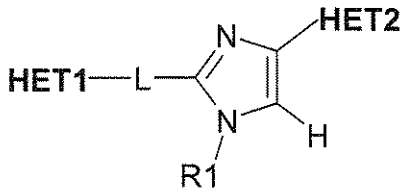
The objective of the present ~~invention~~disclosure is to provide compounds that are selective PDE10A enzyme inhibitors.

A further objective of the present ~~invention~~disclosure is to provide compounds which have such activity, and which have improved solubility, metabolic stability and/or bioavailability compared to prior art compounds.

Another objective of the ~~invention~~disclosure is to provide an effective treatment, in particular long-term treatment, of a human patient, without causing the side effects typically associated with current therapies for neurological and psychiatric disorders.

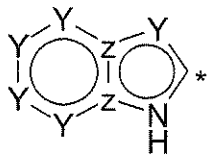
Further objectives ~~of the invention~~ will become apparent upon reading the present specification.

Accordingly, in one aspect the present invention relates to compounds of formula **I:**



I

wherein **HET1** is a heteroaromatic group of formula **II** containing from 2 to 4 nitrogen atoms:

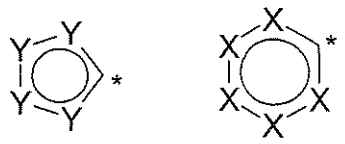


II

wherein Y ~~is~~can ~~be~~ N or CH, Z ~~is~~can ~~be~~ N or C, and wherein **HET1** ~~is~~may optionally ~~be~~ substituted with up to three substituents R2, R3 and R4 individually selected from H; C_1-C_6 alkyl such as Me; halogen such as chlorine and bromine; cyano; halo(C_1-C_6)alkyl such as trifluoromethyl; aryl such as phenyl; alkoxy, such as methoxy, dimethoxy, ethoxy, methoxy-ethoxy and ethoxy-methoxy, and C_1-C_6 hydroxyalkyl

such as CH_2CH_2OH, and wherein * denotes the attachment point,

wherein **HET2** is a heteroaromatic group of formula **III** or formula **IV**:



III **IV**

wherein Y can be N, S, O or CH, X can be N or CH and wherein **HET2** may optionally be substituted with up to three substituents R5, R6 and R7 individually selected from H; C_1-C_6 alkyl such as Me; halogen such as chlorine and bromine; cyano; halo(C_1-C_6)alkyl such as trifluoromethyl; aryl such as phenyl; alkoxy, such as methoxy, dimethoxy, ethoxy, methoxy-ethoxy and ethoxy-methoxy, and C_1-C_6 hydroxyalkyl such as CH_2CH_2OH, and wherein * denotes the attachment point,

-L- is a linker selected from -S-CH_2-, -CH_2-S-, -CH_2-CH_2- , -CH=CH- and $-C\equiv C-$

R1 is selected from H; C_1-C_6 alkyl such as methyl, ethyl, 1-propyl, 2-propyl, isobutyl; C_1-C_6 alkyl(C_3-C_8)cycloalkyl such as cyclopropylmethyl; C_1-C_6 hydroxyalkyl such as hydroxyethyl; CH_2CN; $CH_2C(O)NH_2$; C_1-C_6 arylalkyl such as benzyl and 4-chlorobenzyl; halo(C_1-C_6)alkyl such as trifluoromethyl and C_1-C_6 alkyl-heterocycloalkyl such as tetrahydropyran-4-yl-methyl and 2-morpholin-4-yl-ethyl;

and tautomers and pharmaceutically acceptable acid addition salts thereof, and polymorphic forms thereof, provided that the compound is not 2-(5-phenyl-1H-imidazol-2-ylmethylsulfanyl)-1H-benzoimidazole or 2-(5-phenyl-1H-imidazol-2-yl-sulfanyl-methyl)-1H-benzoimidazole.

In separate embodiments ~~of the invention~~, the compound of formula I is selected among the specific compounds disclosed in the Experimental Section herein.

