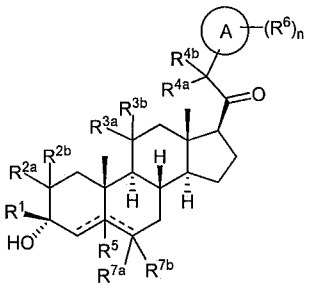
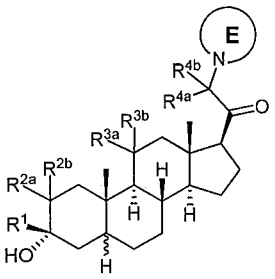
C_{2-6} alkenyl, substituted or unsubstituted C_{2-6} alkynyl, or substituted or unsubstituted C_{3-6} carbocylyl; R^{3a} is hydrogen or $-OR^{A3}$, wherein R^{A3} is hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl, substituted or unsubstituted C_{2-6} 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 one aspect, provided is a compound of the Formula (**I-a**) or Formula (**II-b**):



(I-a)



(II-b)

or a pharmaceutically acceptable salt thereof;

wherein:

Ring E is heterocyclyl or heteroaryl;

Ring A is nitrogen linked heterocyclyl, or heteroaryl;

R^6 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} carbocylyl, C_{1-6} haloalkyl, halogen, cyano, nitro, OR^{A6}, $C(=O)R^{A6}$, $C(=O)OR^{A6}$, SR^{B6}, $S(=O)R^{B6}$, $S(=O)_2R^{B6}$, $N(R^{C6})(R^{D6})$, $C(=O)N(R^{C6})(R^{D6})$, $N(R^{C6})C(=O)R^{A6}$; and

n is 0, 1, 2, or 3;

wherein R^{A6} is hydrogen or C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} carbocylyl, or C_{1-6} haloalkyl; R^{B6} is C_{1-6} alkyl or C_{3-6} carbocylyl; and each of R^{C6} and R^{D6} is independently hydrogen, C_{1-6} alkyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl, or R^{C6} and R^{D6} together with the nitrogen atom to which they are attached form a ring (e.g., a 3-6-membered ring (e.g., carbocycyl or heterocyclyl ring));

R^1 is methyl;

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.

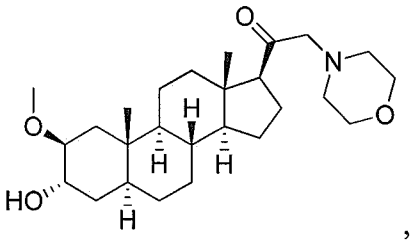
In an embodiment, n is 2 and R^6 is independently selected from halogen (e.g., -F, -Br, -Cl). In an embodiment, n is 2 and one of R^6 is fluorine.

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

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

In another aspect of the present disclosure, the compound is: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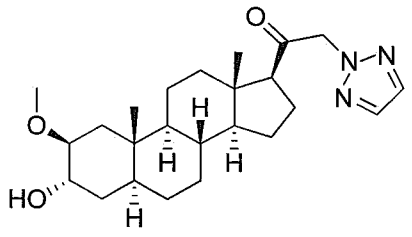
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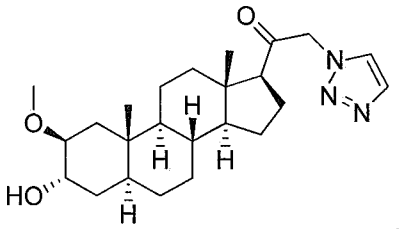
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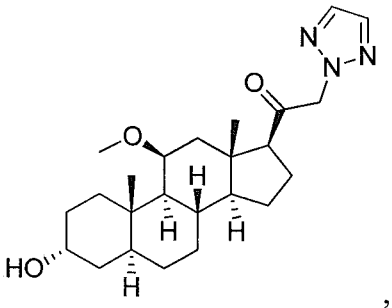
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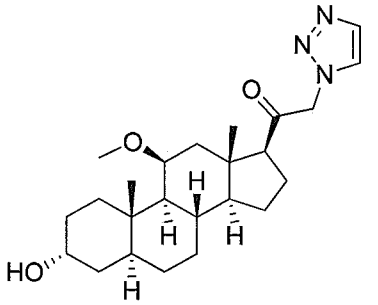
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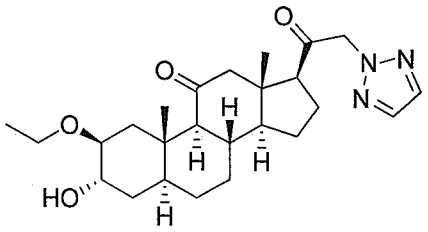
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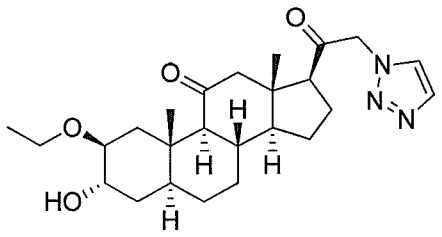
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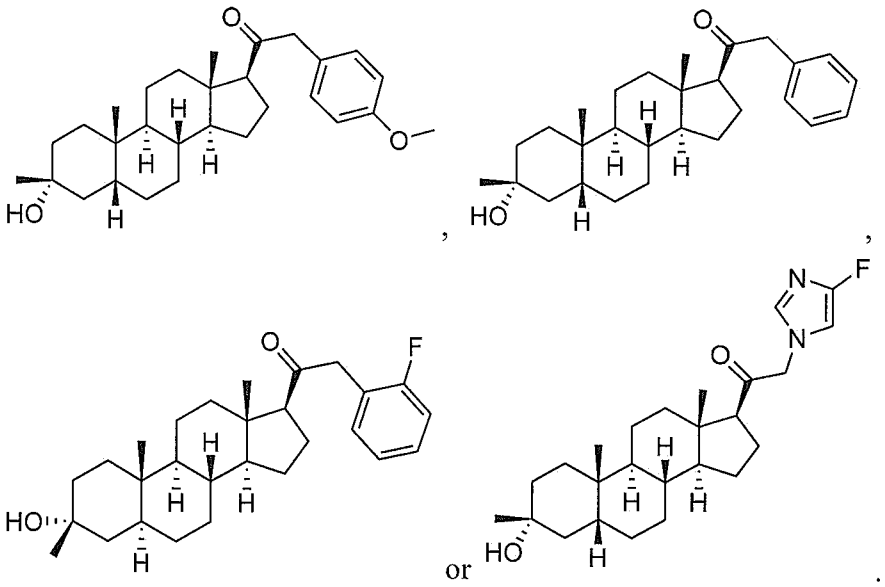


There is also provided a pharmaceutical composition comprising a compound of the Formula (**I**) and a pharmaceutically acceptable excipient.

In another aspect, there is provided a pharmaceutical composition comprising a compound disclosed herein and a pharmaceutically acceptable excipient.

The present disclosure also provides 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 aspect, provided is a use of a compounddisclosed herein in the manufacture of a medicament for inducing sedation and/or anesthesia in a subject.

The present disclosure also provides 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 one aspect, provided is a use of a compound, a pharmaceutically acceptable salt thereof, or pharmaceutical composition of a compound disclosed herein, in the manufacture of a medicament for a method of administration to a subject in need thereof, wherein the subject experiences sedation and/or anesthesia within two hours of administration.

The present disclosure also provides 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 aspect, provided is a use of a compound disclosed herein in the manufacture of a medicament for treating seizure in a subject.

The present disclosure also provides 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 one aspect, provided is a use of a compound disclosed herein in the manufacture of a medicament for treating epilepsy or status or status epilepticus in a subject.

In an embodiment, 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).

The present disclosure also provides 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 aspect, provided is a use of of a compound, a pharmaceutically acceptable salt thereof, or pharmaceutical composition of one of a compound disclosed herein, in the manufacture of a medicament for treating disorders related to GABA function in a subject in need thereof.

The present disclosure also provides 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 one aspect, provided is a use of a compound disclosed herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a CNS-related disorder in a subject in need thereof.

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

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

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

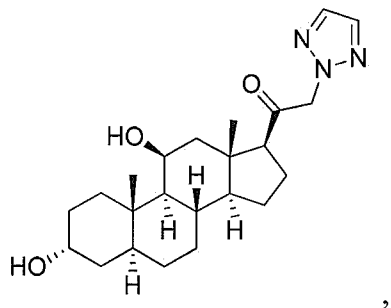
The present disclosure also provides a kit comprising a solid composition comprising a compound of Formula (**I**) and a sterile diluent.

[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 invention/disclosure."

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

[017a] In another aspect of the present disclosure, there is provided a compound, wherein the compound is:



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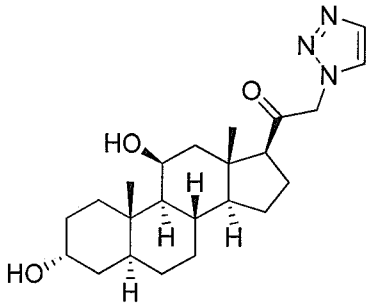

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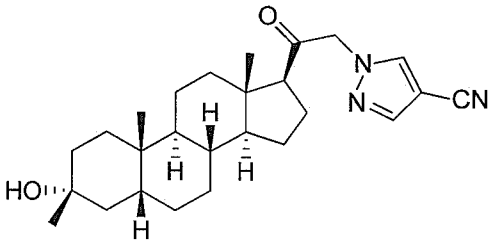

