[10l] In another aspect of the present disclosure, there is provided a use of a compound, the pharmaceutically acceptable salt, or the pharmaceutical composition disclosed herein, in the manufacture of a medicament for treating epilepsy or status epilepticus in a subject.

[10m] In a further aspect of the present disclosure, there is provided a compound, the pharmaceutically acceptable salt, or the pharmaceutical composition disclosed herein, for use in treating a disorder related to GABA function in a subject, wherein the disorder is selected from the group consisting of a sleep disorder, a mood disorder, a schizophrenia spectrum disorder, a convulsive disorder, a disorder of memory and/or cognition, a movement disorder, a personality disorder, autism spectrum disorder (ASD), pain, traumatic brain injury (TBI), a vascular disease, a substance abuse disorder and/or withdrawal syndrome, and tinnitus.

[10n] In another aspect of the present disclosure, there is provided a compound, the pharmaceutically acceptable salt, or the pharmaceutical composition disclosed herein, for use in treating a CNS-related disorder in a subject.

[10o] In a further aspect of the present disclosure, there is provided a use of a compound, the pharmaceutically acceptable salt, or the pharmaceutical composition disclosed herein, in the manufacture of a medicament for treating a disorder related to GABA function in a subject, wherein the disorder is selected from the group consisting of a sleep disorder, a mood disorder, a schizophrenia spectrum disorder, a convulsive disorder, a disorder of memory and/or cognition, a movement disorder, a personality disorder, autism spectrum disorder (ASD), pain, traumatic brain injury (TBI), a vascular disease, a substance abuse disorder and/or withdrawal syndrome, and tinnitus.

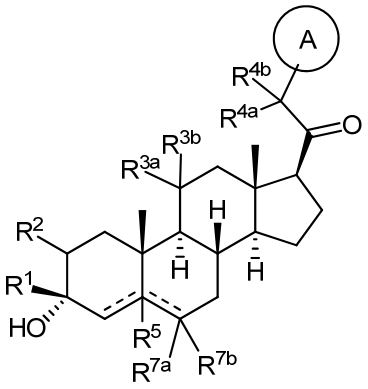
[10p] In another aspect of the present disclosure, there is provided a use of a compound, the pharmaceutically acceptable salt, or the pharmaceutical composition disclosed herein, in the manufacture of a medicament for treating a CNS-related disorder in a subject.

[10q] In another aspect of the present disclosure, there is provided a use of a compound disclosed herein, a pharmaceutically acceptable salt disclosed herein, or a pharmaceutical composition disclosed herein in the manufacture of a medicament for treating Huntington's disease or Parkinson's disease in a subject.

[10r] In another aspect of the present disclosure, there is provided the compound disclosed herein, a pharmaceutically acceptable salt disclosed herein, or a pharmaceutical composition disclosed herein, for use in treating Huntington's disease or Parkinson's disease in a subject

[11] Provided herein are C21-substituted neuroactive steroids designed, for example, to act as GABA modulators. In certain examples, such compounds are envisioned to be useful as therapeutic agents for the inducement of anesthesia and/or sedation in a subject. In some examples, such compounds are envisioned to be useful as therapeutic agents for treating a CNS-related disorder (*e.g.*, sleep disorder, a mood disorder such as depression, a schizophrenia spectrum disorder, a convulsive disorder, a disorder of memory and/or cognition, a movement disorder, a personality disorder, autism spectrum disorder, pain, traumatic brain injury, a vascular disease, a substance abuse disorder and/or withdrawal syndrome, or tinnitus) in a subject in need (*e.g.*, a subject with Rett syndrome, Fragile X syndrome, or Angelman syndrome).

