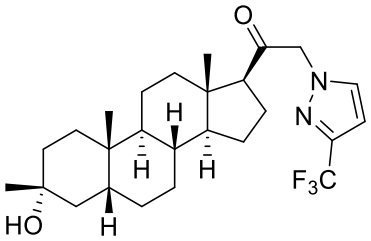
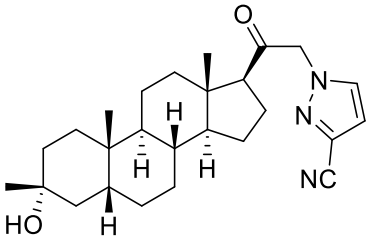
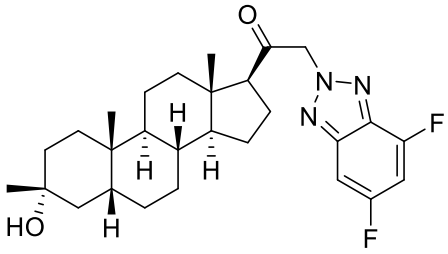
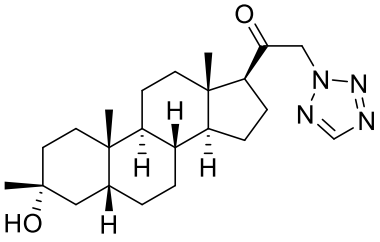
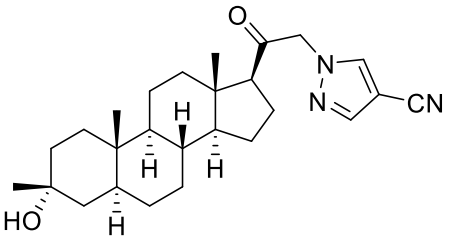
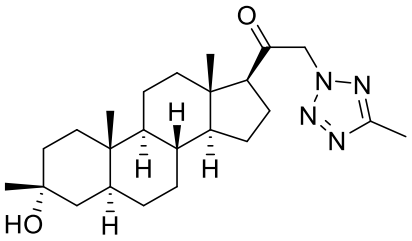
**[10]** New and improved neuroactive steroids are needed that act as modulating agents for brain excitability, as well as agents for the prevention and treatment of CNS-related diseases. The compounds, compositions, and methods described herein are directed toward this end.

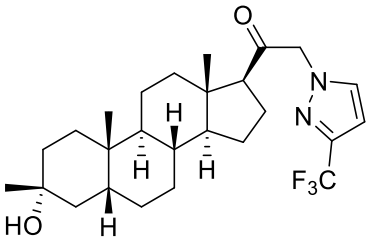
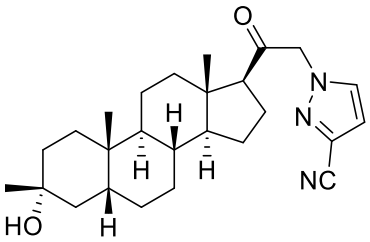
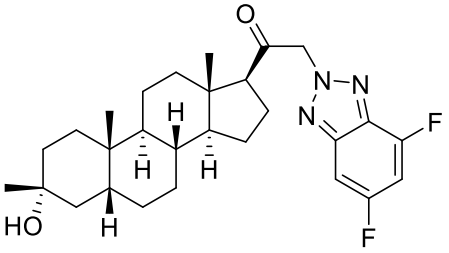
## Summary

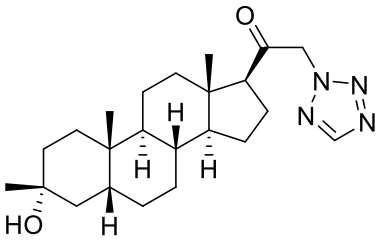
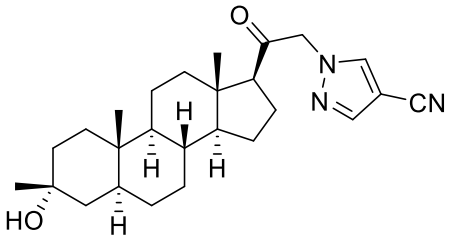
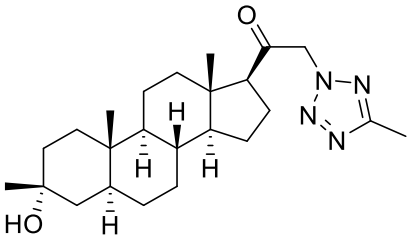
**[10a]** In a first aspect of the present disclosure, there is provided a compound selected from

| Compound No. | Structure |
|---|---|
| 19 |  |
| 24 |  |
| 28 |  |
| 54 |  |

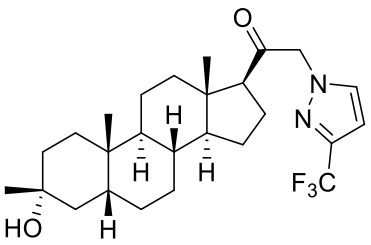
| Compound No. | Structure |
|---|---|
| 79 |  |
| 206 |  |

**[10b]** In another aspect of the present disclosure, there is provided a pharmaceutically acceptable salt of a compound selected from

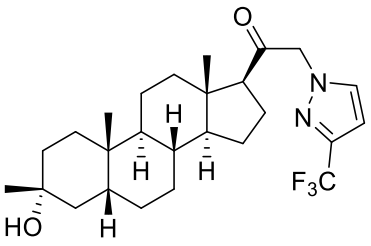
| Compound No. | Structure |
|---|---|
| 19 |  |
| 24 |  |
| 28 |  |

| Compound No. | Structure |
|---|---|
| 54 |  |
| 79 |  |
| 206 |  |

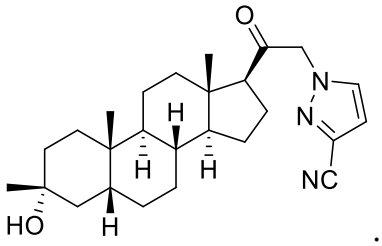
**[10c]** In yet another aspect of the present disclosure, there is provided a compound of the formula



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

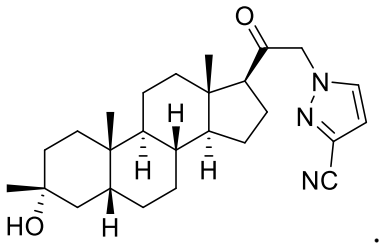


**[10e]** In another aspect of the present disclosure, there is provided a compound of the formula



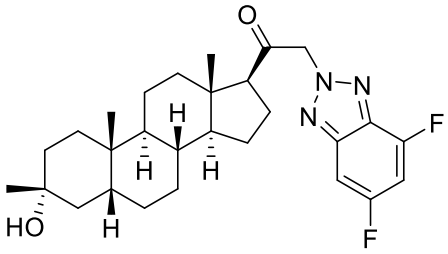
.

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



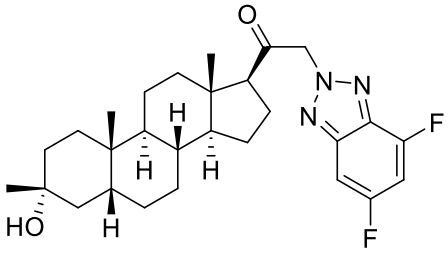
.

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



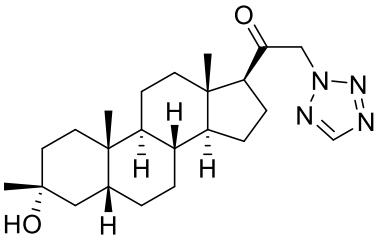
.

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



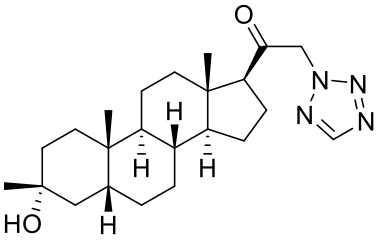
.

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



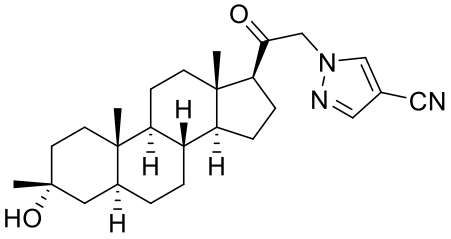
.

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



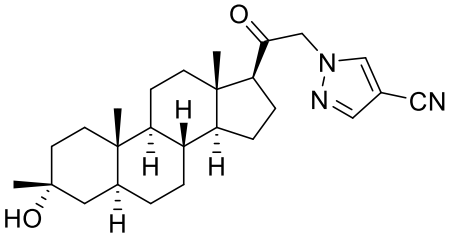
.

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



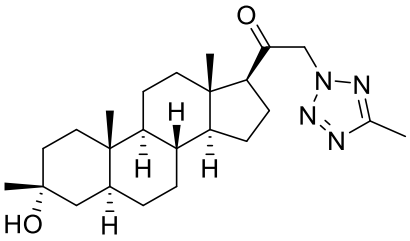
.

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



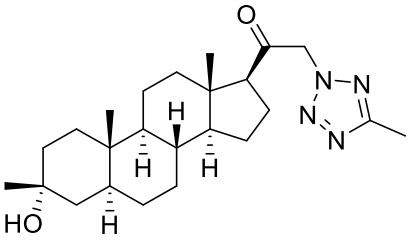
.

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



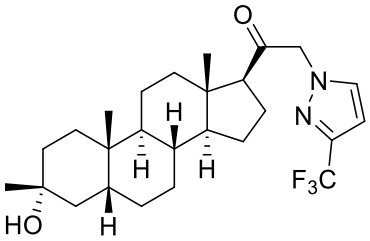
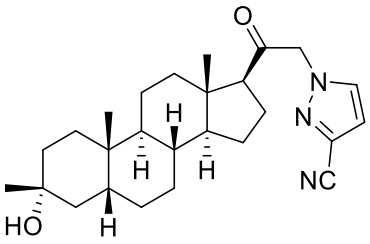
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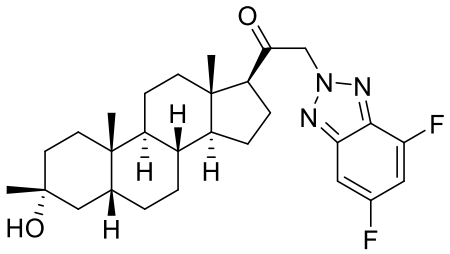
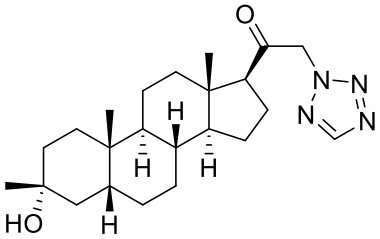
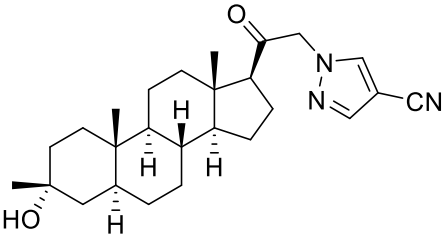
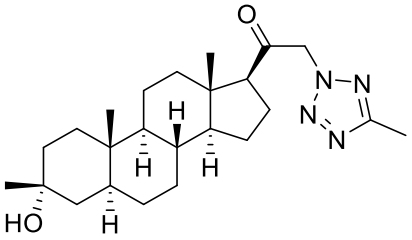
**[10n]** In another aspect of the present disclosure, there is provided a pharmaceutically acceptable salt of a compound of the formula



.

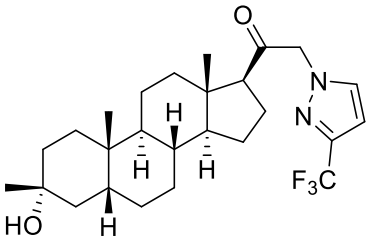
**[10o]** In yet another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound selected from

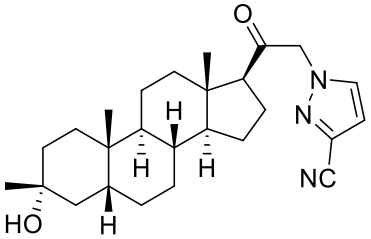
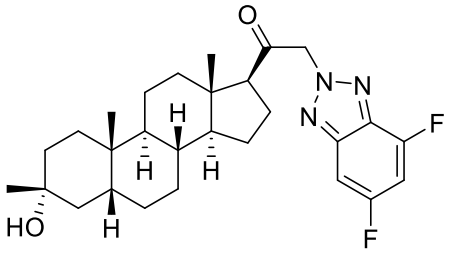
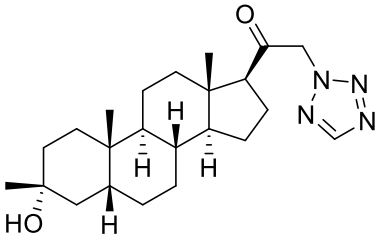
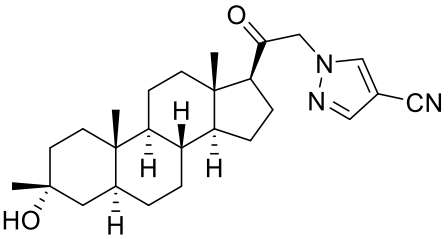
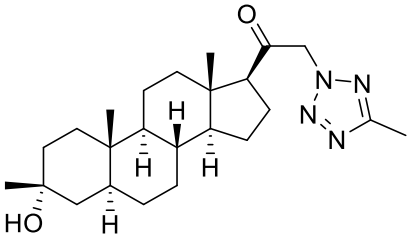
| **Compound No.** | **Structure** |
|---|---|
| 19 |  |
| 24 |  |

| Compound No. | Structure |
|---|---|
| 28 |  |
| 54 |  |
| 79 |  |
| 206 |  , |

and a pharmaceutically acceptable excipient.

