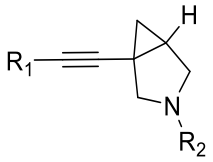
CLAIMS

1. A compound of formula (I):



(I) ,

or a pharmaceutically acceptable salt thereof, wherein:

R_1 is a 5- to 10-membered monocyclic or bicyclic heteroaryl that contains 1, 2 or 3 heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur, wherein the 5- to 10-membered monocyclic or bicyclic heteroaryl is optionally substituted with 1, 2 or 3 substituents independently selected from the group consisting of alkyl, halogen, -OH, -CN, -NO_2, -CF_3, -O-CF_3, -O-alkyl, -O-aryl, -S-alkyl, -S-aryl, -S(O)-alkyl, -S(O)-aryl, -S(O_2)-alkyl, -S(O_2)-aryl, -CH_2-aryl, aryl, heteroaryl, -O-CH_2-aryl, -N(CH_3)$_2$, cycloalkyl, heterocycloalkyl, -C(O)-alkyl, -C(O)-cycloalkyl, -C(O)-heterocycloalkyl, -C(O)-aryl, -C(O)-heteroaryl, -C(O)O-alkyl, -C(O)O-cycloalkyl, -C(O)O-heterocycloalkyl, -C(O)O-aryl, -C(O)O-heteroaryl, -C(O)NH-alkyl, -C(O)NH-cycloalkyl, -C(O)NH-heteroalkyl, -C(O)NH-aryl and -C(O)NH-heteroaryl, wherein the substituents may combine to form a 5-7 membered fused carbocyclyl or heterocyclyl; and

R_2 is -C(O)-alkyl, -C(O)-arylalkyl, -C(O)-aryl, -C(O)-heteroaryl, -S($O)_2$-aryl, -S($O)_2$-heteroaryl, -C(O)O-alkyl, -C(O)O-aryl, -C(O)O-arylalkyl, or -C(O)-NH_2, wherein the aryl or heteroaryl portion of -C(O)-arylalkyl, -C(O)-aryl, -C(O)-heteroaryl, -S($O)_2$-aryl, -S($O)_2$-heteroaryl, -C(O)O-aryl and -C(O)O-arylalkyl are optionally substituted with 1, 2 or 3 substituents independently selected from the group consisting of alkyl, halogen, -OH,

-CN, -NO_2, -CF_3, -OCF_3, -O-alkyl, -O-aryl, -S-alkyl, -S-aryl, -S(O)-alkyl, -S(O)-aryl, -S(O_2)-alkyl, -S(O_2)aryl, -CH_2-aryl, heteroaryl, -O-CH_2-aryl, -N(CH_3)$_2$, cycloalkyl, heterocycloalkyl, -C(O)-alkyl, -C(O)-cycloalkyl, -C(O)-heterocycloalkyl, -C(O)-aryl, -C(O)-heteroaryl, -C(O)O-alkyl, -C(O)O-cycloalkyl, -C(O)O-heterocycloalkyl, -C(O)O-aryl, -C(O)O-heteroaryl, -C(O)NH-alkyl, -C(O)NH-cycloalkyl, -C(O)NH-heteroalkyl, -C(O)NH-aryl and -C(O)NH-heteroaryl, wherein the substituents may combine to form a 5-7 membered fused carbocyclyl or heterocyclyl; or

R_2 is a 5- to 10-membered monocyclic or bicyclic heteroaryl that contains 1, 2 or 3 heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur, wherein the 5- to 10-membered monocyclic or bicyclic heteroaryl is optionally substituted with 1, 2 or 3 substituents independently selected from the group consisting of alkyl, halogen, -OH, -CN, -NO_2, -CF_3, -O-CF_3, -O-alkyl, -O-aryl, -S-alkyl, -S-aryl, -S(O)-alkyl, -S(O)-aryl, -S(O_2)-alkyl, -S(O_2)-aryl, -CH_2-aryl, aryl, heteroaryl, -O-CH_2-aryl, -N(CH_3)$_2$, cycloalkyl, heterocycloalkyl, -C(O)-alkyl, -C(O)-cycloalkyl, -C(O)-heterocycloalkyl, -C(O)-aryl, -C(O)-heteroaryl, -C(O)O-alkyl, -C(O)O-cycloalkyl, -C(O)O-heterocycloalkyl, -C(O)O-aryl, -C(O)O-heteroaryl, -C(O)NH-alkyl, -C(O)NH-cycloalkyl, -C(O)NH-heteroalkyl, -C(O)NH-aryl and -C(O)NH-heteroaryl, wherein the substituents may combine to form a 5-7 membered fused carbocyclyl or heterocyclyl; or

