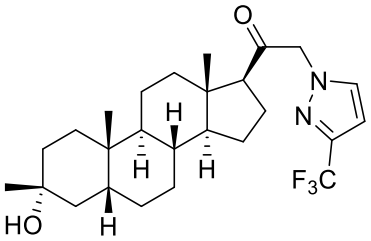
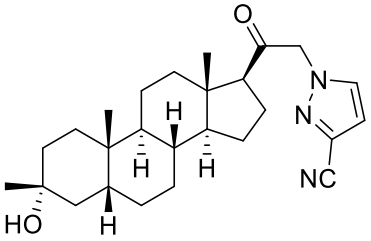
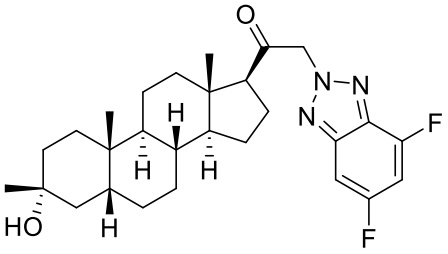
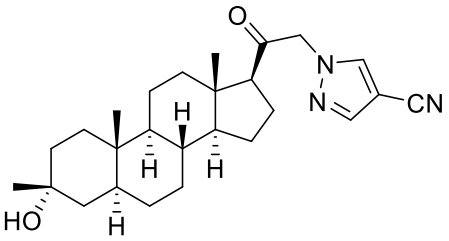
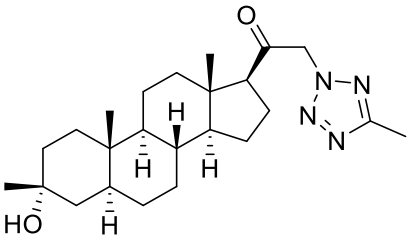
[10] New and improved neuroactive steroids are needed that act as modulating agents for brain excitability, as well as agents for the prevention and treatment of CNS-related diseases. The compounds, compositions, and methods described herein are directed toward this end.

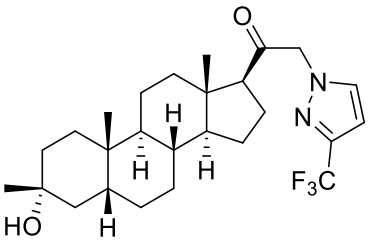
Summary

[10a] In a first aspect of the present disclosure, there is provided a compound selected from

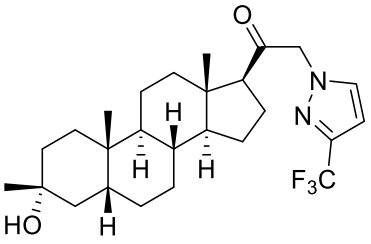
Compound No.	Structure
19	
24	
28	

Compound No.	Structure
79	
206	

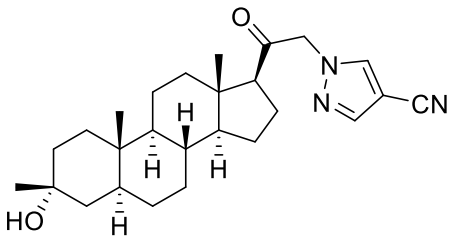
[10c] In yet another aspect of the present disclosure, there is provided a compound of the formula



[10d] In a further aspect of the present disclosure, there is provided a pharmaceutically acceptable salt of a compound of the formula

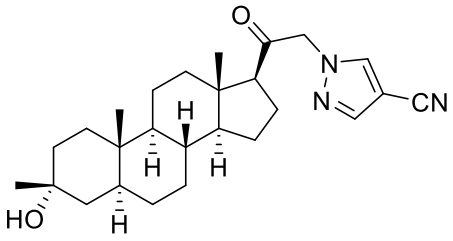


[10i] In another aspect of the present disclosure, there is provided a compound of the formula



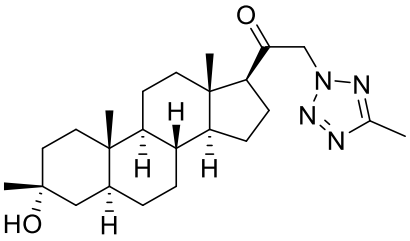
.

[10j] In yet another aspect of the present disclosure, there is provided a pharmaceutically acceptable salt of a compound of the formula



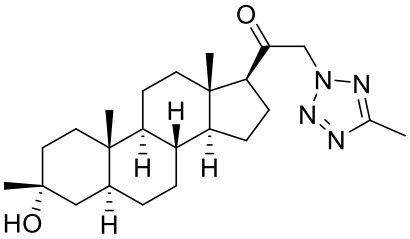
.

[10k] In a further aspect of the present disclosure, there is provided a compound of the formula



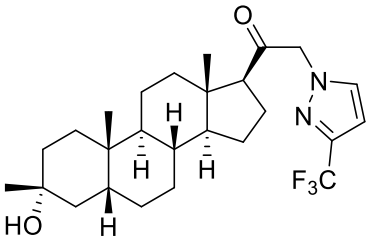
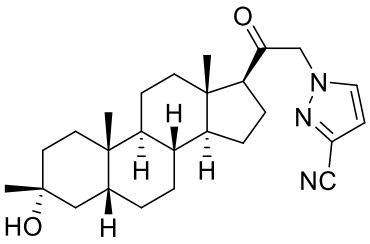
.

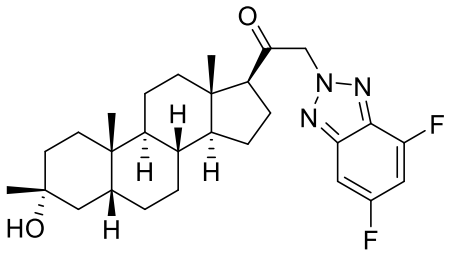
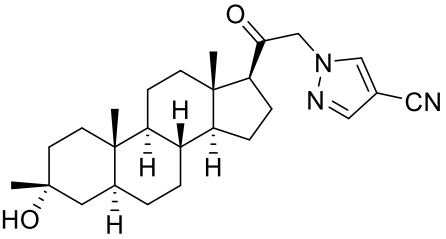
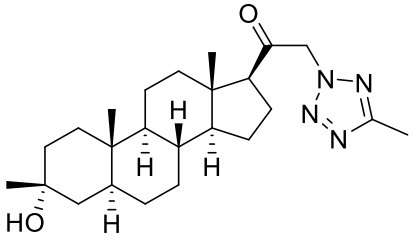
[10l] In another aspect of the present disclosure, there is provided a pharmaceutically acceptable salt of a compound of the formula



.