**[10p]** 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 |  |
| 54 |  |
| 79 |  |
| 206 |  , |

and a pharmaceutically acceptable excipient.

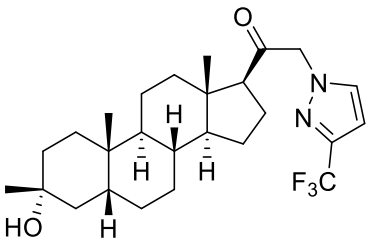
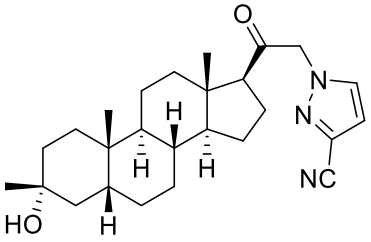
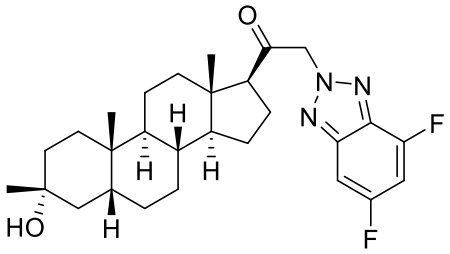
**[10q]** In another aspect of the present disclosure, there is provided the compound, the pharmaceutically acceptable salt, or the pharmaceutical composition as disclosed herein, for use in inducing sedation and/or anesthesia in a subject.

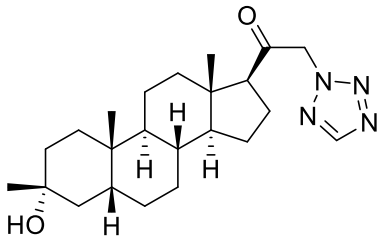
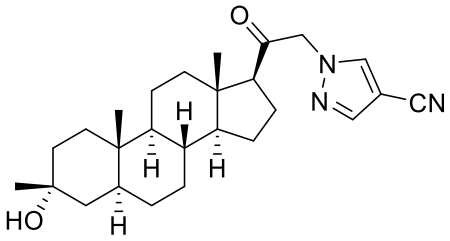
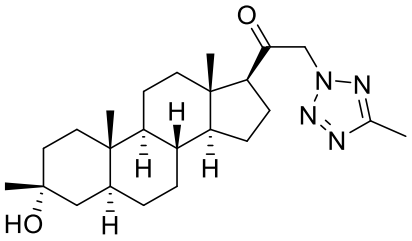
**[10r]** In yet another aspect of the present disclosure, there is provided the compound, the pharmaceutically acceptable salt, or the pharmaceutical composition as disclosed herein, for use in tremor in a subject.

**[10s]** 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.

**[10t]** 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.

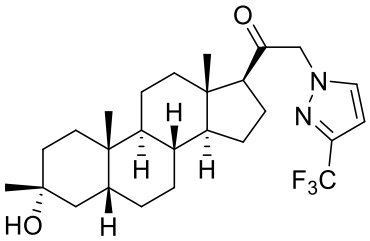
**[10u]** In yet another aspect of the present disclosure, there is provided a use of a compound selected from

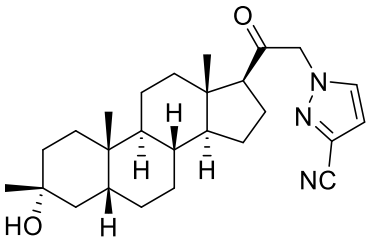
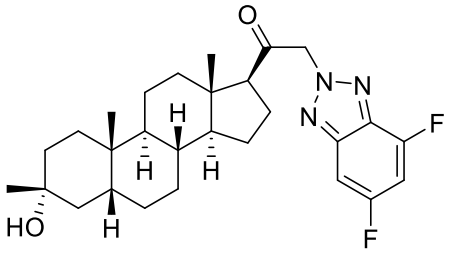
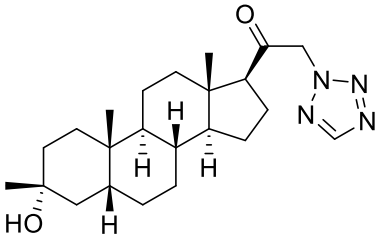
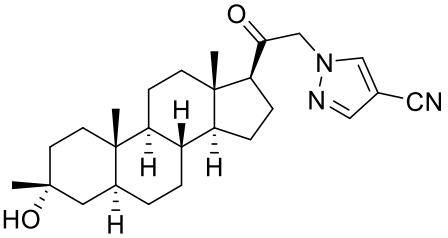
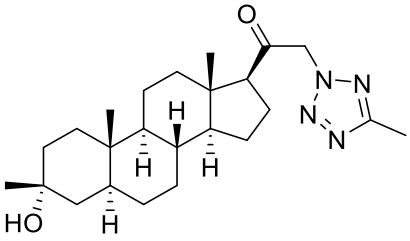
| **Compound No.** | **Structure** |
|---|---|
| 19 |  |
| 24 |  |
| 28 |  |

| Compound No. | Structure |
|---|---|
| 54 |  |
| 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.

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

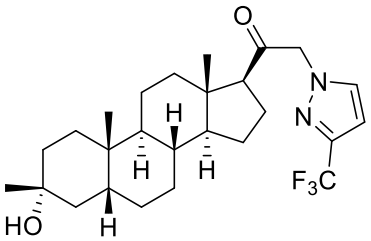
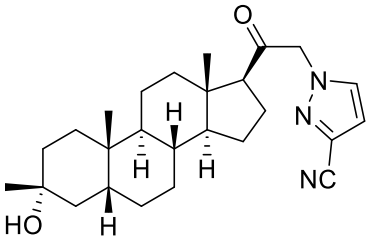
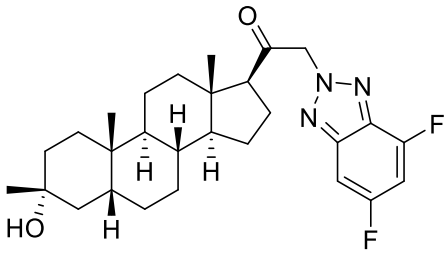
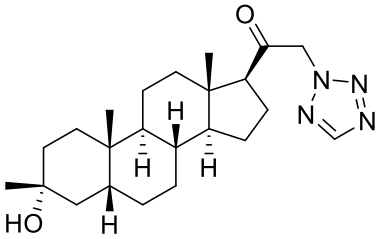
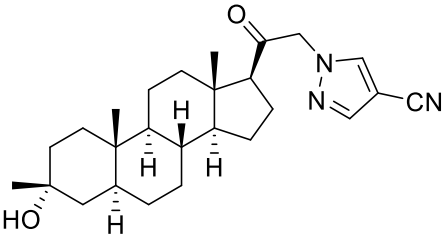
| Compound No. | Structure |
|---|---|
| 19 |  |

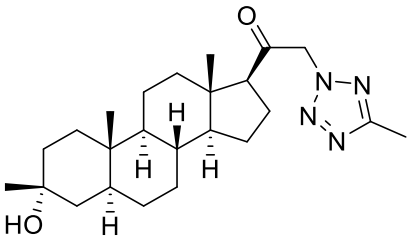
| Compound No. | Structure |
|---|---|
| 24 |  |
| 28 |  |
| 54 |  |
| 79 |  |
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,

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

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

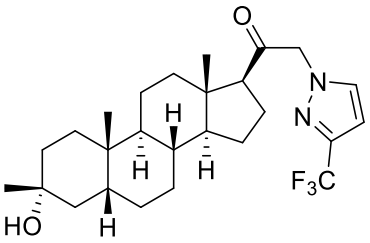
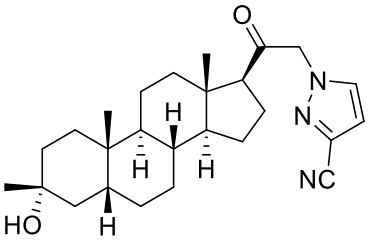
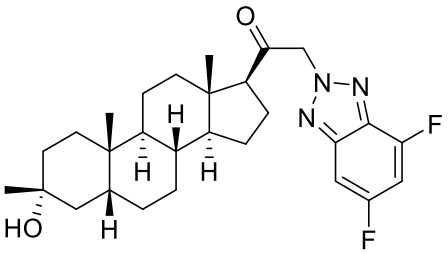
| Compound No. | Structure |
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| 19 |  |
| 24 |  |
| 28 |  |
| 54 |  |
| 79 |  |

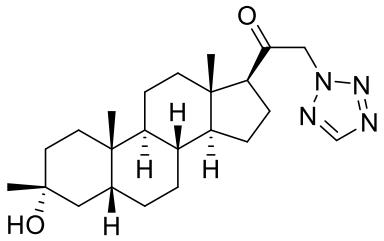
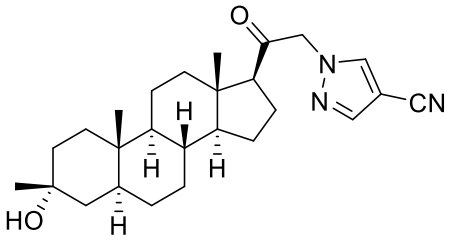
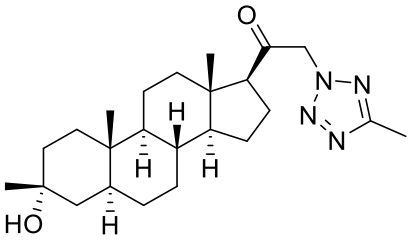
| Compound No. | Structure |
|---|---|
| 206 |  |

,

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

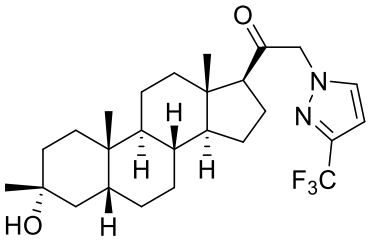
**[10x]** In yet another aspect of the present disclosure, there is provided a use of a compound selected from

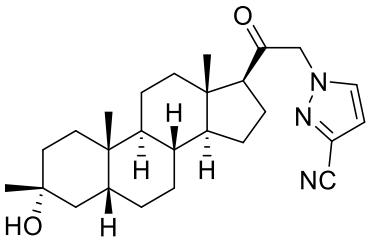
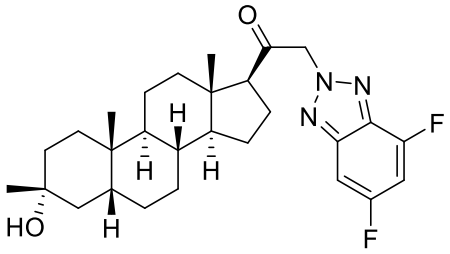
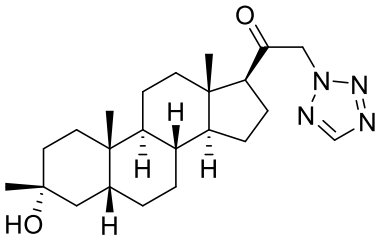
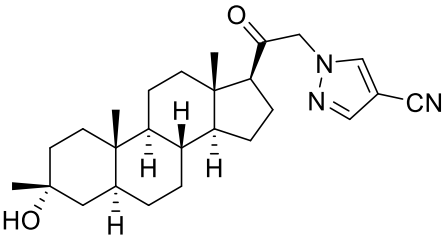
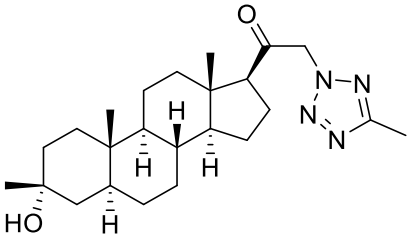
| Compound No. | Structure |
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| 19 |  |
| 24 |  |
| 28 |  |

| Compound No. | Structure |
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| 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.

