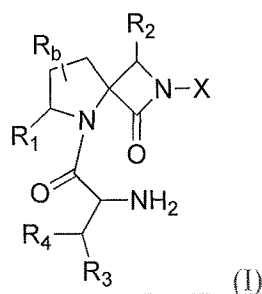


substituted with from 1-3 independently selected C₁-C₃ alkyl; -CH₂-C₃-C₁₀ cycloalkyl wherein the C₃-C₁₀ cycloalkyl is optionally substituted with from 1-3 independently selected C₁-C₃ alkyl; -CH₂-phenyl, wherein the phenyl is optionally substituted with from 1-2 substituents independently selected from C₁-C₃ alkyl; C₁-C₃ haloalkyl; C₁-C₃ alkoxy; C₁-C₃ haloalkoxy; nitro; halo; SO₂Me, cyano; and -OC(O)CH₃; and -CH₂-pyridyl; and

R₃₂ is selected from the group consisting of: H; C₁-C₆ alkyl; C₁-C₆ haloalkyl; phenyl, wherein the phenyl is optionally substituted with from 1-2 substituents independently selected from C₁-C₃ alkyl; C₁-C₃ haloalkyl; C₁-C₃ alkoxy; C₁-C₃ haloalkoxy; nitro; halo; SO₂Me, cyano; and -OC(O)CH₃; and pyridyl.

[0008a] In one aspect of the present disclosure, there is provided a compound represented by formula I:



or a pharmaceutically acceptable salt thereof, wherein

R_b is selected from the group consisting of H, halogen, hydroxyl, cyano and C₁-C₆ alkyl;

R₁ is H or C₁-C₆ alkyl;

R₂ is H or C₁-C₆ alkyl;

R₃ is selected from the group consisting of H, C₁-C₆alkyl, -OH, C₁-C₆alkoxy, -OC(O)-C₁-C₆ alkyl and -OC(O)-phenyl (optionally substituted by one, two or three substituents independently selected from the group consisting of halogen, hydroxyl, C₁-C₆alkyl, and C₁-C₆alkoxy);

R₄ is H or C₁-C₆ alkyl;

X is selected from the group consisting of:

(i) hydrogen;

(ii) -C₁₋₆alkylene-C₃₋₆cycloalkyl;

(iii) -C₁₋₆alkylene- heterocyclyl including from 3 to 6 ring atoms wherein 1, 2, or 3 of the ring atoms are independently selected from the group consisting of N, NH, N(C₁₋₃ alkyl), O, and S; wherein the heterocyclyl is optionally substituted by one, two or three substituents independently selected from the group consisting of

halogen, hydroxyl, C₁₋₆alkyl, and C₁₋₆alkoxy);

(iv) -C₁₋₆alkylene- C(O)-heterocyclyl including from 3 to 6 ring atoms wherein 1, 2, or 3 of the ring atoms are independently selected from the group consisting of N, NH, N(C₁₋₃ alkyl), O, and S; wherein the heterocyclyl is optionally substituted by one, two or three substituents independently selected from the group consisting of

halogen, hydroxyl, C₁₋₆alkyl, and C₁₋₆alkoxy);

(v) -C₁₋₆alkylene- heteroaryl including from 5 to 6 ring atoms wherein 1, 2, or 3 of the ring atoms are independently selected from the group consisting of N, NH, N(C₁₋₃ alkyl), O, and S; wherein the heteroaryl is optionally substituted by one, two or three substituents independently selected from the group consisting of

halogen, hydroxyl, C₁₋₆alkyl, and C₁₋₆alkoxy;

(vi) branched unsubstituted C₃₋₆ alkyl; and

(vii) branched C₃₋₆ alkyl substituted with -C(O)NH₂ on one carbon and -OH on another carbon;