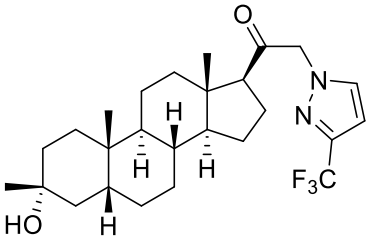
[10m] In yet another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound selected from

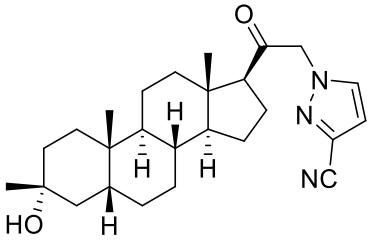
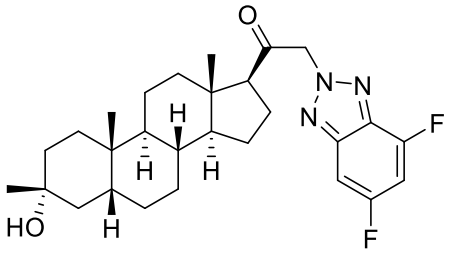
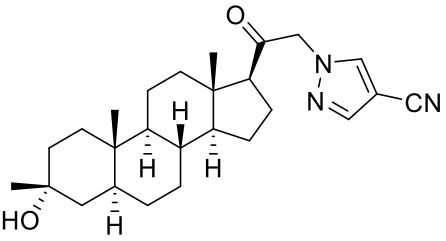
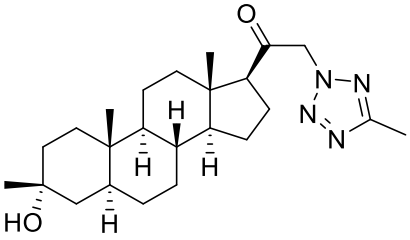
Compound No.	**Structure**
19	
24	

Compound No.	Structure
28	
79	
206	 ,

and a pharmaceutically acceptable excipient.

[10n] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising a pharmaceutically acceptable salt of a compound selected from

Compound No.	Structure
19	

Compound No.	Structure
24	
28	
79	
206	 ,

and a pharmaceutically acceptable excipient.

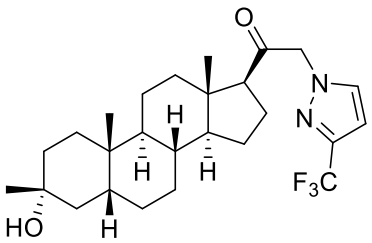
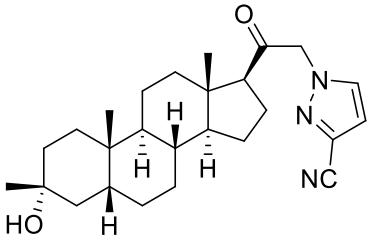
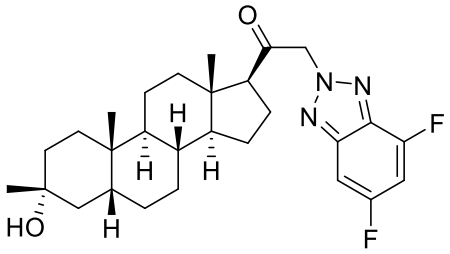
[10o] In another aspect of the present disclosure, there is provided the compound, the pharmaceutically acceptable salt, or the pharmaceutical composition as disclosed herein, for use in inducing sedation and/or anesthesia in a subject.

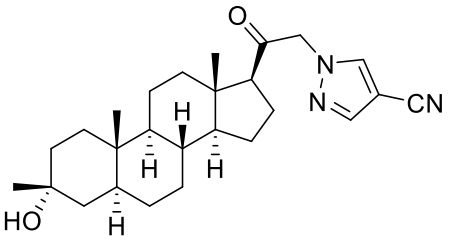
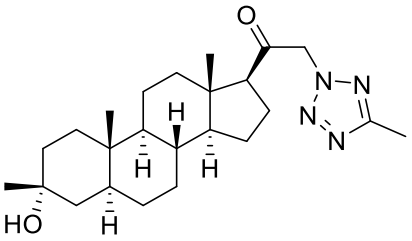
[10p] In yet another aspect of the present disclosure, there is provided the compound, the pharmaceutically acceptable salt, or the pharmaceutical composition as disclosed herein, for use in tremor in a subject.

[10q] In a further aspect of the present disclosure, there is provided the compound, the pharmaceutically acceptable salt, or the pharmaceutical composition as disclosed herein, for use in treating seizure in a subject.

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

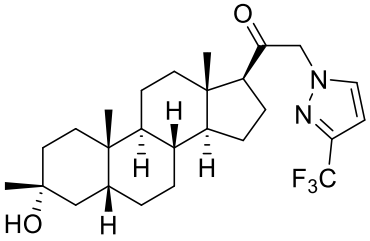
[10s] In yet another aspect of the present disclosure, there is provided a use of a compound selected from

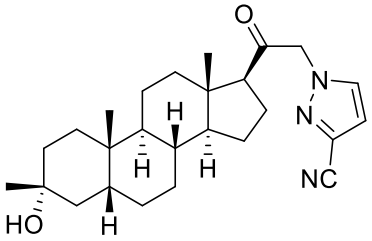
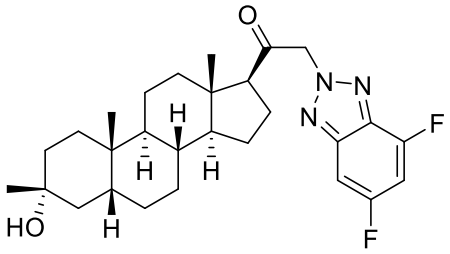
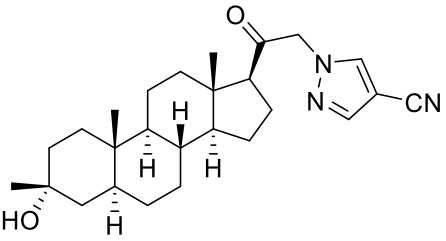
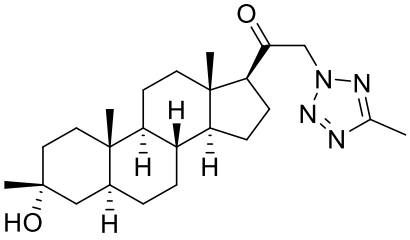
Compound No.	**Structure**
19	
24	
28	

Compound No.	Structure
79	
206	 ,

or pharmaceutically acceptable salt thereof in the manufacture of a medicament for inducing sedation and/or anesthesia in a subject in need thereof.

