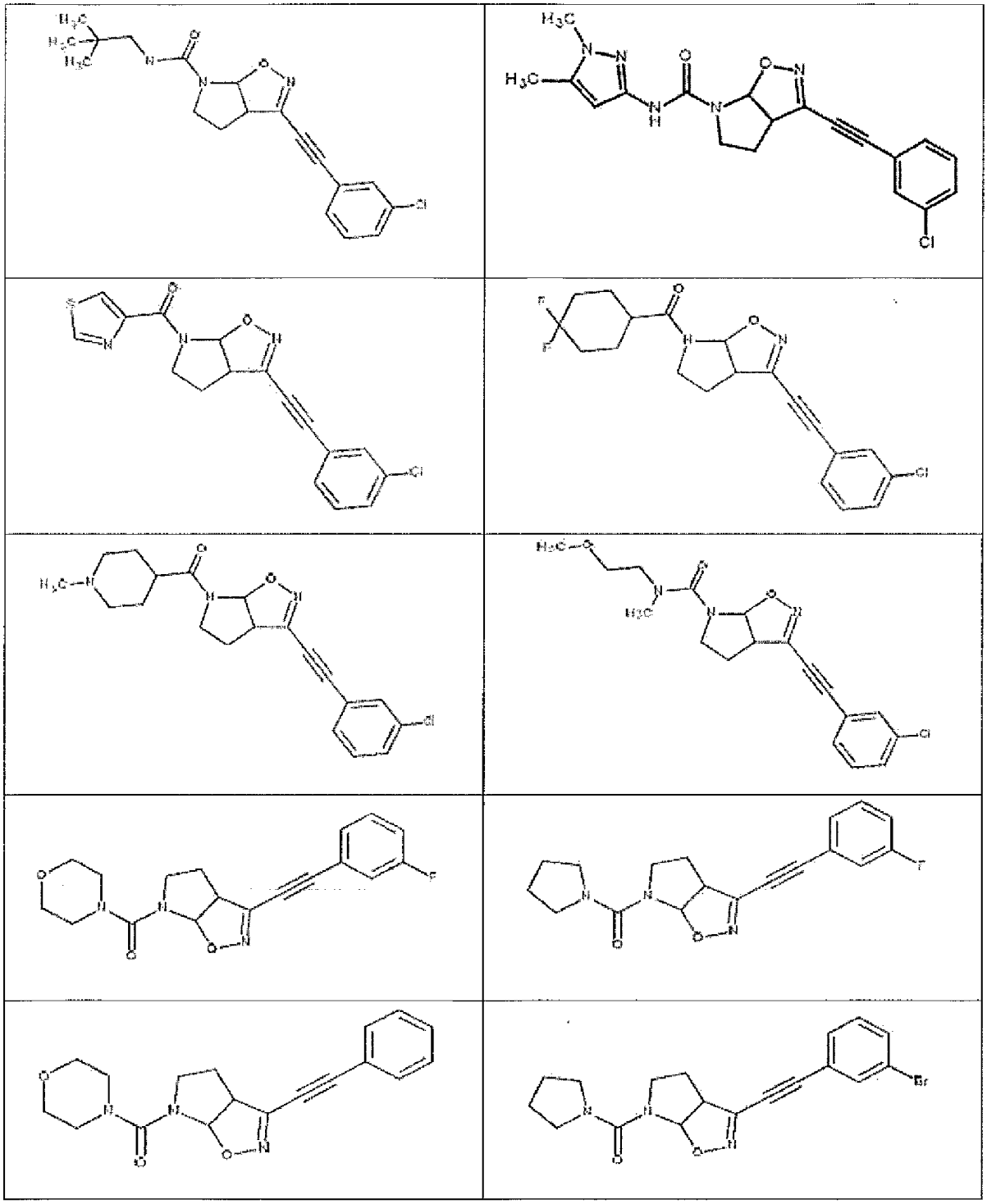


[0039] In a further embodiment of the invention, a pharmaceutical composition is preferably provided comprising a compound of Formula I,