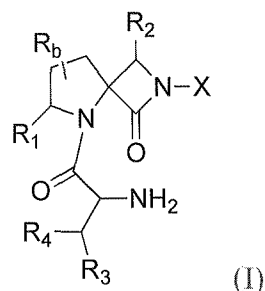
and wherein the -NH₂ group attached to the carbon adjacent to -CH(R₃)(R₄) is optionally substituted with a substituent selected from -C(O)OR₃₁ and -C(O) R₃₂, wherein:

R₃₁ is selected from the group consisting of: C₁₋₆ alkyl; C₁₋₆ haloalkyl; C₂₋₆ alkenyl; C₂₋₆ alkynyl; C₃₋₁₀ cycloalkyl, wherein the C₃₋₁₀ cycloalkyl is optionally substituted with from 1-3 independently selected C₁₋₃ alkyl; -CH₂-C₃₋₁₀ cycloalkyl wherein the C₃₋₁₀ cycloalkyl is optionally substituted with from 1-3 independently selected C₁₋₃ alkyl; -CH₂-phenyl, wherein the phenyl is optionally substituted with from 1-2 substituents independently selected from C₁₋₃ alkyl; C₁₋₃ haloalkyl; C₁₋₃ alkoxy; C₁₋₃ haloalkoxy; nitro; halo; SO₂Me, cyano; and -OC(O)CH₃; and -CH₂-pyridyl; and

R₃₂ is selected from the group consisting of: H; C₁₋₆ alkyl; C₁₋₆ haloalkyl; phenyl, wherein the phenyl is optionally substituted with from 1-2 substituents independently selected from

C₁-C₃ alkyl; C₁-C₃ haloalkyl; C₁-C₃ alkoxy; C₁-C₃ haloalkoxy; nitro; halo; SO₂Me, cyano; and -OC(O)CH₃; and pyridyl.

[0008b] In another aspect of the present disclosure, there is provided a compound represented by formula I:



and pharmaceutically acceptable salts, stereoisomers, and N-oxides thereof, wherein

R_b is selected from the group consisting of H, halogen, hydroxyl, cyano and C₁-C₆ alkyl;

R₁ is H or C₁-C₆ alkyl;

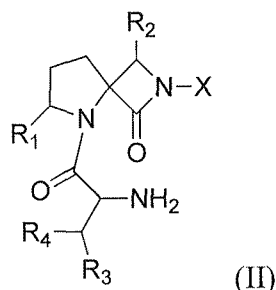
R₂ is H or C₁-C₆ alkyl;

R₃ is selected from the group consisting of H, C₁-C₆alkyl, -OH, C₁-C₆alkoxy, -OC(O)-C₁-C₆ alkyl and -OC(O)-phenyl (optionally substituted by one, two or three substituents selected from the group consisting of halogen, hydroxyl, C₁-C₆alkyl, and C₁-C₆alkoxy);

R₄ is H or C₁-C₆ alkyl; and

X is selected from the group consisting of hydrogen, -C₁₋₆alkylene-C₃₋₆cycloalkyl; C₁₋₆alkylene- heterocycle (optionally substituted by one, two or three substituents selected from the group consisting of halogen, hydroxyl, C₁-C₆alkyl, and C₁-C₆alkoxy), and -C₁₋₆alkylene- heteroaryl (optionally substituted by one, two or three substituents selected from the group consisting of halogen, hydroxyl, C₁-C₆alkyl, and C₁-C₆alkoxy).

[0009] In another aspect, ~~Further~~ disclosed herein are compounds represented by the formula:



and pharmaceutically acceptable salts, stereoisomers, and N-oxides thereof, wherein

R_1 is H or C_1 - C_6 alkyl;

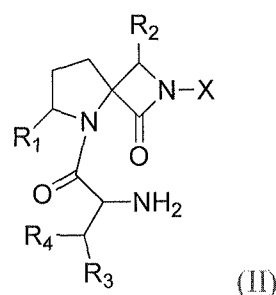
R_2 is H or C_1 - C_6 alkyl;

- 5 R_3 is selected from the group consisting of H, C_1 - C_6 alkyl, -OH, C_1 - C_6 alkoxy, -OC(O)- C_1 - C_6 alkyl and -OC(O)-phenyl;

R_4 is H or C_1 - C_6 alkyl; and

X is $-C_1$ - C_6 alkylene- X' , wherein X' is a 4- to 6-membered heteroaryl having 1, 2, or 3 heteroatoms selected from O, N, or S, where X' is optionally substituted on a free carbon by
 10 one, two or three substituents selected from the group consisting of halogen, hydroxyl, C_1 - C_6 alkyl, and C_1 - C_6 alkoxy.