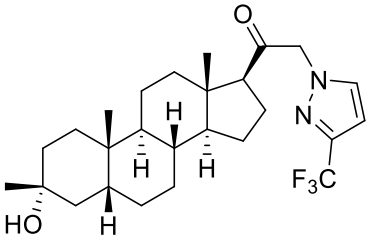
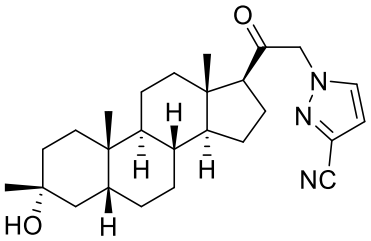
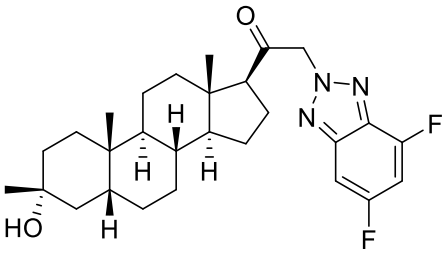
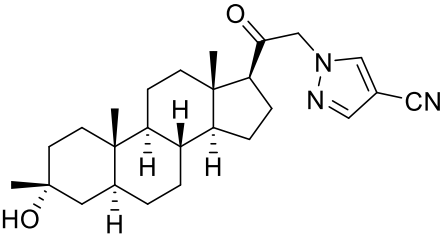
[10t] In a further aspect of the present disclosure, there is provided a use of a compound selected from

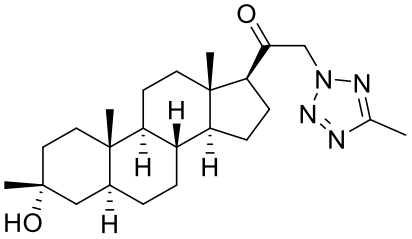
Compound No.	Structure
19	

Compound No.	Structure
24	
28	
79	
206	 ,

or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating tremor in a subject in need thereof.

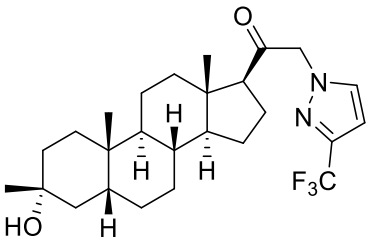
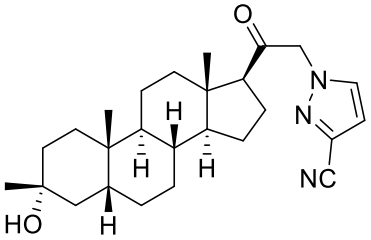
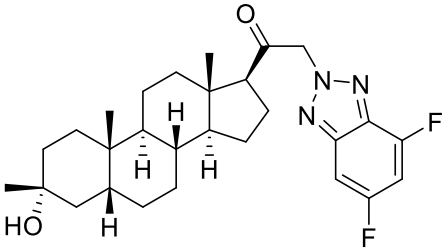
[10u] In another aspect of the present disclosure, there is provided a use of a compound selected from

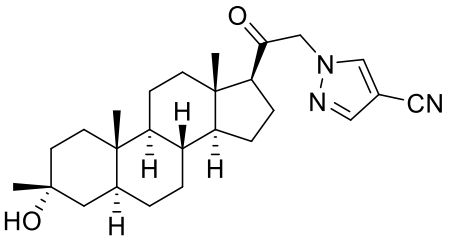
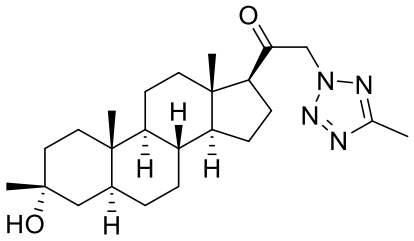
Compound No.	Structure
19	
24	
28	
79	

Compound No.	Structure
206	

or pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating seizure in a subject in need thereof.

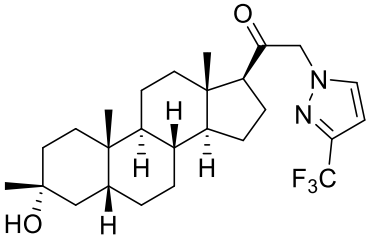
[10v] In yet another aspect of the present disclosure, there is provided a use of a compound selected from

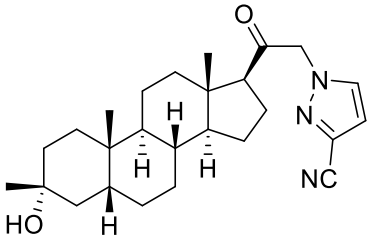
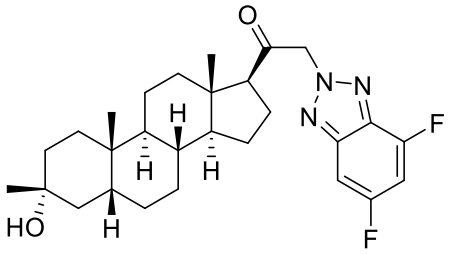
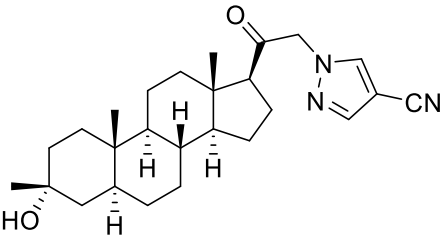
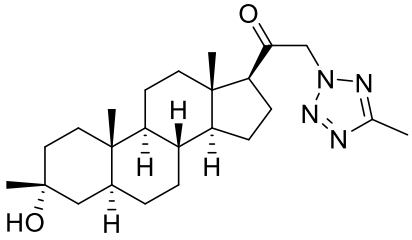
Compound No.	Structure
19	
24	
28	

Compound No.	Structure
79	
206	 ,

or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating epilepsy or status epilepticus in a subject in need thereof.

