In recent years there have been significant advantages in understanding the pathophysiology of several disorders of brain development, suggesting that protein synthesis at synapses is triggered by activation of group I metabotropic glutamate receptors. Such disorders include fragile X syndrome, autism, idiopatic autism, tuberous sclerosis complex disorder, neurofibromatosis type 1 or Rett syndrome (*Annu. Rev. Med., 2011, 62, 31.1 – 31.19 and Neuroscience 156, 2008, 203-215).*

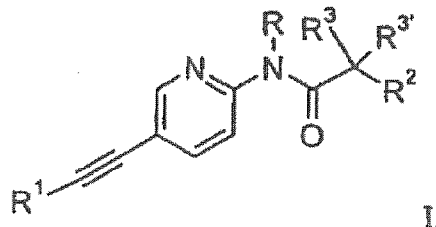
Described in the prior art are positive allosteric modulators. They are compounds that do not directly activate receptors by themselves, but markedly potentiate agonist-stimulated responses, increase potency and maximum of efficacy. The binding of these compounds increases the affinity of a glutamate-site agonist at its extracellular N-terminal binding site. Allosteric modulation is thus an attractive mechanism for enhancing appropriate physiological receptor activation. There is a scarcity of selective allosteric modulators for the mGluR5 receptor. Conventional mGluR5 receptor modulators typically lack satisfactory aqueous solubility and exhibit poor oral bioavailability.
Therefore, there remains a need for compounds that overcome these deficiencies and that effectively provide selective allosteric modulators for the mGluR5 receptor.

Compounds of formula I are distinguished by having valuable therapeutic properties. They can be used in the treatment or prevention of disorders, relating to allosteric modulators for the mGluR5 receptor.

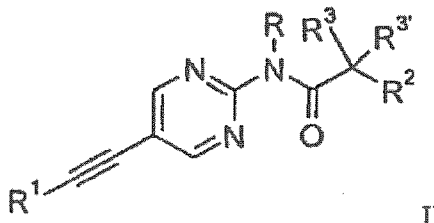
The most preferred indications for compounds which are allosteric modulators are schizophrenia and cognition.

The present ~~invention~~ disclosure relates to compounds of formula I and to their pharmaceutically acceptable salts, in cases where this applies to mixtures of enantiomers or diastereomers or their enantiomerically or diastereomerically pure forms, to these compounds as pharmaceutically active substances, to the processes for their production as well as to the use in the treatment or prevention of disorders, relating to allosteric modulators for the mGluR5 receptor, such as schizophrenia, cognition, fragile X syndrome or autism, and to pharmaceutical compositions containing the compounds of formula I.

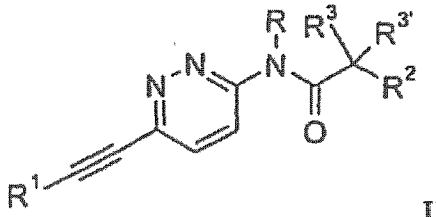
In one aspect, there is provided ethynyl derivatives of formula IA, IB and ID



IA



IB and



ID

wherein

R^1 is phenyl or heteroaryl, which are optionally substituted by halogen, lower alkyl or lower alkoxy;

R is hydrogen or lower alkyl;

R^2 is hydrogen, lower alkyl, lower alkoxy, CF_3 or S-lower alkyl;

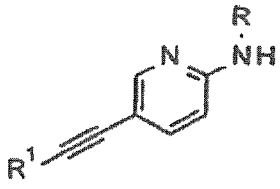
$R^3/R^{3'}$ are independently from each other hydrogen, lower alkyl or lower alkoxy;

or R^3 and $R^{3'}$ form together a C_{3-5}-cycloalkyl-, tetrahydrofuran- or an oxetane-ring;

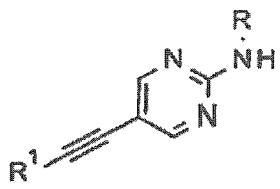
or a pharmaceutically acceptable acid addition salt thereof, a racemic mixture, or its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof, with the exception of the compound N-(5-((1H-pyrrolo[2,3-B]pyridine-2-yl)ethynyl)pyridine-2-yl)acetamide.

In another aspect, there is provided a process for preparation of a compound of formula I as defined herein, comprising the variant

