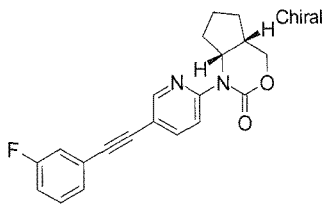
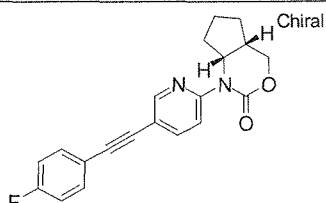
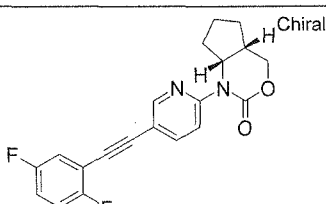


|       |                                                                                   |    |    |            |
|-------|-----------------------------------------------------------------------------------|----|----|------------|
| Ex. 2 |  | 10 | 43 | NO<br>FLAG |
| Ex. 3 |  | 10 | 40 | NO<br>FLAG |
| Ex. 4 |  | 15 | 35 | No<br>FLAG |

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.

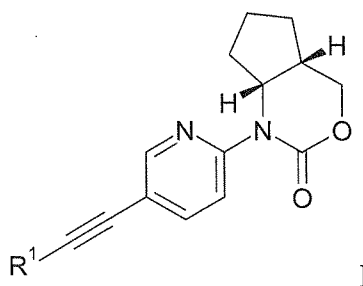
- 5        The most preferred indications for compounds which are allosteric modulators are schizophrenia and cognition.

The present ~~invention~~ disclosure relates to compounds of formula I and to their pharmaceutically acceptable salts, 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  
10 disorders, relating to allosteric modulators for the mGluR5 receptor, such as schizophrenia and cognition and to pharmaceutical compositions containing the compounds of formula I.

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.

The term "pharmaceutically acceptable salt" or "pharmaceutically acceptable acid addition  
15 salt" 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.

The embodiment of the ~~invention~~ disclosure are compounds of formula I



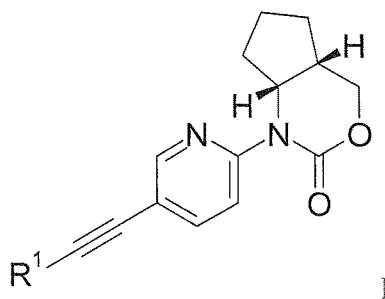
wherein

R<sup>1</sup> is phenyl, 3-fluorophenyl, 4-fluorophenyl or 2,5-di-fluorophenyl;

or a pharmaceutically acceptable acid addition salt, in enantiomerically pure form with the

5 absolute configuration as shown in formula I.

In a first aspect, there are provided ethynyl derivatives of formula I



wherein

R<sup>1</sup> is phenyl, 3-fluorophenyl, 4-fluorophenyl or 2,5-di-fluorophenyl;

10 or a pharmaceutically acceptable acid addition salt in enantiomerically pure form.

Compounds of formula I are the followings:

(4aS,7aR)-1-(5-Phenylethynyl-pyridin-2-yl)-hexahydro-cyclopenta[d][1,3]oxazin-2-one

(4aS,7aR)-1-[5-(3-Fluorophenylethynyl)-pyridin-2-yl]-hexahydro-cyclopenta[d][1,3]oxazin-2-one

15 (4aS,7aR)-1-(5-((4-Fluorophenyl)ethynyl)-pyridin-2-yl)hexahydro-cyclopenta[d][1,3]oxazin-2(1H)-one

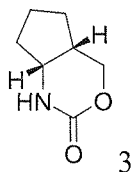
(4aS,7aR)-1-[5-(2,5-Difluorophenylethynyl)-pyridin-2-yl]-hexahydro-cyclopenta[d][1,3]oxazin-2-one

The preparation of compounds of formula I of the present ~~disclosure invention~~ may be  
 20 carried out in sequential or convergent synthetic routes. Syntheses of the compounds of the  
~~disclosure invention~~ are shown in the following schemes 1 to 3. The skills required for carrying  
 out the reaction and purification of the resulting products are known to those skilled in the art.  
 The substituents and indices used in the following description of the processes have the  
 significance given herein before.

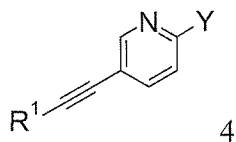
The compounds of formula I can be manufactured by the methods given below, by the methods given in the examples or by analogous methods. Appropriate reaction conditions for the individual reaction steps are known to a person skilled in the art. The reaction sequence is not limited to the one displayed in the schemes, however, depending on the starting materials and  
5 their respective reactivity the sequence of reaction steps can be freely altered. Starting materials are either commercially available or can be prepared by methods analogous to the methods given below, by methods described in references cited in the description or in the examples, or by methods known in the art.