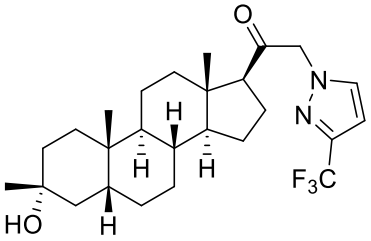
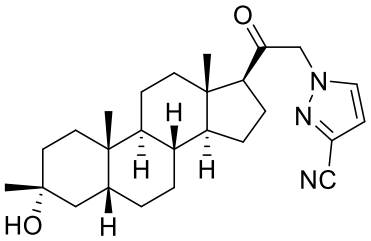
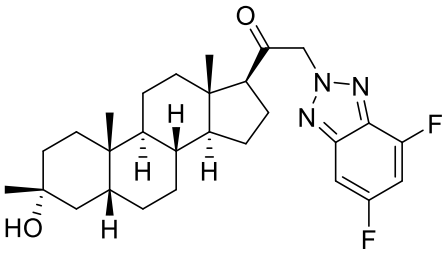
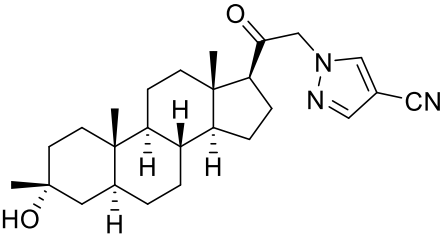
[10w] In a further aspect of the present disclosure, there is provided a use of a compound selected from

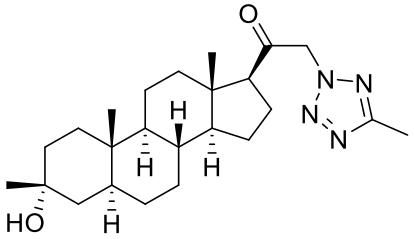
Compound No.	Structure
19	

Compound No.	Structure
24	
28	
79	
206	 ,

in the manufacture of a medicament for treating a CNS-related disorder related to GABA function in a subject in need thereof, 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 disorders and/or withdrawal syndromes, and tinnitus.

[10x] In another aspect of the present disclosure, there is provided a use of a compound selected from

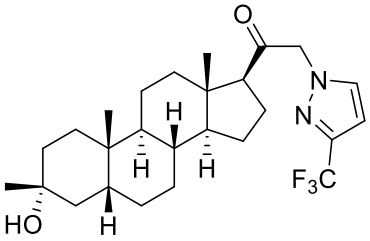
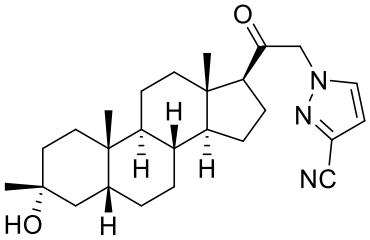
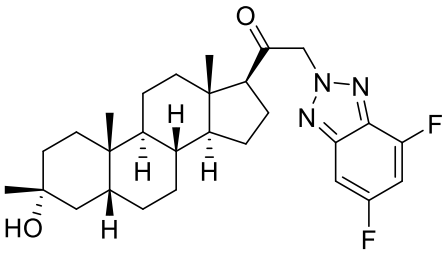
Compound No.	Structure
19	
24	
28	
79	

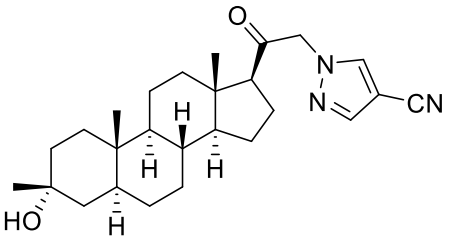
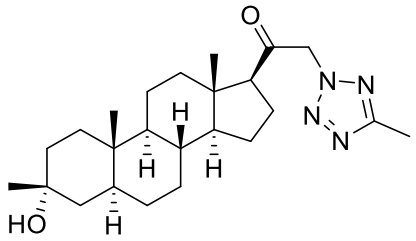
Compound No.	Structure
206	

,

or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating an eating disorder in a subject in need thereof, wherein the eating disorder is selected from anorexia nervosa, bulimia nervosa, binge-eating disorder, and cachexia.

[10y] In yet another aspect of the present disclosure, there is provided a use of a compound selected from

Compound No.	Structure
19	
24	
28	

Compound No.	Structure
79	
206	

or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating Angelman's syndrome in a subject in need thereof.

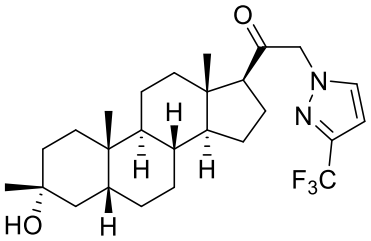
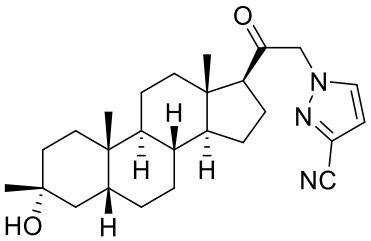
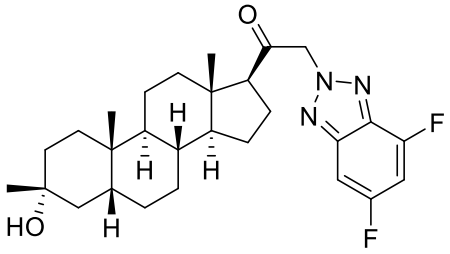
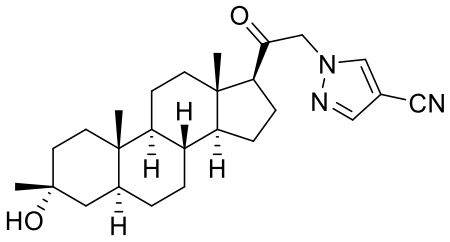
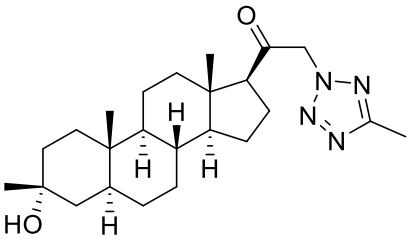
[11] Provided herein are C21-substituted neuroactive steroids designed, for example, to act as GABA modulators. In certain examples, such compounds are envisioned to be useful as therapeutic agents for the inducement of anesthesia and/or sedation in a subject. In some examples, such compounds are envisioned 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**):