[0009a] In one aspect of the present disclosure, there is provided a compound represented by formula II:



15 and pharmaceutically acceptable salts, stereoisomers, and N-oxides thereof, wherein

R_1 is H or C_1 - C_6 alkyl;

R_2 is H or C_1 - C_6 alkyl;

R_3 is selected from the group consisting of H, C_1 - C_6 alkyl, -OH, C_1 - C_6 alkoxy, -OC(O)- C_1 - C_6 alkyl and -OC(O)-phenyl;

20 R_4 is H or C_1 - C_6 alkyl; and

X is -C₁-C₆alkylene-X', wherein X' is a 4- to 6-membered heteroaryl having 1, 2, or 3 heteroatoms selected from O, N, or S, where X' is optionally substituted on a free carbon by one, two or three substituents selected from the group consisting of halogen, hydroxyl, C₁-C₆alkyl, and C₁-C₆alkoxy.

5 **[0009b]** In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound defined above, and a pharmaceutically acceptable excipient.

[0009c] In a further aspect of the present disclosure, there is provided a use of a compound defined above in the manufacture of a medicament for treating depression, Alzheimer's disease, attention deficit disorder, schizophrenia, or anxiety, in a patient in need thereof.

10

[0010] Also provided herein are pharmaceutically acceptable compositions comprising a disclosed compound, and a pharmaceutically acceptable excipient. For example, such compositions may be suitable for oral or intravenous administration to a patient.

[0011] ~~The present disclosure also relates to In another aspect,~~ a method of treating a condition selected from the group consisting of autism, anxiety, depression, bipolar disorder, attention deficit disorder, attention deficit hyperactivity disorder (ADHD), schizophrenia, a psychotic disorder, a psychotic symptom, social withdrawal, obsessive-compulsive disorder, phobia, post-traumatic stress syndrome, a behavior disorder, an impulse control disorder, a substance abuse disorder, a sleep disorder, a memory disorder, a learning disorder, urinary incontinence, multiple system atrophy, progressive supra-nuclear palsy, Friedrich's ataxia, Down's syndrome, fragile X syndrome, tuberous sclerosis, olivio-ponto-cerebellar atrophy, cerebral palsy, drug-induced optic neuritis, ischemic retinopathy, diabetic retinopathy, glaucoma, dementia, AIDS dementia, Alzheimer's disease, Huntington's chorea, spasticity, myoclonus, muscle spasm, Tourette's syndrome, epilepsy, cerebral ischemia, stroke, a brain tumor, traumatic brain injury, cardiac arrest, myelopathy, spinal cord injury, peripheral neuropathy, acute neuropathic pain, and chronic neuropathic, in a patient in need thereof is provided. Such methods may comprise administering to the patient a pharmaceutically effective amount of a disclosed compound or pharmaceutically acceptable salts, stereoisomers, N-oxides, and hydrates thereof.

[0012] In some embodiments, a contemplated method includes treating depression. For example, depression may include one or more of major depressive disorder, dysthymic disorder, psychotic depression, postpartum depression, seasonal affective disorder, bipolar disorder, mood disorder, or depression caused by a chronic medical condition. In other embodiments, a contemplated method may treat schizophrenia. Such schizophrenia may be, for example, paranoid type schizophrenia, disorganized type schizophrenia, catatonic type schizophrenia, undifferentiated type schizophrenia, residual type schizophrenia, post-schizophrenic depression, or simple schizophrenia.