In one example, provided is a compound of Formula (**I**):



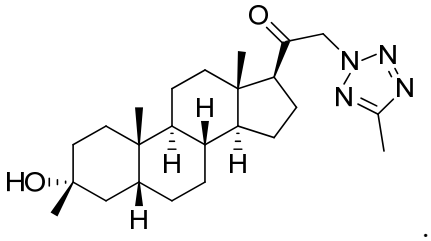
(**I**)

or a pharmaceutically acceptable salt thereof; wherein: ring A is substituted or unsubstituted carbocyclyl, heterocyclyl, aryl, or heteroaryl; R^1 is hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl, or substituted or unsubstituted C_{3-6} carbocylyl; R^2 is hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl, substituted or unsubstituted C_{2-6} alkynyl, substituted or unsubstituted C_{3-6} carbocylyl, or $–OR^{A2}$, wherein R^{A2} is hydrogen or substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted

Claims

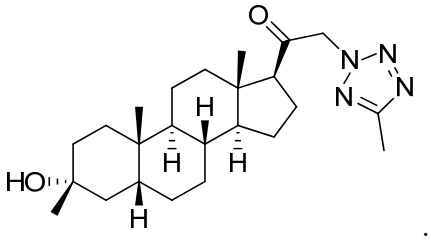
What is claimed is:

1. A compound of the formula



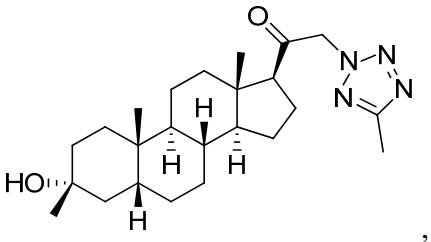
.

2. A pharmaceutically acceptable salt of a compound of the formula



.

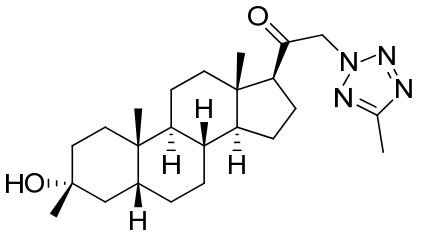
3. A pharmaceutical composition comprising a compound of the formula



, and

a pharmaceutically acceptable excipient.

4. A pharmaceutical composition comprising a pharmaceutically acceptable salt of a compound of the formula



, and

a pharmaceutically acceptable excipient.

5. The compound of claim 1, the pharmaceutically acceptable salt of claim 2, or the pharmaceutical composition of claim 3 or claim 4, for use in inducing sedation and/or anesthesia in a subject.

6. The compound of claim 1, the pharmaceutically acceptable salt of claim 2, or the pharmaceutical composition of claim 3 or claim 4, for use in treating essential tremor in a subject.

7. The compound of claim 1, the pharmaceutically acceptable salt of claim 2, or the pharmaceutical composition of claim 3 or claim 4, for use in treating seizure in a subject.

8. The compound of claim 1, the pharmaceutically acceptable salt of claim 2, or the pharmaceutical composition of claim 3 or claim 4, for use in treating epilepsy or status epilepticus in a subject.

9. Use of a compound of claim 1, a pharmaceutically acceptable salt of claim 2, or a pharmaceutical composition of claim 3 or 4, in the manufacture of a medicament for inducing sedation and/or anesthesia in a subject.

10. Use of a compound of claim 1, a pharmaceutically acceptable salt of claim 2, or a pharmaceutical composition of claim 3 or 4, in the manufacture of a medicament for treating essential tremor in a subject.

11. Use of a compound of claim 1, a pharmaceutically acceptable salt of claim 2, or a pharmaceutical composition of claim 3 or 4, in the manufacture of a medicament for treating seizure in a subject.

12. Use of a compound of claim 1, a pharmaceutically acceptable salt of claim 2, or a pharmaceutical composition of claim 3 or 4, in the manufacture of a medicament for treating epilepsy or status epilepticus in a subject.

13. The compound of claim 1, the pharmaceutically acceptable salt of claim 2, or the pharmaceutical composition of claim 3 or claim 4, for use in treating a disorder related to GABA function in a subject, wherein the disorder is selected from the group consisting of a sleep disorder, a mood disorder, a schizophrenia spectrum disorder, a convulsive disorder, a disorder of memory and/or cognition, a movement disorder, a personality disorder, autism spectrum disorder (ASD), pain, traumatic brain injury (TBI), a vascular disease, a substance abuse disorder and/or withdrawal syndrome, and tinnitus.