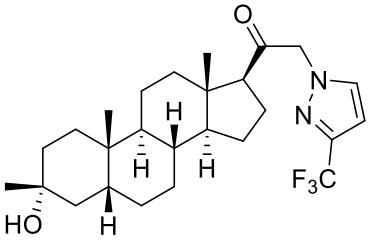
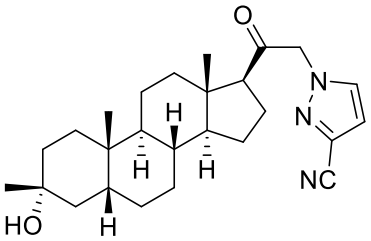
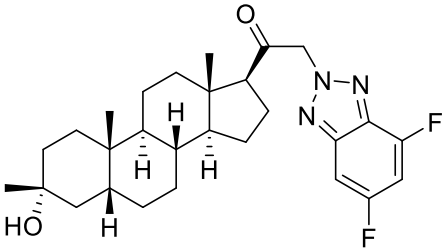
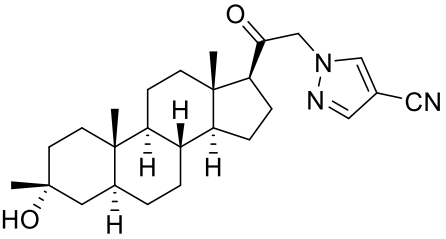
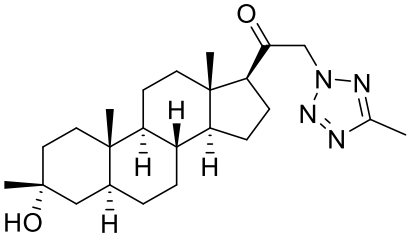
Claims

What is claimed is:

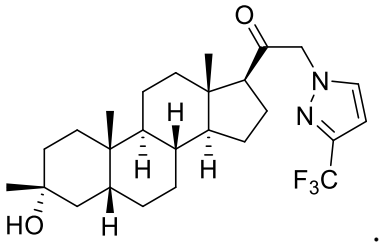
1. A compound selected from

Compound No.	Structure
19	
24	
28	
79	
206	

2. A pharmaceutically acceptable salt of a compound selected from

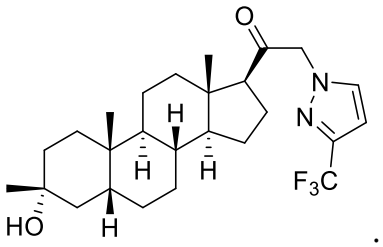
Compound No.	Structure
19	
24	
28	
79	
206	

3. A compound of the formula



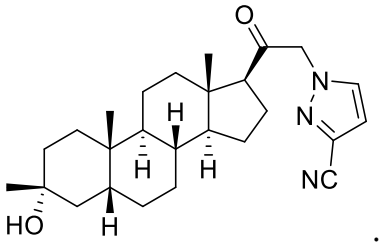
.

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



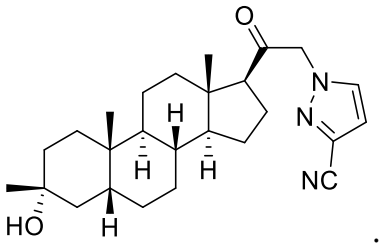
.

5. A compound of the formula



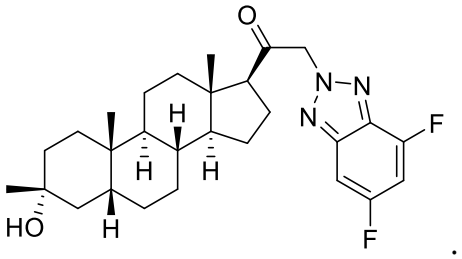
.

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



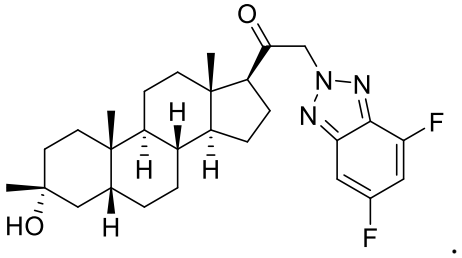
.

7. A compound of the formula



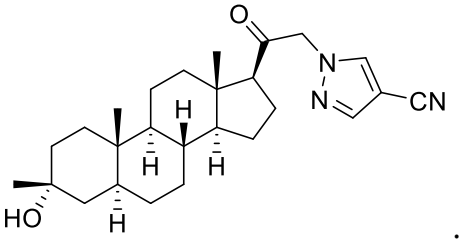
.

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



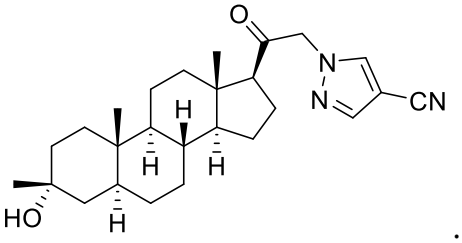
.

9. A compound of the formula



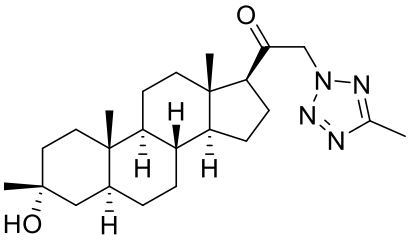
.

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



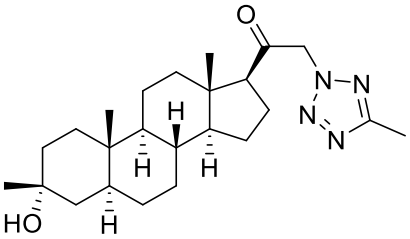
.

11. A compound of the formula



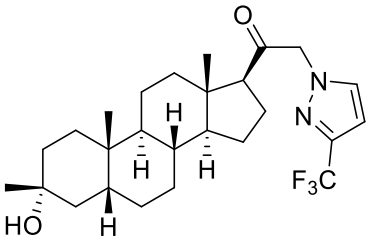
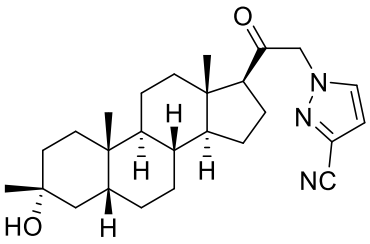
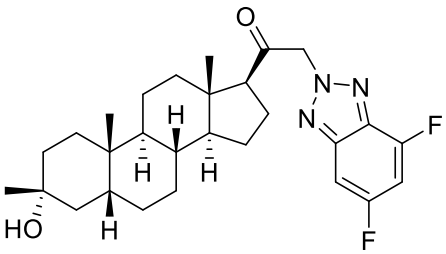
.

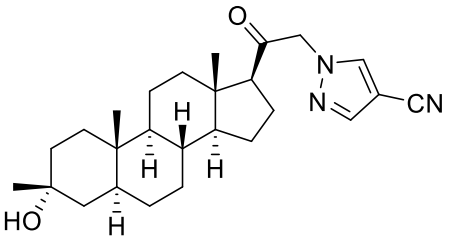
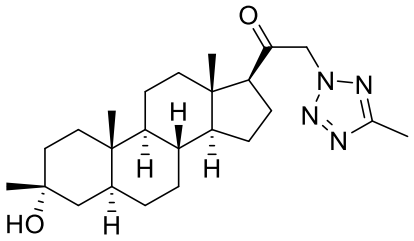
12. A pharmaceutically acceptable salt of a compound of the formula



.