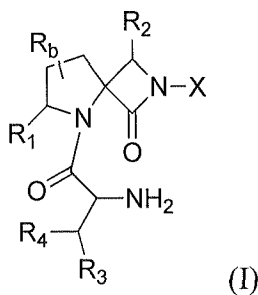
BRIEF DESCRIPTION OF THE DRAWINGS

[0013] **Figure 1** shows the potentiation of [³H]MK-801 binding in the presence of Compound X.

DETAILED DESCRIPTION

[0014] This disclosure is generally directed to compounds that are capable of modulating NMDA, e.g., NMDA antagonists or partial agonists, and compositions and/or methods of using the disclosed compounds.

21. The compound of claim 20, wherein R_{31} is C_1 - C_6 alkyl.
22. The compound of claim 21, wherein R_{31} is *tert*-butyl.
23. The compound of claim 19, wherein the $-NH_2$ group attached to the carbon adjacent to $-CH(R_3)(R_4)$ is substituted with $-C(O)R_{32}$.
24. The compound of claim 23, wherein R_{32} is C_1 - C_6 alkyl.
25. The compound of claim 23, wherein R_{32} is $-CH_3$ or *iso*-propyl.
26. The compound of claim 1, wherein the compound is selected from the compounds delineated in Table 1.
27. A pharmaceutical composition comprising a compound of any one of claims 1-26, and a pharmaceutically acceptable excipient.
28. The pharmaceutical composition of claim 27, suitable for oral administration.
29. The pharmaceutical composition of claim 27, suitable for intravenous administration.
30. Use of a compound of any one of claims 1-26 in the manufacture of a medicament for A
~~method of treating or~~ treating depression, Alzheimer's disease, attention deficit disorder, schizophrenia, or anxiety, in a patient in need thereof, ~~comprising administering to said patient:~~
~~a pharmaceutically effective amount of a compound of any one of claims 1-26.~~
31. A compound represented by formula I:

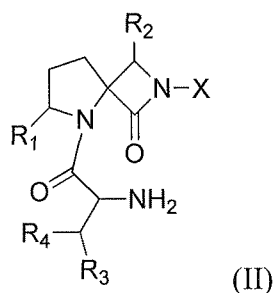


and pharmaceutically acceptable salts, stereoisomers, and N-oxides thereof, wherein

R_b is selected from the group consisting of H, halogen, hydroxyl, cyano and C_1 - C_6 alkyl;

R_1 is H or C_1 - C_6 alkyl;

R_2 is H or C_1 - C_6 alkyl;



and pharmaceutically acceptable salts, stereoisomers, and N-oxides thereof, wherein

R₁ is H or C₁-C₆ alkyl;

R₂ is H or C₁-C₆ alkyl;

R₃ is selected from the group consisting of H, C₁-C₆ alkyl, -OH, C₁-C₆ alkoxy, -OC(O)-C₁-C₆ alkyl and -OC(O)-phenyl;

R₄ is H or C₁-C₆ alkyl; and

X is -C₁-C₆alkylene-X', wherein X' is a 4- to 6-membered heteroaryl having 1, 2, or 3 heteroatoms selected from O, N, or S, where X' is optionally substituted on a free carbon by one, two or three substituents selected from the group consisting of halogen, hydroxyl, C₁-C₆alkyl, and C₁-C₆alkoxy.

44. A pharmaceutical composition comprising a compound of any one of claims 31-43, and a pharmaceutically acceptable excipient.

45. The pharmaceutical composition of claim 44, suitable for oral administration.

46. The pharmaceutical composition of claim 44, suitable for intravenous administration.

47. Use of a compound of any one of claims 31-43 in the manufacture of a medicament for
~~A method of treating or treating depression, Alzheimer's disease, attention deficit disorder,~~
~~schizophrenia, or anxiety, in a patient in need thereof, comprising administering to said patient:~~
~~a pharmaceutically effective amount of a compound of any one of claims 31-43.~~