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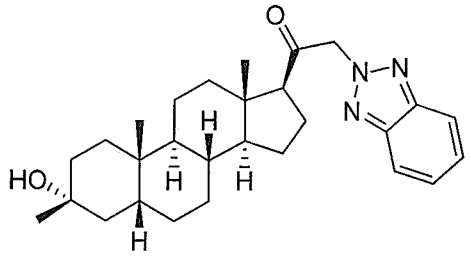
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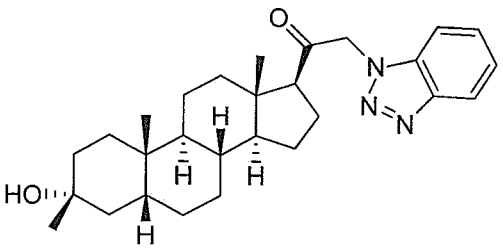
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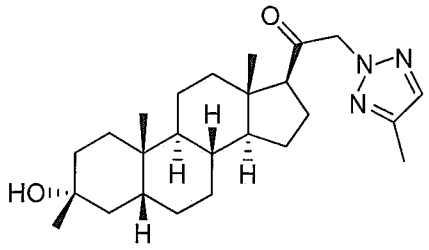
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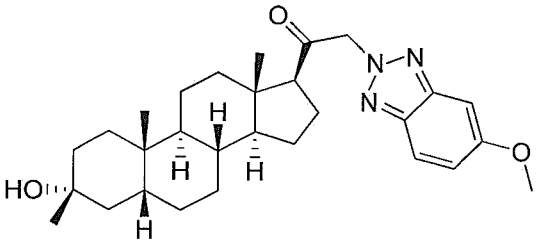
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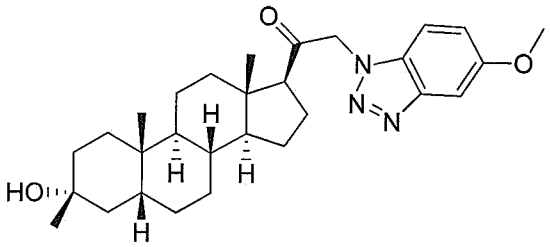
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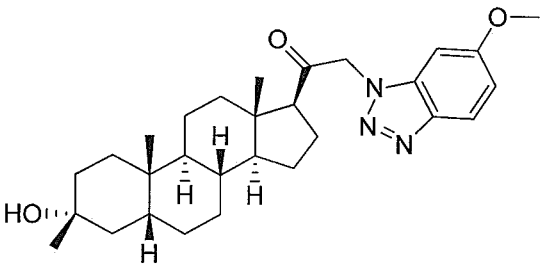
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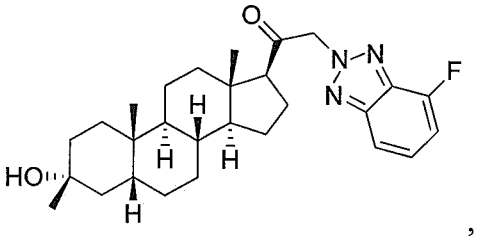
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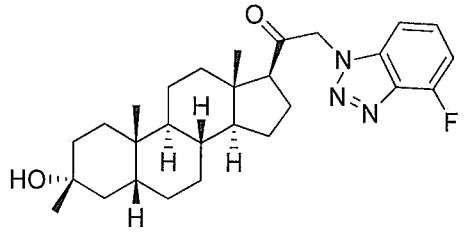
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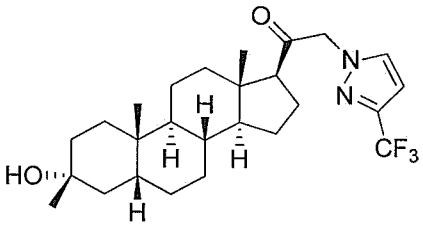
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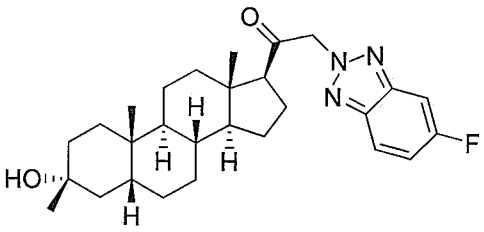
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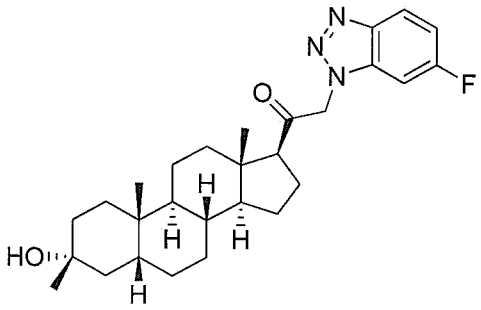
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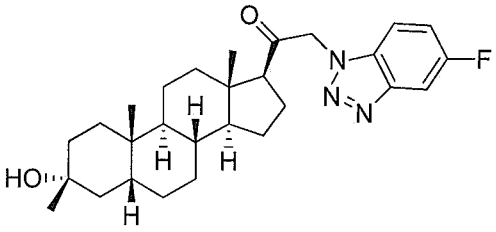
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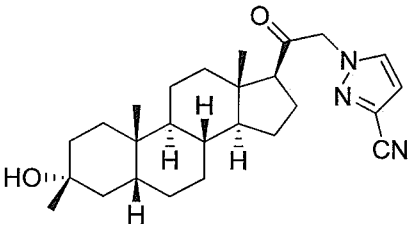
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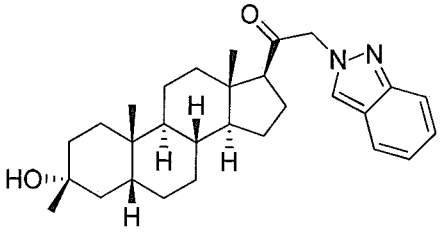
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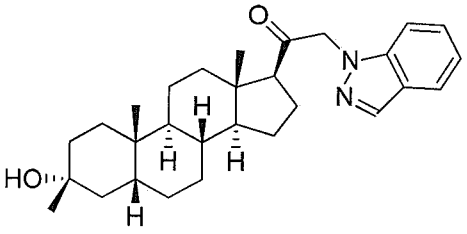
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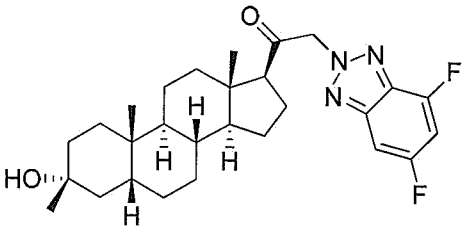
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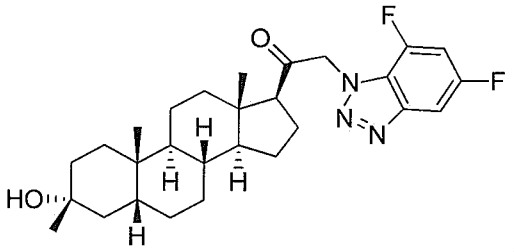
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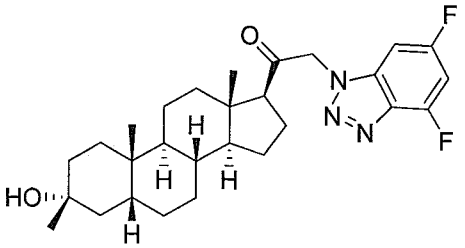
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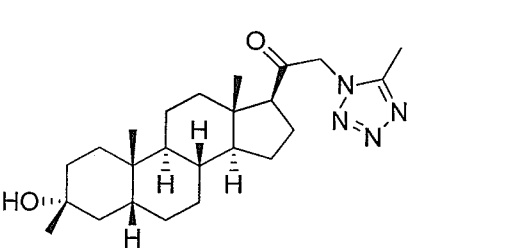
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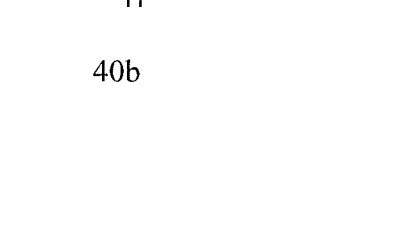
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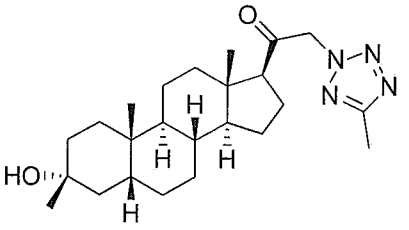
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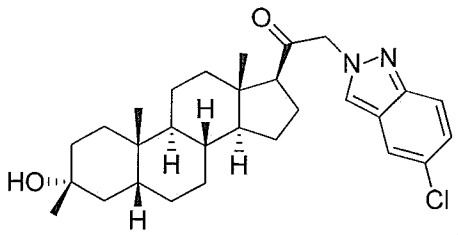
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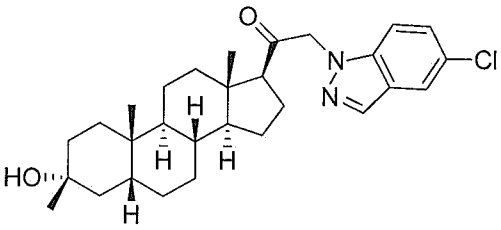
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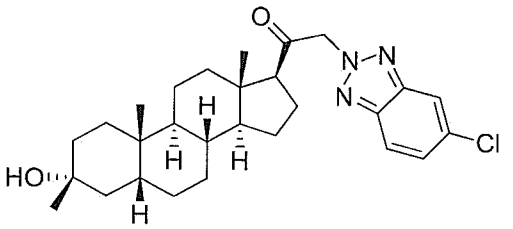
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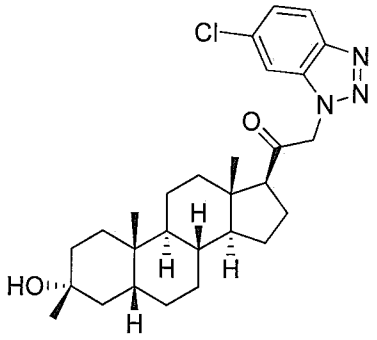
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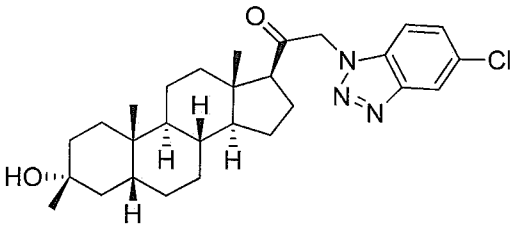
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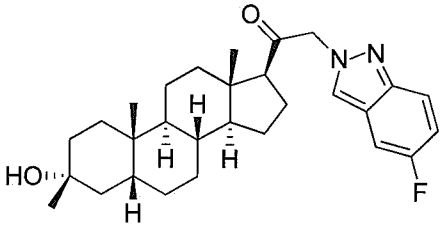
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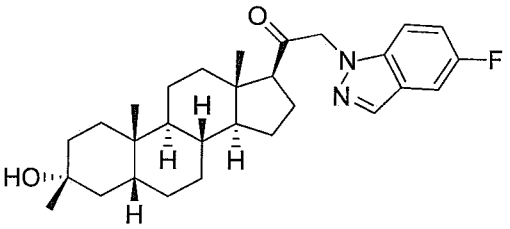
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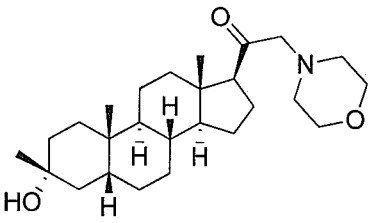
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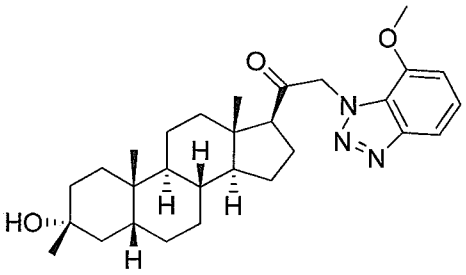
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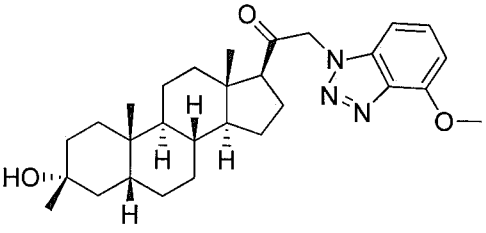
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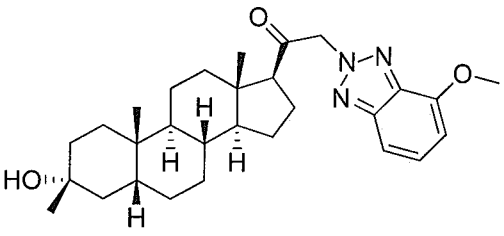
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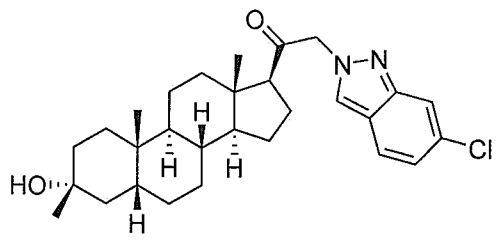
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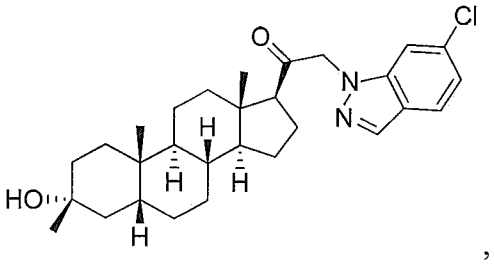
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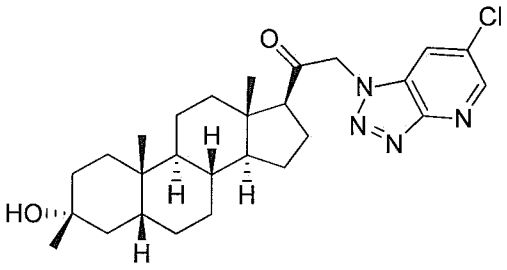
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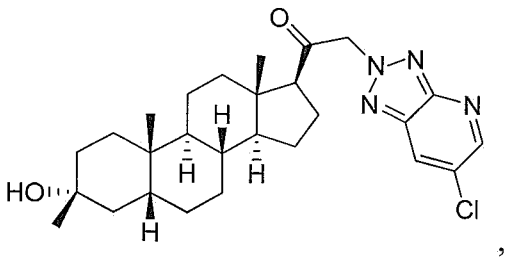
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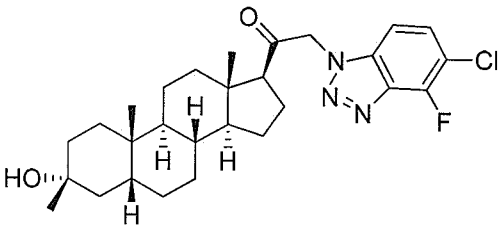
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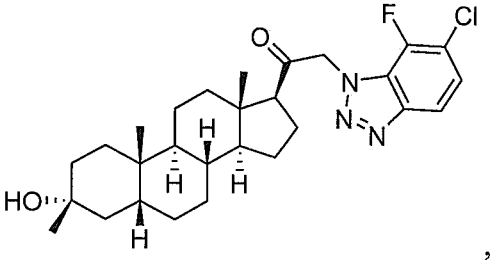
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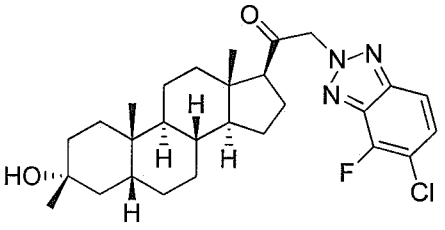
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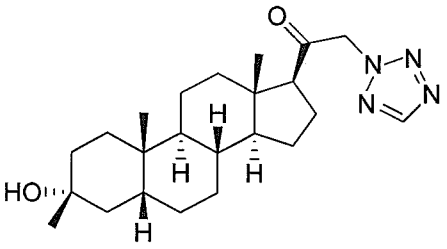
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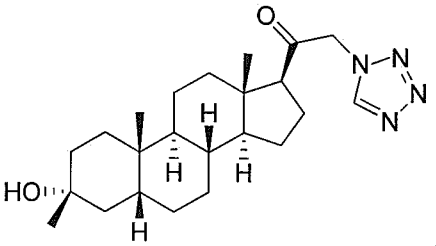
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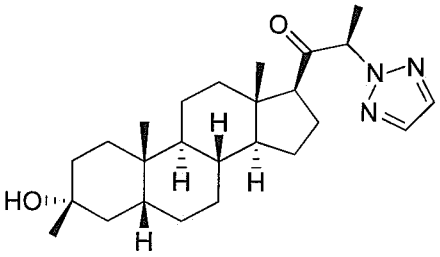
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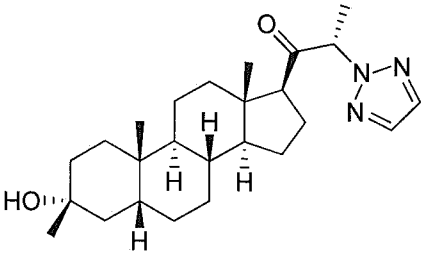
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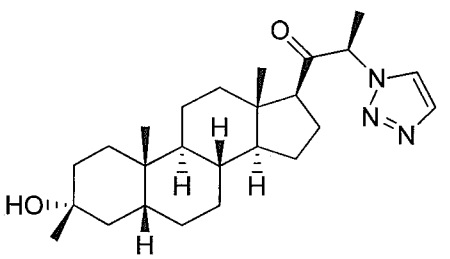
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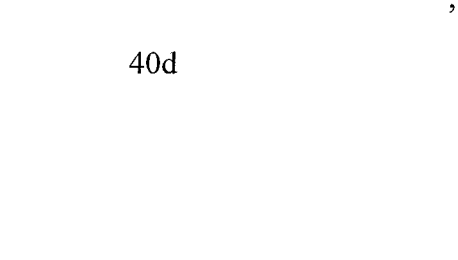
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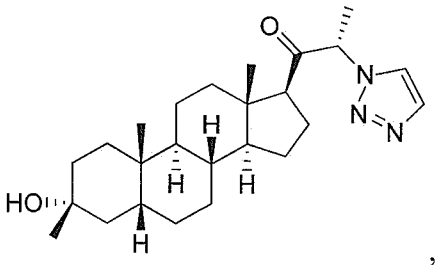
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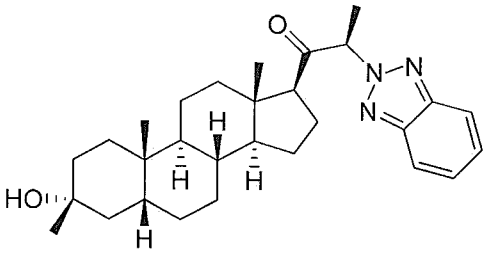
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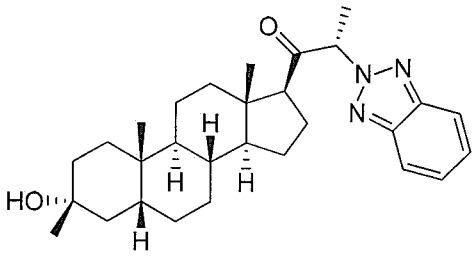
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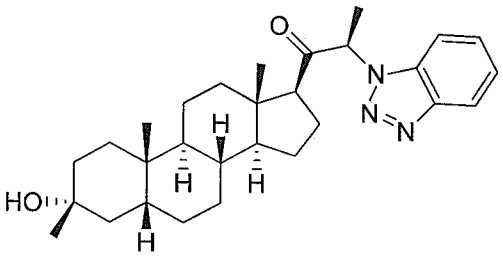
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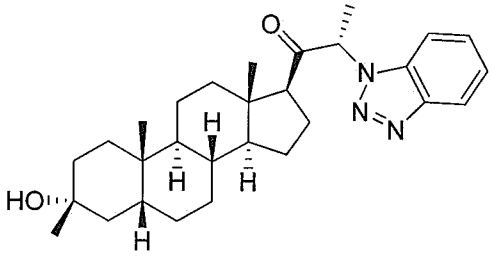
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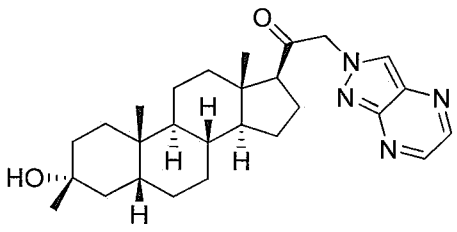
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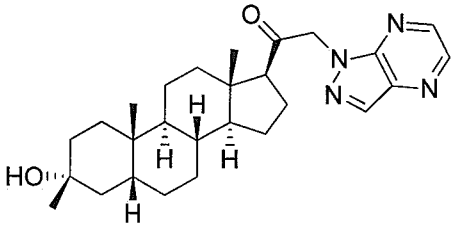
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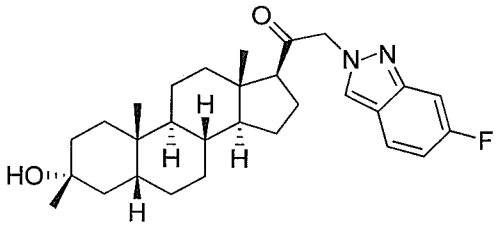
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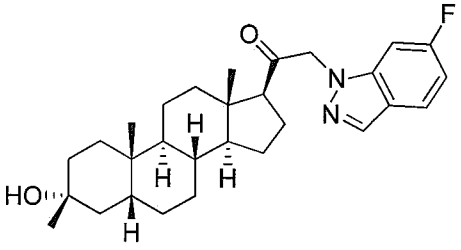
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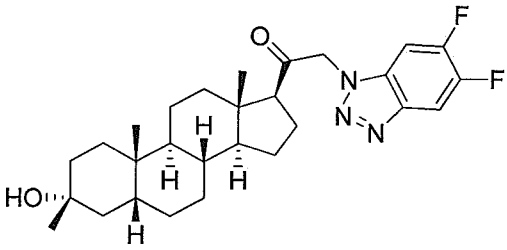
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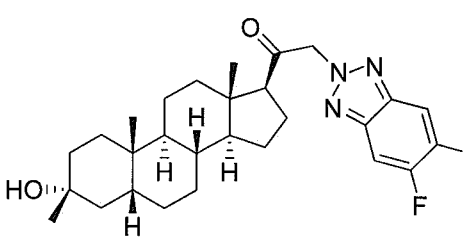
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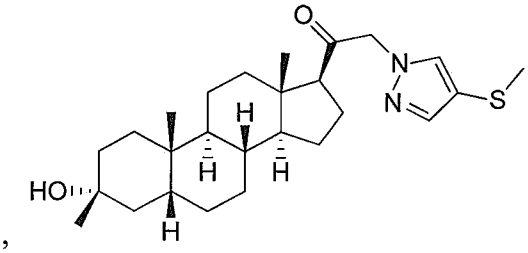
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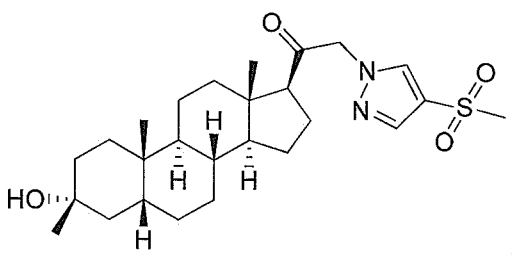
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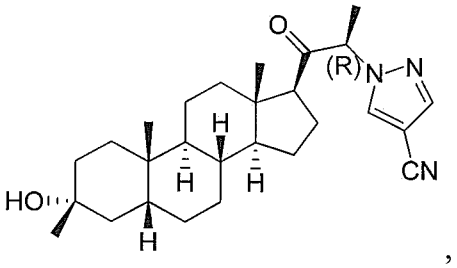
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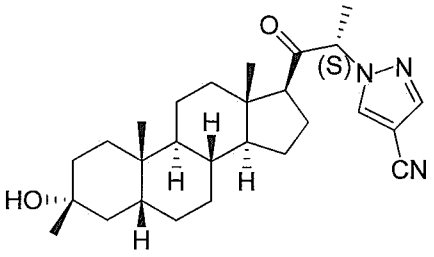
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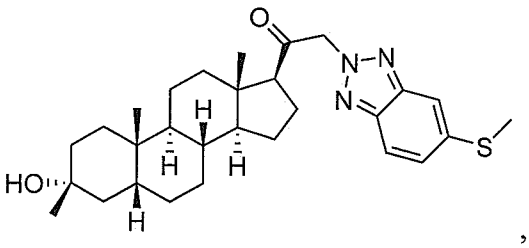