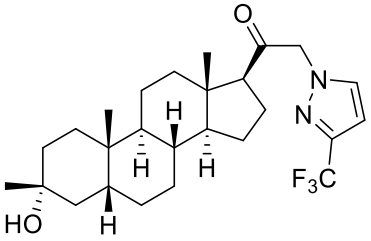
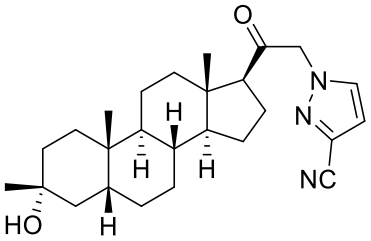
13. A pharmaceutical composition comprising a compound selected from

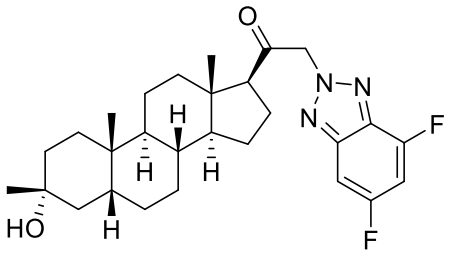
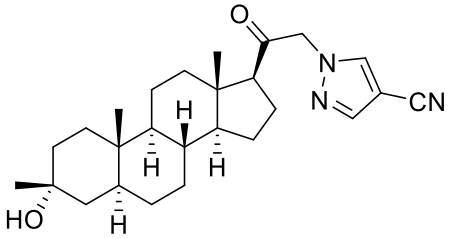
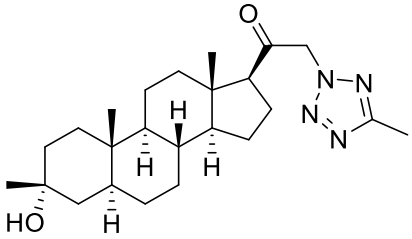
Compound No.	**Structure**
19	
24	
28	

Compound No.	Structure
79	
206	 ,

and a pharmaceutically acceptable excipient.

14. A pharmaceutical composition comprising a pharmaceutically acceptable salt of a compound selected from

Compound No.	Structure
19	
24	

Compound No.	Structure
28	
79	
206	 ,

and a pharmaceutically acceptable excipient.

15. The compound of any one of claims 1, 3, 5, 7, 9, or 11, the pharmaceutically acceptable salt of claim 2, 4, 6, 8, 10, or 12, or the pharmaceutical composition of claim 13 or 14, for use in inducing sedation and/or anesthesia in a subject.

16. The compound of any one of claims 1, 3, 5, 7, 9, or 11, the pharmaceutically acceptable salt of claim 2, 4, 6, 8, 10, or 12, or the pharmaceutical composition of claim 13 or 14, for use in tremor in a subject.

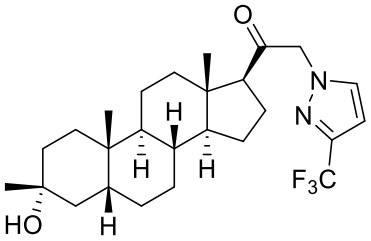
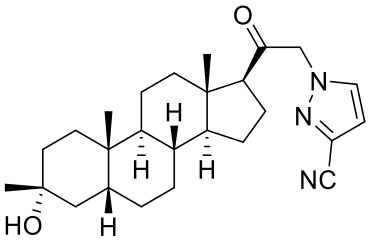
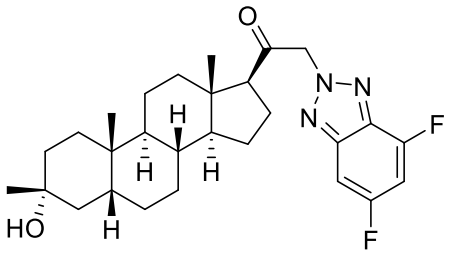
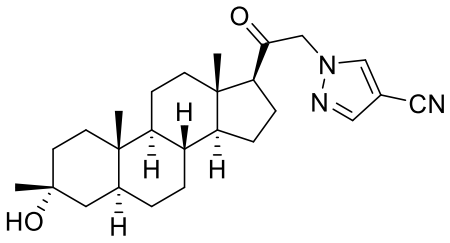
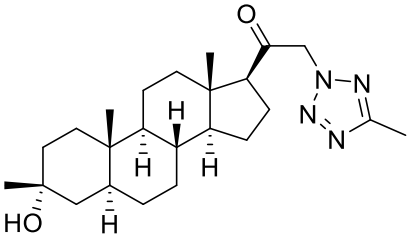
17. The compound of any one of claims 1, 3, 5, 7, 9, or 11, the pharmaceutically acceptable salt of claim 2, 4, 6, 8, 10, or 12, or the pharmaceutical composition of claim 13 or 14, for use of claim 16, wherein the tremor is essential tremor.

18. The compound of any one of claims 1, 3, 5, 7, 9, or 11, the pharmaceutically acceptable salt of claim 2, 4, 6, 8, 10, or 12, or the pharmaceutical composition of claim 13 or 14, for use of claim 16, wherein the tremor is parkinsonian tremor.

19. The compound of any one of claims 1, 3, 5, 7, 9, or 11, the pharmaceutically acceptable salt of claim 2, 4, 6, 8, 10, or 12, or the pharmaceutical composition of claim 13 or 14, for use in treating seizure in a subject.