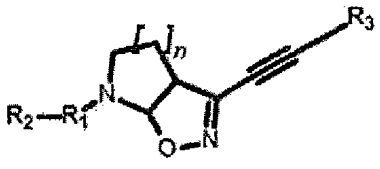
psychiatric disorder associated with glutamate dysfunction is preferably provided, wherein R_1 is an alkyl group, an optionally substituted mono-, bi- or tricyclic C_1-C_{13} heterocyclic group containing 1 to 5 heteroatoms selected from N, O, and S; an optionally substituted mono-, bi- or tricyclic C_6-C_{14} aryl group, an optionally substituted C_3-C_6 cycloalkyl group, or an optionally substituted C_3-C_6 cycloalkenyl group; or a bond, CO, CS, CH, CH_2, SO_2 group optionally substituted by one or more R_2 group or substituent; R_2 is absent or is an optionally substituted mono- or bicyclic C_1-C_9 heterocyclic group containing from 1 to 3 heteroatoms selected from nitrogen, oxygen and sulfur, an optionally substituted mono-, bi- or tricyclic C_6-C_{14} aryl group, or an optionally substituted group chosen from alkyl, cycloalkyl, alkoxy, cycloalkyloxy, aryloxy, heteroaryloxy, alkylthio, amino, N-alkylamino, N,N-dialkylamino or N-alkyl-N-alkoxyamino; R_3 is an optionally substituted alkyl group, an optionally substituted mono-, bi- or tricyclic C_1-C_{13} heterocyclic group containing 1 to 5 heteroatoms selected from N, O, and S; an optionally substituted mono-, bi- or tricyclic C_6-C_{14} aryl group, an optionally substituted C_3-C_6 cycloalkyl group, or an optionally substituted C_3-C_6 cycloalkenyl group; and n is 1-3.

[0041] In an embodiment of the invention, a compound according to Formula I is used in the treatment and/or prevention of a neurological disorder, psychotic disorder, or a psychiatric disorder associated with glutamate dysfunction.

[0042] Preferably the neurological disorder, psychotic disorder, or psychiatric disorder associated with glutamate dysfunction is schizophrenia, schizoaffective disorder, substance induced psychotic disorder, age-associated learning and memory impairments or losses, post stroke dementia, deficits in concentration, mild cognitive impairment, cognitive dysfunction in Alzheimer's disease, cognitive dysfunction of schizophrenia, cognitive decline, dementia or cognitive impairment.

[0043] More preferably the disorder is Fragile-X syndrome, Rett syndrome, Phelan-McDermid syndrome, or tuberous sclerosis.

[0043a] In an embodiment of the invention, use of a compound of Formula I,



(I),

or an enantiomer, diastereomer, N-oxide, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment and/or prevention of a neurological disorder, psychotic disorder, or a psychiatric disorder associated with glutamate dysfunction in a patient in need thereof, wherein:

R_1 is an alkyl group, an optionally substituted mono-, bi- or tricyclic C_1-C_{13} heterocyclic group containing 1 to 5 heteroatoms selected from N, O, and S; an optionally substituted mono-, bi- or tricyclic C_6-C_{14} aryl group, an optionally substituted C_3-C_6 cycloalkyl group, or an optionally substituted C_3-C_6 cycloalkenyl group; or a bond, CO, CS, CH, CH_2, SO_2 group optionally substituted by one or more R_2 group or substituent;

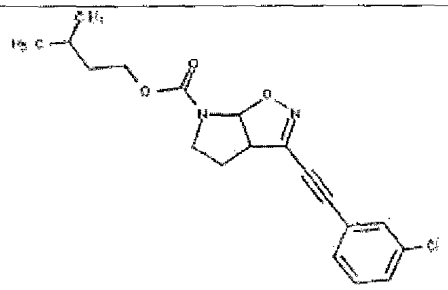
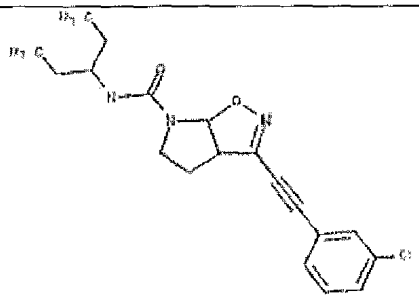
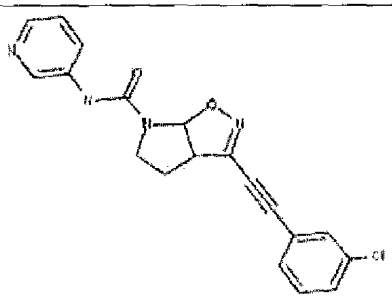
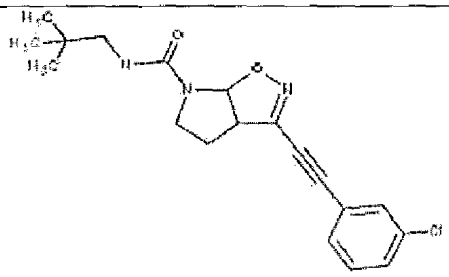
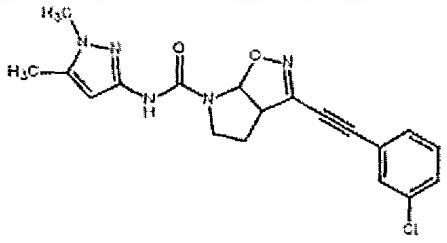
R_2 is absent or is an optionally substituted mono- or bicyclic C_1-C_9 heterocyclic group containing from 1 to 3 heteroatoms selected from nitrogen, oxygen and sulfur, an optionally substituted mono-, bi- or tricyclic C_6-C_{14} aryl group, or an optionally substituted group chosen from alkyl, cycloalkyl, alkoxy, cycloalkyloxy, aryloxy, heteroaryloxy, alkylthio, amino, N-alkylamino, N,N-dialkylamino or N-alkyl-N-alkoxyamino;