14. The compound of claim 1, the pharmaceutically acceptable salt of claim 2, or the pharmaceutical composition of claim 3 or claim 4 for use in treating a CNS-related disorder in a subject.

15. Use of a compound of claim 1, a pharmaceutically acceptable salt of claim 2, or a pharmaceutical composition of claim 3 or 4, in the manufacture of a medicament for treating a disorder related to GABA function in a subject, wherein the disorder is selected from the group consisting of a sleep disorder, a mood disorder, a schizophrenia spectrum disorder, a convulsive disorder, a disorder of memory and/or cognition, a movement disorder, a personality disorder, autism spectrum disorder (ASD), pain, traumatic brain injury (TBI), a vascular disease, a substance abuse disorder and/or withdrawal syndrome, and tinnitus.

16. Use of a compound of claim 1, a pharmaceutically acceptable salt of claim 2, or a pharmaceutical composition of claim 3 or 4, in the manufacture of a medicament for treating a CNS-related disorder in a subject.

17. The compound ~~of claim 1~~, ~~the~~ pharmaceutically acceptable salt ~~of claim 2~~, or ~~the~~ pharmaceutical composition ~~of claim 3 or claim 4,~~ for use according to ~~claim 13 or~~ claim 14~~,~~ or the use according to ~~claim 15 or~~ claim 16, wherein the disorder is selected from the group consisting of a sleep disorder, a mood disorder, a schizophrenia spectrum disorder, a convulsive disorder, a disorder of memory and/or cognition, a movement disorder, a personality disorder, autism spectrum disorder (ASD), pain, traumatic brain injury (TBI), a vascular disease, a substance abuse disorder and/or withdrawal syndrome, and tinnitus.

18. The compound, pharmaceutically acceptable salt, or pharmaceutical composition for use according to any one of claims 13 or 17, or the use according to claim 15, wherein the disorder is a movement disorder.

19. The compound, pharmaceutically acceptable salt, or pharmaceutical composition for use according to any one of claims 13 or 17, or the use according to claim 15, wherein the disorder is a mood disorder.

20. The compound, pharmaceutically acceptable salt, or the pharmaceutical composition for use or use according to claim 19, wherein the mood disorder is depression.

21. The compound, pharmaceutically acceptable salt, or the pharmaceutical composition for use or use according to claim 20, wherein the depression is post-partum depression.

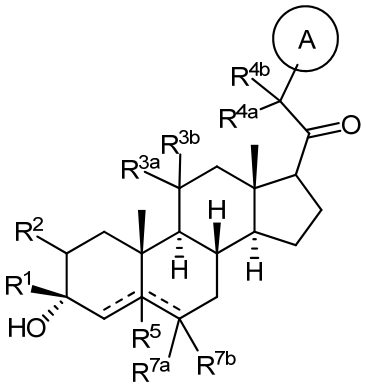
22. Use of a compound of claim 1, a pharmaceutically acceptable salt of claim 2, or a pharmaceutical composition of claim 3 or 4 in the manufacture of a medicament for treating Huntington's disease or Parkinson's disease in a subject.

23. The compound of claim 1, a pharmaceutically acceptable salt of claim 2, or a pharmaceutical composition of claim 3 or 4, for use in treating Huntington's disease or Parkinson's disease in a subject.

COMPOSITIONS AND METHODS FOR TREATING CNS DISORDERS

Abstract

Described herein are neuroactive steroids of the Formula (**I**):



(**I**)

or a pharmaceutically acceptable salt thereof; wherein ------, A, R^1, R^2, R^{3a}, R^{4a}, R^{4b}, R^5, R^{7a}, and R^{7b} are as defined herein. Such compounds are envisioned, in certain embodiments, to behave as GABA modulators. The present invention also provides pharmaceutical compositions comprising a compound of the present invention and methods of use and treatment, *e.g.*, such for inducing sedation and/or anesthesia.

[No available figure]