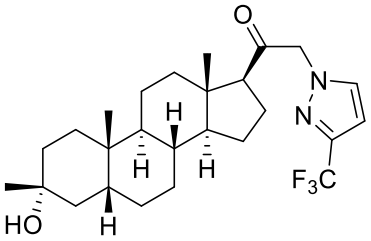
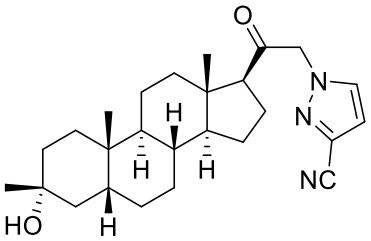
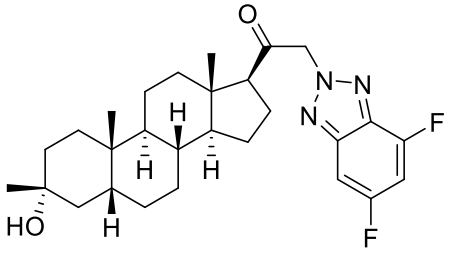
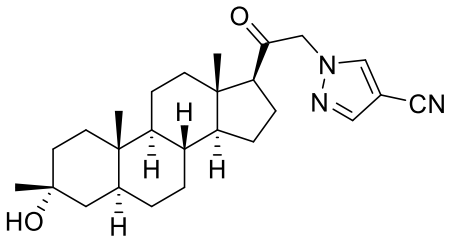
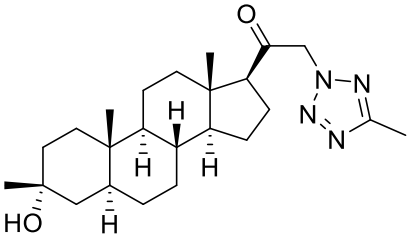
20. The compound of any one of claims 1, 3, 5, 7, 9, or 11, the pharmaceutically acceptable salt of claim 2, 4, 6, 8, 10, or 12, or the pharmaceutical composition of claim 13 or 14, for use in treating epilepsy or status epilepticus in a subject.

21. Use of a compound selected from

Compound No.	Structure
19	
24	
28	
79	
206	 ,

or pharmaceutically acceptable salt thereof in the manufacture of a medicament for inducing sedation and/or anesthesia in a subject in need thereof.

22. Use of a compound selected from

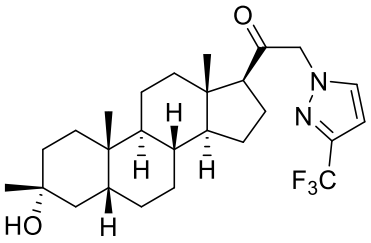
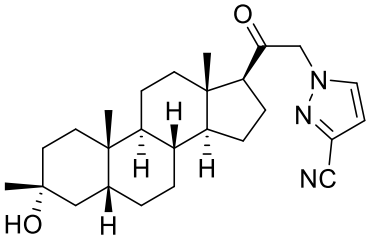
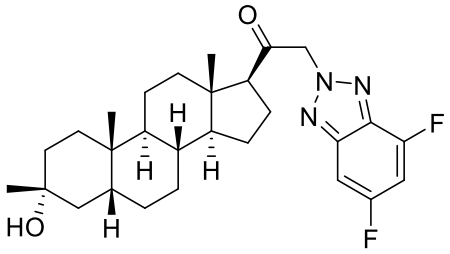
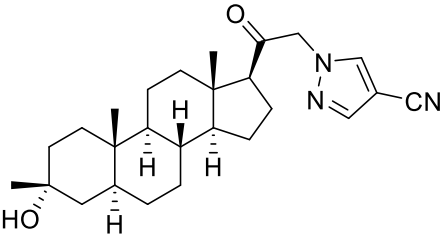
Compound No.	Structure
19	
24	
28	
79	
206	 ,

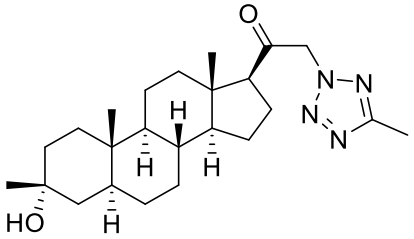
or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating tremor in a subject in need thereof.

23. The use of claim 22, wherein the tremor is essential tremor.

24. The use of claim 22, wherein the tremor is parkinsonian tremor.

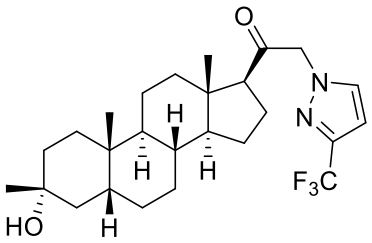
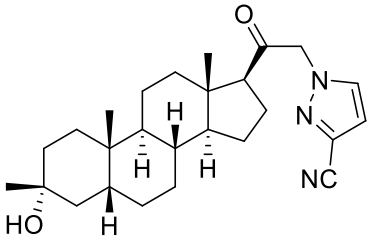
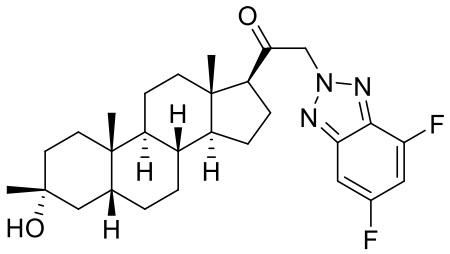
25. Use of a compound selected from

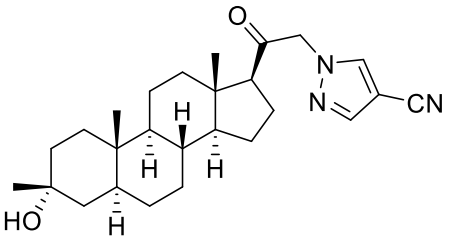
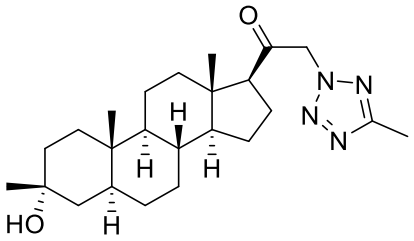
Compound No.	Structure
19	
24	
28	
79	

Compound No.	Structure
206	

or pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating seizure in a subject in need thereof.

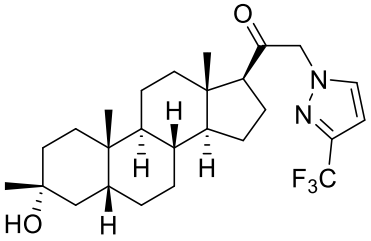
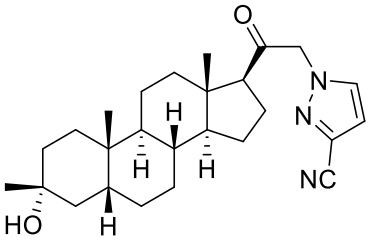
26. Use of a compound selected from

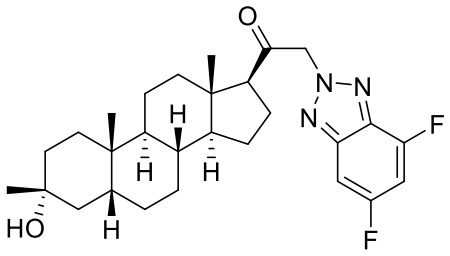
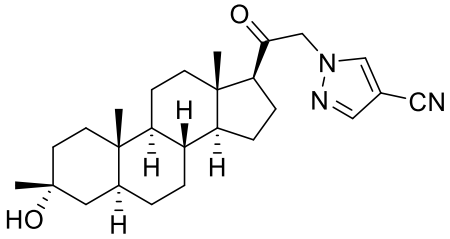
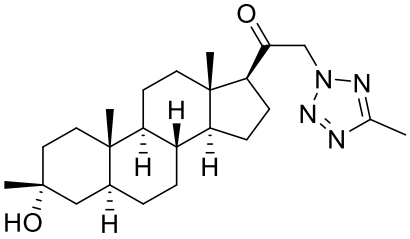
Compound No.	Structure
19	
24	
28	

Compound No.	Structure
79	
206	 ,

or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating epilepsy or status epilepticus in a subject in need thereof.