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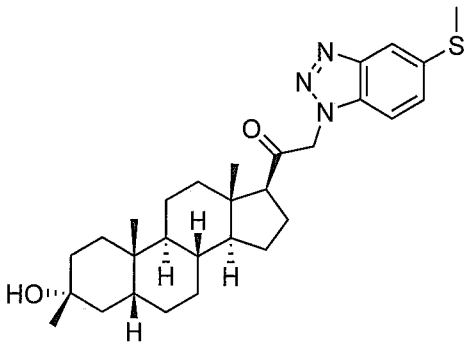
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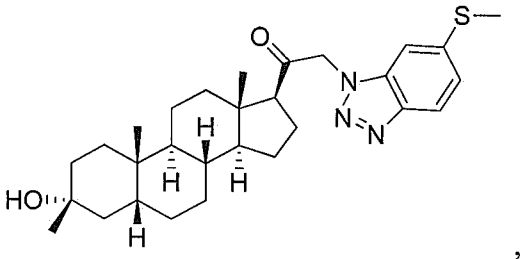
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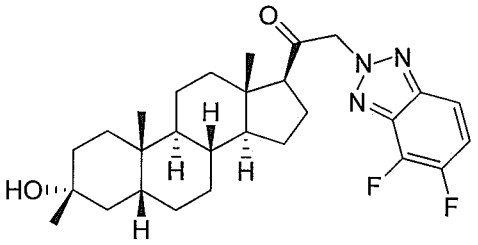
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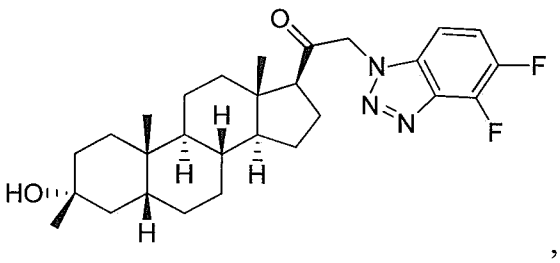
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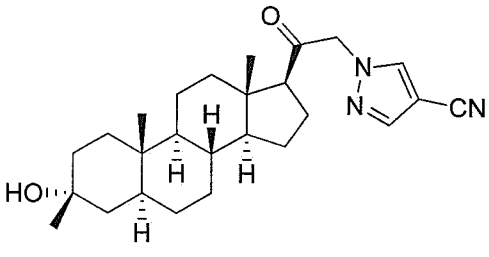
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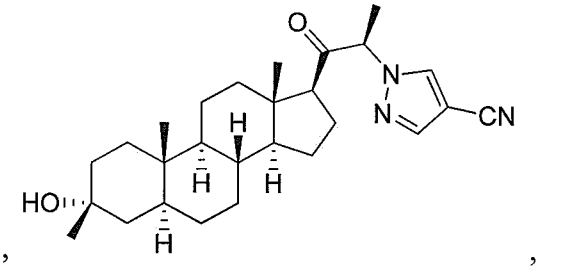
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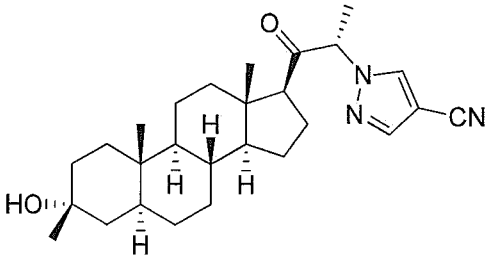
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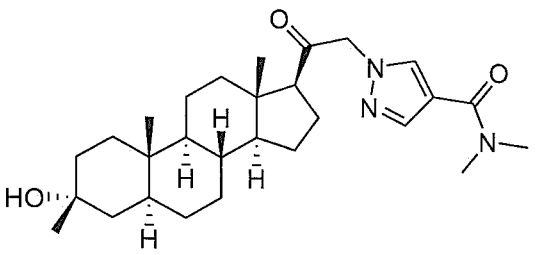
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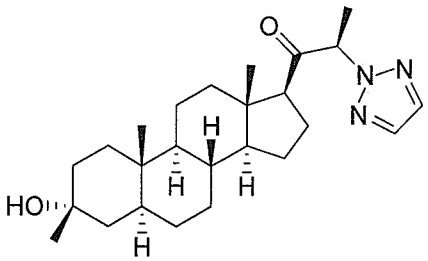
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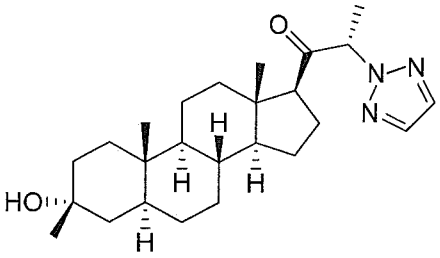
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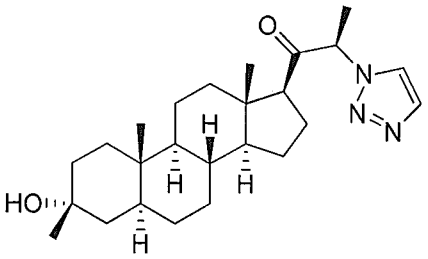
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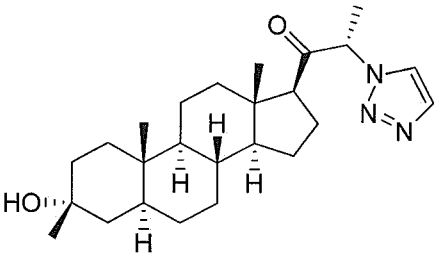
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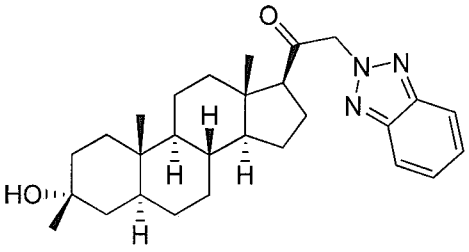
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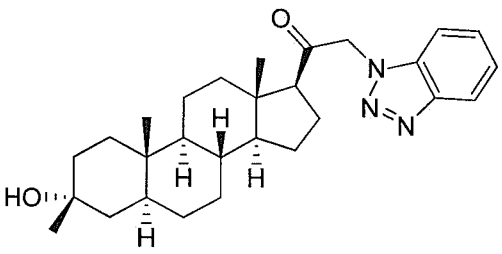
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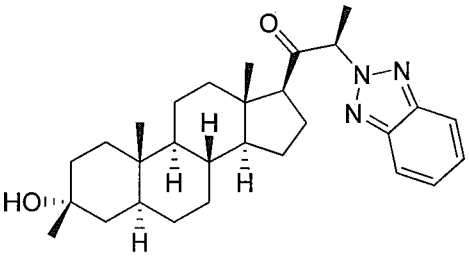
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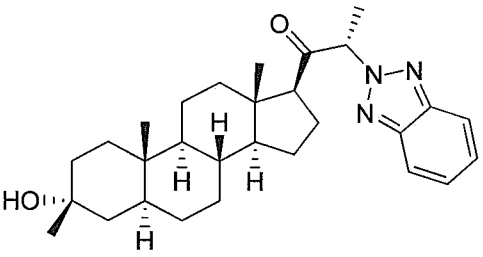
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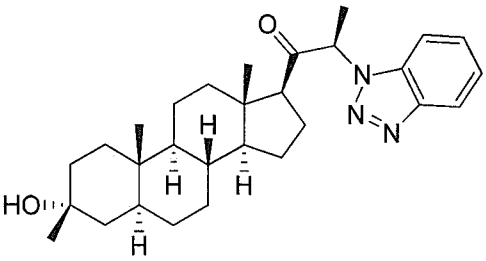
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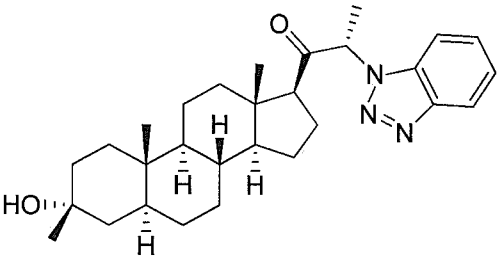
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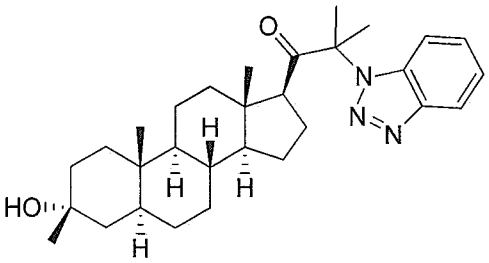
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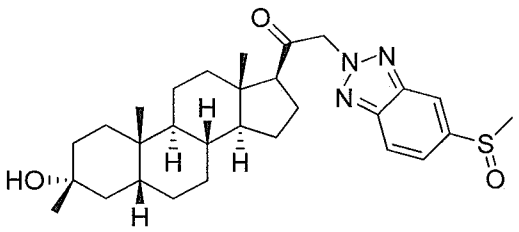
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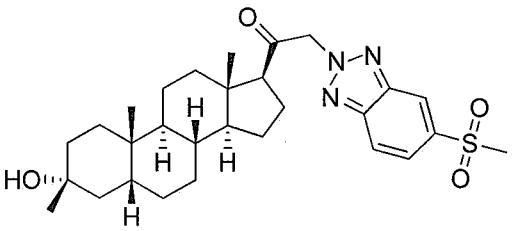
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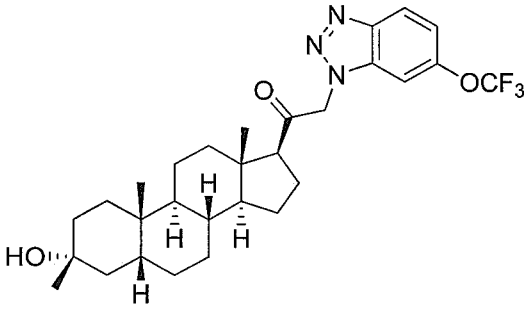
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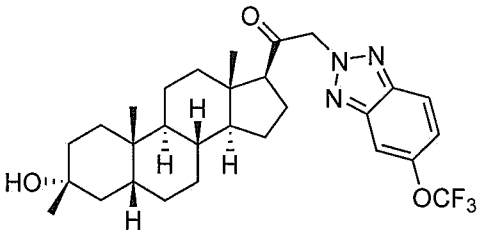
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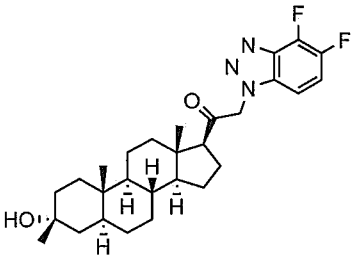
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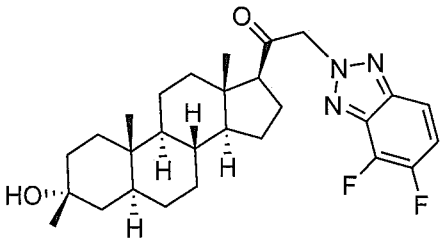
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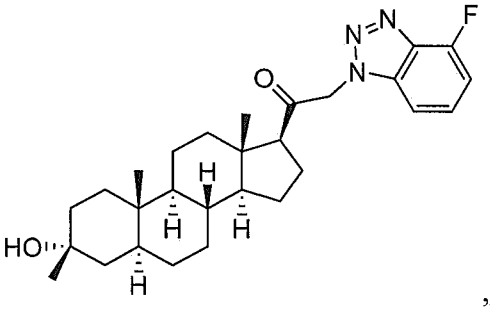
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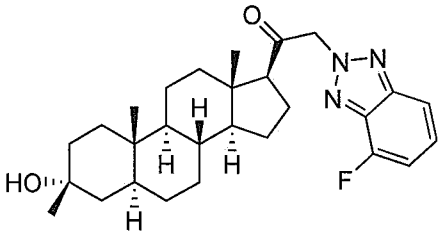
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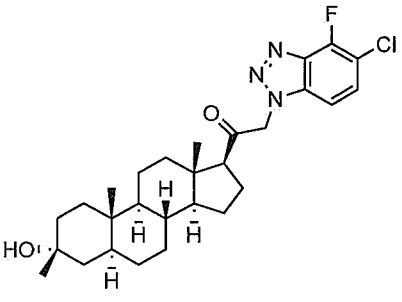
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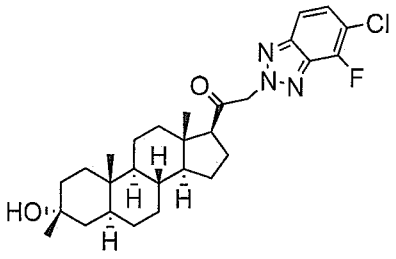
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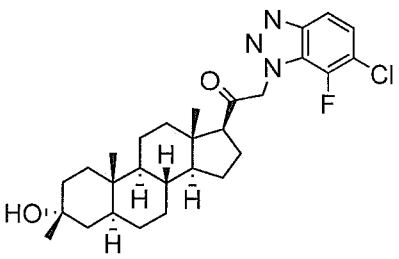
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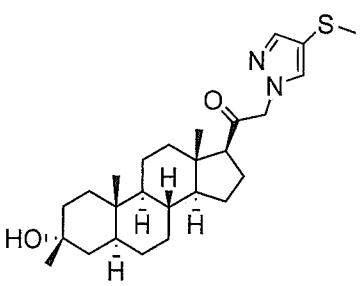
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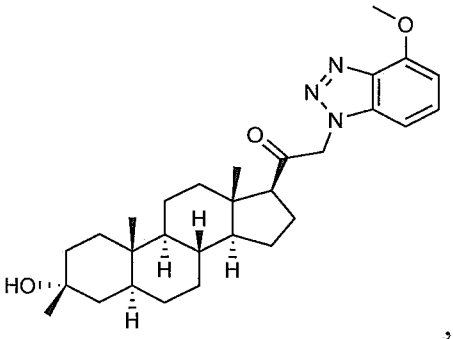
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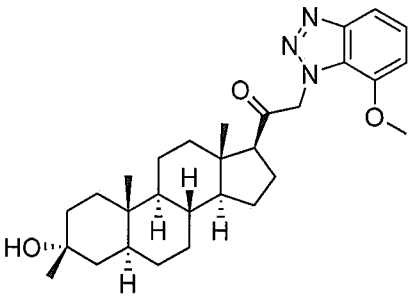
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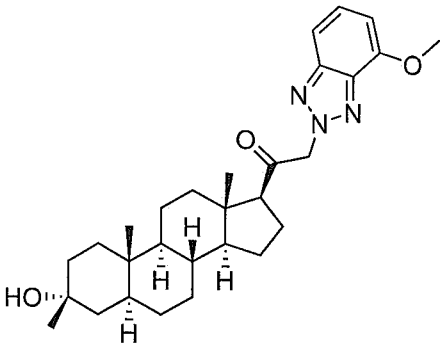
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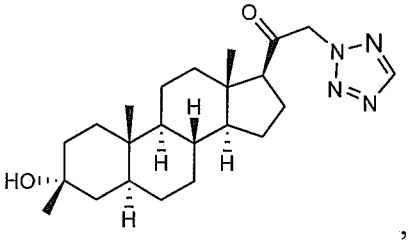
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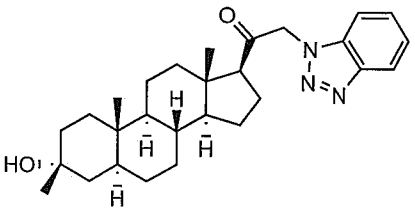
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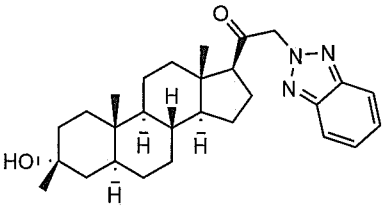
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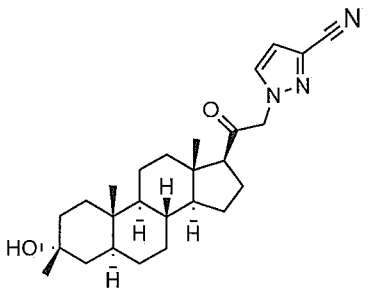
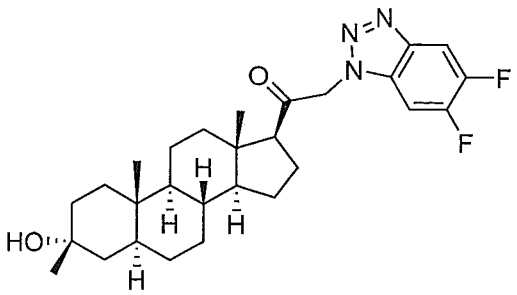
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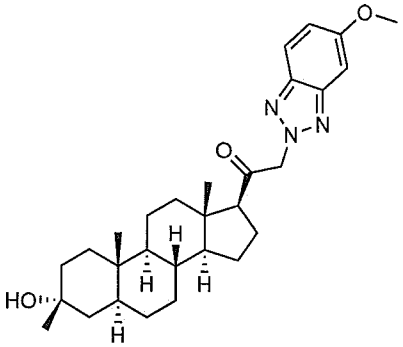
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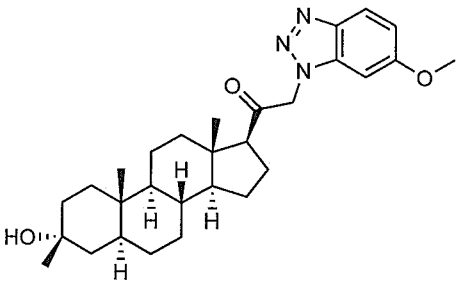
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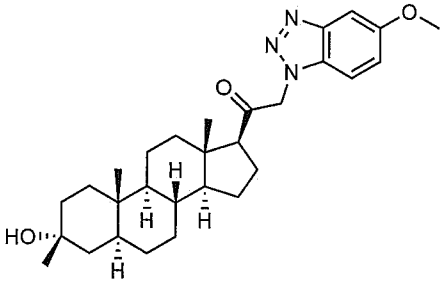
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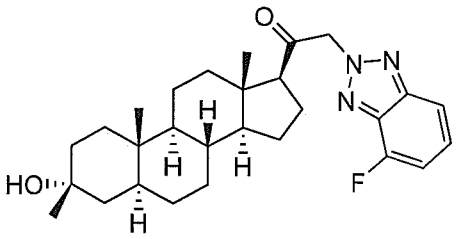
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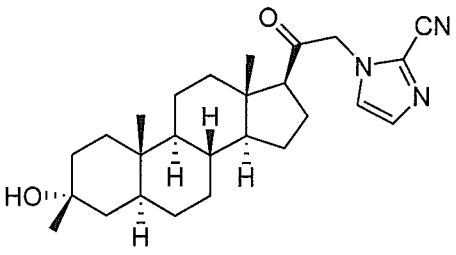
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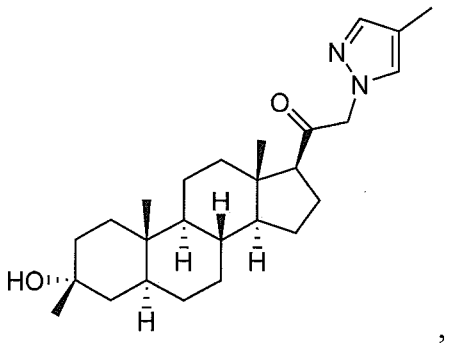
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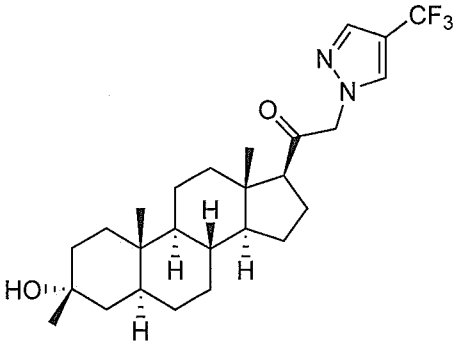
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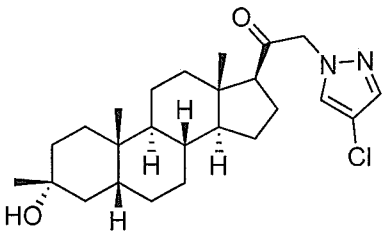
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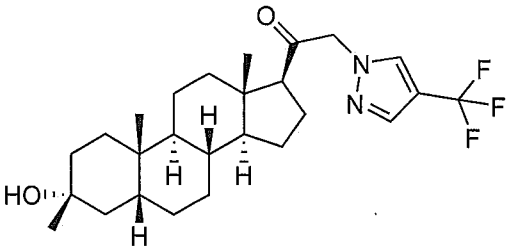
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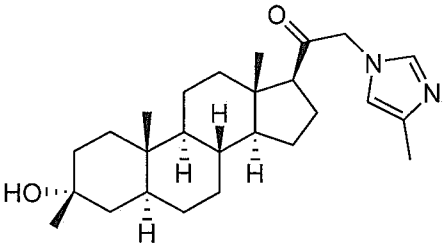
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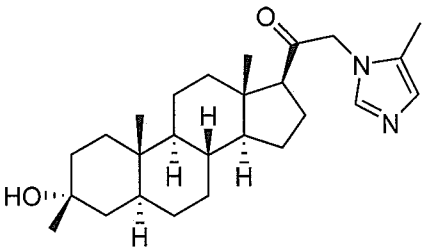
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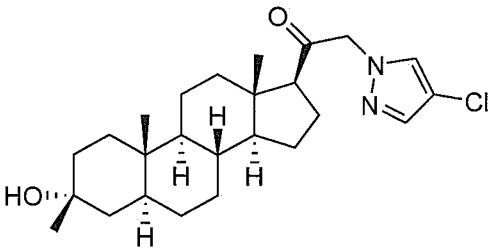
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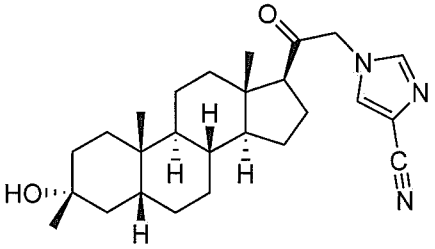
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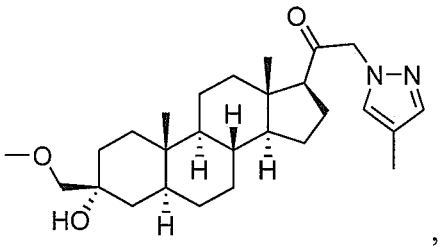
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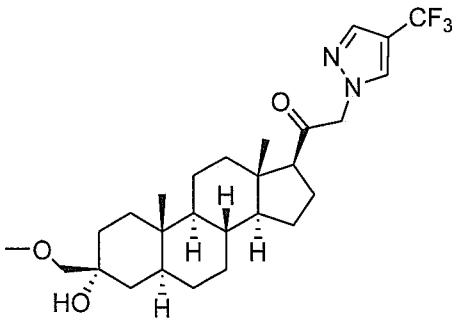
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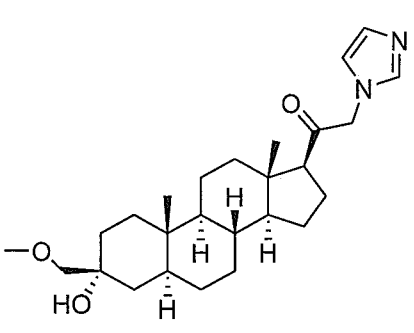
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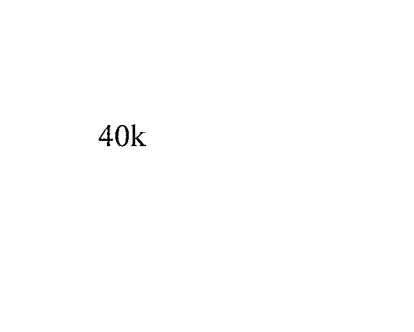
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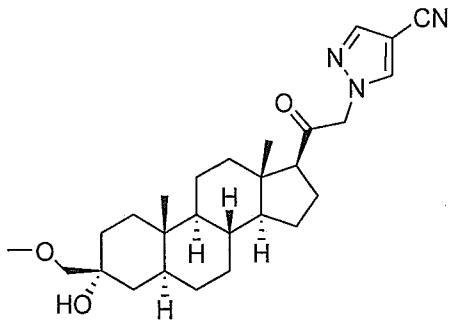
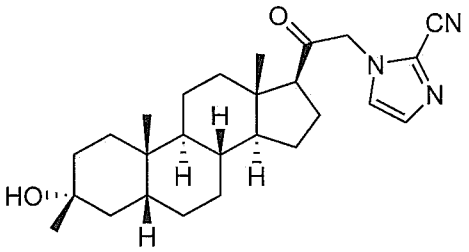
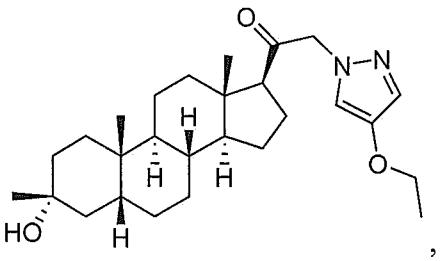
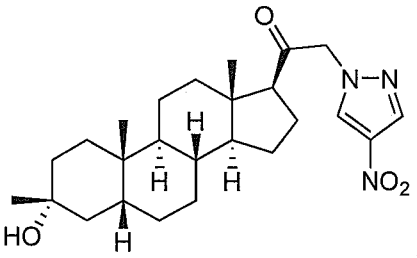
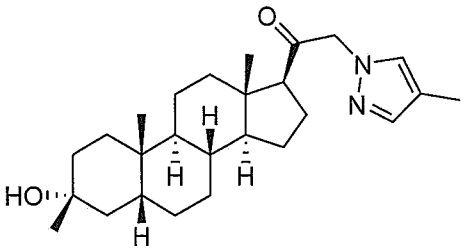
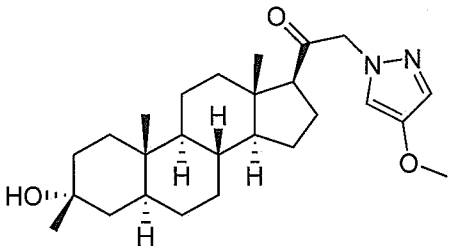
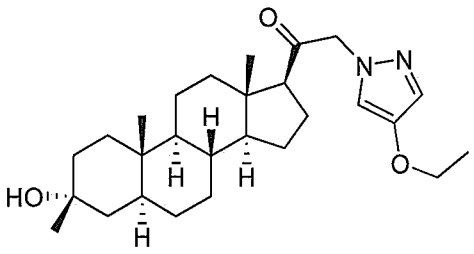
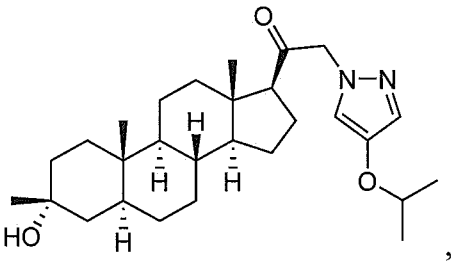
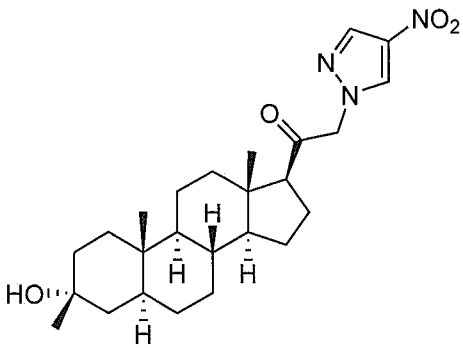
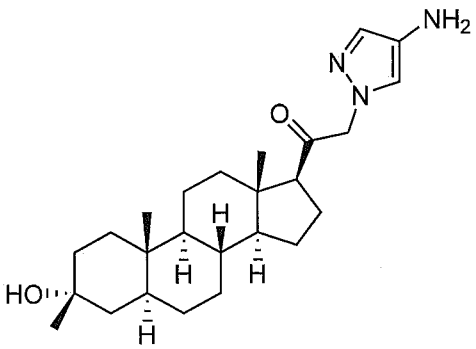