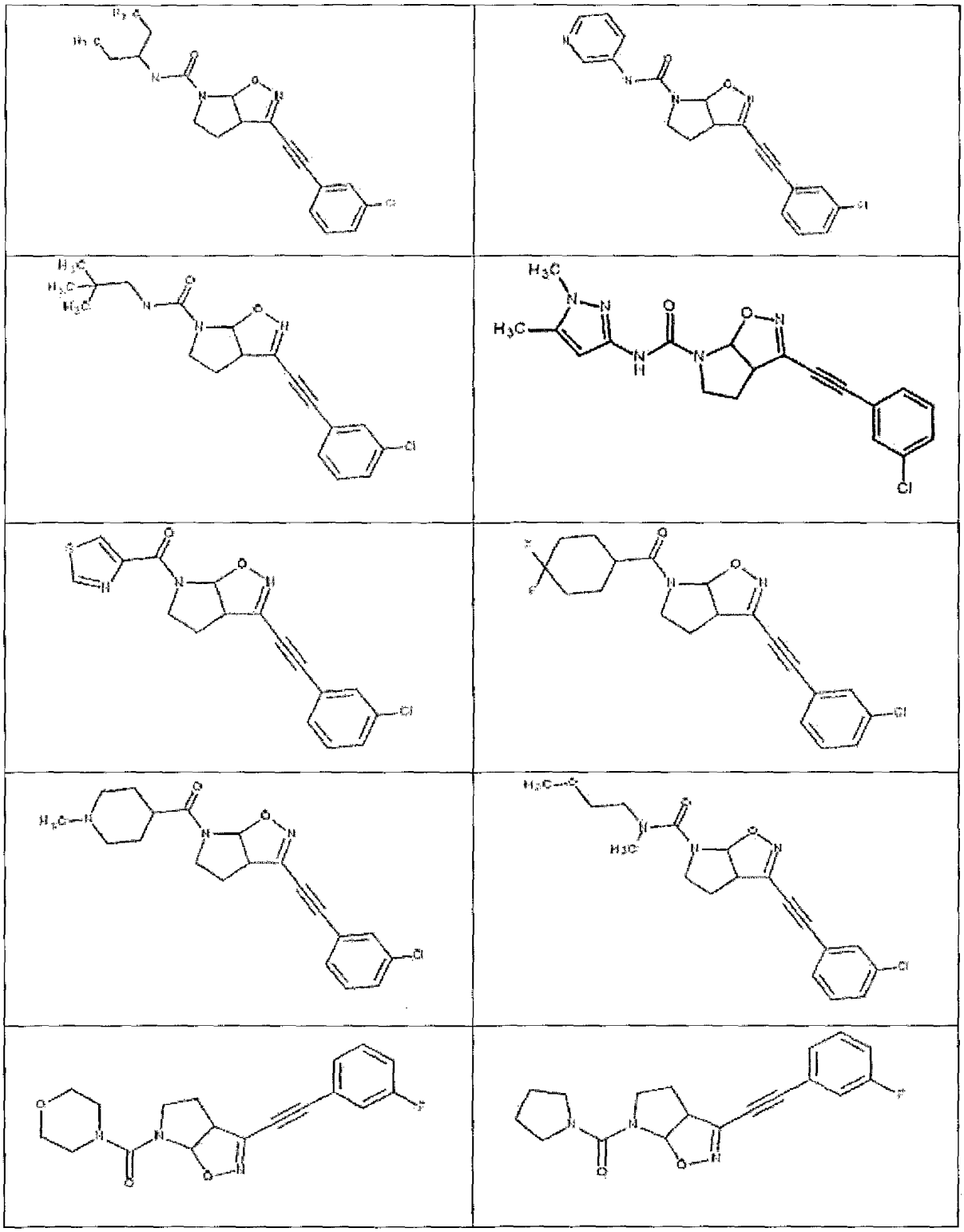
R_3 is an optionally substituted alkyl group, an optionally substituted mono-, bi- or tricyclic C_1-C_{13} heterocyclic group containing 1 to 5 heteroatoms selected from N, O, and S; an optionally substituted mono-, bi- or tricyclic C_6-C_{14} aryl group, an optionally substituted C_3-C_6 cycloalkyl group, or an optionally substituted C_3-C_6 cycloalkenyl group; and