R_2 is a 5- to 10-membered monocyclic or bicyclic aryl, wherein the 5- to 10-membered monocyclic or bicyclic aryl is optionally substituted with 1, 2 or 3 substituents independently selected from the group consisting of alkyl, halogen, -OH, -CN, -NO_2, -CF_3, -OCF_3, -O-alkyl, -O-aryl, -S-alkyl, -S-aryl, -S(O)-alkyl, -S(O)-aryl, -S(O_2)-alkyl, -S(O_2)aryl, -CH_2-aryl, aryl, heteroaryl, -O-CH_2-aryl, -N(CH_3)$_2$, cycloalkyl, heterocycloalkyl, -C(O)-alkyl,

-C(O)cycloalkyl, -C(O)-heterocycloalkyl, -C(O)-aryl, -C(O)-heteroaryl, -C(O)O-alkyl, -C(O)O-cycloalkyl, -C(O)O-heterocycloalkyl, -C(O)O-aryl, -C(O)O-heteroaryl, -C(O)NH-alkyl, -C(O)NH-cycloalkyl, -C(O)NH-heteroalkyl, -C(O)NH-aryl and -C(O)NH-heteroaryl, wherein the substituents may combine to form a 5-7 membered fused carbocyclyl or heterocyclyl.

2. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein:

R_1 is a 5- to 6-membered monocyclic heteroaryl that contains 1, 2 or 3 heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur, optionally substituted with 1 or 2 substituents; and

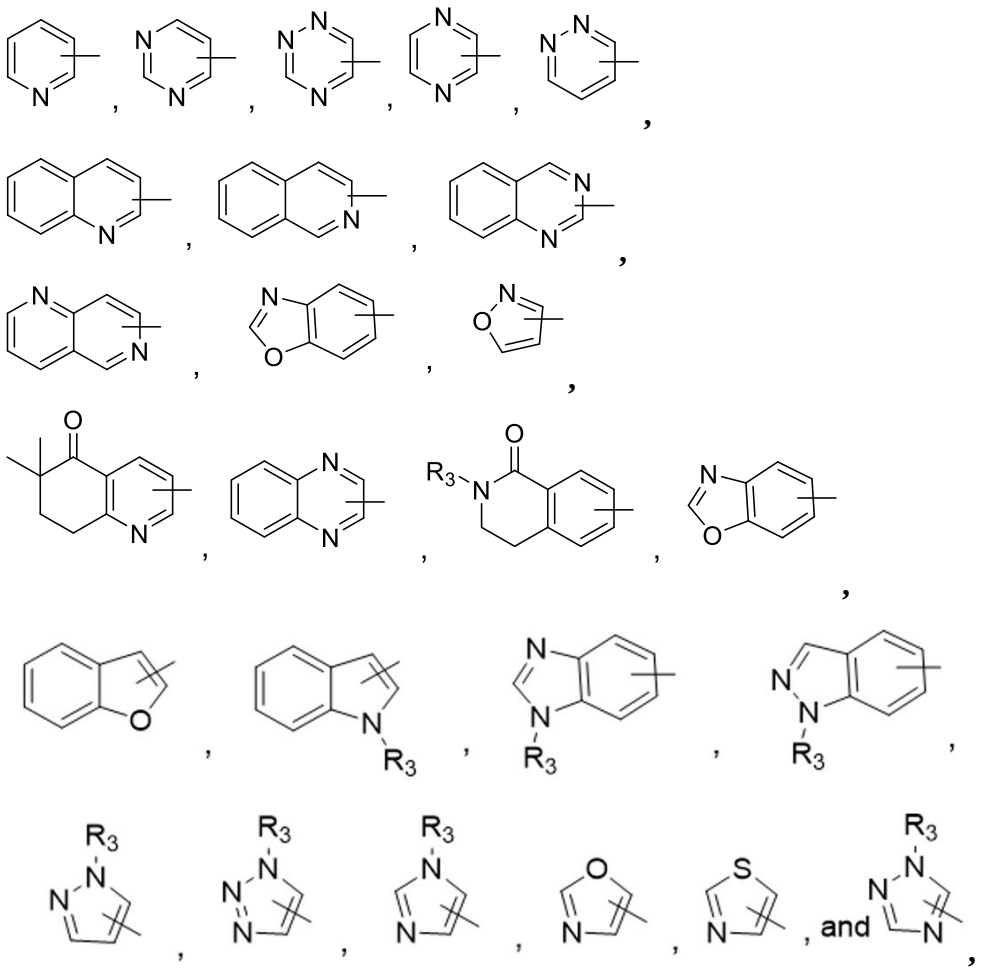
R_2 is -C(O)-C_1-C_5-alkyl, -C(O)-C_1-C_5-alkylaryl, -C(O)-aryl, -C(O)-heteroaryl, -C(O)O-C_1-C_5-alkyl, -C(O)O-C_1-C_5-alkylaryl or -$S(O)_2$-phenyl, wherein the aryl, phenyl or heteroaryl portion of the -C(O)-C_1-C_5-alkylaryl, -C(O)-aryl, -C(O)-heteroaryl, -C(O)O-C_1-C_5-arylalkyl and -$S(O)_2$-phenyl is optionally substituted; or