The present compounds of formula I and their pharmaceutically acceptable salts may be prepared by methods, known in the art, for example by the process variant described below. In a second aspect, there is provided a process for preparation of a compound of formula I as described herein, comprising the variants which process comprises

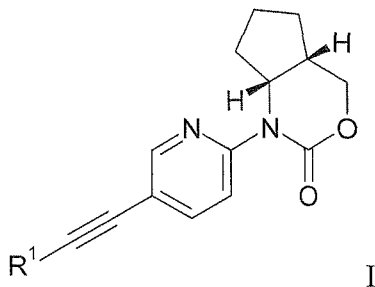
- 5 a) reacting a compound of formula 3



where the compound of formula 3 is a racemic mixture or in enantiomerically pure form with a suitable arylacetylene halo-pyridine compound of formula 4, where Y is halogen, preferably fluorine, bromine or iodine

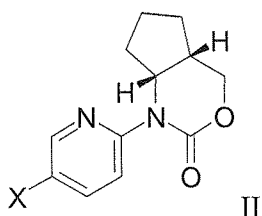


to form a compound of formula I in enantiomerically pure form or as a racemic mixture, where the enantiomers can be separated using methods known to persons skilled in the art,

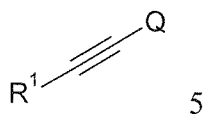


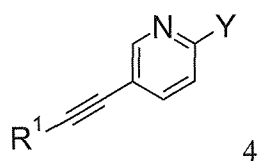
wherein the substituents are described above, or if desired, converting the compounds obtained into pharmaceutically acceptable acid addition salts or by

- b) reacting a compound of formula II in enantiomerically pure form or as a racemic mixture, where X is halogen, preferably iodine or bromine

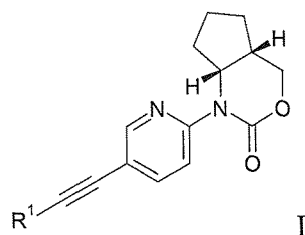


with an acetylene compound of formula 5, where Q is hydrogen or a trialkylsilyl group

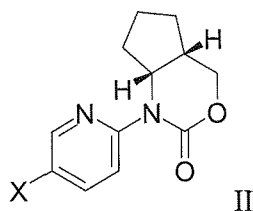




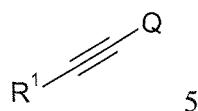
to form a compound of formula I in enantiomerically pure form or as a racemic mixture, where the enantiomers can be separated using methods known to persons skilled in the art,



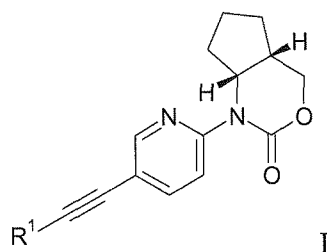
- 5 wherein the substituents are described ~~above~~ in claim 1, or if desired, converting the compounds obtained into pharmaceutically acceptable acid addition salts or by  
be) reacting a compound of formula II in enantiomerically pure form or as a racemic mixture, where X is halogen, preferably iodine or bromine



- 10 with an acetylene compound of formula 5, where Q is hydrogen or a trialkylsilyl group



to form a compound of formula I in enantiomerically pure form or as a racemic mixture which can be separated using methods known to persons skilled in the art,



- 15 wherein the substituents are described in claim 1, or if desired, converting the compounds obtained into pharmaceutically acceptable acid addition salts.

4. A compound according to any one of claims 1 to 2 for use as therapeutically active substance.

5. A pharmaceutical composition comprising at least one of the compounds according to any one of claims 1 to 2 as well as its pharmaceutically acceptable salt.

5           6. A compound of any one of claims 1 to 2, when applicable as mixtures of enantiomers, diastereomers, or in enantiomerically pure form; as well as its pharmaceutically acceptable salt, for use as a medicament.

7. The use of a compound according to any one of claims 1 to 2 as well as its pharmaceutically acceptable salt ~~for~~in the manufacture of a medicament for the treatment or  
10   prevention of diseases relating to allosteric modulators of mGluR<sup>5</sup> receptors.

8. The use of a compound according to claim 7 for the treatment or prevention of schizophrenia, cognitive diseases, fragile X syndrome or autism.

9. A compound according to any one of claims 1 to 2 for use in the treatment or prevention of schizophrenia, cognitive diseases, fragile X syndrome or autism.

15           ~~10. A method for the treatment of schizophrenia, cognitive diseases, fragile X syndrome or autism, which method comprises administering an effective amount of a compound as defined in any one of claims 1 to 2.~~