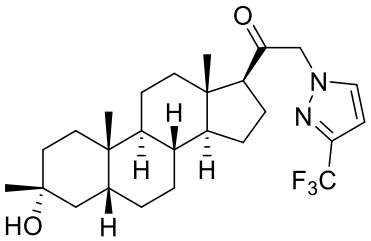
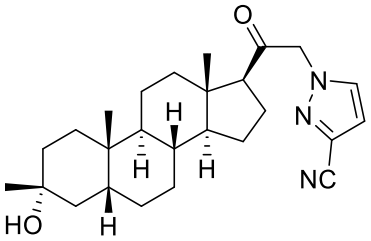
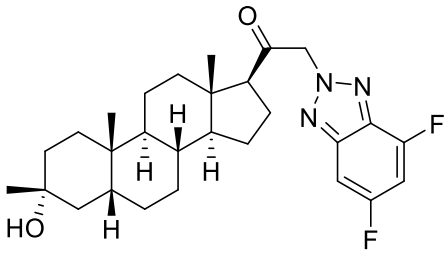
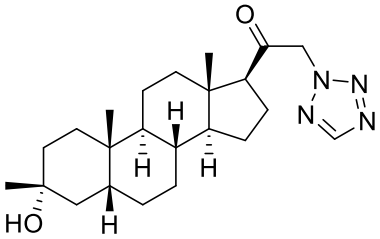
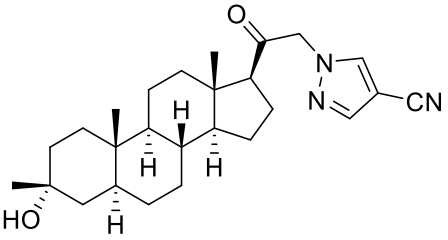
**[10y]** In a further aspect of the present disclosure, there is provided a use of a compound selected from

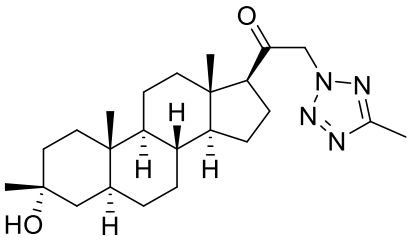
| Compound No. | Structure |
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| Compound No. | Structure |
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| 24 |  |
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| 54 |  |
| 79 |  |
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in the manufacture of a medicament for treating a CNS-related disorder related to GABA function in a subject in need thereof.

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

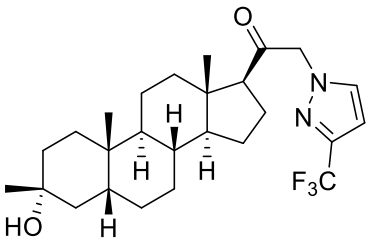
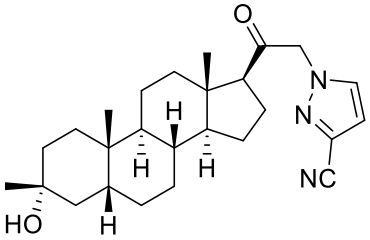
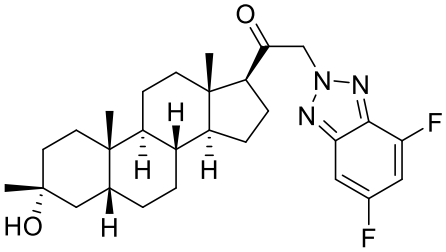
| Compound No. | Structure |
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| 19 |  |
| 24 |  |
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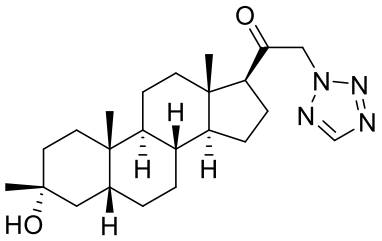
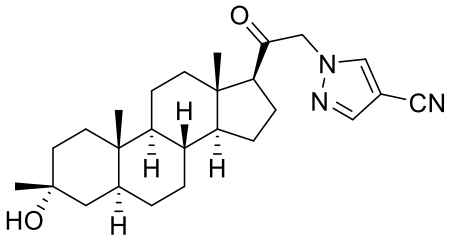
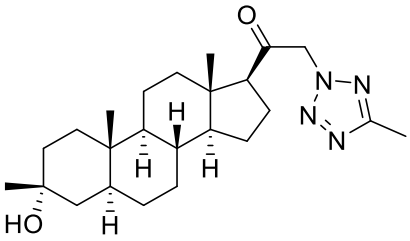
| Compound No. | Structure |
|---|---|
| 206 |  |

,

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.

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

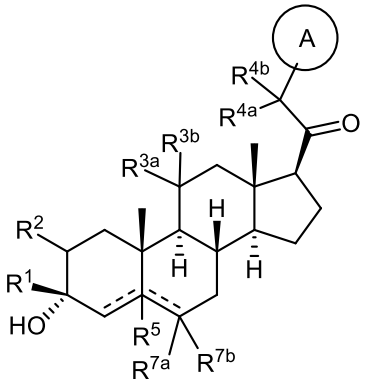
| Compound No. | Structure |
|---|---|
| 19 |  |
| 24 |  |
| 28 |  |

| Compound No. | Structure |
|---|---|
| 54 |  |
| 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**):




(**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

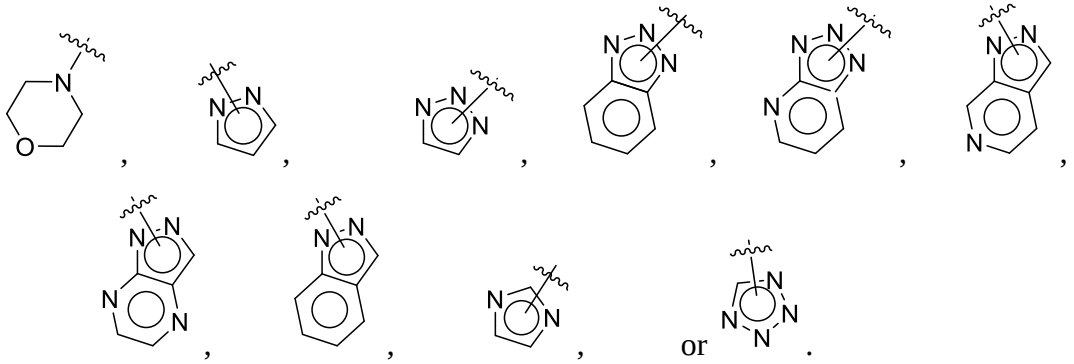
$C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, or substituted or unsubstituted $C_{3-6}$ carbocylyl; $R^{3a}$ is hydrogen or $–OR^{A3}$, wherein $R^{A3}$ is hydrogen, substituted or unsubstituted $C_{1-6}$ alkyl, substituted or unsubstituted $C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, or substituted or unsubstituted $C_{3-6}$ carbocylyl, and $R^{3b}$ is hydrogen; or $R^{3a}$ and $R^{3b}$ are joined to form an oxo (=O) group; $R^{4a}$ is hydrogen, substituted or unsubstituted $C_{1-6}$ alkyl, or $–OR^{A4}$, wherein $R^{A4}$ is hydrogen, substituted or unsubstituted $C_{1-6}$ alkyl, substituted or unsubstituted $C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, or substituted or unsubstituted $C_{3-6}$ carbocylyl, and $R^{4b}$ is hydrogen or substituted or unsubstituted $C_{1-6}$ alkyl; $R^{4a}$ and $R^{4b}$ are joined to form an oxo (=O) group; or $R^{4a}$ and $R^{4b}$ together with the carbon atom to which they are attached form a ring (e.g., a 3-6-membered ring (e.g., carbocycyl or heterocyclyl ring). $R^{7a}$ is hydrogen or halogen; $R^{7b}$ is hydrogen; $R^5$ is absent or hydrogen; and ------ represents a single or double bond, wherein when one of ------ is a double bond, the other ------ is a single bond; and when one of the ------ is a double bond, $R^5$ is absent.

In an example, A is Ring A is substituted or unsubstituted nitrogen containing heterocyclyl, or nitrogen containing heteroaryl. In an example, A is attached through a nitrogen atom. In an example, A is monocyclic heteroaryl or heterocylcyl, for example, a substituted monocyclic heteroaryl. In an example, A is bicyclic heteroaryl, for example, a substituted bicyclic heteroaryl. Exemplary substituents are described herein.

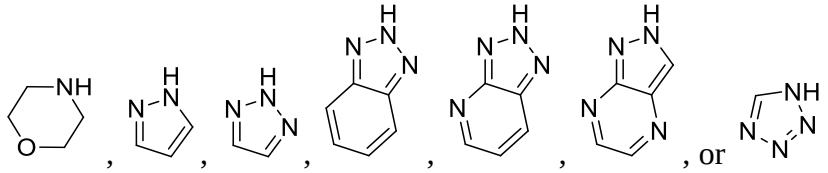
In an example, ring A is substituted carbocyclyl, heterocyclyl, aryl, or heteroaryl, for example, a substituted heterocyclyl or heteroaryl. In some examples, the heterocyclyl or heteroaryl is attached through a nitrogen atom. In an example, A is a substituted heterocyclyl linked through a nitrogen atom. In an example, A is an unsubstituted heterocyclyl linked through a nitrogen atom. In an example, A is a substituted heteroaryl linked through a nitrogen atom. In an example, A is an unsubstituted heteroaryl linked through a nitrogen atom.

In an example, A is substituted or unsubstituted imidiaole or benzimidazole (e.g., a substituted imidazole or benzimidazole). In some examples the imidazole or benzimidazole is attached through a nitrogen atom.

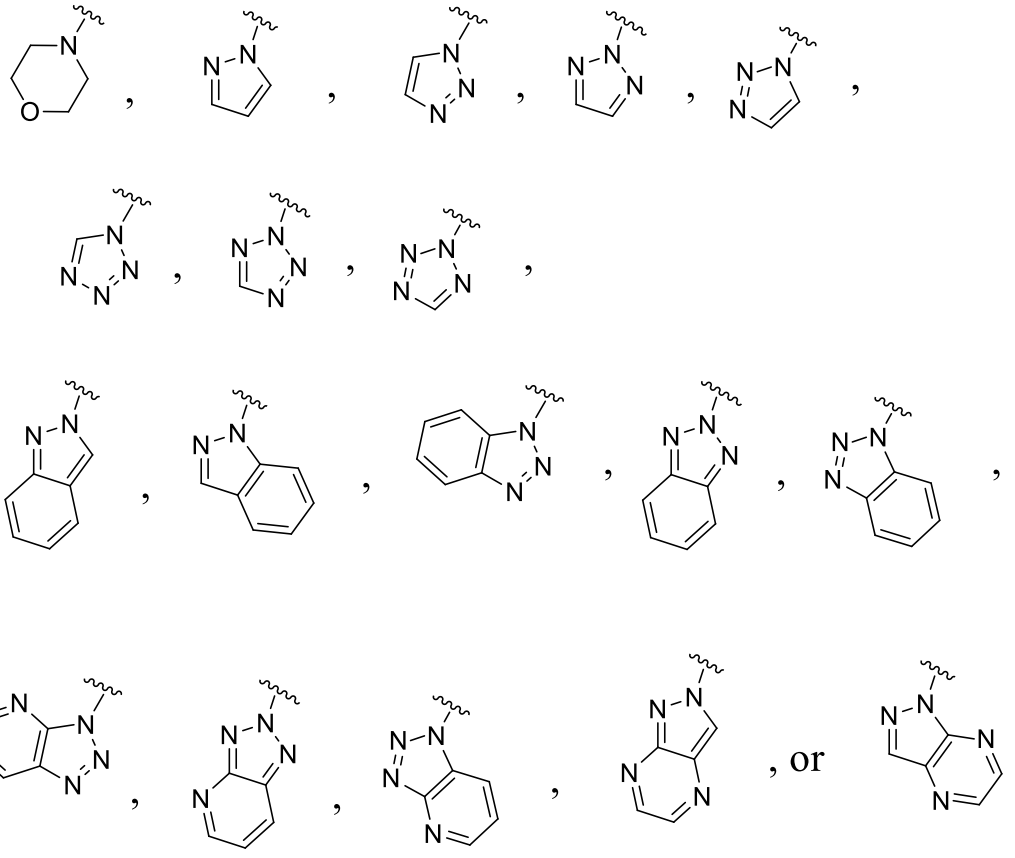
In an example, A is substituted or unsubstituted and is selected from:



In an example, A is substituted or unsubstituted and is selected from:



In an example A is substituted or unsubstituted and is selected from:



In an example, $R^1$ is hydrogen, methyl, ethyl, or propyl (e.g., methyl). In an example, $R^1$ is unsubstituted $C_{1-3}$ alkyl. In an example, $R^1$ is substituted $C_{1-6}$ alkyl (e.g., haloalkyl or alkoxyalkyl such as methoxymethyl).