The invention further provides a compound of formula I, or a pharmaceutically acceptable acid addition salt thereof, for use as a medicament.

In another aspect, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound of formula I and a pharmaceutically acceptable carrier, diluent or excipient.

The ~~invention~~disclosure further provides the use of a compound of formula I, or a pharmaceutically acceptable acid addition salt thereof, for the preparation of a medicament for the treatment of a neurodegenerative or psychiatric disorder.

Furthermore, in yet another ~~aspect~~embodiment, the present ~~invention~~disclosure provides a method of treating a subject suffering from a neurodegenerative disorder, comprising administering to the subject a therapeutically effective amount of a compound of formula I. In a still further ~~aspect~~embodiment, the present ~~invention~~disclosure provides a method of treating a subject suffering from a psychiatric disorder, comprising administering to the subject a therapeutically effective amount of a compound of formula I. In another embodiment, the present ~~invention~~disclosure provides a method of treating a subject suffering from a drug addiction, such as an alcohol, amphetamine, cocaine, or opiate addiction.

In another aspect, there is provided the use of a compound as defined above, in the manufacture of a medicament for the treatment of a neurodegenerative or psychiatric disorder, alone or in combination with one or more neuroleptic agents, wherein the neurodegenerative disorder is selected from the group consisting of Alzheimer's disease, multi-infarct dementia, alcoholic dementia or other drug-related dementia, dementia associated with intracranial tumors or cerebral trauma, dementia associated with Huntington's disease or Parkinson's disease, or AIDS-related dementia; delirium; amnestic disorder; post-traumatic stress disorder; mental retardation; a learning disorder, or a disorder of written expression; attention-deficit/hyperactivity disorder; and age-related cognitive decline, and the psychiatric disorder is selected from the group consisting of schizophrenia, schizophreniform disorder; schizoaffective disorder, for example of the delusional type or the depressive type; delusional disorder; substance-induced psychotic disorder, for example psychosis; personality disorder of the paranoid type; and personality disorder of the schizoid type.

Detailed Description of the Invention

Definition of Substitutents

As used in the context of the present invention, the terms "halo" and "halogen" are used interchangeably and refer to fluorine, chlorine, bromine or iodine.

The term "C_1-C_6 alkyl" refers to a straight-chain or branched saturated hydrocarbon having from one to six carbon atoms, inclusive. Examples of such groups include, but are not limited to, methyl, ethyl, 1-propyl, 2-propyl, 1-butyl, 2-butyl, 2-methyl-2-propyl, 2-methyl-1-butyl, and n-hexyl. The expression "C_1-C_6 hydroxyalkyl" refers to a C_1-C_6 alkyl group as defined above which is substituted with one hydroxy group. The term "halo(C_1-C_6)alkyl" refers to a C_1-C_6 alkyl group as defined above which is substituted with up to three halogen atoms, such as trifluoromethyl.

25. The use according to claim 24, wherein the neuroleptic agent is selected from the group consisting of sertindole, olanzapine, risperidone, quetiapine, aripiprazole, haloperidol, clozapine, ziprasidone and osanetant.

26. The use according to claim 24, wherein the learning disorder is reading disorder or mathematics disorder.

27. The use according to claim 24, wherein schizophrenia is of the paranoid, disorganized, catatonic, undifferentiated, or residual type.

28. The use according to claim 24, wherein the psychosis is induced by alcohol, amphetamine, cannabis, cocaine, hallucinogens, inhalants, opioids, or phencyclidine.

29. Use of a compound of any one of claims 1 to 22, in the manufacture of a medicament for the treatment of a drug addiction in a mammal, including a human.

30. The use according to claim 29, wherein the drug addiction is an alcohol, amphetamine, cocaine, or opiate addiction.

31. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1 to 22, and one or more pharmaceutically acceptable carriers, diluents and excipients.

31. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1 to 22, and one or more pharmaceutically acceptable carriers, diluents and excipients.