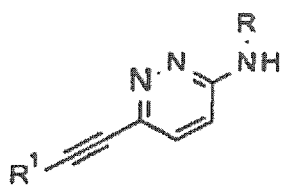
a) reacting a compound of formula



3A,

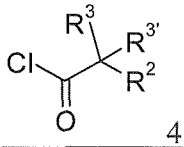


3B or

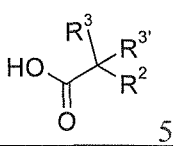


3D

with a suitable compound of formula

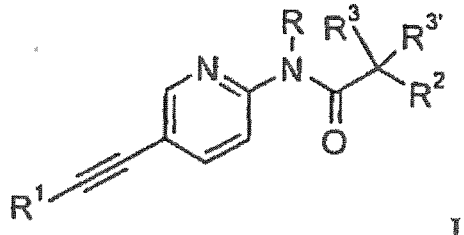


4 or

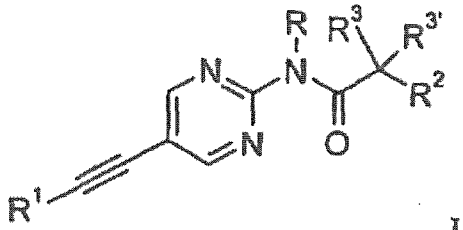


5

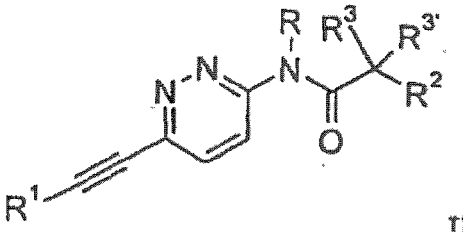
to a compound of formulas



IA



IB or

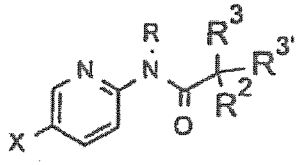


ID

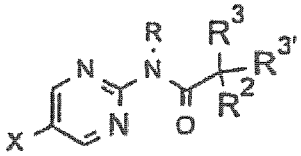
wherein the substituents are described above, or

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

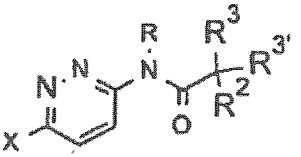
b)reacting a compound of formulas



6A,

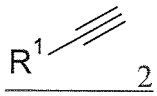


6B or



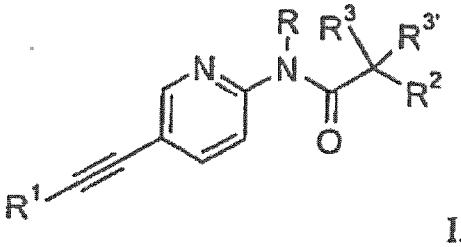
6D

with a suitable compound of formula

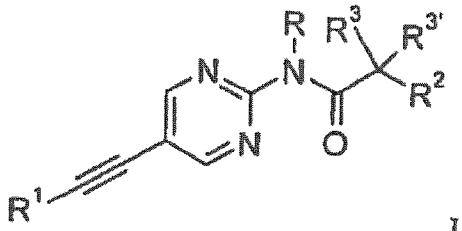


2

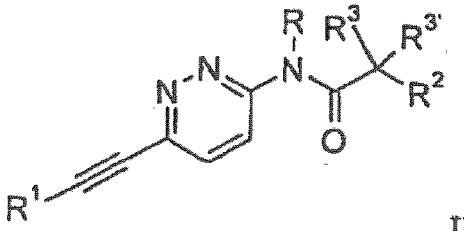
to a compound of formulas



IA



IB or

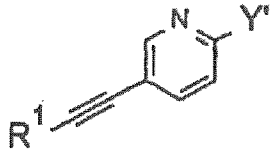


ID

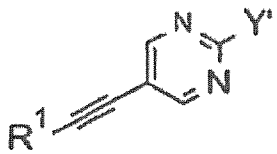
wherein the substituents are described above, or

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

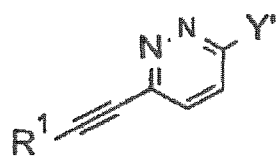
c) reacting a compound of formulas



13A,

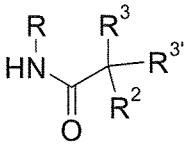


13B or

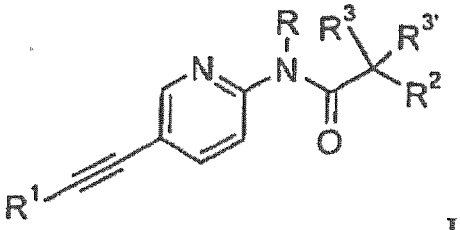


13D

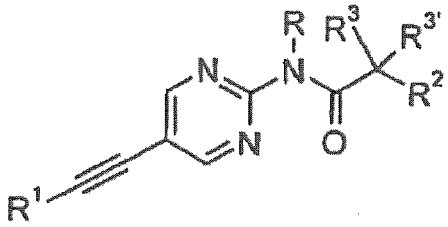
with a suitable compound of formula



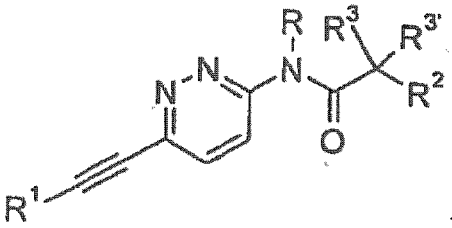
to a compound of formula



IA



IB or



ID

wherein the substituents are described above, or

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

In another aspect, there is provided a compound as defined herein for use as therapeutically active substance.

In another aspect, there is provided a pharmaceutical composition comprising at least one of the compounds as defined herein as well as its pharmaceutically acceptable salt.

In another aspect, there is provided a compound as defined herein, when applicable as mixtures of enantiomers, diastereomers, or in enantiomerically pure form; as well as its pharmaceutically acceptable salt, for use as a medicament.

In another aspect, there is provided the use of a compound as defined herein as well as its pharmaceutically acceptable salt for the manufacture of a medicament for the treatment or prevention of diseases relating to allosteric modulators of $mGluR^5$ receptors.

In another aspect, there is provided a compound as defined herein for use in the treatment or prevention of schizophrenia, cognitive diseases, fragile X syndrome or autism.

The following definitions of the general terms used in the present description apply irrespective of whether the terms in question appear alone or in combination.