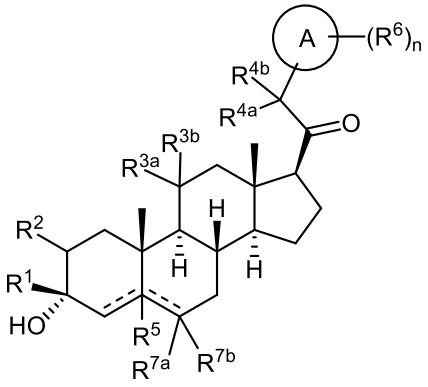
**[12]** In an example, at least one of $R^2$, $R^{3a}$, $R^{4a}$ or $R^{4b}$ is not hydrogen. For example, in an example, at least 2 of $R^2$, $R^{3a}$, $R^{4a}$ or $R^{4b}$ is not hydrogen.

In an example, $R^2$ is 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 $C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, or substituted or unsubstituted $C_{3-6}$ carbocylyl. In an example, $R^2$ is $–OR^{A2}$, wherein $R^{A2}$ is hydrogen or substituted or unsubstituted $C_{1-6}$ alkyl, substituted or unsubstituted $C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, or substituted or unsubstituted $C_{3-6}$ carbocylyl, for example, hydroxyl or alkoxy.

In an example, $R^{3a}$ is $–OR^{A3}$, wherein $R^{A3}$ is hydrogen, substituted or unsubstituted $C_{1-6}$ alkyl, substituted or unsubstituted $C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, or substituted or unsubstituted $C_{3-6}$ carbocylyl, and $R^{3b}$ is hydrogen; or $R^{3a}$ and $R^{3b}$ are joined to form an oxo (=O) group. In an example, $R^{3a}$ is $–OR^{A3}$, wherein $R^{A3}$ is hydrogen, substituted or unsubstituted $C_{1-6}$ alkyl, substituted or unsubstituted $C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, or substituted or unsubstituted $C_{3-6}$ carbocylyl, for example, hydroxyl or alkoxy

In an example, $R^{4a}$ is substituted or unsubstituted $C_{1-6}$ alkyl, or $–OR^{A4}$, wherein $R^{A4}$ is hydrogen, substituted or unsubstituted $C_{1-6}$ alkyl, substituted or unsubstituted $C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, or substituted or unsubstituted $C_{3-6}$ carbocylyl, and $R^{4b}$ is hydrogen or substituted or unsubstituted $C_{1-6}$ alkyl; or $R^{4a}$ and $R^{4b}$ are joined to form an oxo (=O) group.

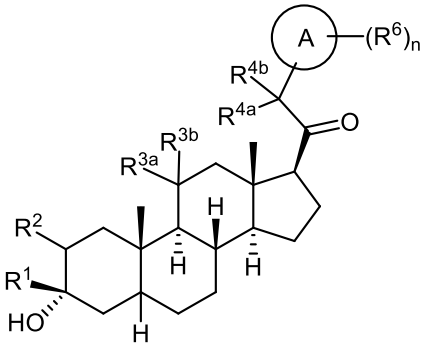
In an example, the compound is of the Formula (**I-a**):




(**I-a**)

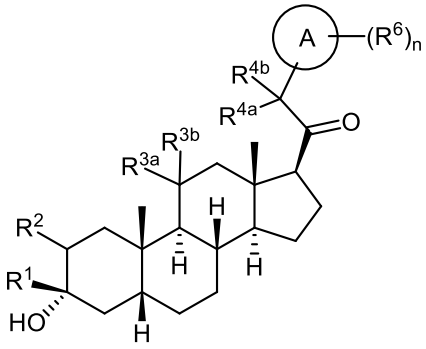
wherein: $R^6$ is substituted or unsubstituted $C_{1-6}$ alkyl, substituted or unsubstituted $C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, substituted or unsubstituted $C_{3-6}$ carbocylyl, $C_{1-6}$ haloalkyl, halogen, cyano,–$OR^{A6}$, -C(=O)$OR^{A6}$, -$SR^{B6}$, -S(=O)$R^{B6}$, or S(=O)$_2R^{B6}$, wherein $R^{A6}$ is hydrogen or 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 $C_{1-6}$ haloalkyl, and $R^{B6}$ is substituted or unsubstituted $C_{1-6}$ alkyl or substituted or unsubstituted $C_{3-6}$ carbocylyl; and n is 0, 1, 2, or 3.

In an example, the compound is of the Formula (**I-b**):

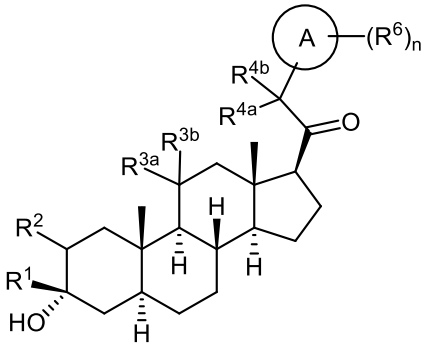



(**I-b**).

In an example, the compound is of the Formula (**I-c1**) or (**I-c2**):

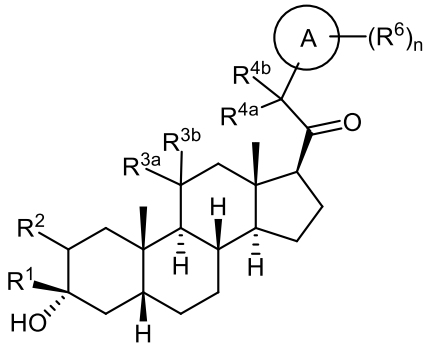



(**I-c1**)




(**I-c2**).

In an example, the compound is of the Formula (**I-c1**):




(**I-c1**)

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 $C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, or substituted or unsubstituted $C_{3-6}$ carbocylyl; $R^{3a}$ is hydrogen or $–OR^{A3}$, wherein $R^{A3}$ is hydrogen, substituted or unsubstituted $C_{1-6}$ alkyl, substituted or unsubstituted $C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, or substituted or unsubstituted $C_{3-6}$ carbocylyl, and $R^{3b}$ is hydrogen; or $R^{3a}$ and $R^{3b}$ are joined to form an oxo (=O) group; $R^{4a}$ is hydrogen, substituted or unsubstituted $C_{1-6}$ alkyl, or $–OR^{A4}$, wherein $R^{A4}$ is hydrogen, substituted or unsubstituted $C_{1-6}$ alkyl, substituted or unsubstituted $C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, or substituted or unsubstituted $C_{3-6}$ carbocylyl,

and $R^{4b}$ is hydrogen or substituted or unsubstituted $C_{1-6}$ alkyl; $R^{4a}$ and $R^{4b}$ are joined to form an oxo (=O) group; or $R^{4a}$ and $R^{4b}$ together with the carbon atom to which they are attached form a ring (e.g., a 3-6-membered ring (e.g., carbocycyl or heterocyclyl ring); $R^6$ is 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, $C_{1-6}$ haloalkyl, halogen, cyano,$–OR^{A6}$, $-C(=O)OR^{A6}$, $-SR^{B6}$, $-S(=O)R^{B6}$, or $S(=O)_2R^{B6}$, wherein $R^{A6}$ is hydrogen or 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 $C_{1-6}$ haloalkyl, and $R^{B6}$ is substituted or unsubstituted $C_{1-6}$ alkyl or substituted or unsubstituted $C_{3-6}$ carbocylyl; and n is 0, 1, 2, or 3.

In an example, A is a carbon bound (e.g., A linked through a carbon atom) substituted or unsubstituted 5 or 6-membered heteroaryl, or 6-membered aryl.

In an example, A is Ring A is substituted or unsubstituted nitrogen containing heterocyclyl, or nitrogen containing heteroaryl. In an example, A is attached through a nitrogen. In an example, A is monocyclic heteroaryl or heterocylcyl, for example, a substituted monocyclic heteroaryl. In an example, A is bicyclic heteroaryl, for example, a substituted bicyclic heteroaryl. Exemplary substituents are described herein.

**[13]** In an example, $R^1$ is hydrogen. In an example, $R^1$ is substituted or unsubstituted $C_{1-6}$ alkyl, for example, methyl.

**[14]** In an example, at least one of $R^2$, $R^{3a}$, $R^{4a}$ or $R^{4b}$ is not hydrogen. For example, in an example, at least 2 of $R^2$, $R^{3a}$, $R^{4a}$ or $R^{4b}$ is not hydrogen.

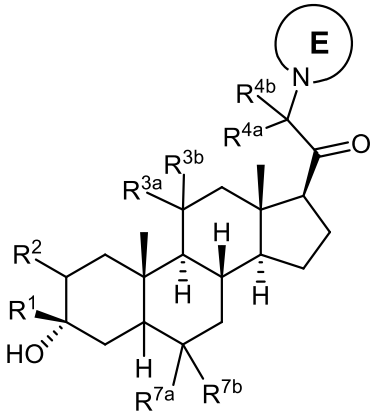
In an example, $R^2$ is substituted or unsubstituted $C_{1-6}$ alkyl, substituted or unsubstituted $C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, substituted or unsubstituted $C_{3-6}$ carbocylyl, or $–OR^{A2}$, wherein $R^{A2}$ is hydrogen or substituted or unsubstituted $C_{1-6}$ alkyl, substituted or unsubstituted $C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, or substituted or unsubstituted $C_{3-6}$ carbocylyl. In an example, $R^2$ is $–OR^{A2}$, wherein $R^{A2}$ is hydrogen or substituted or unsubstituted $C_{1-6}$ alkyl, substituted or unsubstituted $C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, or substituted or unsubstituted $C_{3-6}$ carbocylyl, for example, hydroxyl or alkoxy.

In an example, $R^{3a}$ is $–OR^{A3}$, wherein $R^{A3}$ is hydrogen, substituted or unsubstituted $C_{1-6}$ alkyl, substituted or unsubstituted $C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, or

substituted or unsubstituted $C_{3-6}$ carbocylyl, and $R^{3b}$ is hydrogen; or $R^{3a}$ and $R^{3b}$ are joined to form an oxo (=O) group. In an example, $R^{3a}$ is $–OR^{A3}$, wherein $R^{A3}$ is hydrogen, substituted or unsubstituted $C_{1-6}$ alkyl, substituted or unsubstituted $C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, or substituted or unsubstituted $C_{3-6}$ carbocylyl, for example, hydroxyl or alkoxy

In an example, $R^{4a}$ is substituted or unsubstituted $C_{1-6}$ alkyl, or $–OR^{A4}$, wherein $R^{A4}$ is hydrogen, substituted or unsubstituted $C_{1-6}$ alkyl, substituted or unsubstituted $C_{2-6}$ alkenyl, substituted or unsubstituted $C_{2-6}$ alkynyl, or substituted or unsubstituted $C_{3-6}$ carbocylyl, and $R^{4b}$ is hydrogen or substituted or unsubstituted $C_{1-6}$ alkyl; or $R^{4a}$ and $R^{4b}$ are joined to form an oxo (=O) group.

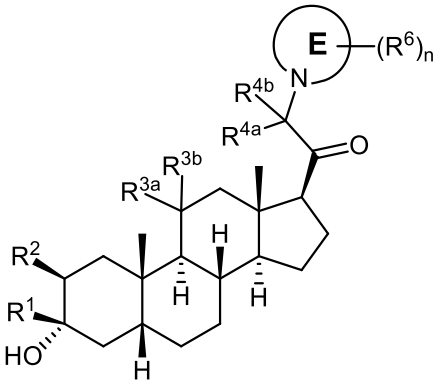
In an example, the compound is of the Formula (**II**):



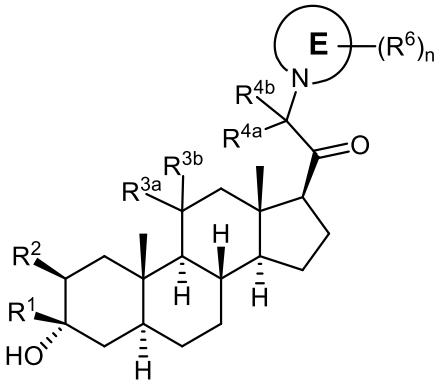

(**II**)

wherein: Ring E is substituted or unsubstituted heterocyclyl or heteroaryl.

In an example, the compound is of the Formula (**II-a1**) or (**II-a2**):




(**II-a1**)

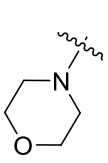
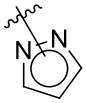
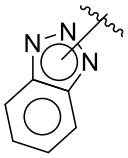
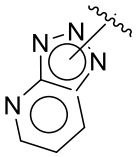
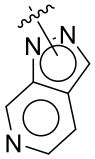
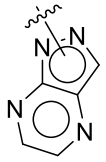
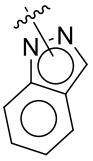



(**II-a2**).