R_2 is a 5- to 10-membered monocyclic or bicyclic heteroaryl that contains 1, 2 or 3 heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur, wherein the 5- to 10-membered monocyclic or bicyclic heteroaryl is optionally substituted with 1 or 2 substituents; or

R_2 is a 5- to 10-membered monocyclic or bicyclic aryl, wherein the 5- to 10-membered monocyclic or bicyclic aryl is optionally substituted with 1 or 2 substituents.

3. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein:

R_1 is selected from the group consisting of:



R_3 is -H or lower alkyl.

4. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein: R_1 is optionally substituted thiazolyl, optionally substituted 4-pyridinyl, optionally substituted pyridazinyl, optionally substituted pyrimidinyl, or optionally substituted pyrazinyl.

5. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein: R_1 is optionally substituted 2-pyridinyl.

6. The compound according to claim 1, wherein the compound is selected from the group consisting of:

3-fluoro-5-(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0] hexan-3-yl)benzonitrile,
3-(4-fluorophenyl)-1-(pyridin-2-ylethynyl)-3-azabicyclo [3.1.0]hexane,
1-(pyridin-2-ylethynyl)-3-(4-(trifluoromethoxy)phenyl)-3-azabicyclo [3.1.0]hexane,
3-phenyl-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane,
3-(2-fluorophenyl)-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane,
3-(2-chlorophenyl)-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane,
3-(3-chlorophenyl)-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane,
3-(4-chlorophenyl)-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane,
3-(3-chloro-5-fluorophenyl)-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane,
3-(4-chloro-2-fluorophenyl)-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane,
3-(4-chloro-3-fluorophenyl)-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane，
3-(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)benzonitrile,
3-(3,5-difluorophenyl)-1-(pyrimidin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane,
3-(3-fluorophenyl)-1-(pyrimidin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane,
3-(1-((2-methylthiazol-4-yl)ethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)benzonitrile,
4-(3-(5-fluoropyridin-3-yl)-3-azabicyclo[3.1.0]hexan-1-yl)ethynyl)-2-methylthiazole,
and
3-(1-(pyrimidin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)benzonitrile,
or a pharmaceutically acceptable salt thereof.

7. The compound according to claim 1, wherein the compound is selected from the group consisting of:

3-(5-fluoropyridin-3-yl)-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane,

3-(5-fluoropyridin-2-yl)-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane,
2-(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)isonicotinonitrile,
5-(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-pyrrolo[3,2-b]pyridine,
5-(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-benzo[d]imidazole,
6-(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)picolinonitrile,
3-(5-fluoropyridin-3-yl)-1-((6-methylpyridin-2-yl)ethynyl)-3-azabicyclo[3.1.0]hexane
,
5-(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)nicotinonitrile, and
3-(5-fluoropyridin-3-yl)-1-(pyrimidin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane,
or a pharmaceutically acceptable salt thereof.