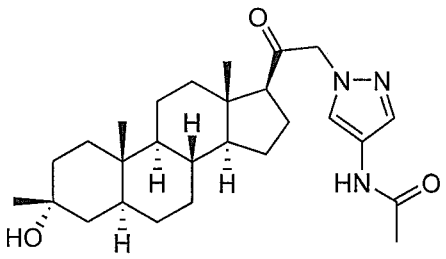
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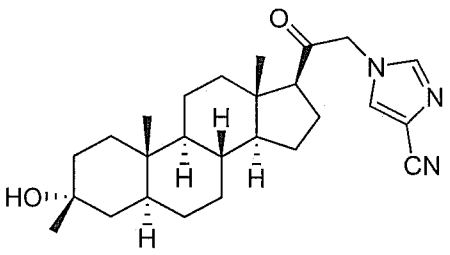
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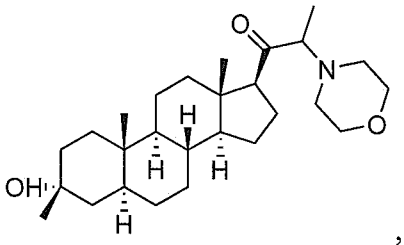
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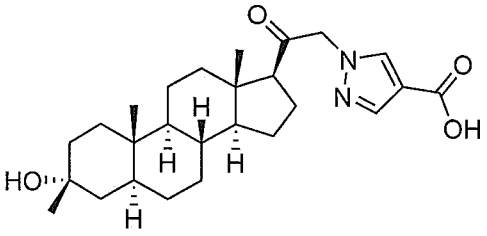
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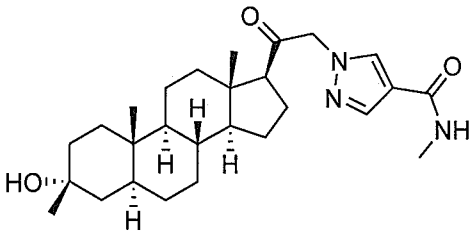
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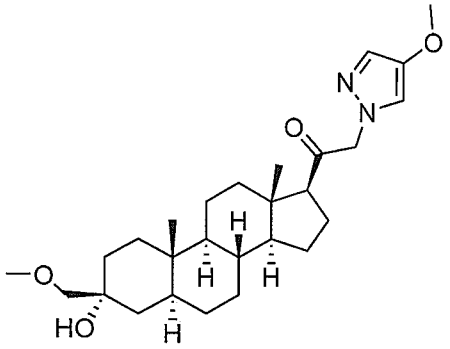
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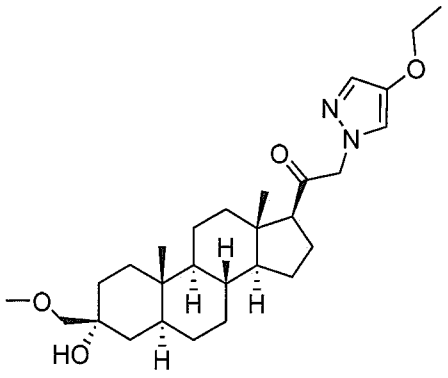
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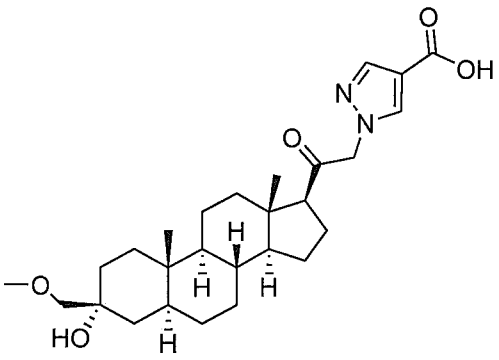
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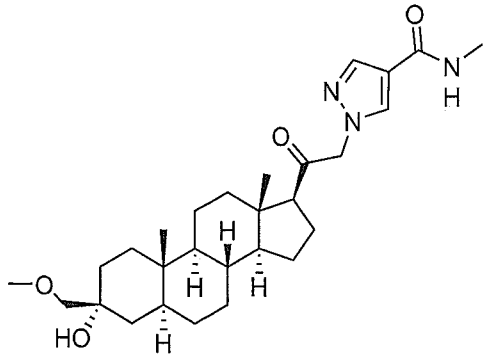
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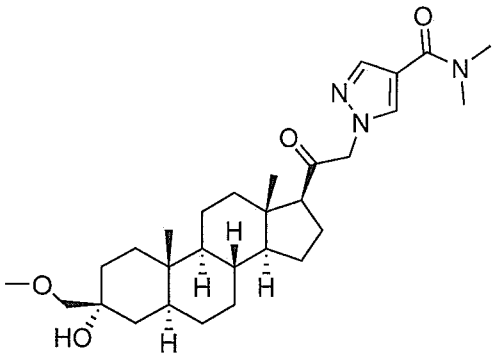
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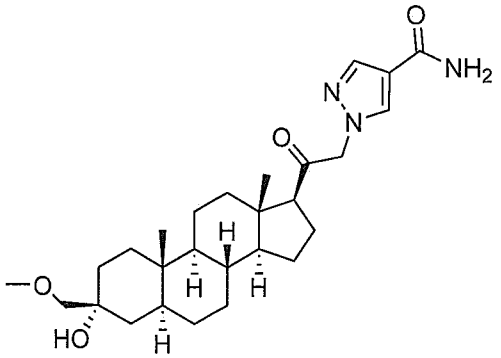
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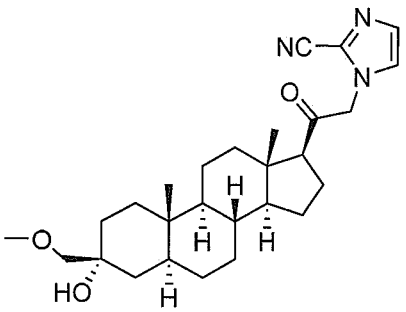
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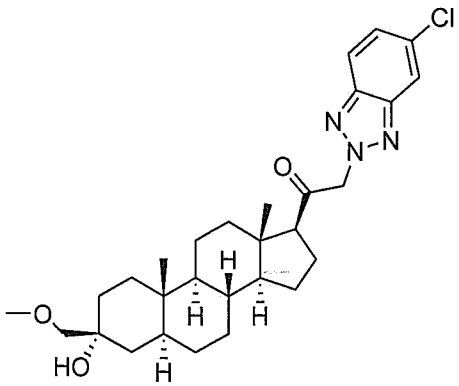
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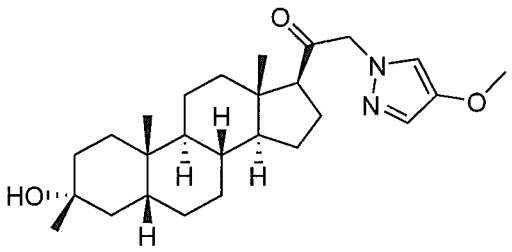
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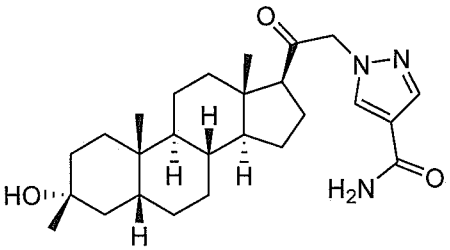
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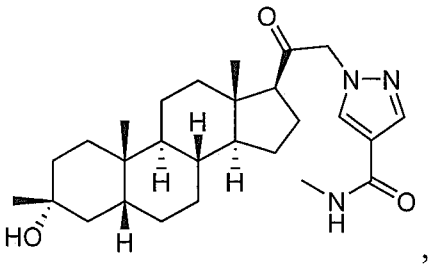
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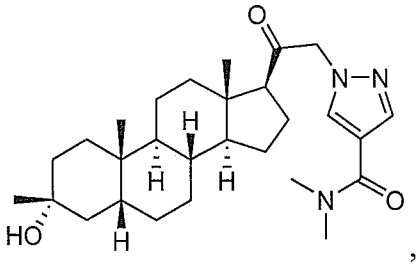
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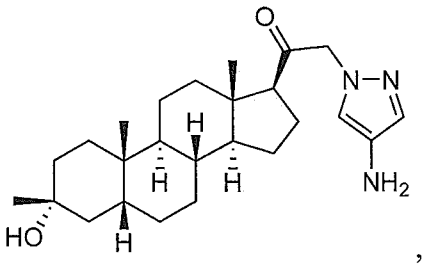
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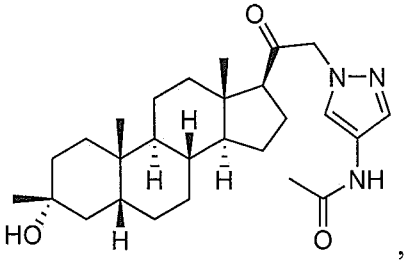
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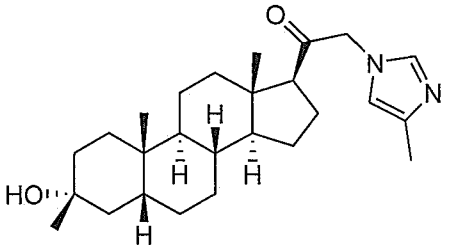
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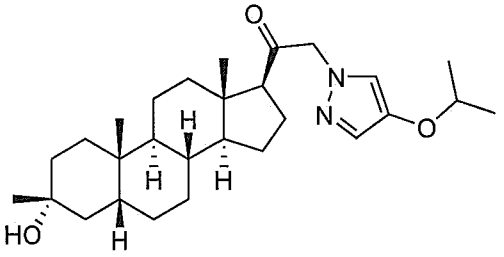
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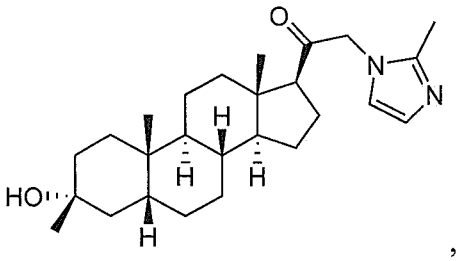
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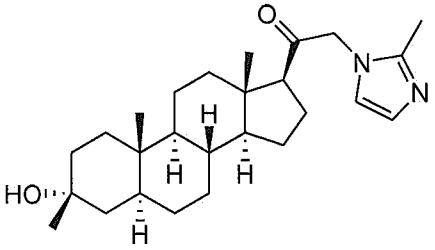
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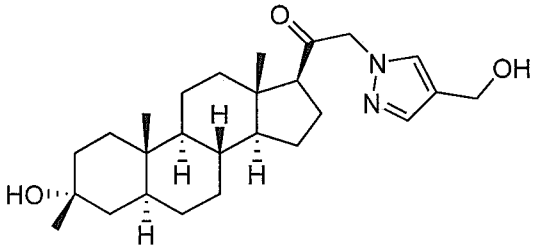
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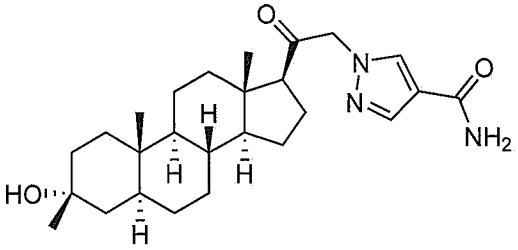
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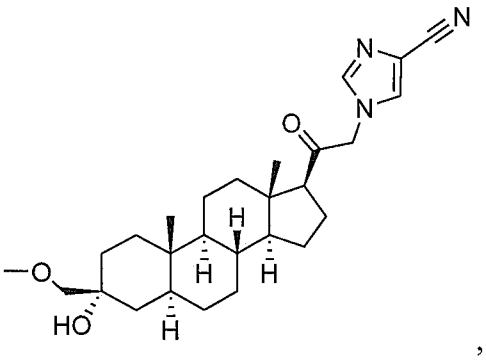