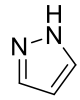
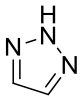
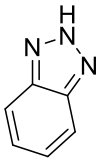
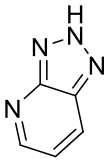
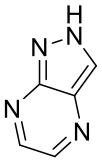
In an example, E is a ring comprising at least one nitrogen atom.

In an example, A is a ring comprising at least one nitrogen atom.

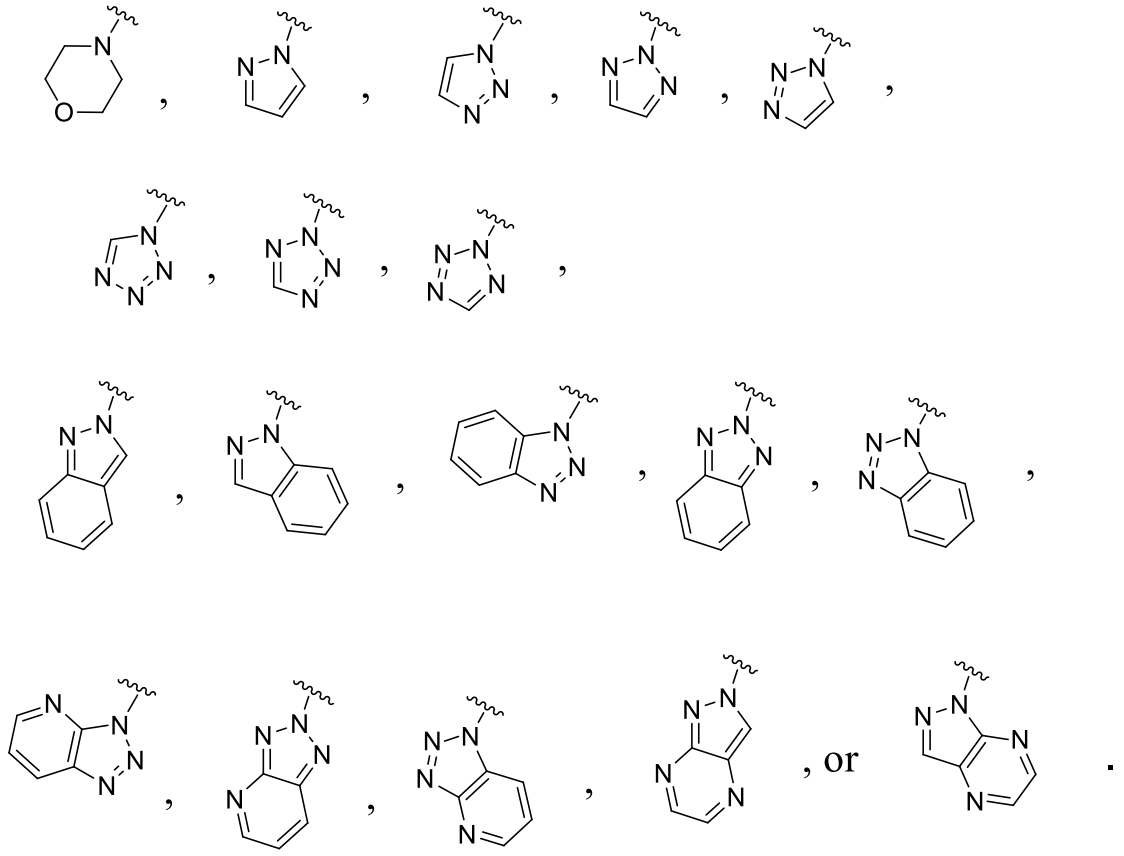
In an example, E is selected from:

, , , , , , , , , or .

In an example, E is selected from:

, , , , , , , or .

In an example, A is:



In an example, E is a ring comprising at least two nitrogen atoms. In an example, E is a ring comprising at least two nitrogen atoms and $R^1$ is substituted or unsubstituted $C_{2-6}$ alkyl. In an example, E is a ring comprising at least two nitrogen atoms and at least one of $R^2$, $R^{3a}$, $R^{4a}$ or $R^{4b}$ is not hydrogen.

In an example, E is a ring comprising at least three nitrogen atoms. In an example, E is a ring comprising four nitrogen atoms.

In an example, $R^1$ is substituted or unsubstituted $C_{2-6}$ alkyl.

In an example, at least one of $R^2$, $R^{3a}$, $R^{4a}$ or $R^{4b}$ is not hydrogen.

In an example, E is a ring comprising 2, 3 or 4 nitrogen atoms.

In an example, E is a ring selected from pyrazole, triazole, tetrazole, indazole, benzotriazole, triazolopyridine, triazolopyrazine, pyrazolopyrazine.

In an example, A is a 6-membered heterocyclyl ring (e.g., a 6-membered heterocyclyl ring comprising at least two heteroatoms).

In an example, A is a 5-6-membered heterocyclyl ring, and n is 1 or 2.

In an example, E is morpholine and n is 1 or 2.

In an example, $R^1$ is hydrogen or unsubstituted $C_{1-6}$ alkyl. In an example, $R^1$ is or methyl. In an example, $R^1$ is substituted or unsubstituted $C_{2-6}$ alkyl.

In an example, $R^2$ is hydrogen, $–OR^{A2}$, wherein $R^{A2}$ is hydrogen, or substituted or unsubstituted $C_{1-6}$ alkyl (e.g., methyl, ethyl).

In an example, $R^{3a}$ is $–OR^{A3}$, wherein $R^{A3}$ is hydrogen, or substituted or unsubstituted $C_{1-6}$ alkyl (e.g., methyl).

In an example, $R^{3a}$ and $R^{3b}$ are joined to form an oxo (=O) group.

In an example, $R^{4a}$ is hydrogen, or substituted or unsubstituted $C_{1-6}$ alkyl (e.g., methyl).

In an example, $R^{4b}$ is hydrogen, or substituted or unsubstituted $C_{1-6}$ alkyl (e.g., methyl).

In an example, $R^{4a}$ is hydrogen, and $R^{4b}$ is substituted or unsubstituted $C_{1-6}$ alkyl (e.g., methyl).

In an example, $R^5$ is hydrogen.

In an example, n is 0.

In an example, n is 1 and $R^6$ is substituted or unsubstituted $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, halogen (e.g., -F, -Br, -Cl), cyano, $–OR^{A6}$, $-C(=O)OR^{A6}$, $-SR^{B6}$, $-S(=O)R^{B6}$, or $S(=O)_2R^{B6}$, wherein $R^{A6}$ is hydrogen or substituted or unsubstituted $C_{1-6}$ alkyl (e.g., methyl, ethyl), $C_{1-6}$ haloalkyl (e.g., $-CF_3$), and $R^{B6}$ is substituted or unsubstituted $C_{1-6}$ alkyl.

In an example, n is 1 and $R^6$ is halogen (e.g., -F, -Br, -Cl) or cyano. In an example, n is 1 and $R^6$ is substituted or unsubstituted $C_{1-6}$ alkyl (e.g., methyl). In an example, n is 1 and $R^6$ is $C_{1-6}$ haloalkyl, $–OR^{A6}$, or $–C(=O)OR^{A6}$, wherein $R^{A6}$ is hydrogen or substituted or unsubstituted $C_{1-6}$ alkyl (e.g., methyl, ethyl), $C_{1-6}$ haloalkyl (e.g., $-CF_3$). In an example, n is 1 and $R^6$ is $SR^{B6}$, $-S(=O)R^{B6}$, or $S(=O)_2R^{B6}$, wherein $R^{B6}$ is substituted or unsubstituted $C_{1-6}$ alkyl (e.g., methyl).

In an example, n is 2 and $R^6$ is independently selected from substituted or unsubstituted $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, halogen (e.g., -F, -Br, -Cl), cyano,$–OR^{A6}$, $-C(=O)OR^{A6}$, -

$SR^{B6}$, $-S(=O)R^{B6}$, or $S(=O)_2R^{B6}$, wherein $R^{A6}$ is hydrogen or substituted or unsubstituted $C_{1-6}$ alkyl (e.g., methyl, ethyl), $C_{1-6}$ haloalkyl (e.g., $-CF_3$), and $R^{B6}$ is substituted or unsubstituted $C_{1-6}$ alkyl.

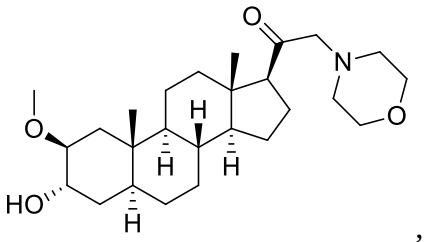
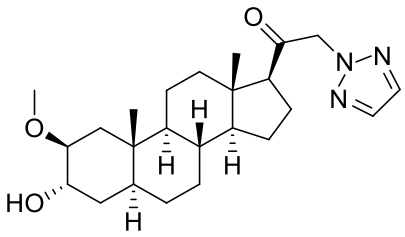
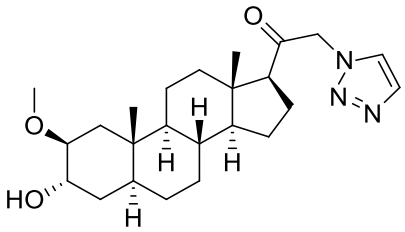
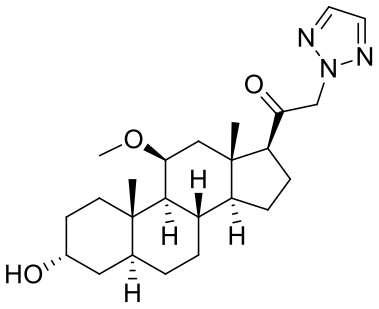
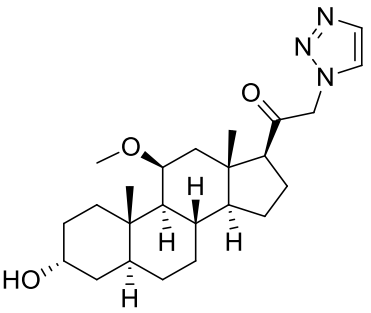
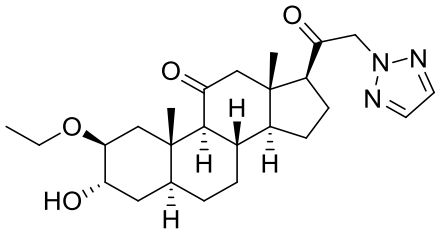
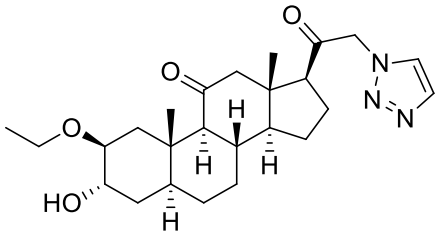
In an example, n is 2 and $R^6$ is independently selected from halogen (e.g., -F, -Br, -Cl). In an example, n is 2 and one of $R^6$ is fluorine.

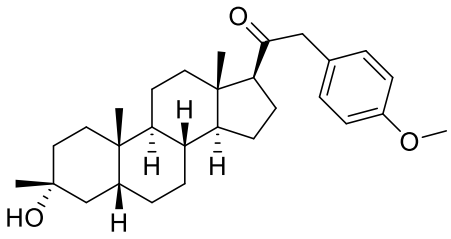
In an example, n is 0 and $R^1$ is substituted or unsubstituted $C_{2-6}$ alkyl.

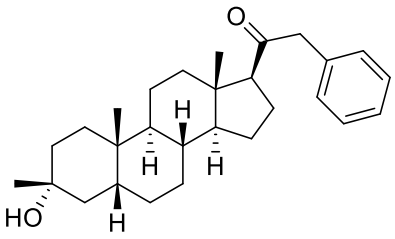
In an example, $R^1$ is substituted or unsubstituted $C_{1-6}$ alkyl and at least one of $R^2$, $R^{3a}$, $R^{4a}$ or $R^{4b}$ is not hydrogen.

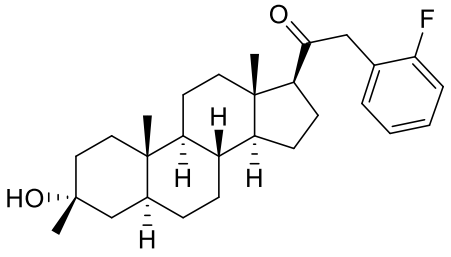
In an example, the compound is of the Formula (**II-a1**) and E is a heteroaryl ring comprising at least 3 nitrogen atoms.

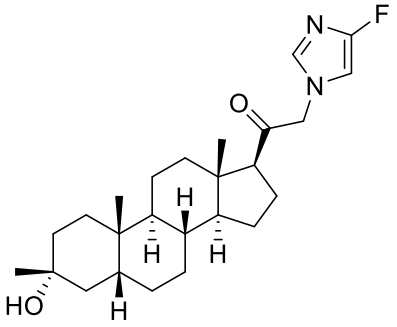
In an example, the compound is:


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or


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In one example, provided is a pharmaceutical composition comprising a compound of the Formula (**I**) and a pharmaceutically acceptable excipient.