27. Use of a compound selected from

Compound No.	Structure
19	
24	

Compound No.	Structure
28	
79	
206	 ,

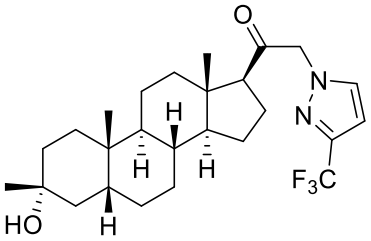
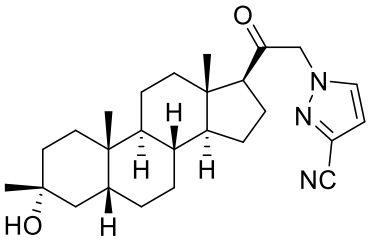
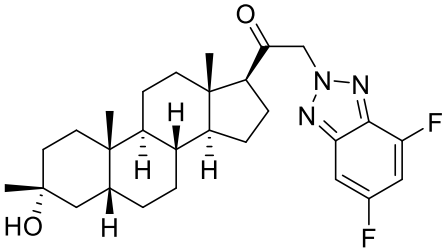
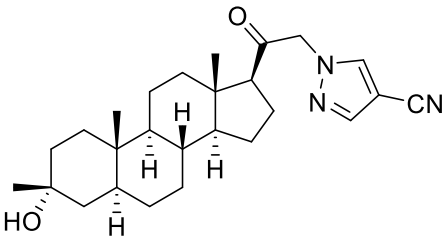
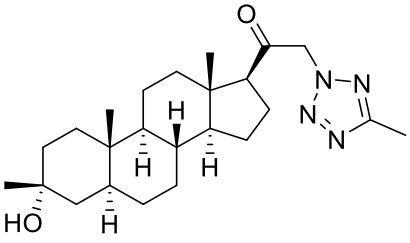
in the manufacture of a medicament for treating a CNS-related disorder related to GABA function in a subject in need thereof, wherein the disorder is selected from the group consisting of a sleep disorder, a mood disorder, a schizophrenia spectrum disorder, a convulsive disorder, a disorder of memory and/or cognition, a movement disorder, a personality disorder, autism spectrum disorder (ASD), pain, traumatic brain injury (TBI), a vascular disease, a substance abuse disorders and/or withdrawal syndromes, and tinnitus.

28. The use of claim 27, wherein the CNS-related disorder is depression.

29. The use of claim 28, wherein the depression is postpartum depression.

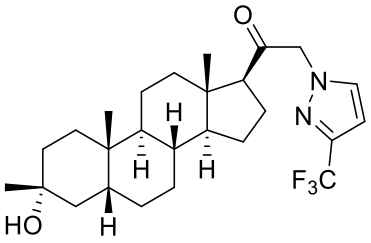
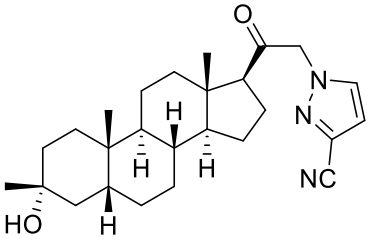
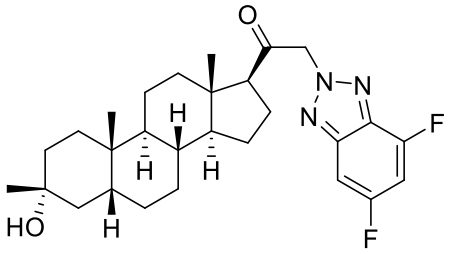
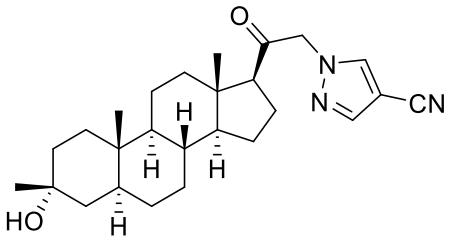
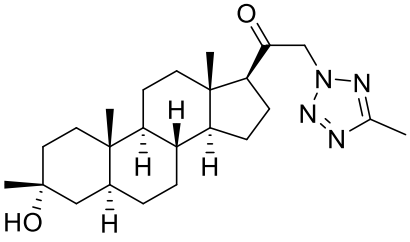
30. The use of claim 28, wherein the depression is a major depressive disorder.

31. Use of a compound selected from

Compound No.	Structure
19	
24	
28	
79	
206	 ,

or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating an eating disorder in a subject in need thereof, wherein the eating disorder is selected from anorexia nervosa, bulimia nervosa, binge-eating disorder, and cachexia.

32. Use of a compound selected from

Compound No.	Structure
19	
24	
28	
79	
206	 ,

or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating Angelman's syndrome in a subject in need thereof.

33. The use of any one of claims 21-32, wherein the medicament is to be administered orally or intramuscularly.

34. The use of claim 33, wherein the medicament is to be administered orally.

35. The use of claim 34, wherein the medicament is a tablet.

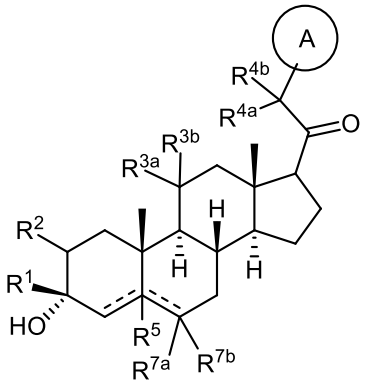
36. The use of claim 33, wherein the medicament is to be administered intramuscularly.

37. The use of any one of claims 21-36, wherein the medicament is to be administered chronically.

38. The use of any one of claims 21-37, wherein the subject is a human.

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]