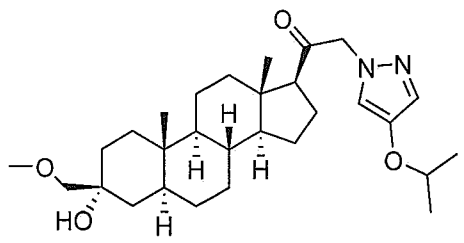
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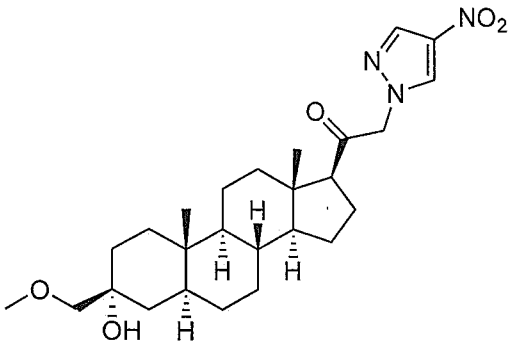
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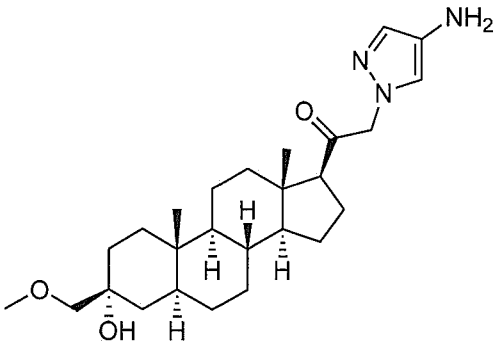
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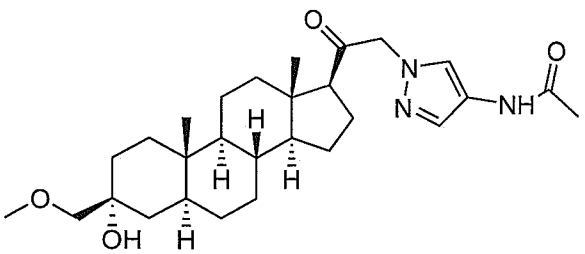
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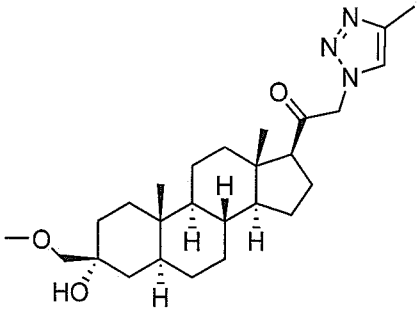
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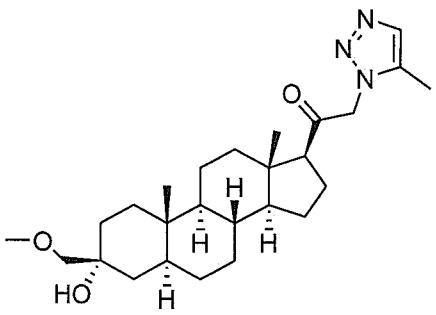
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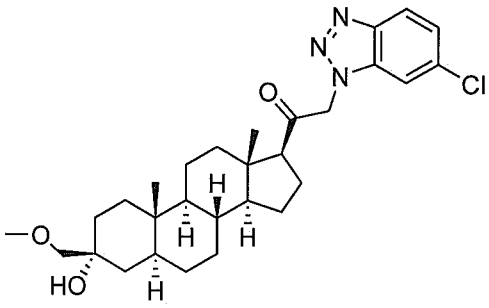
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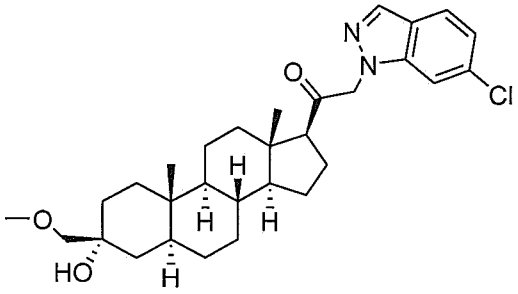
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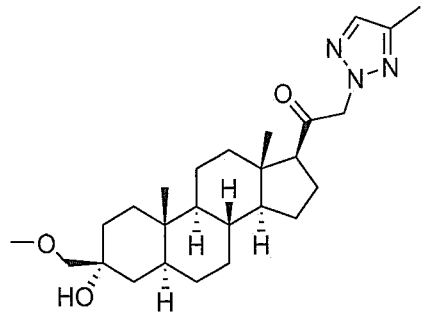
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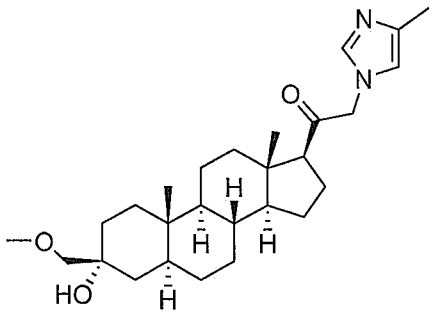
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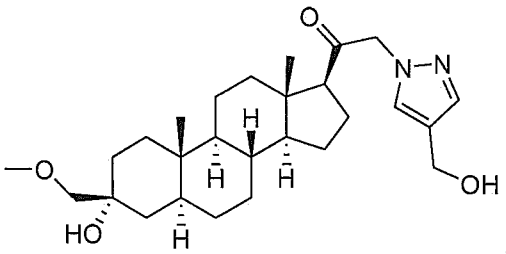
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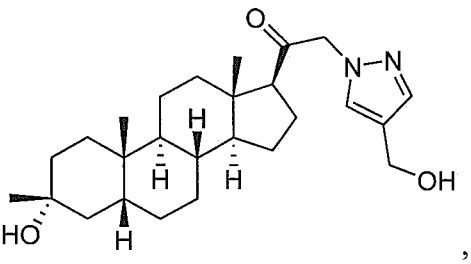
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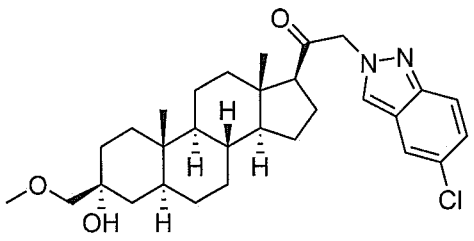
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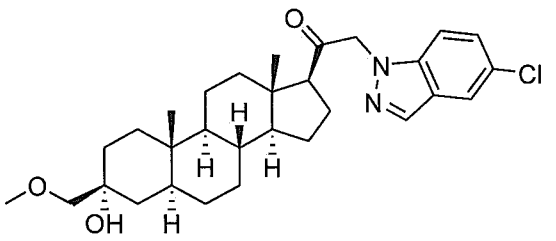
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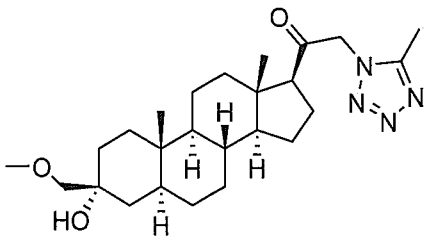
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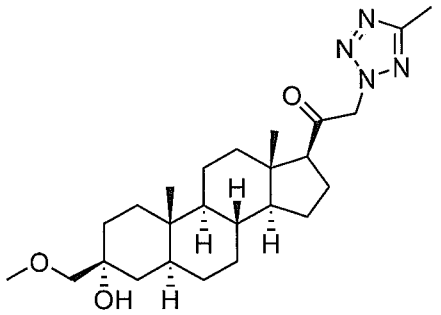
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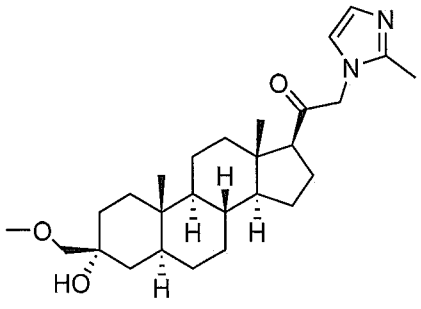
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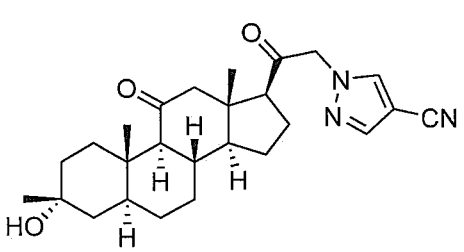
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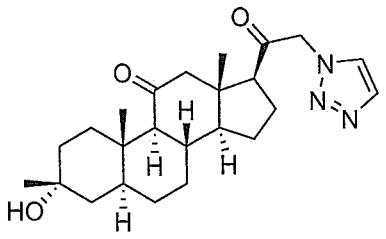
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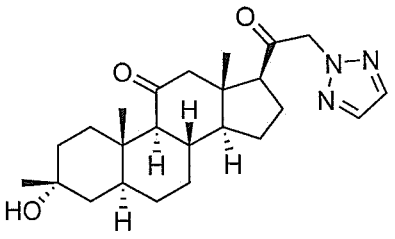
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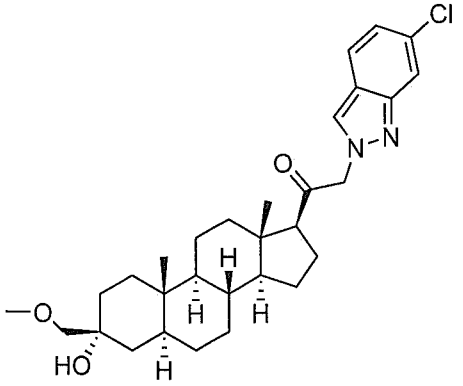
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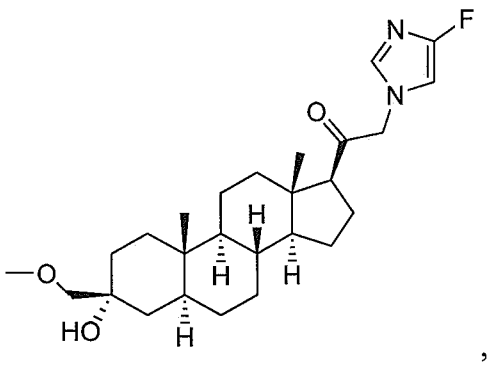
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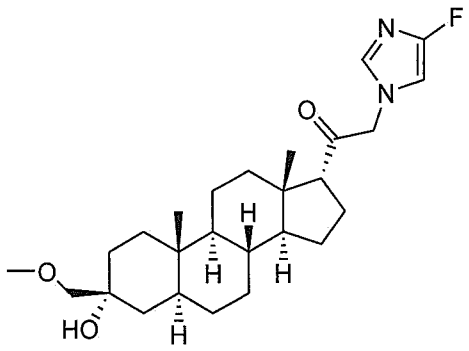
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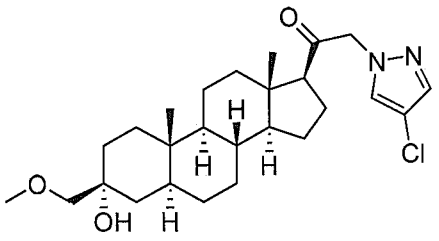
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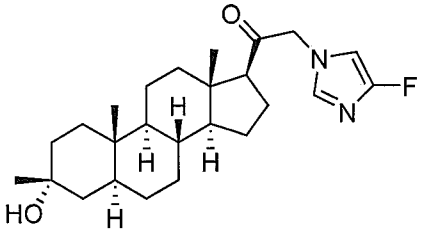
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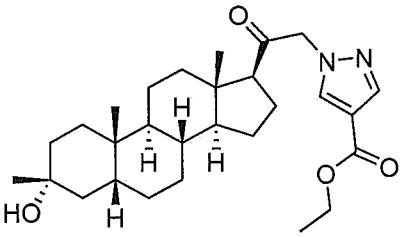
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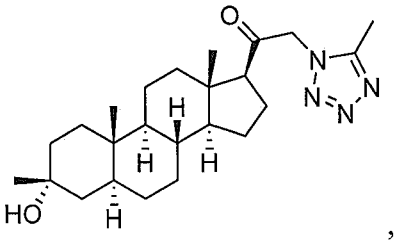
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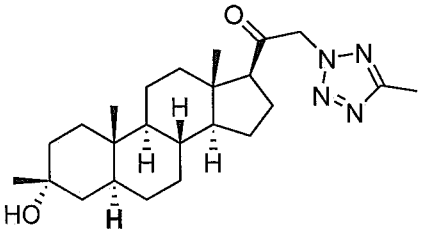
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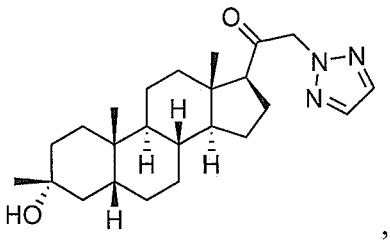
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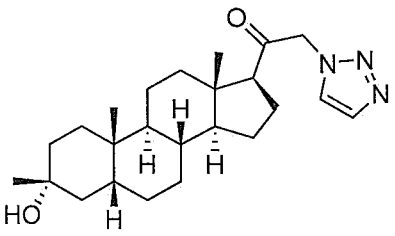
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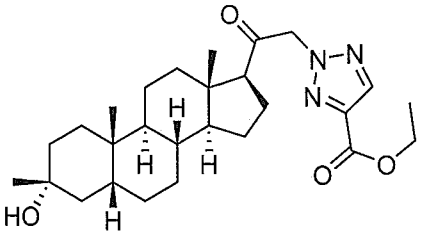
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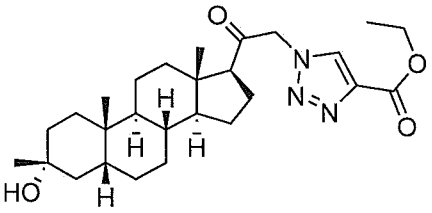
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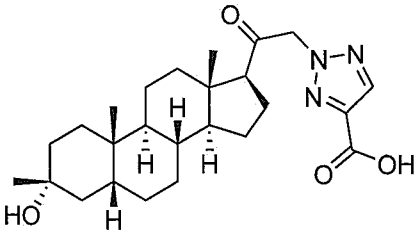
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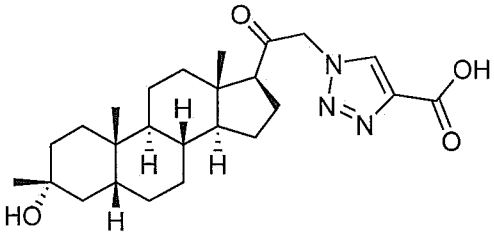
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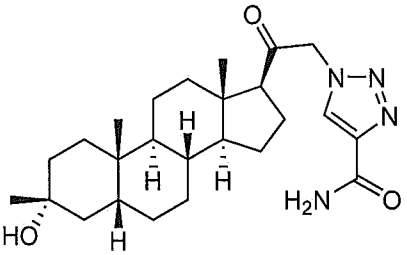
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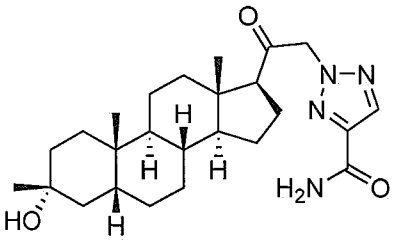
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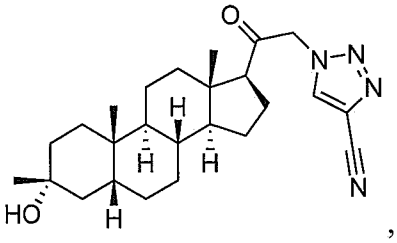
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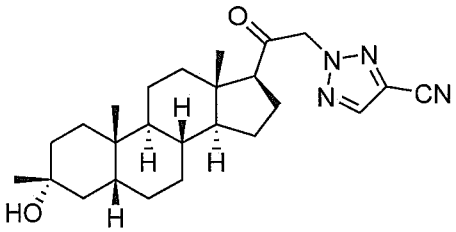
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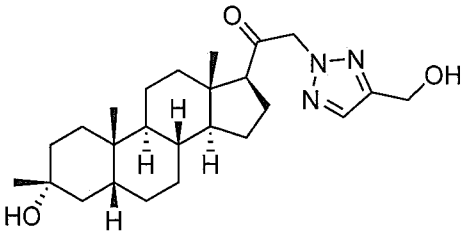
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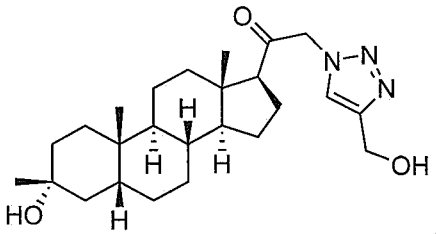
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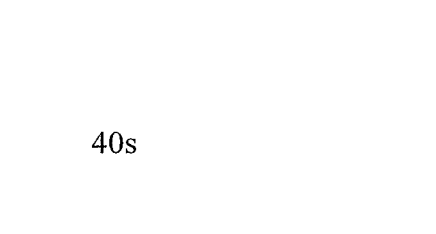
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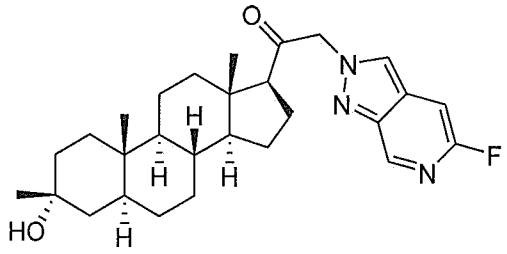
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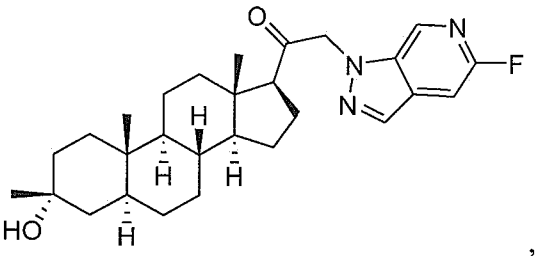
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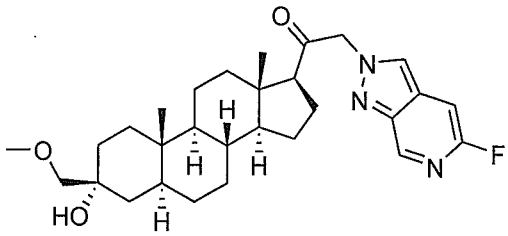
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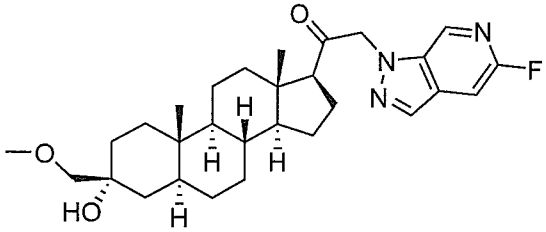
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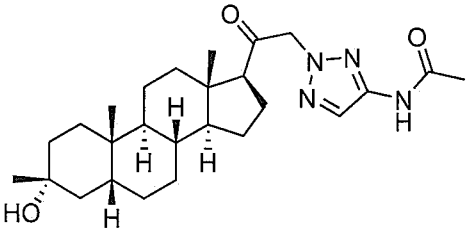
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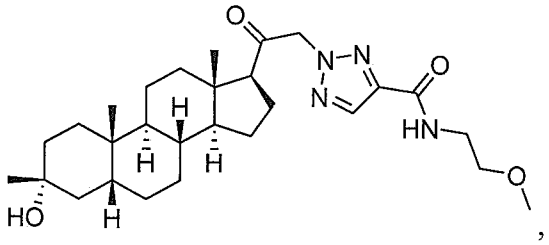
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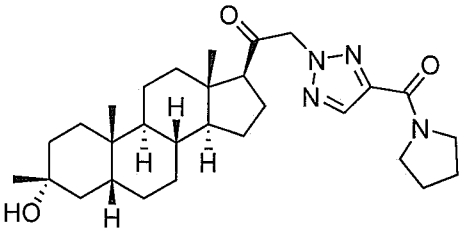
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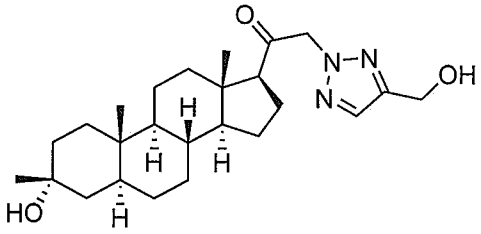
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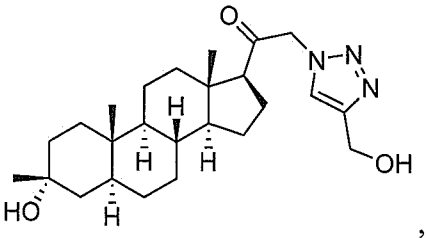
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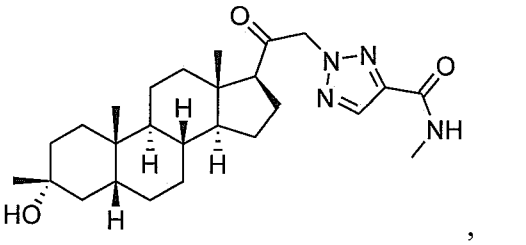
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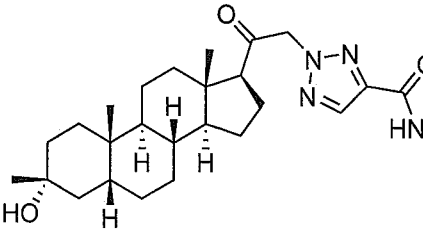
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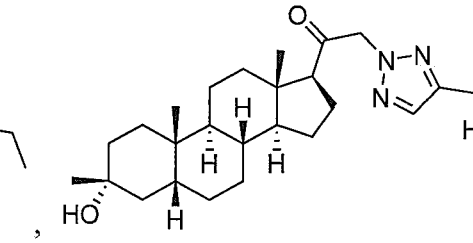
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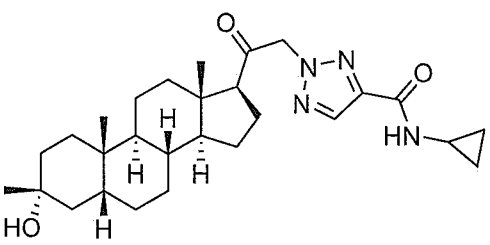
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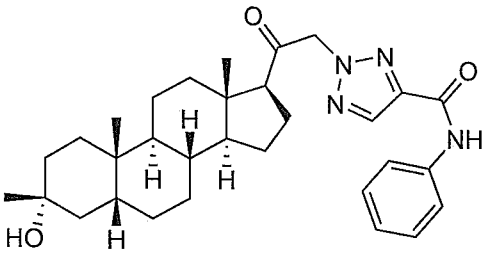
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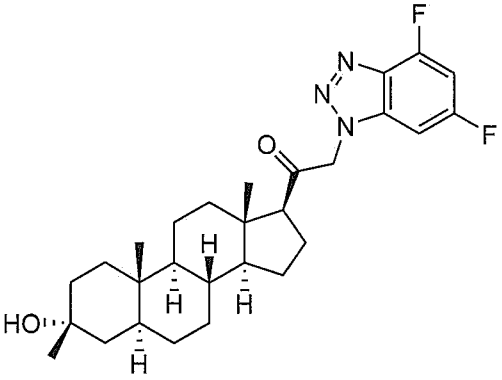
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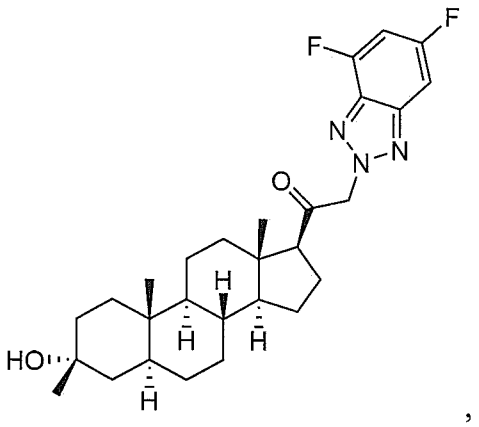
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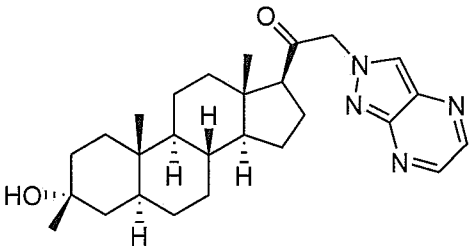
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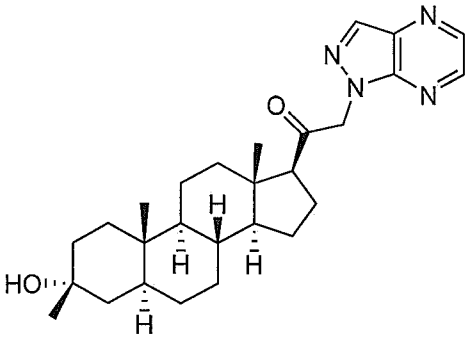
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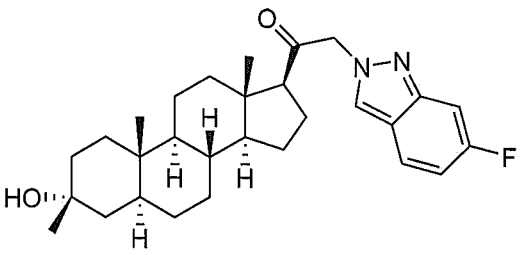
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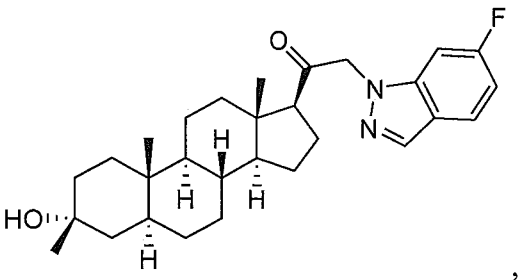
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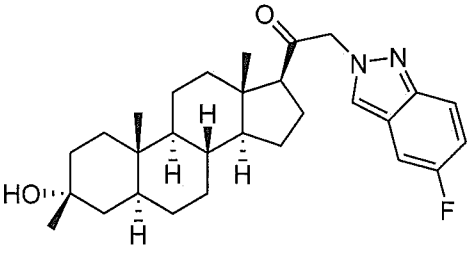
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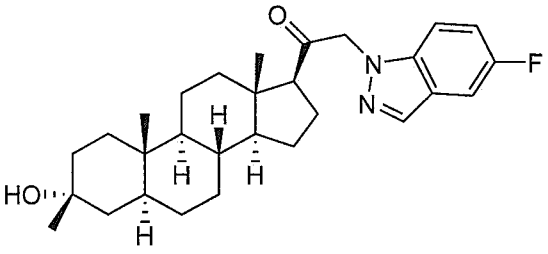
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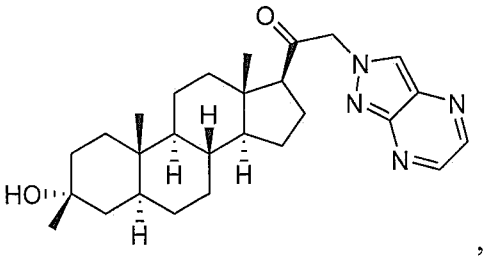
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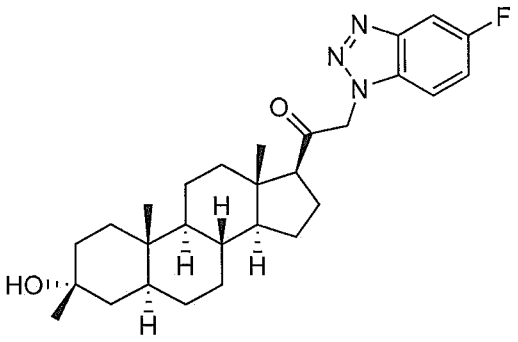
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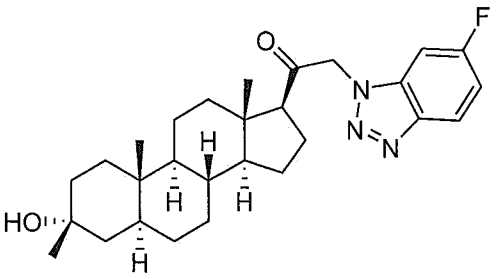
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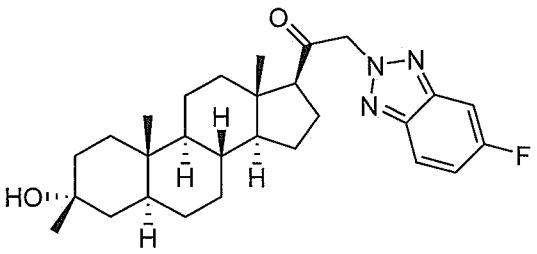
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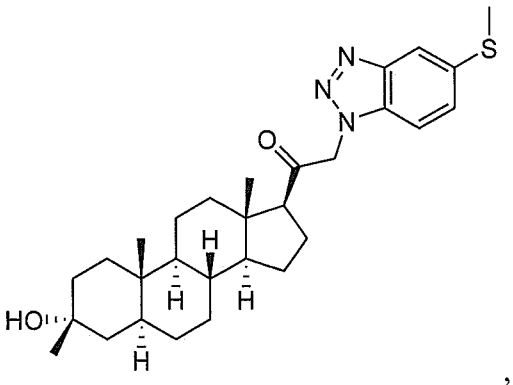
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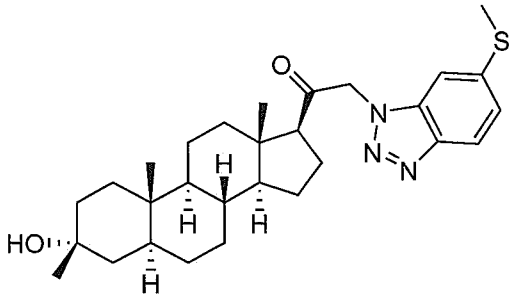
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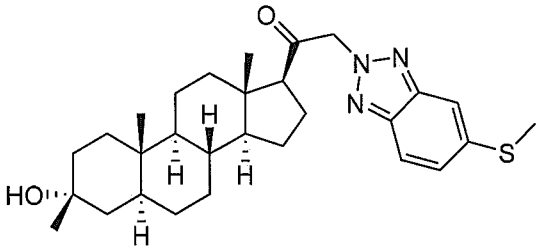
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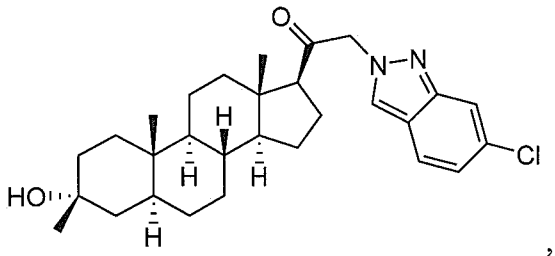
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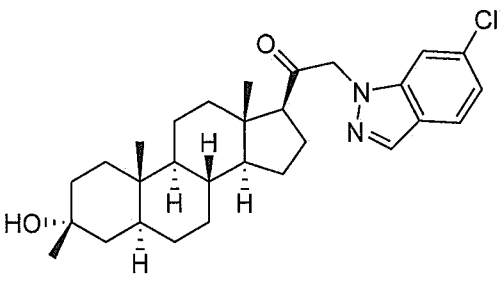
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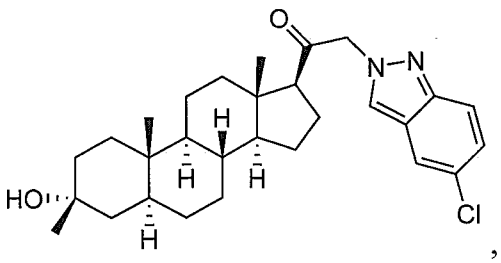
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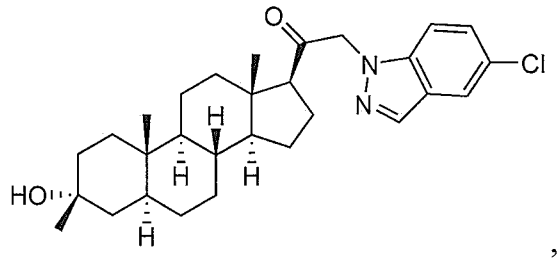
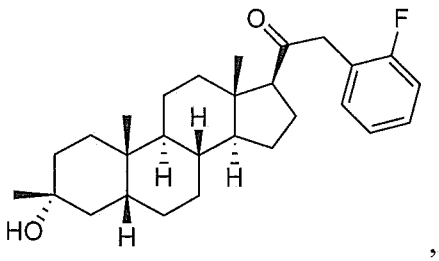
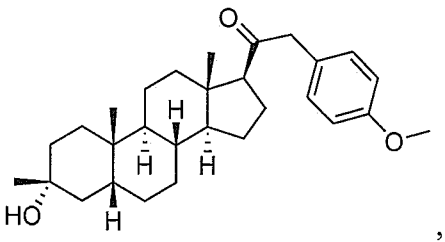
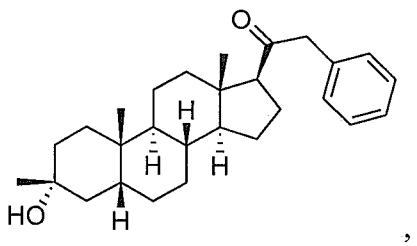
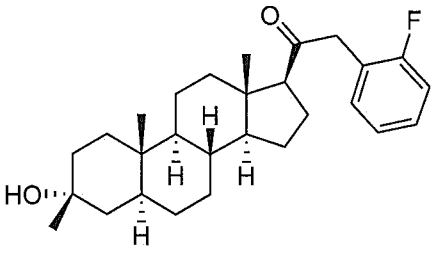
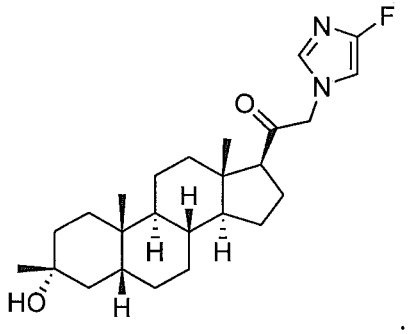
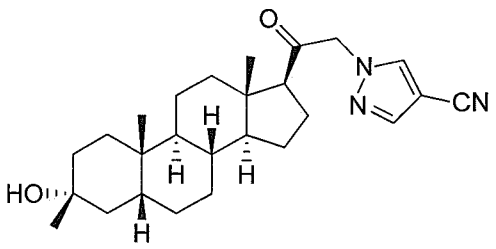
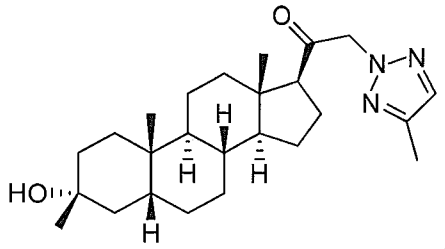
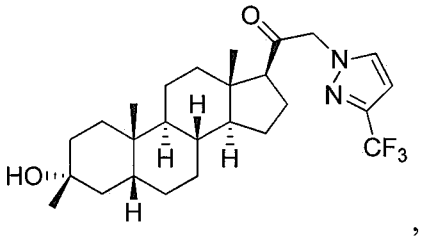
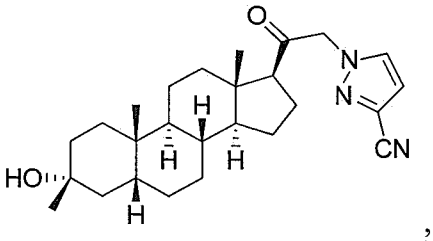
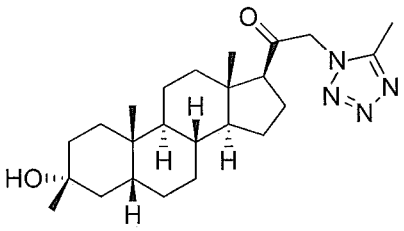