In one example, provided is a method of inducing sedation and/or anesthesia in a subject, comprising administering to the subject an effective amount of a compound of the Formula (**I**), or a pharmaceutically acceptable salt thereof.

In one example, provided is a method of administering an effective amount of a compound, a pharmaceutically acceptable salt thereof, or pharmaceutical composition of a compound of Formula (**I**), to a subject in need thereof, wherein the subject experiences sedation and/or anesthesia within two hours of administration.

In an example, the subject experiences sedation and/or anesthesia within one hour of administration.

In an example, the subject experiences sedation and/or anesthesia instantaneously.

In an example, the compound is administered by intravenous administration.

In an example, the compound is administered chronically.

In an example, the subject is a mammal. In an example, the subject is a human.

In an example, the compound is administered in combination with another therapeutic agent.

In one example, provided is a method for treating seizure in a subject, comprising administering to the subject an effective amount of a compound of the Formula (**I**) or a pharmaceutically acceptable salt thereof.

In one example, provided is a method for treating epilepsy or status or status epilepticus in a subject, the method comprising administering to the subject an effective amount of a compound of the Formula (**I**) or a pharmaceutically acceptable salt thereof. In an example, the status epilepticus is convulsive status epilepticus (*e.g.*, early status epilepticus, established status epilepticus, refractory status epilepticus, super-refractory status epilepticus) or non-convulsive status epilepticus, (*e.g.*, generalized status epilepticus, complex partial status epilepticus).

In one example, provided is a method for treating disorders related to GABA function in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a compound, a pharmaceutically acceptable salt thereof, or pharmaceutical composition of one of a compound of the Formula (**I**).

In one example, provided is a method for treating a CNS-related disorder in a subject in need thereof, comprising administering to the subject an effective amount of a compound of the Formula (**I**) or a pharmaceutically acceptable salt thereof.

In an example, the CNS-related disorder is a 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 an example, the subject is a subject with Rett syndrome, Fragile X syndrome, or Angelman syndrome. In an example, the CNS–related disorder is a sleep disorder, an eating 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 an example, the CNS-related disorder is depression (e.g., post-partum depression). In an example, the CNS-related disorder is

tremor (e.g., essential tremor). In an example, the CNS-related disorder is an eating disorder (e.g., anorexia nervosa, bulimia nervosa, binge-eating disorder, cachexia).

In an example, the compound is administered orally. In an example, the compound is administered intramuscularly.

In one example, provided is a kit comprising a solid composition comprising a compound of Formula (**I**) and a sterile diluent.

**[15]** The present disclosure also provides pharmaceutical compositions comprising a compound of the present disclosure and methods of use and treatment, *e.g.*, such as for inducing sedation and/or anesthesia, for treating a CNS-related disorder.

**[16]** Steroids of Formula (**I**), sub-genera thereof, and pharmaceutically acceptable salts thereof are collectively referred to herein as "compounds of the present disclosure."

**[17]** In another example, provided is a pharmaceutical composition comprising a compound of the present disclosure and a pharmaceutically acceptable excipient. In certain examples, the compound of the present disclosure is provided in an effective amount in the pharmaceutical composition. In certain examples, the compound of the present disclosure is provided in a therapeutically effective amount. In certain examples, the compound of the present disclosure is provided in a prophylactically effective amount.

**[18]** Compounds of the present disclosure as described herein, act, in certain examples, as GABA modulators, *e.g.*, effecting the $GABA_A$ receptor in either a positive or negative manner. As modulators of the excitability of the central nervous system (CNS), as mediated by their ability to modulate $GABA_A$ receptor, such compounds are expected to have CNS-activity.

**[19]** Thus, in another example, provided are methods of treating a CNS–related disorder in a subject in need thereof, comprising administering to the subject an effective amount of a compound of the present disclosure. In certain examples, the CNS–related disorder is selected from the group consisting of a sleep disorder, a mood disordersuch 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, and tinnitus. In certain examples, the compound is administered orally, subcutaneously, intravenously, or

intramuscularly. In certain examples, the compound is administered chronically. In certain examples, the compound is administered continuously, *e.g.*, by continuous intravenous infusion.

**[20]** Other objects and advantages will become apparent to those skilled in the art from a consideration of the ensuing **Detailed Description**, **Examples**, and **Claims**.

## Definitions

*Chemical definitions*

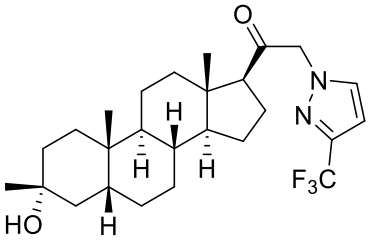
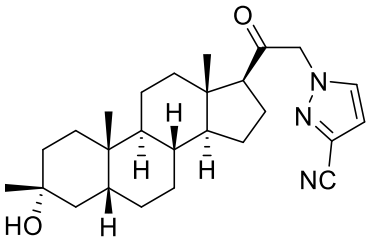
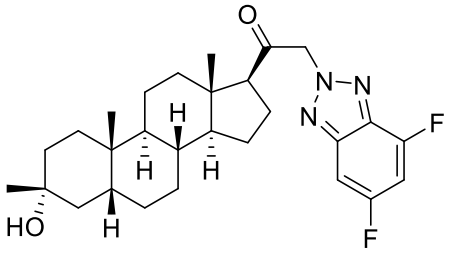
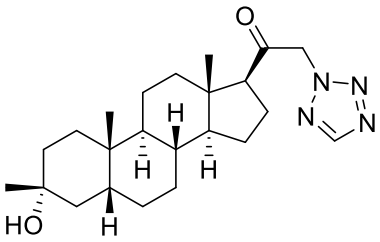
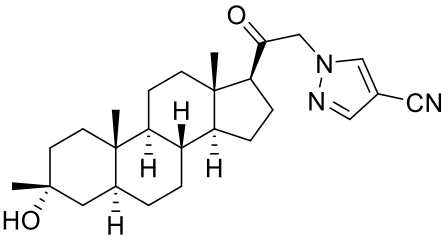
**[21]** Definitions of specific functional groups and chemical terms are described in more detail below. The chemical elements are identified in accordance with the Periodic Table of the Elements, CAS version, *Handbook of Chemistry and Physics*, 75th Ed., inside cover, and specific functional groups are generally defined as described therein. Additionally, general principles of organic chemistry, as well as specific functional moieties and reactivity, are described in Thomas Sorrell, *Organic Chemistry*, University Science Books, Sausalito, 1999; Smith and March, *March's Advanced Organic Chemistry*, 5th Edition, John Wiley & Sons, Inc., New York, 2001; Larock, *Comprehensive Organic Transformations*, VCH Publishers, Inc., New York, 1989; and Carruthers, *Some Modern Methods of Organic Synthesis*, 3rd Edition, Cambridge University Press, Cambridge, 1987.

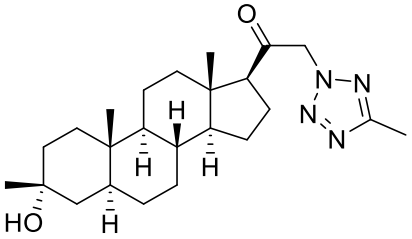
**[22]** Compounds described herein can comprise one or more asymmetric centers, and thus can exist in various isomeric forms, *e.g.*, enantiomers and/or diastereomers. For example, the compounds described herein can be in the form of an individual enantiomer, diastereomer or geometric isomer, or can be in the form of a mixture of stereoisomers, including racemic mixtures and mixtures enriched in one or more stereoisomer. Isomers can be isolated from mixtures by methods known to those skilled in the art, including chiral high pressure liquid chromatography (HPLC) ), supercritical fluid chromatography (SFC), and the formation and crystallization of chiral salts; or preferred isomers can be prepared by asymmetric syntheses. See, for example, Jacques *et al.*, *Enantiomers, Racemates and Resolutions* (Wiley Interscience, New York, 1981); Wilen *et al.*, *Tetrahedron* 33:2725 (1977); Eliel, *Stereochemistry of Carbon Compounds* (McGraw–Hill, NY, 1962); and Wilen, *Tables of Resolving Agents and Optical*

## Claims

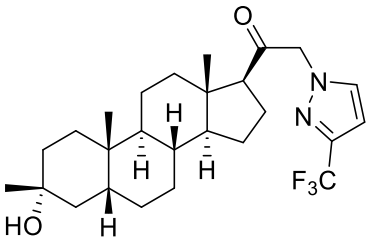
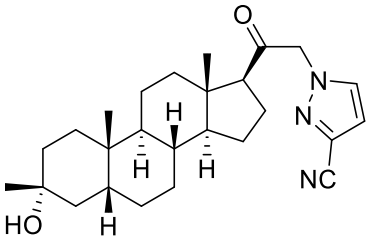
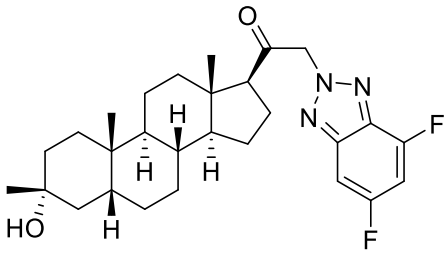
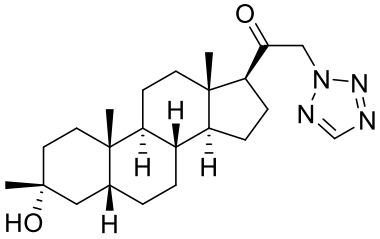
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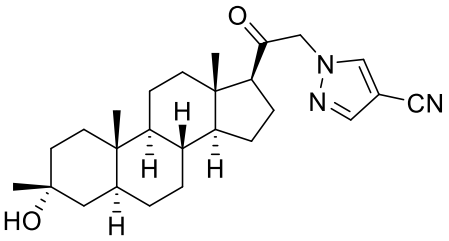
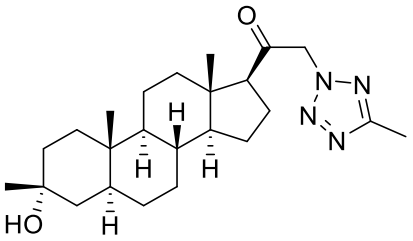
1. A compound selected from

| Compound No. | Structure |
|---|---|
| 19 |  |
| 24 |  |
| 28 |  |
| 54 |  |
| 79 |  |

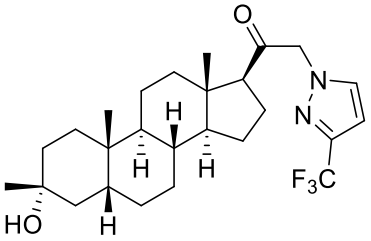
| Compound No. | Structure |
|---|---|
| 206 |  |

2. A pharmaceutically acceptable salt of a compound selected from

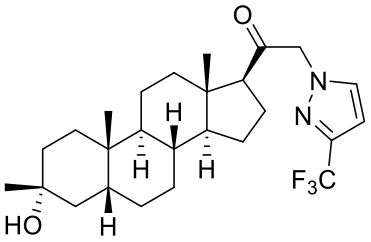
| Compound No. | Structure |
|---|---|
| 19 |  |
| 24 |  |
| 28 |  |
| 54 |  |

| Compound No. | Structure |
|---|---|
| 79 |  |
| 206 |  |

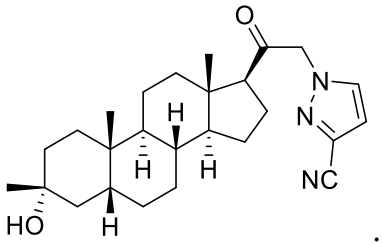
3. A compound of the formula



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

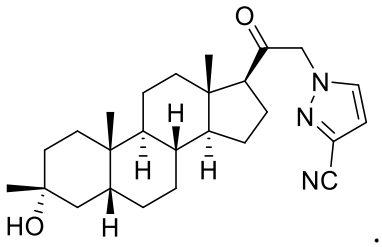


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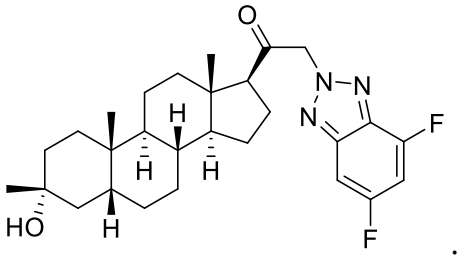
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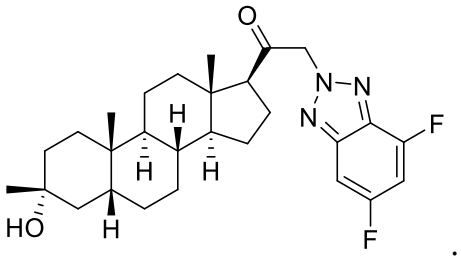
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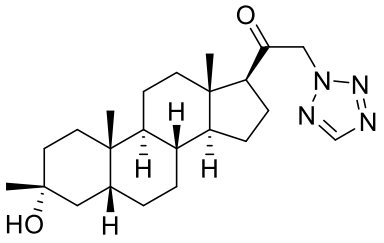
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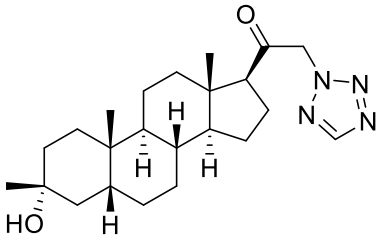
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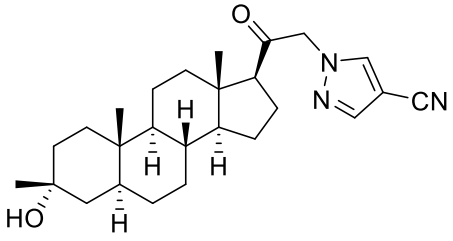
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10. A pharmaceutically acceptable salt of a compound of the formula