8. The compound according to claim 1, wherein the compound is selected from the group consisting of:

3-(phenylsulfonyl)-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0] hexane,
(3-chlorophenyl)(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)methanone,
pyridin-2-yl(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)methanone,
phenyl(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)methanone,
2-phenyl-1-(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)ethanone,
(2-chlorophenyl)(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)methanone,
1-(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)pentan-1-one,
3-phenyl-1-(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)propan-1-one,
(4-chlorophenyl)(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)methanone,
3-((3-chlorophenyl)sulfonyl)-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane,
3-((4-chlorophenyl)sulfonyl)-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane,
3-((2-chlorophenyl)sulfonyl)-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane,
1-(pyridin-2-ylethynyl)-3-tosyl-3-azabicyclo[3.1.0]hexane,
(3-fluorophenyl)(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)methanone,
3-((2-fluorophenyl)sulfonyl)-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane,

(3-fluorophenyl)(1-((6-methylpyridin-2-yl)ethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)methanone,
(3-chlorophenyl)(1-((2-methylthiazol-4-yl)ethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)methanone,
cyclopentyl(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)methanone,
2,2-dimethyl-1-(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)propan-1-one,
methyl-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane-3-carboxylate
(5-chloropyridin-3-yl)-(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)methanone,
(4-chloropyridin-2-yl)(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)methanone,
(6-chloropyridin-3-yl)(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)methanone,
(3-chlorophenyl)(1-(pyrimidin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)methanone,
2-methyl-1-(1-((6-methylpyridin-2-yl)ethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)propan-1-one,
1-(1-((6-chloropyridin-2-yl)ethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)-2-methylpropan-1-one,
(1-((2-methylthiazol-4-yl)ethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)(phenyl)methanone,
1-(1-((2-methylthiazol-4-yl)ethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)pentan-1-one,
2-methyl-1-(1-((2-methylthiazol-4-yl)ethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)propan-1-one, and
2,2-dimethyl-1-(1-((2-methylthiazol-4-yl)ethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)propan-1-one,
or a pharmaceutically acceptable salt thereof.

9. The compound according to claim 1, wherein the compound is selected from the group :

3-fluoro-5-(1-(pyrazin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)benzonitrile,
3-fluoro-5-(1-(pyrimidin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)benzonitrile,
3-fluoro-5-(1-((3-methylpyridin-2-yl)ethynyl)-3-azabicyclo
[3.1.0]hexan-3-yl)benzonitrile,
3-fluoro-5-(1-(pyridazin-3-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)benzonitrile,
3-(1-((2-chloropyridin-4-yl)ethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)-5-fluorobenzonitrile,
3-fluoro-5-(1-((6-methylpyridin-2-yl)ethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)benzonitrile,
3-(1-(6-chloropyridin-2-yl)-3-azabicyclo[3.1.0]hexan-3-yl)-5-fluorobenzonitrile,
3-fluoro-5-(1-((6-methoxypyridin-2-yl)ethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)benzonitrile, and
3-fluoro-5-(1-((2-methylthiazol-4-yl)ethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)benzonitrile,
or a pharmaceutically acceptable salt thereof.

10. A pharmaceutical composition comprising a compound of claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

11. A pharmaceutical composition comprising a compound according to claim 6, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

12. A pharmaceutical composition comprising a compound according to claim 7, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

13. A pharmaceutical composition comprising a compound according to claim 8, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

14. A pharmaceutical composition comprising a compound according to claim 9, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

15. A compound selected from the group consisting of:
N-phenyl-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane-3-carboxamide,
N-propyl-1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexane-3-carboxamide,
(1-(pyridin-2-ylethynyl)-3-azabicyclo[3.1.0]hexan-3-yl)(pyrrolidin-1-yl)methanone, and
1-(pyridin-2-ylethynyl)-N-(2,2,2-trifluoroethyl)-3-azabicyclo[3.1.0]hexane-3-carboxamide,
or a pharmaceutically acceptable salt thereof.

16. A pharmaceutical composition comprising a compound according to claim 15, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

17. A compound according to any one of claims 1, 6 to 9 and 15, or a pharmaceutically acceptable salt thereof, for use in antagonizing metabotropic glutamate receptor 5 activity in a subject.

18. A pharmaceutical composition according to claim 10 or 16 for use in antagonizing metabotropic glutamate receptor 5 activity in a subject.