[017b] In a further aspect of the present disclosure, there is provided a compound, wherien the compound is: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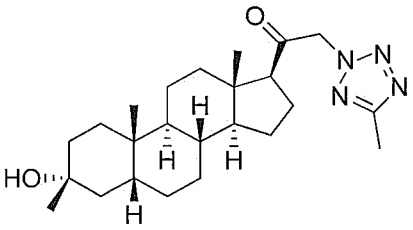
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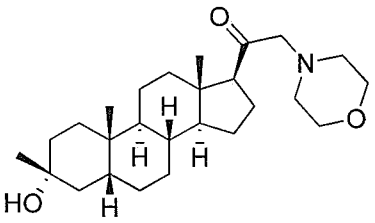
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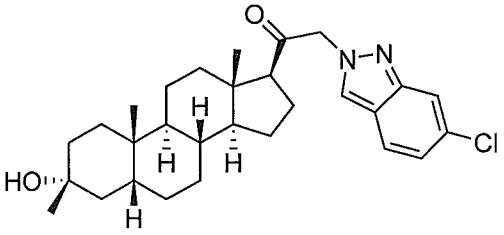
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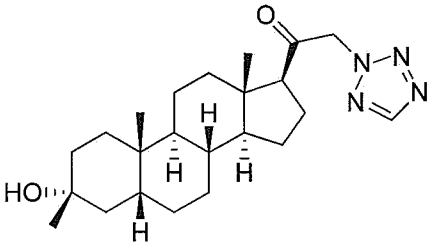
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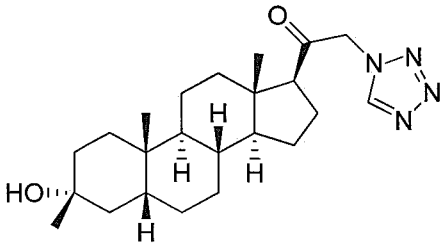
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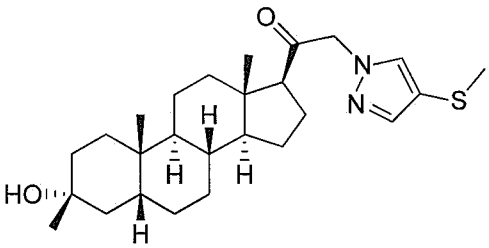
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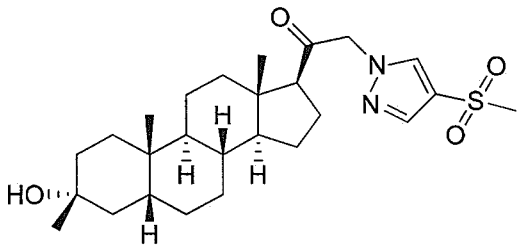
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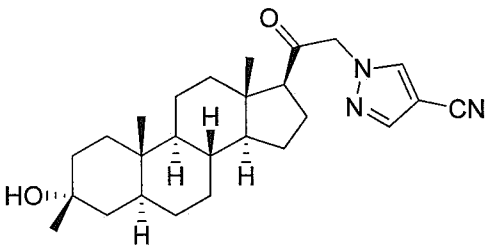
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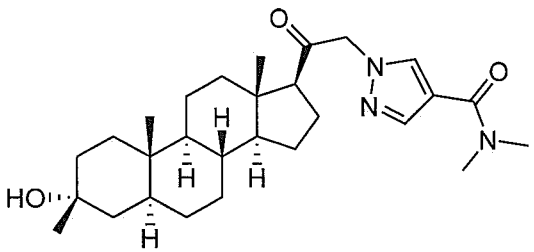
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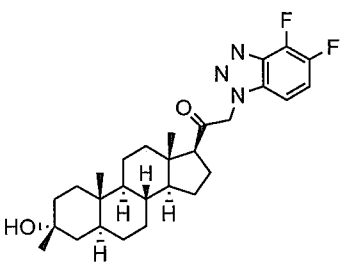
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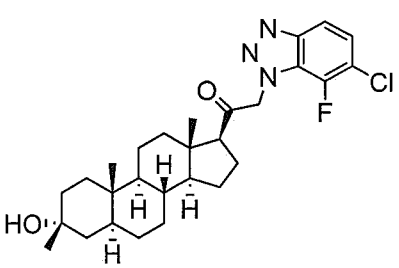
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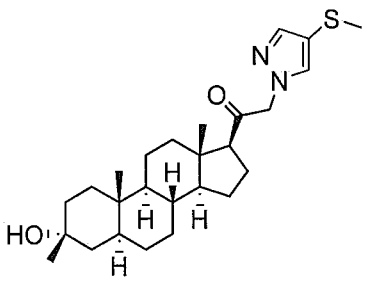
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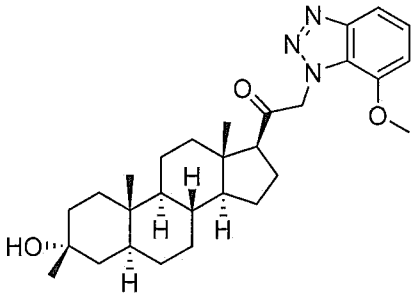
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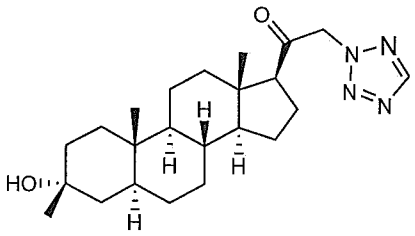
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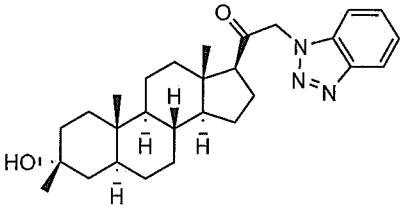
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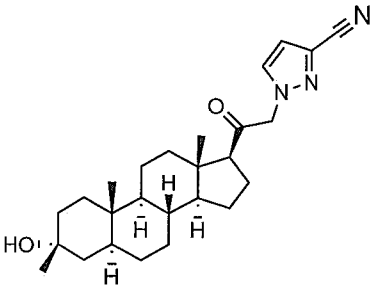
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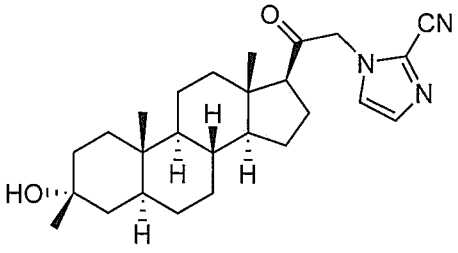
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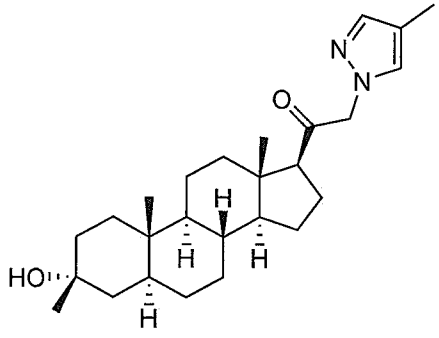
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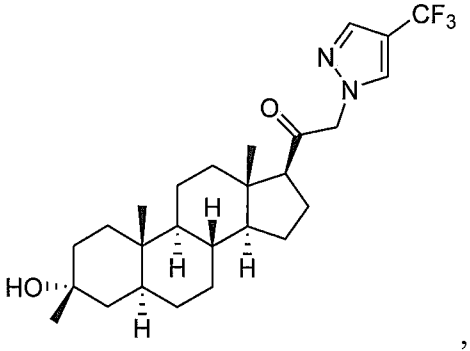
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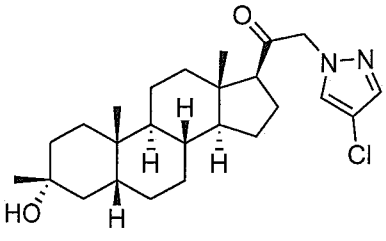
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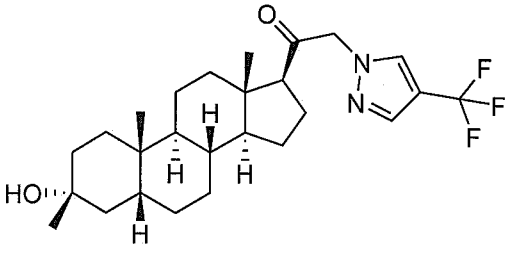
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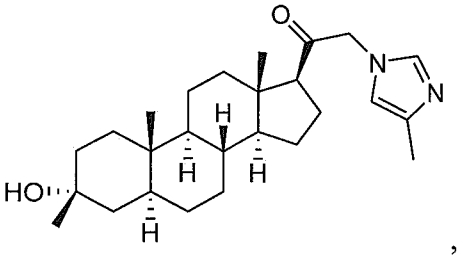
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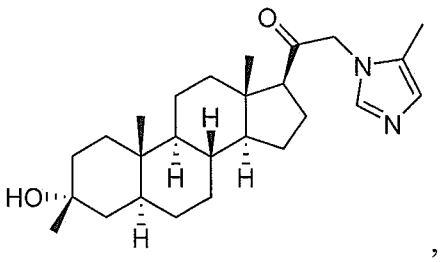
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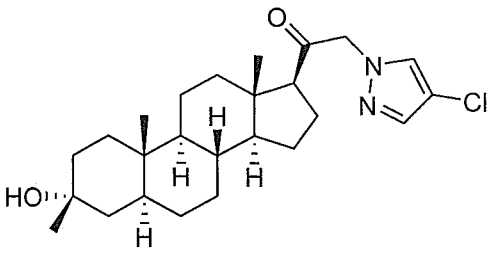
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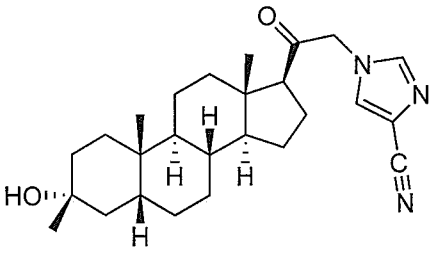
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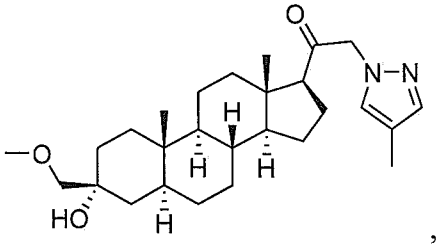
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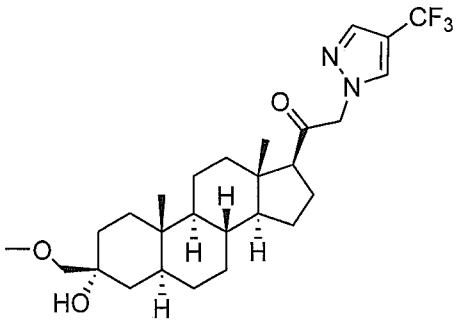
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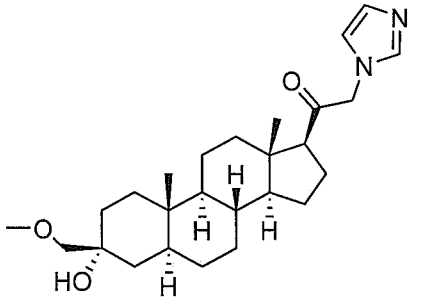
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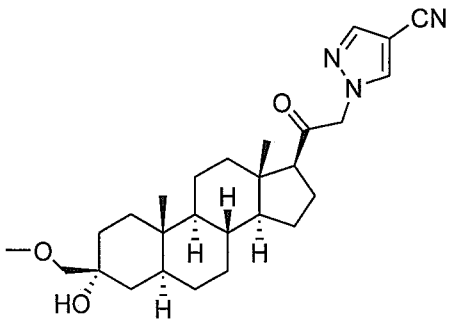
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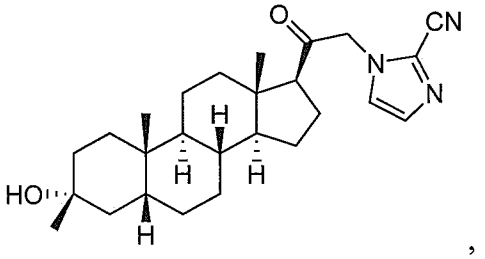
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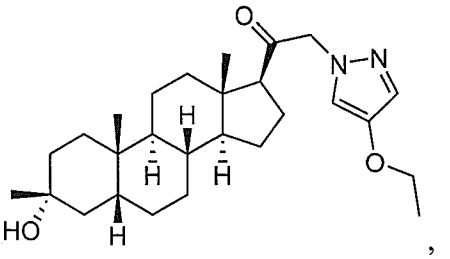
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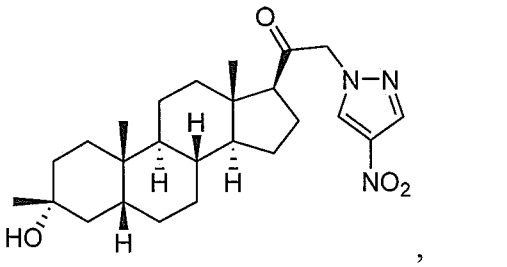
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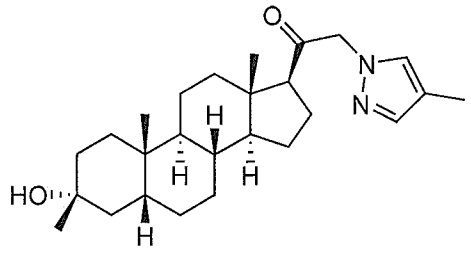
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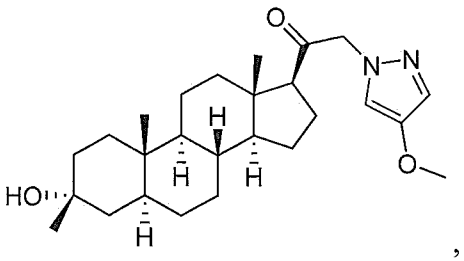
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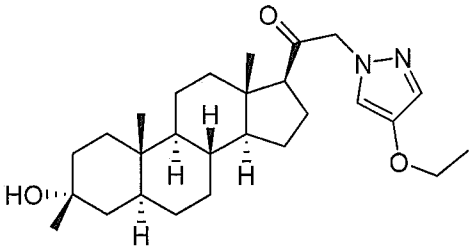
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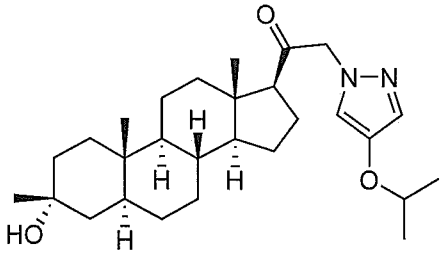
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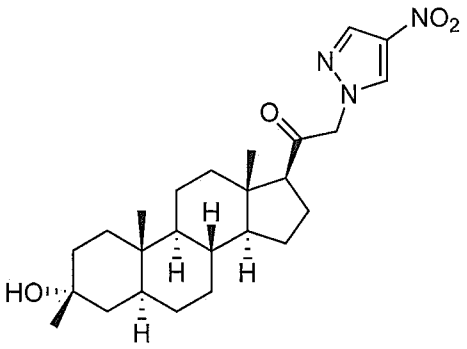
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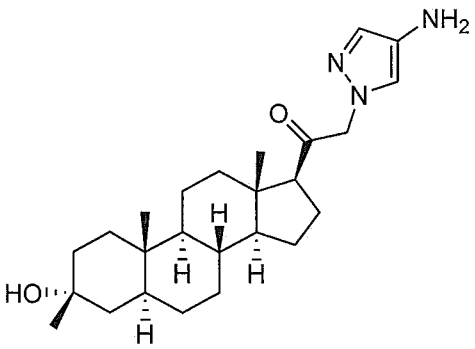
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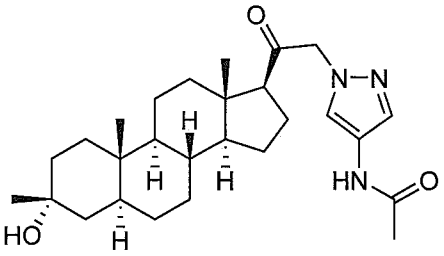
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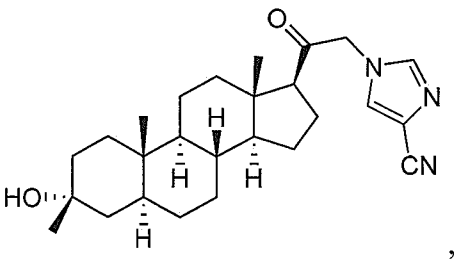
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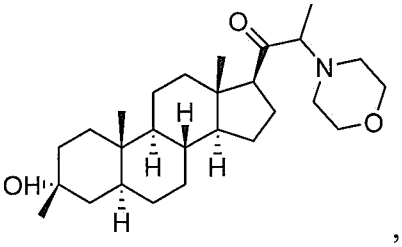
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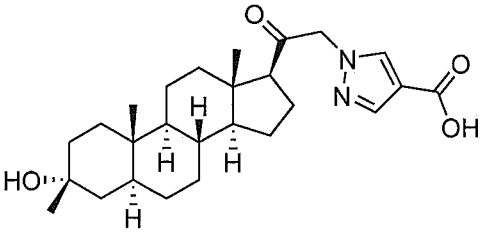
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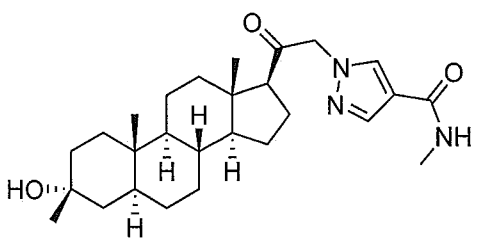
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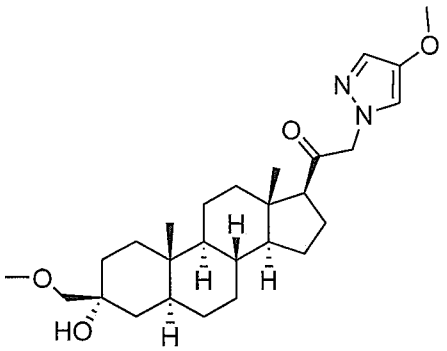
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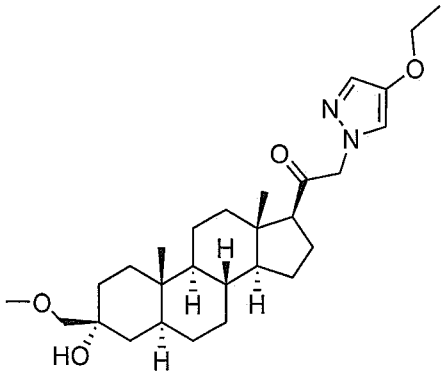
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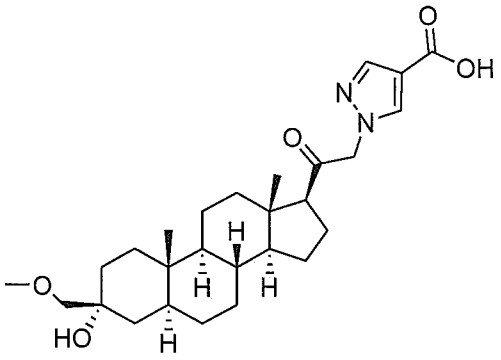
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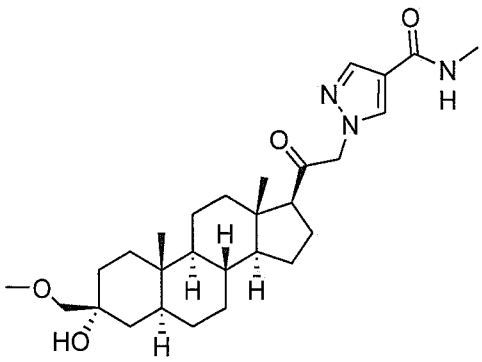
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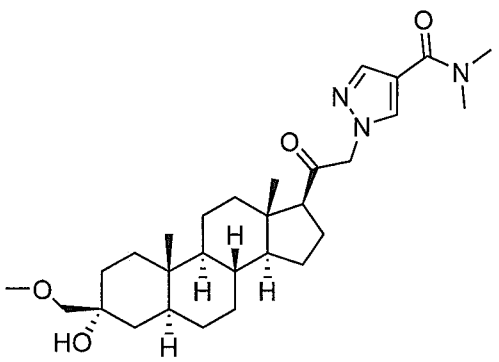
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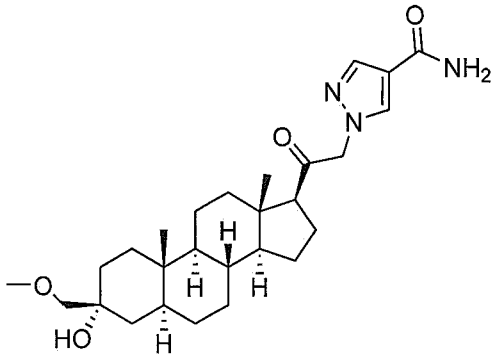
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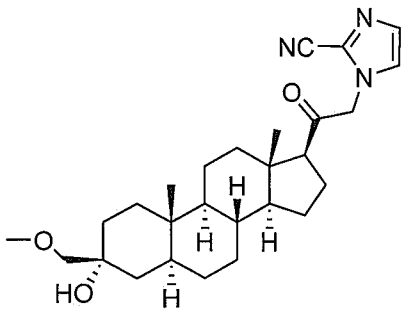
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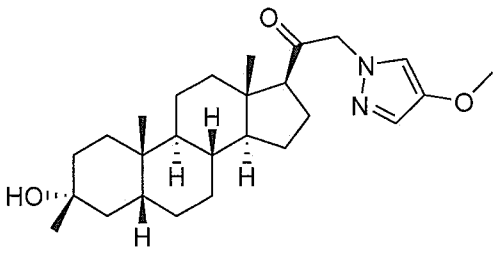
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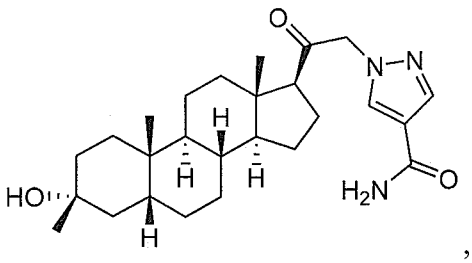
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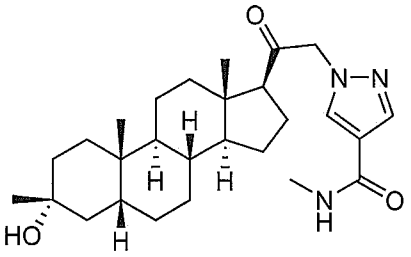
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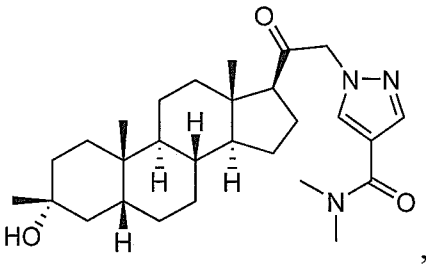
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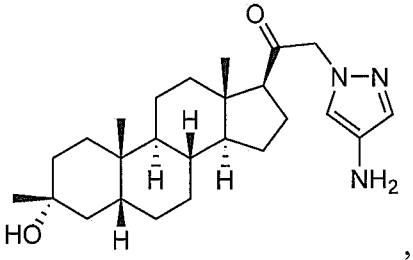
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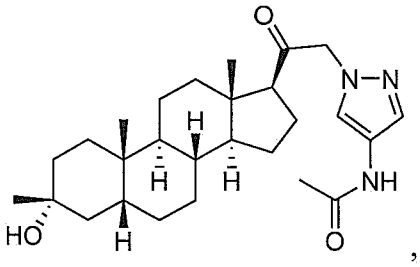
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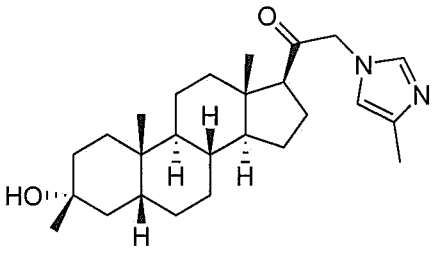
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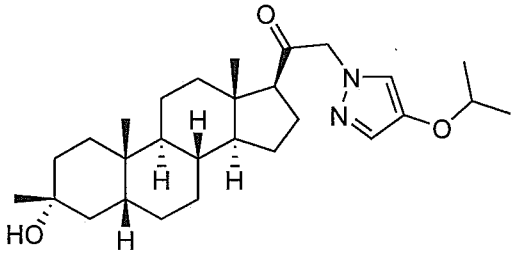
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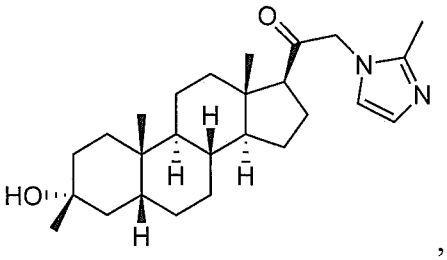
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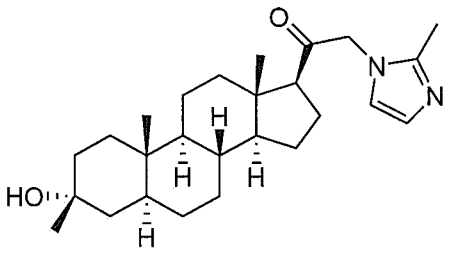
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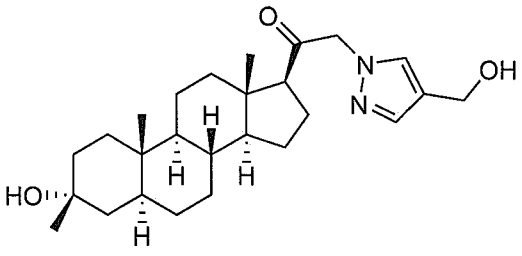
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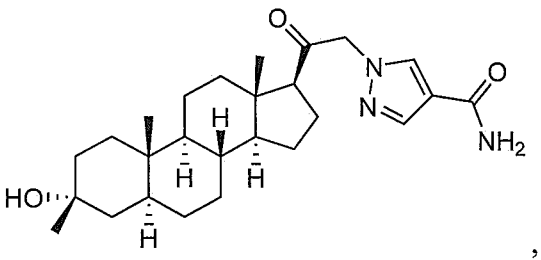
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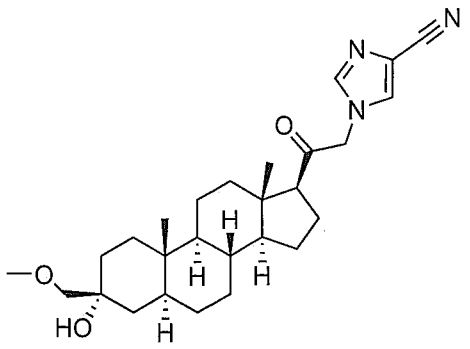
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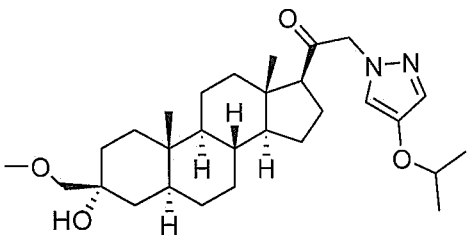
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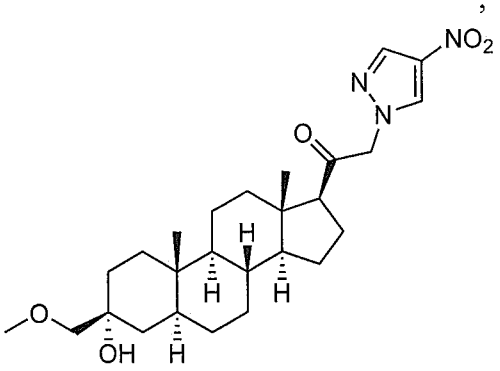
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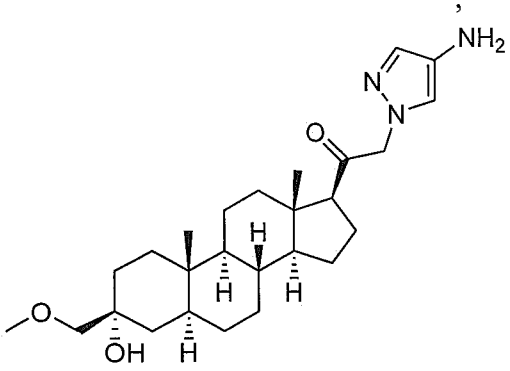
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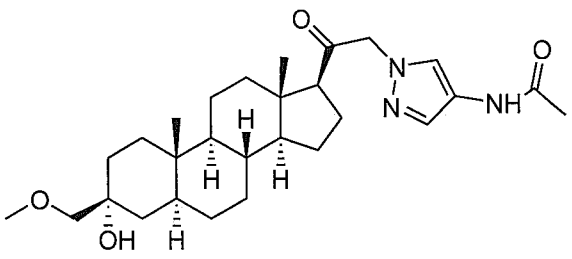
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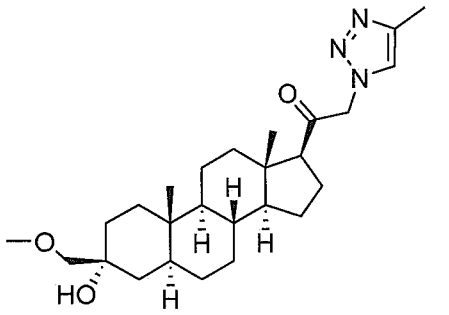
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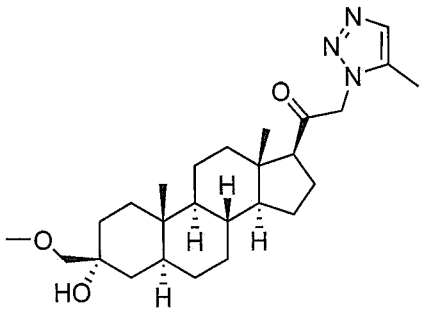
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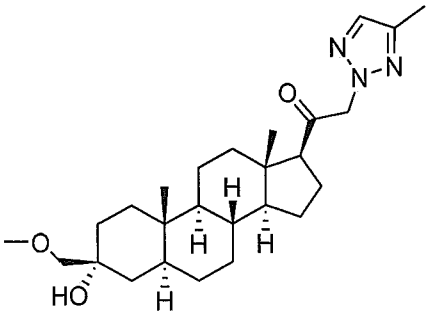
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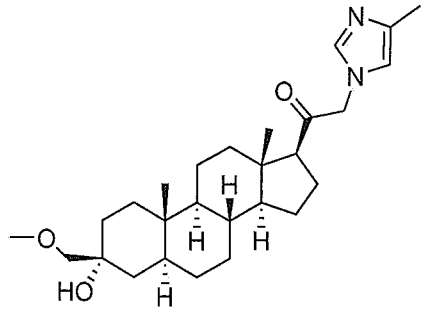
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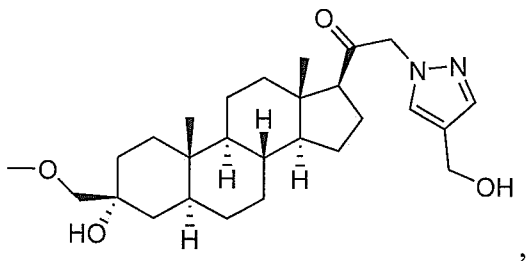
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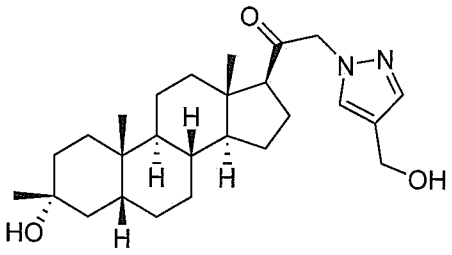
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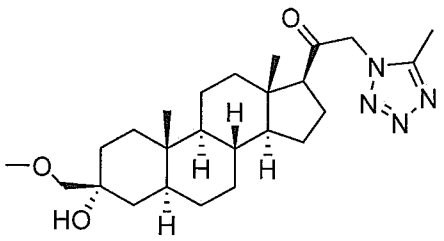
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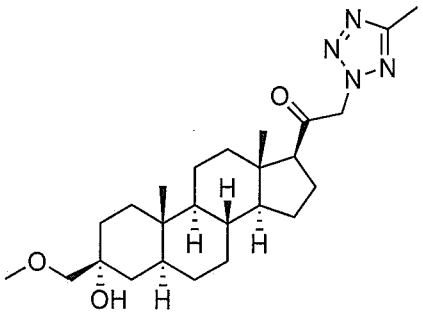
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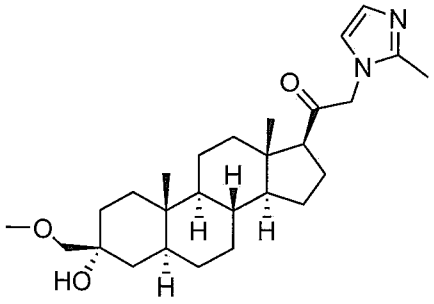
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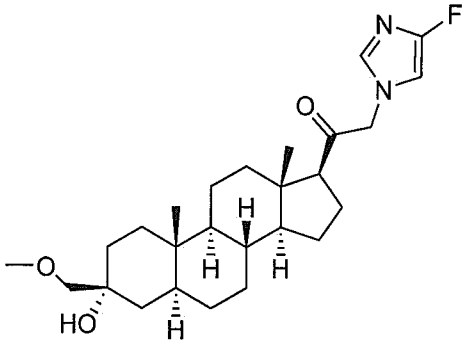
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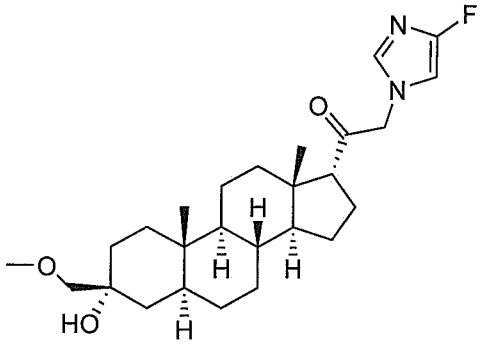
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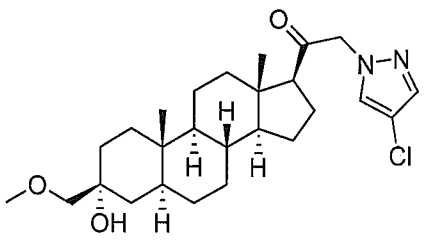
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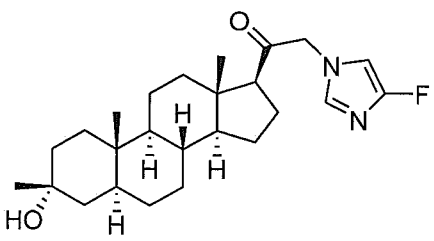
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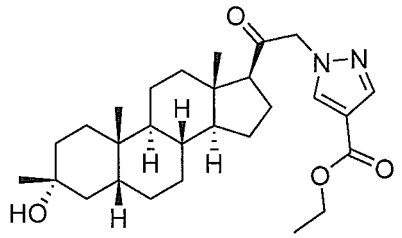
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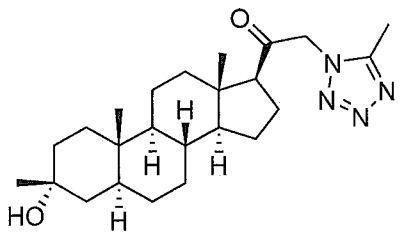
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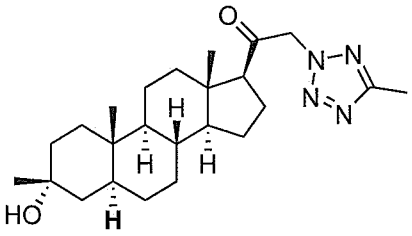
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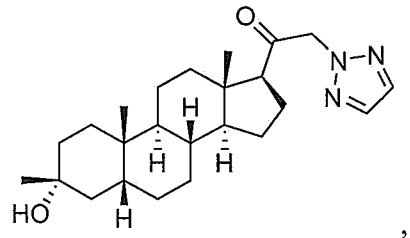
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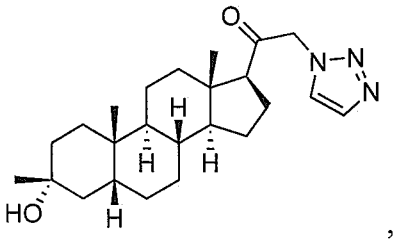
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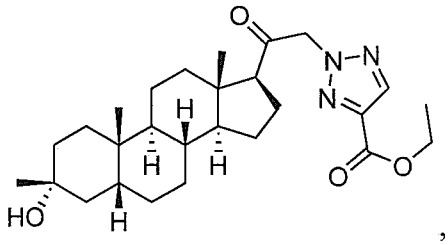
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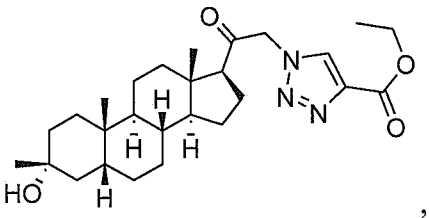
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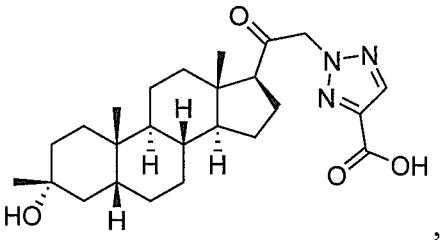
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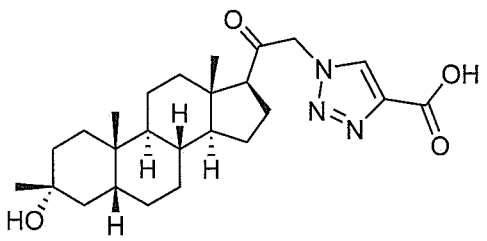
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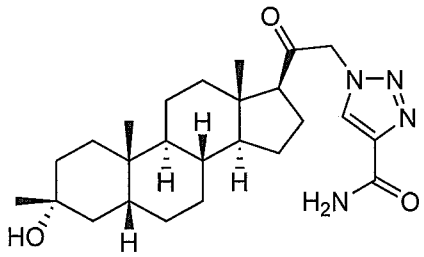
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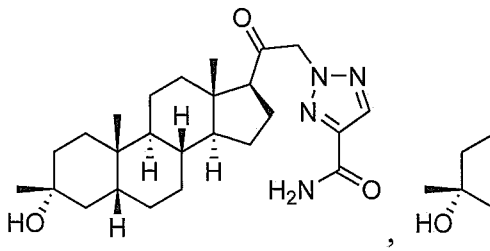
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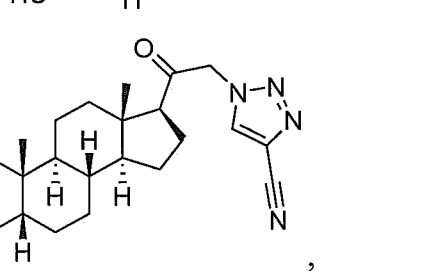
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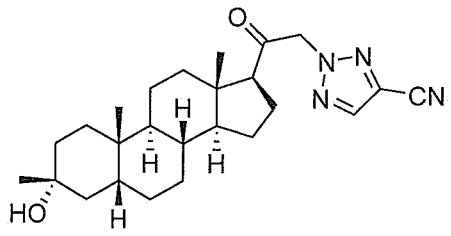
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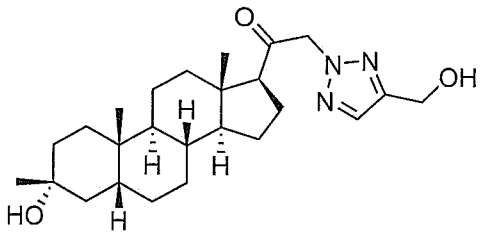
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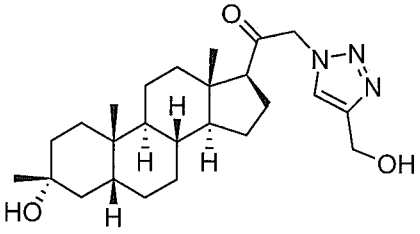
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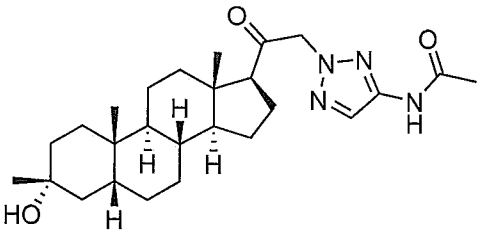
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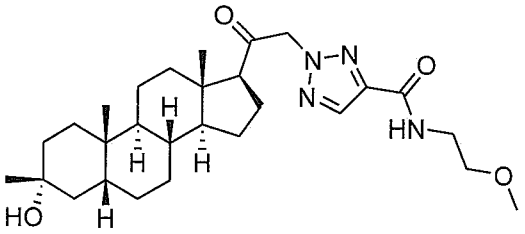
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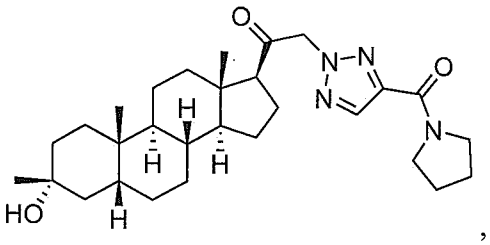
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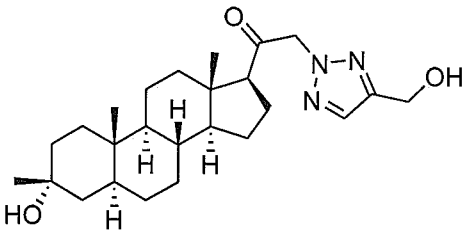
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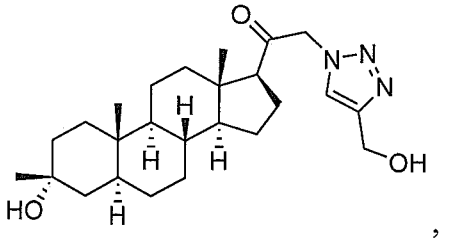
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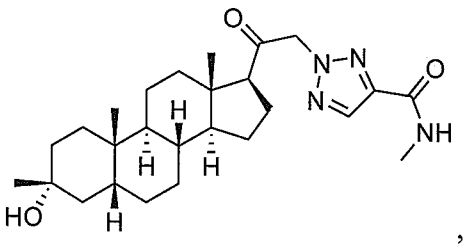
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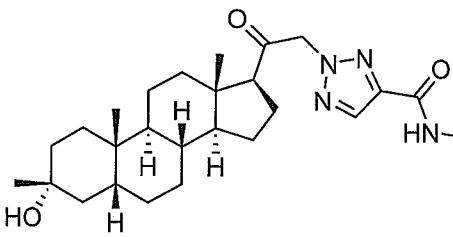
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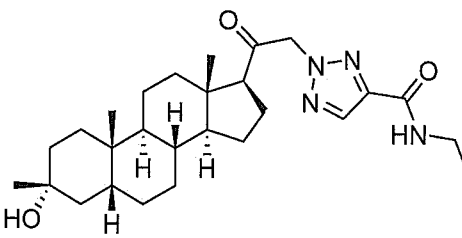
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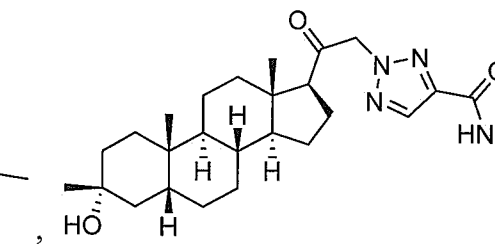
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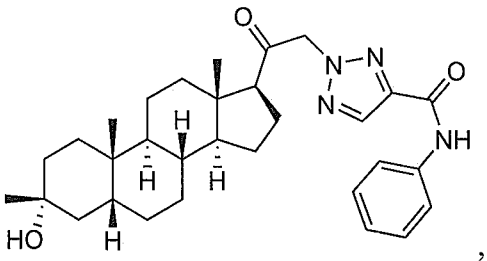