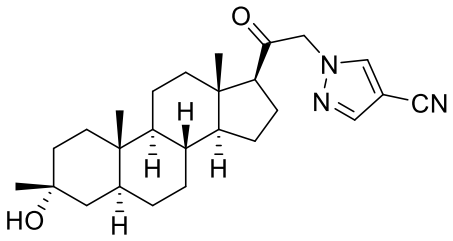
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11. A compound of the formula



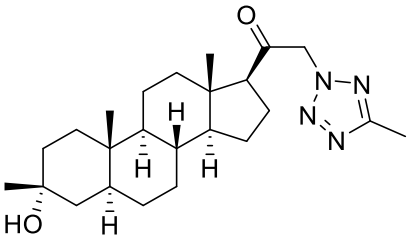
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12. A pharmaceutically acceptable salt of a compound of the formula



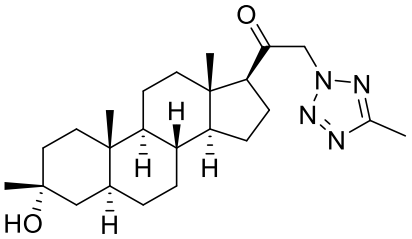
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13. A compound of the formula



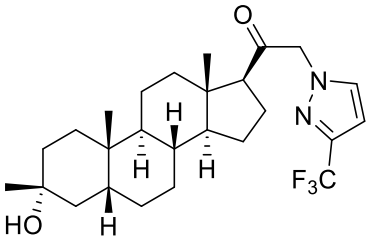
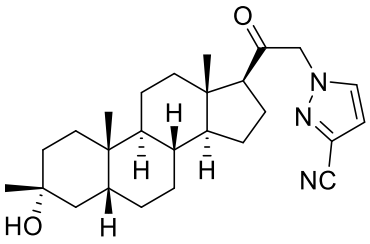
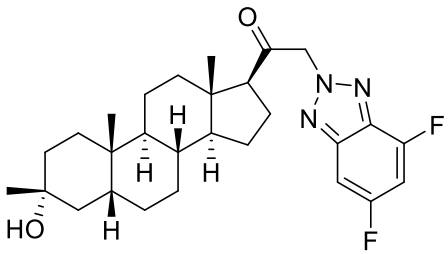
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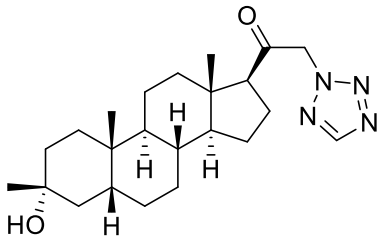
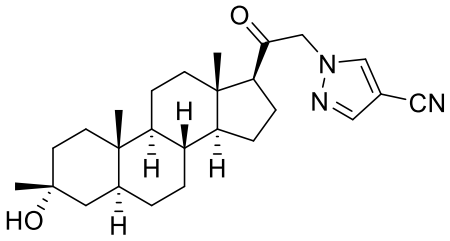
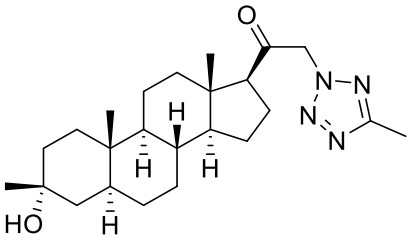
14. A pharmaceutically acceptable salt of a compound of the formula



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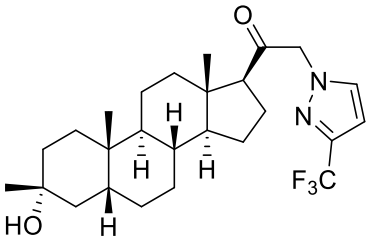
15. A pharmaceutical composition comprising a compound selected from

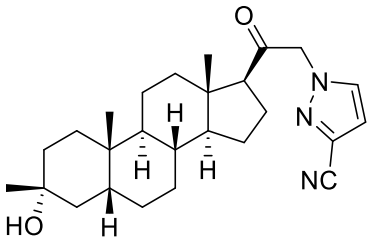
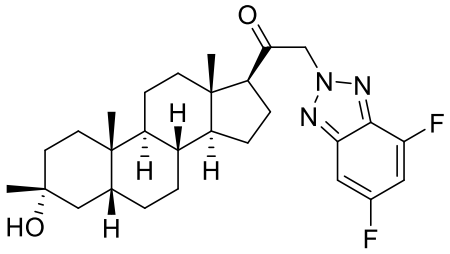
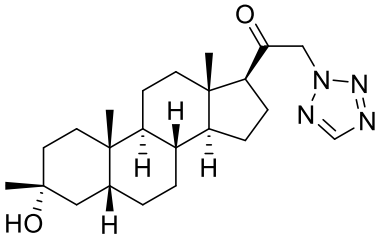
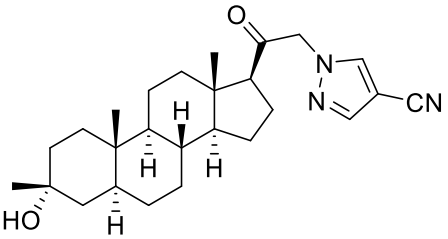
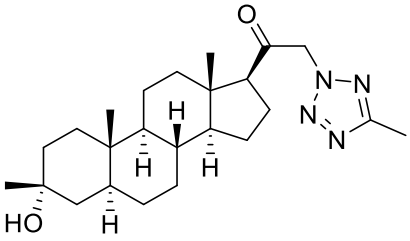
| **Compound No.** | **Structure** |
|---|---|
| 19 |  |
| 24 |  |
| 28 |  |

| Compound No. | Structure |
|---|---|
| 54 |  |
| 79 |  |
| 206 |  , |

and a pharmaceutically acceptable excipient.

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

| Compound No. | Structure |
|---|---|
| 19 |  |

| Compound No. | Structure |
|---|---|
| 24 |  |
| 28 |  |
| 54 |  |
| 79 |  |
| 206 |  , |

and a pharmaceutically acceptable excipient.

17. The compound of any one of claims 1, 3, 5, 7, 9, 11, or 13, the pharmaceutically acceptable salt of claim 2, 4, 6, 8, 10, 12, or 14, or the pharmaceutical composition of claim 15 or 16, for use in inducing sedation and/or anesthesia in a subject.

18. The compound of any one of claims 1, 3, 5, 7, 9, 11, or 13, the pharmaceutically acceptable salt of claim 2, 4, 6, 8, 10, 12, or 14, or the pharmaceutical composition of claim 15 or 16, for use in tremor in a subject.

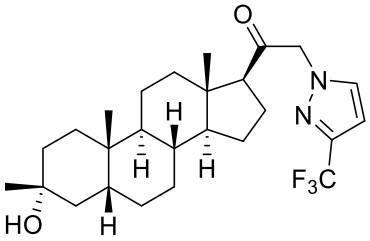
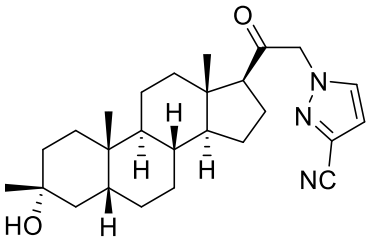
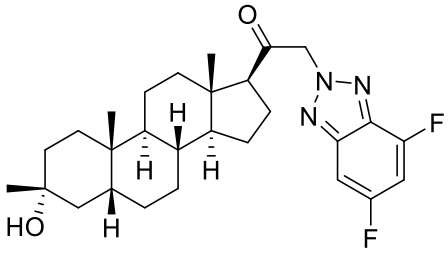
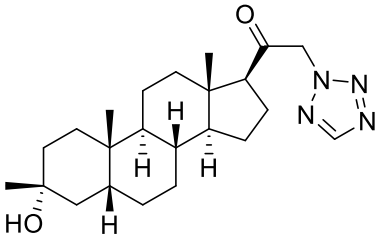
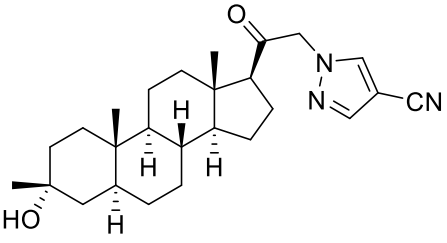
19. The compound of any one of claims 1, 3, 5, 7, 9, 11, or 13, the pharmaceutically acceptable salt of claim 2, 4, 6, 8, 10, 12, or 14, or the pharmaceutical composition of claim 15 or 16, for use of claim 18, wherein the tremor is essential tremor.

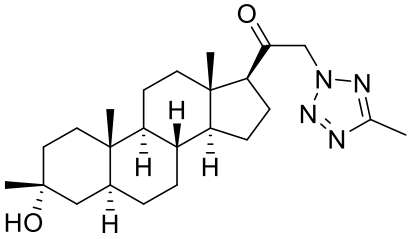
20. The compound of any one of claims 1, 3, 5, 7, 9, 11, or 13, the pharmaceutically acceptable salt of claim 2, 4, 6, 8, 10, 12, or 14, or the pharmaceutical composition of claim 15 or 16, for use of claim 18, wherein the tremor is parkinsonian tremor.

21. The compound of any one of claims 1, 3, 5, 7, 9, 11, or 13, the pharmaceutically acceptable salt of claim 2, 4, 6, 8, 10, 12, or 14, or the pharmaceutical composition of claim 15 or 16, for use in treating seizure in a subject.

22. The compound of any one of claims 1, 3, 5, 7, 9, 11, or 13, the pharmaceutically acceptable salt of claim 2, 4, 6, 8, 10, 12, or 14, or the pharmaceutical composition of claim 15 or 16, for use in treating epilepsy or status epilepticus in a subject.

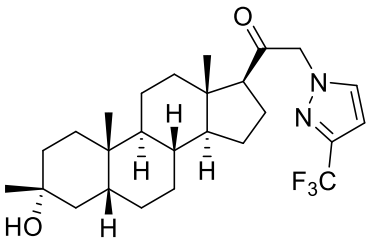
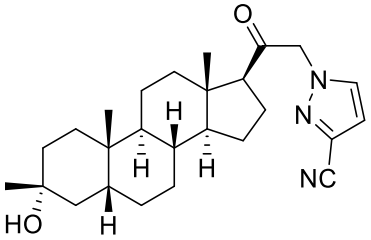
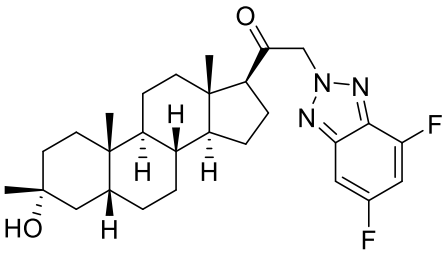
23. Use of a compound selected from