n is 1-3.

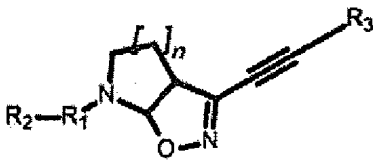
Terms and Definitions Used

[0044] Except where stated otherwise, the following definitions apply throughout the present specification and claims. These definitions apply regardless of whether a term is used

34		3-methylbutyl-3-(3-chlorophenylethynyl)-3a,4,5,6a-tetrahydropyrrolo[3,2-d]isoxazole-6-carboxylate	[2M+Na] = 743.3
35		3-(3-chlorophenylethynyl)-N-(pentan-3-yl)-3a,4,5,6a-tetrahydropyrrolo[3,2-d]isoxazole-6-carboxamide	360
36		3-(3-chlorophenylethynyl)-N-(pyridin-3-yl)-3a,4,5,6a-tetrahydropyrrolo[3,2-d]isoxazole-6-carboxamide	367.2
37		3-(3-chlorophenylethynyl)-N-(2,2-dimethylpropyl)-3a,4,5,6a-tetrahydropyrrolo[3,2-d]isoxazole-6-carboxamide	360.2
38		3-(3-chlorophenylethynyl)-3a,4,5,6a-tetrahydropyrrolo[3,2-d]isoxazol-6-yl-(1,5-dimethyl-1H-pyrazol-3-yl)methanone	369.1



13. Use of a compound of Formula I,



(I),

or an enantiomer, diastereomer, N-oxide, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment and/or prevention of a neurological disorder, psychotic disorder, or a psychiatric disorder associated with glutamate dysfunction in a patient in need thereof, wherein:

R_1 is an alkyl group, an optionally substituted mono-, bi- or tricyclic C_1-C_{13} heterocyclic group containing 1 to 5 heteroatoms selected from N, O, and S; an optionally substituted mono-, bi- or tricyclic C_6-C_{14} aryl group, an optionally substituted C_3-C_6 cycloalkyl group, or an optionally substituted C_3-C_6 cycloalkenyl group; or a bond, CO, CS, CH, CH_2, SO_2 group optionally substituted by one or more R_2 group or substituent;

R_2 is absent or is an optionally substituted mono- or bicyclic C_1-C_9 heterocyclic group containing from 1 to 3 heteroatoms selected from nitrogen, oxygen and sulfur, an optionally substituted mono-, bi- or tricyclic C_6-C_{14} aryl group, or an optionally substituted group chosen from alkyl, cycloalkyl, alkoxy, cycloalkyloxy, aryloxy, heteroaryloxy, alkylthio, amino, N-alkylamino, N,N-dialkylamino or N-alkyl-N-alkoxyamino;

R_3 is an optionally substituted alkyl group, an optionally substituted mono-, bi- or tricyclic C_1-C_{13} heterocyclic group containing 1 to 5 heteroatoms selected from N, O, and S; an optionally substituted mono-, bi- or tricyclic C_6-C_{14} aryl group, an optionally substituted C_3-C_6 cycloalkyl group, or an optionally substituted C_3-C_6 cycloalkenyl group; and

n is 1-3.

14. The use according to claim 13, wherein the disorder associated with glutamate dysfunction is schizophrenia, schizoaffective disorder, substance induced psychotic disorder, age-associated learning and memory impairments or losses, post stroke dementia, deficits in

concentration, mild cognitive impairment, cognitive dysfunction in Alzheimer's disease, cognitive dysfunction of schizophrenia, cognitive decline, dementia, cognitive impairment, Fragile-X syndrome, Rett syndrome, Phelan-McDermid syndrome, or tuberous sclerosis.

15. The use according to claim 13, wherein the disorder is Fragile-X syndrome, Rett syndrome, Phelan-McDermid syndrome, or tuberous sclerosis.