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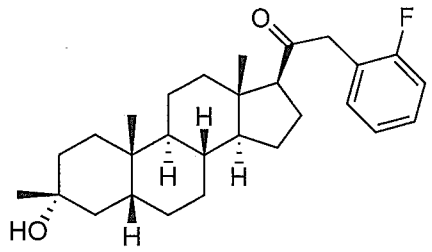

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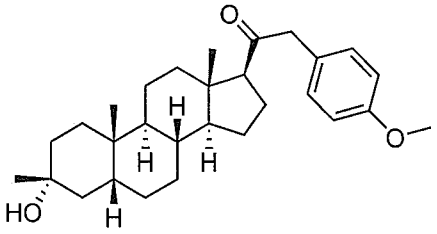

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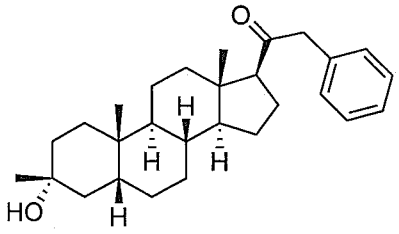

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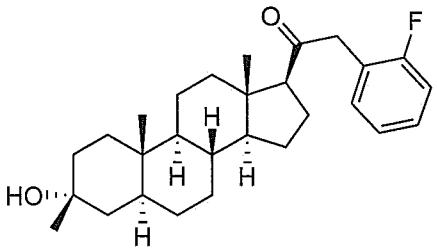

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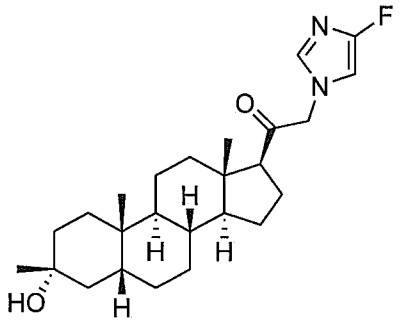

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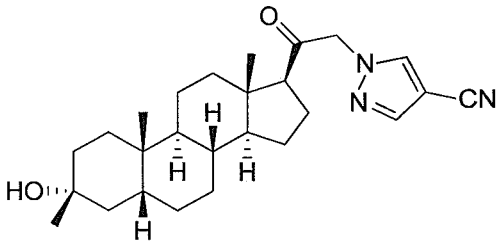
[017c] In another aspect of the present disclosure, there is provided a compound, wherein the compound is:


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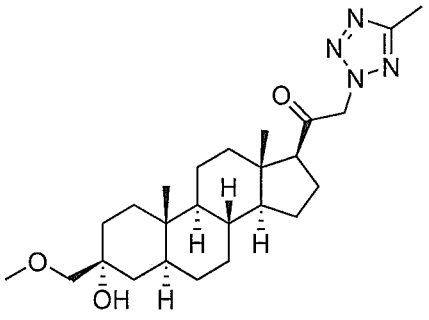
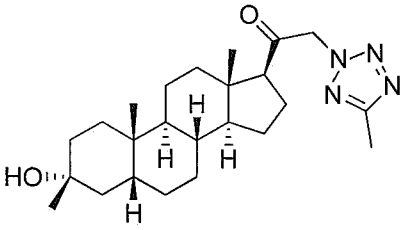
[017d] In a further aspect of the present disclosure, there is provided a compound, wherein the compound is:  .

[017e] In another aspect of the present disclosure, there is provided a compound, wherein the compound is:  .