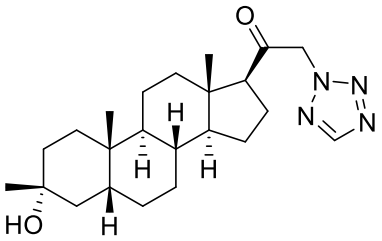
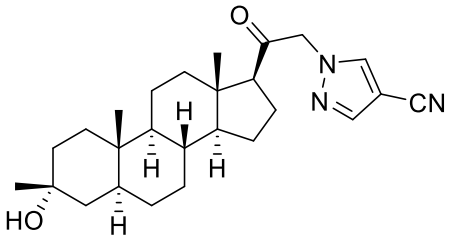
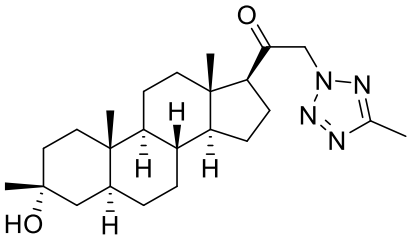
| Compound No. | Structure |
|---|---|
| 19 |  |
| 24 |  |
| 28 |  |
| 54 |  |
| 79 |  |

| Compound No. | Structure |
|---|---|
| 206 |  |

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

24. Use of a compound selected from

| Compound No. | Structure |
|---|---|
| 19 |  |
| 24 |  |
| 28 |  |

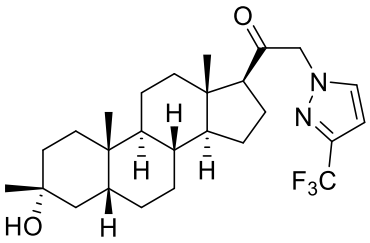
| Compound No. | Structure |
|---|---|
| 54 |  |
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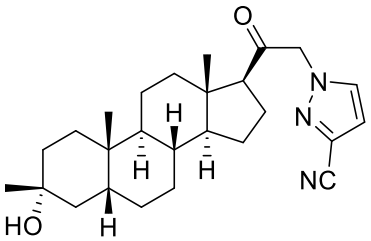
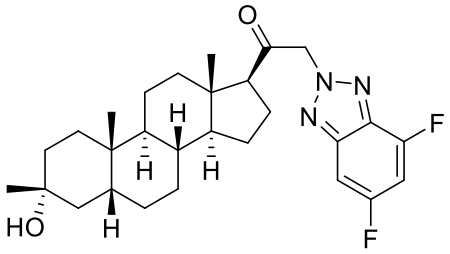
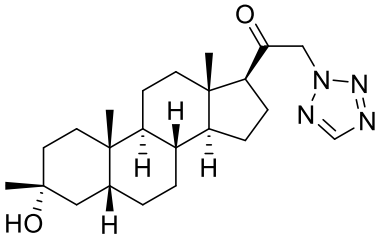
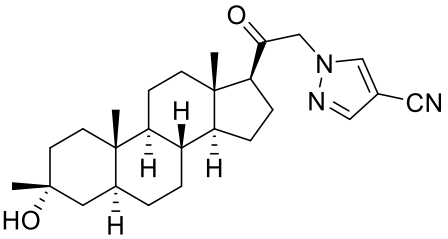
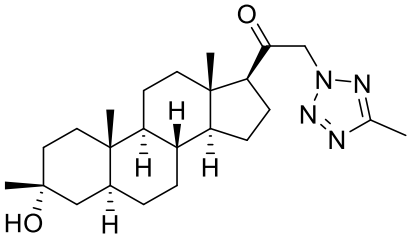
or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating tremor in a subject in need thereof.

25. The use of claim 24, wherein the tremor is essential tremor.

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

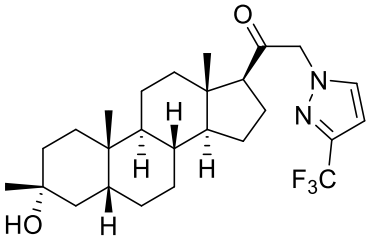
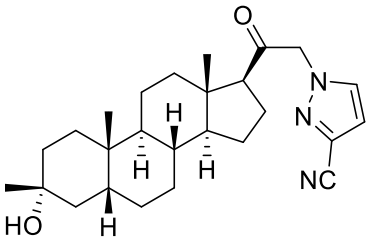
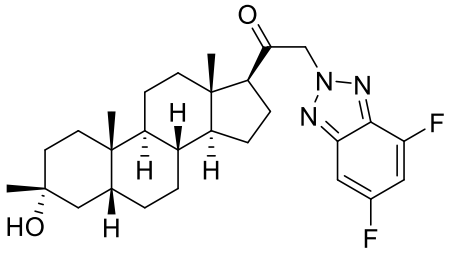
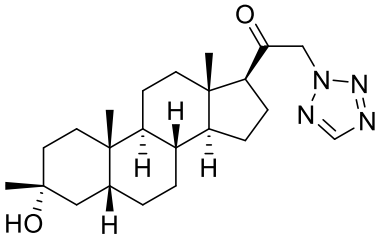
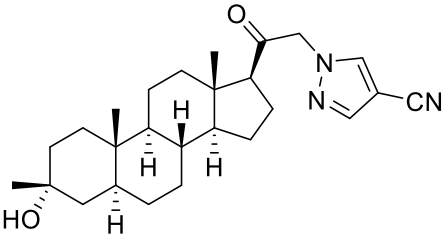
27. Use of a compound selected from

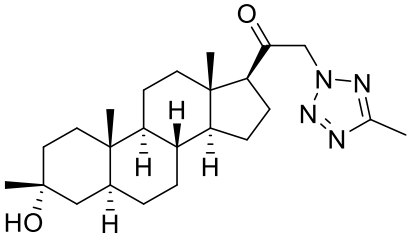
| Compound No. | Structure |
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| Compound No. | Structure |
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or pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating seizure in a subject in need thereof.

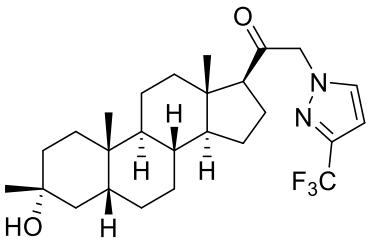
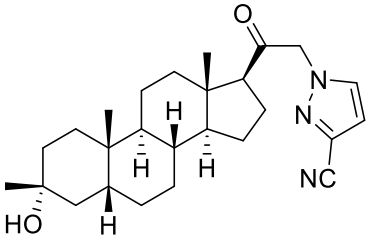
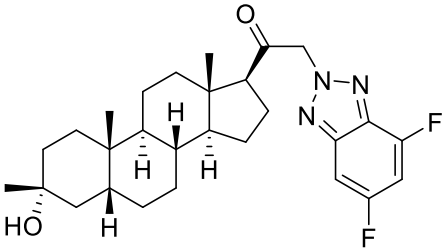
28. Use of a compound selected from

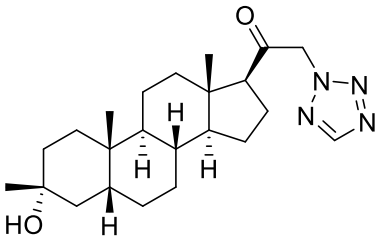
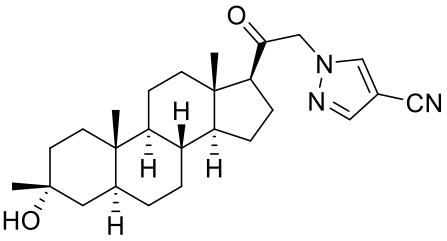
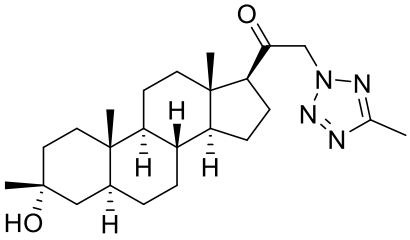
| Compound No. | Structure |
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or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating epilepsy or status epilepticus in a subject in need thereof.

29. Use of a compound selected from

| Compound No. | Structure |
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| Compound No. | Structure |
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in the manufacture of a medicament for treating a CNS-related disorder related to GABA function in a subject in need thereof.

30. The use of claim 29, wherein the CNS-related disorder is selected from the group consisting of sleep disorders, mood disorders, schizophrenia spectrum disorders, convulsive disorders, disorders of memory and/or cognition, movement disorders, personality disorders, autism spectrum disorders (ASD), pain, traumatic brain injury (TBI), vascular diseases, substance abuse disorders and/or withdrawal syndromes, and tinnitus.

31. The use of claim 29, wherein the CNS-related disorder is depression.

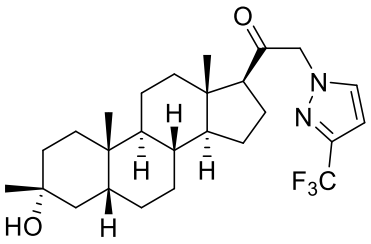
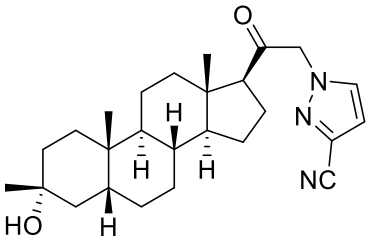
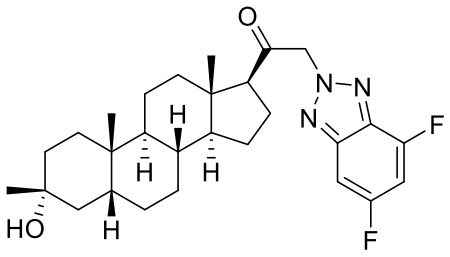
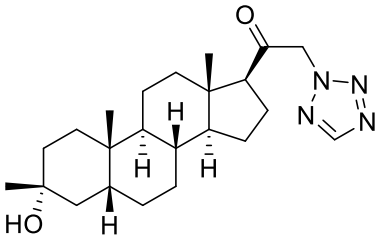
32. The use of claim 31, wherein the depression is postpartum depression.

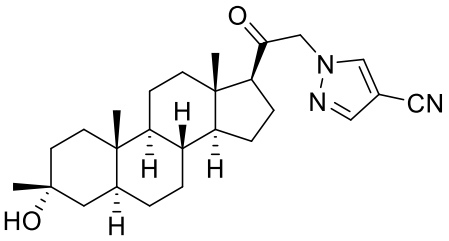
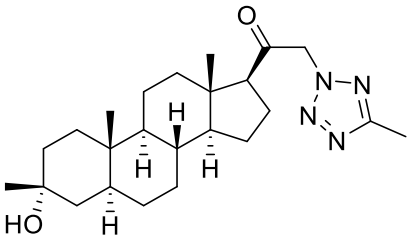
33. The use of claim 31, wherein the depression is a major depressive disorder.

34. The use of claim 33, wherein the major depressive disorder is a severe major depressive disorder.

35. The use of claim 33, wherein the major depressive disorder is a moderate major depressive disorder.

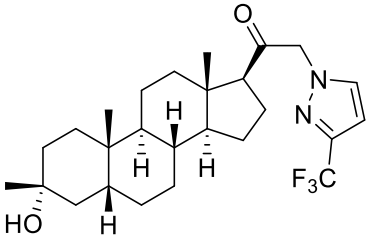
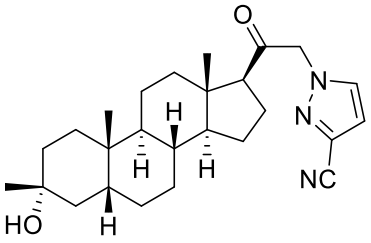
36. Use of a compound selected from

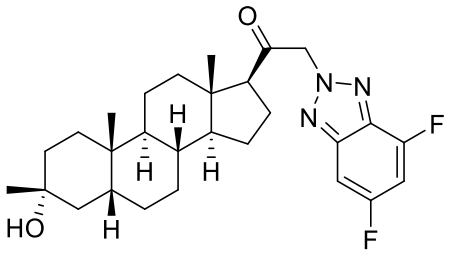
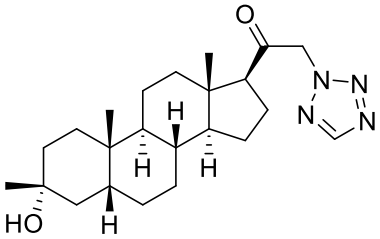
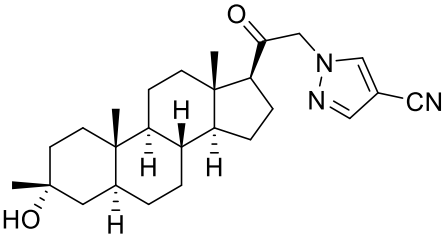
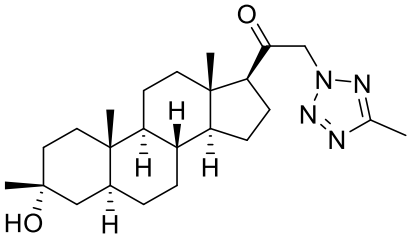
| Compound No. | Structure |
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or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating an eating disorder in a subject in need thereof, wherein the eating disorder is selected from anorexia nervosa, bulimia nervosa, binge-eating disorder, and cachexia.

37. Use of a compound selected from

| Compound No. | Structure |
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| Compound No. | Structure |
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or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating Angelman's syndrome in a subject in need thereof.

38. The use of any one of claims 23-38, wherein the medicament is to be administered orally or intramuscularly.

39. The use of claim 38, wherein the medicament is to be administered orally.

40. The use of claim 39, wherein the medicament is a tablet.

41. The use of claim 38, wherein the medicament is to be administered intramuscularly.

42. The use of any one of claims 23-41, wherein the medicament is to be administered chronically.

43. The use of any one of claims 23-42, wherein the subject is a human.