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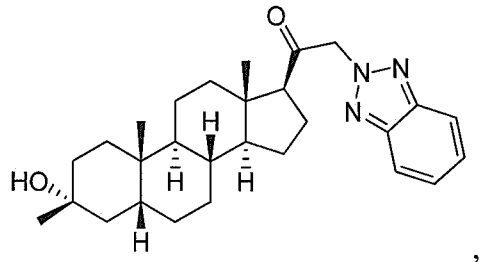
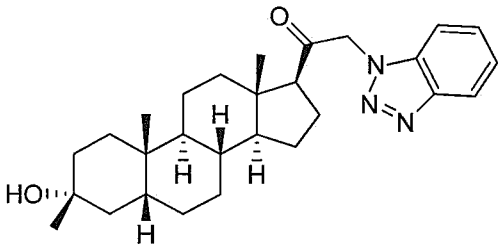
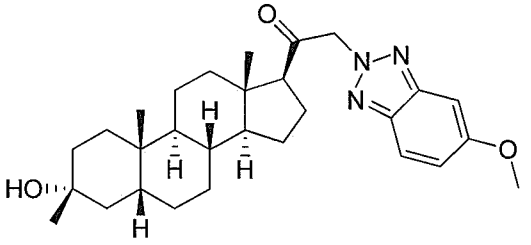
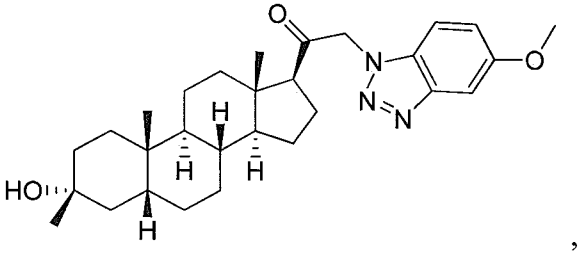
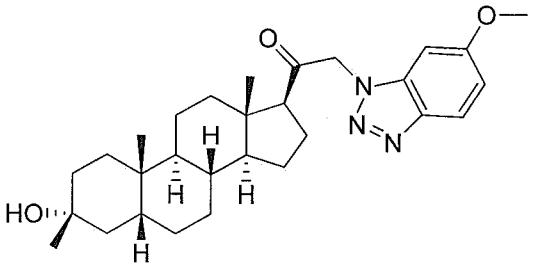
 ,  ,  ,  .



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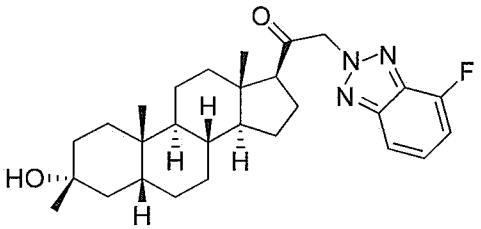

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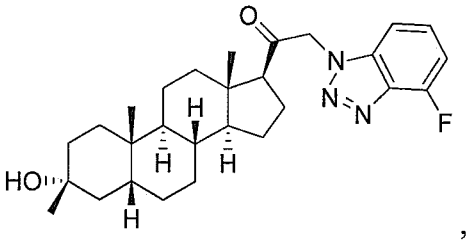

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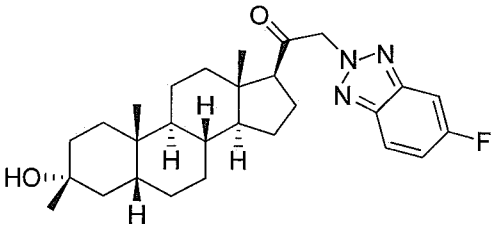

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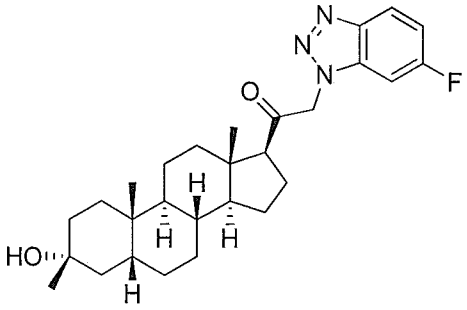
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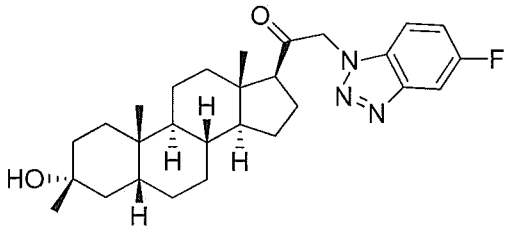
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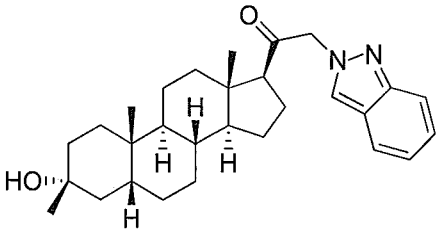
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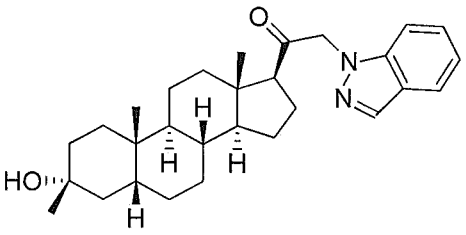
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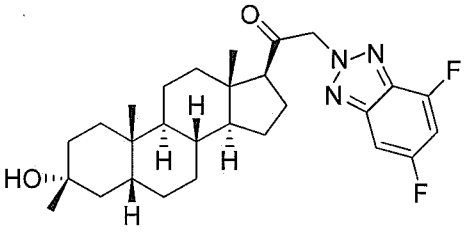
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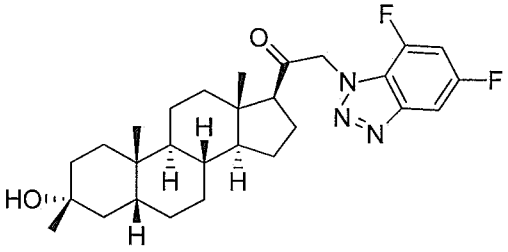
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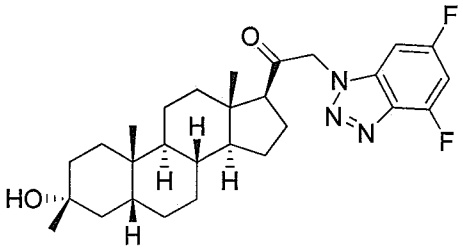
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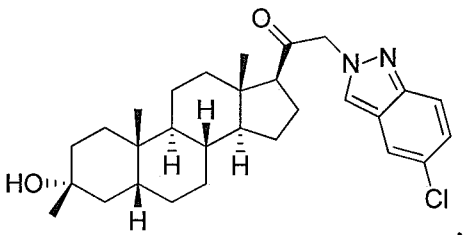
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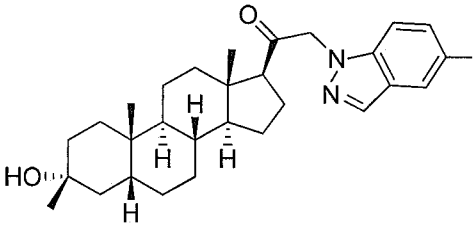
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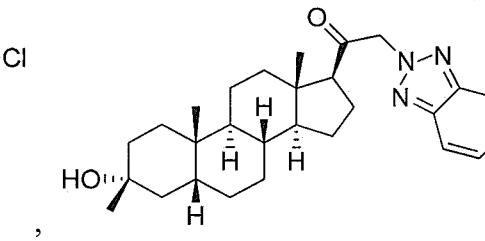
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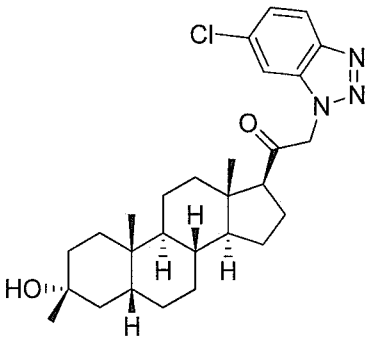
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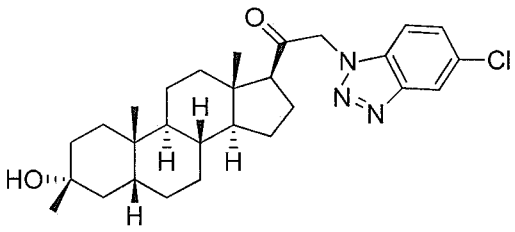
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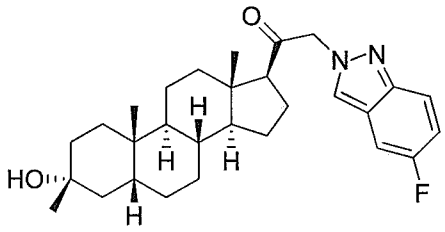
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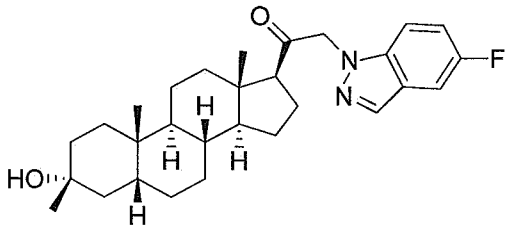
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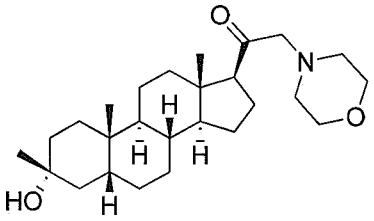
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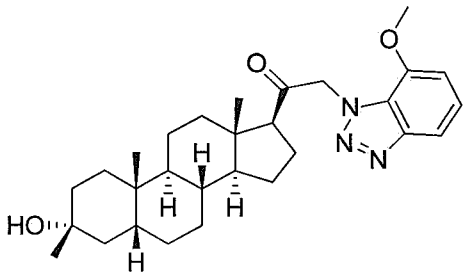
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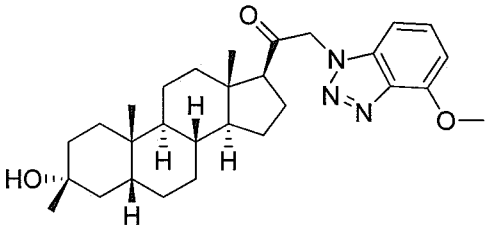
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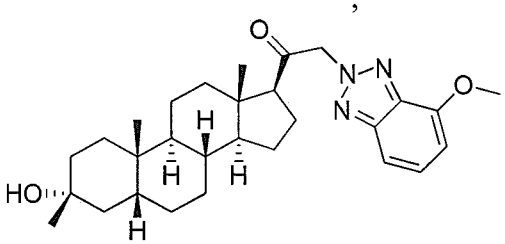
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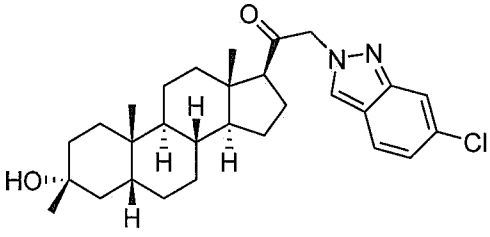
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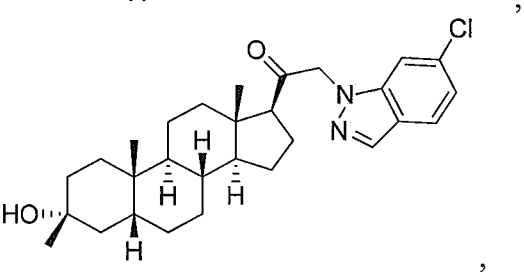
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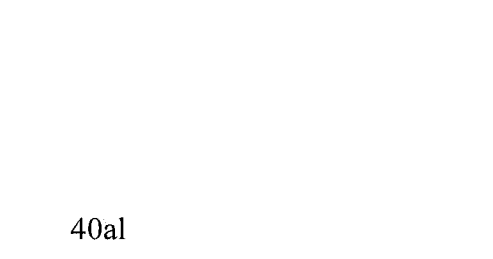
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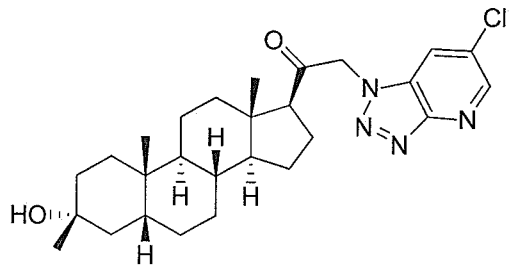
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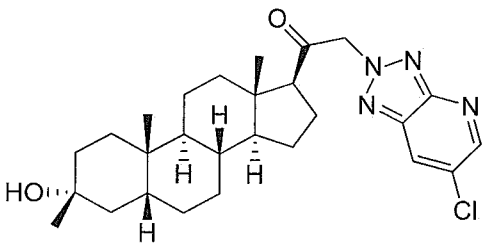
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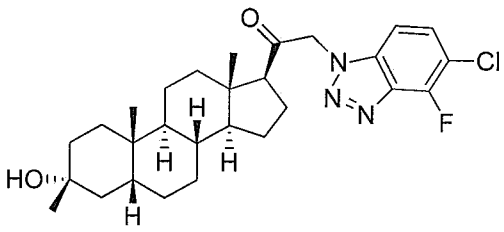
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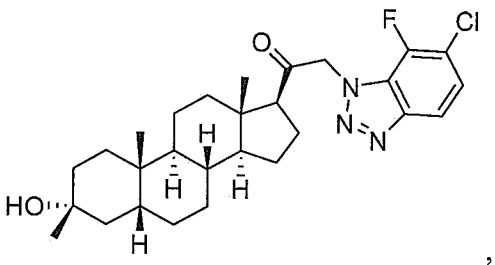
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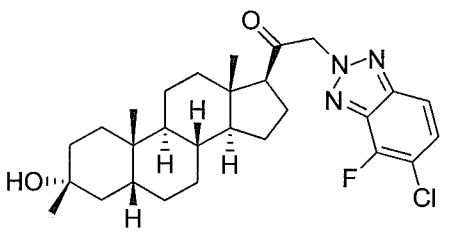
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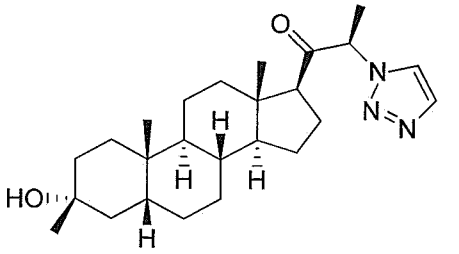
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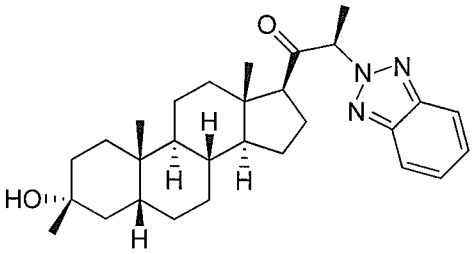
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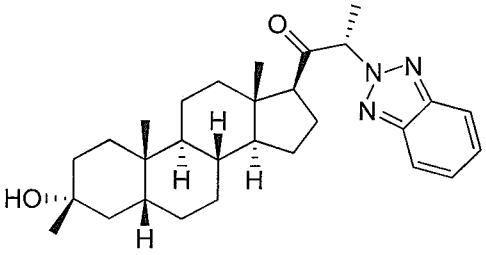
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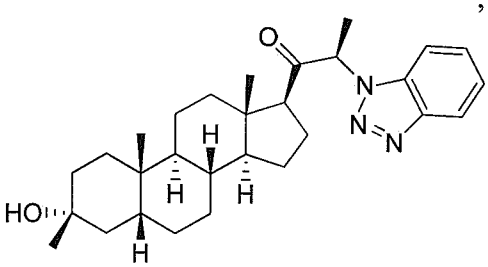
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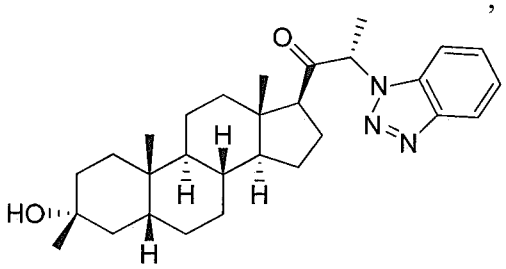
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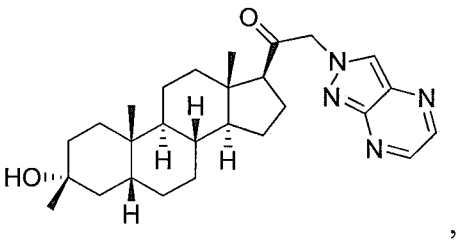
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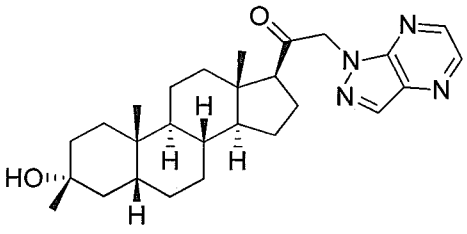
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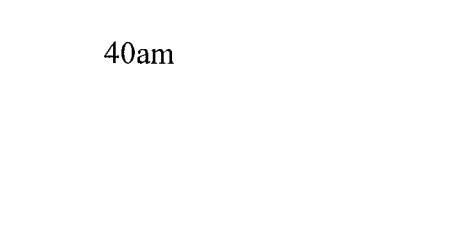
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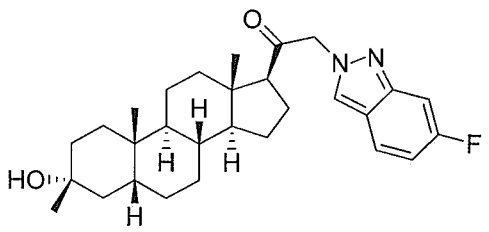
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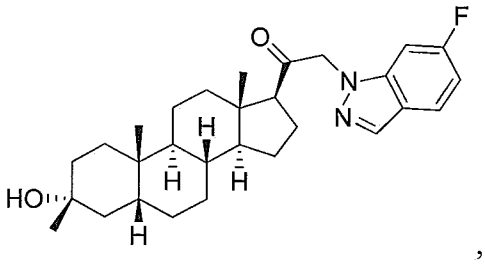
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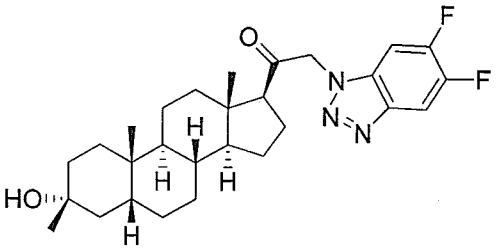
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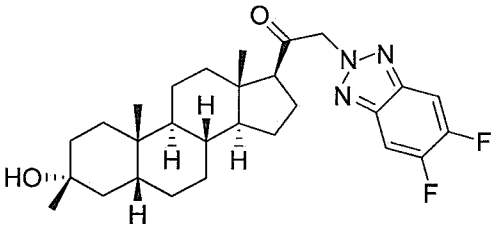
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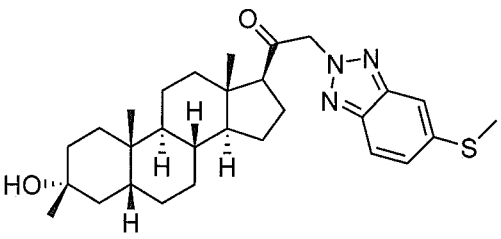
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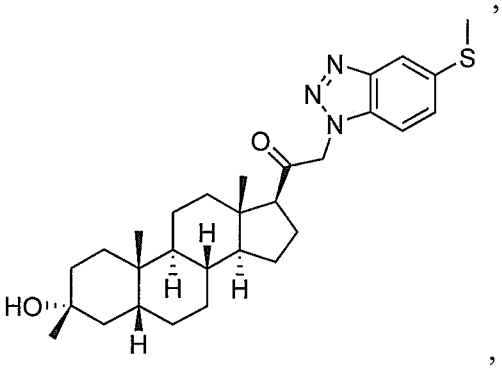
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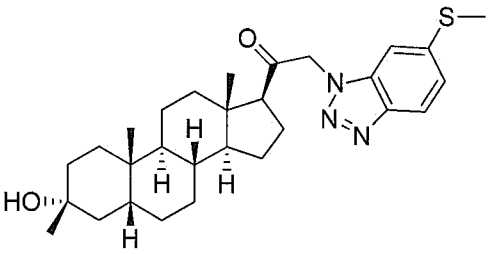
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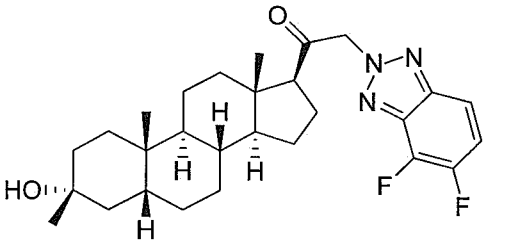
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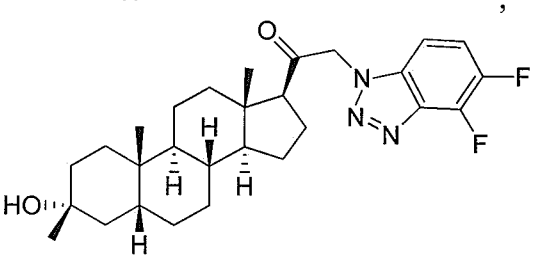
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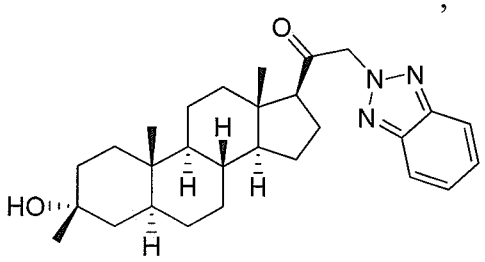
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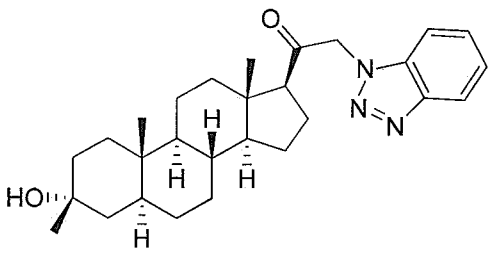
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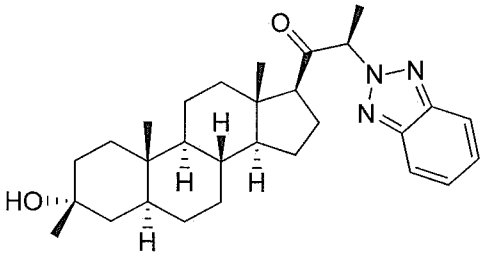
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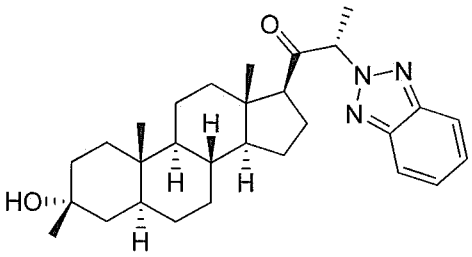
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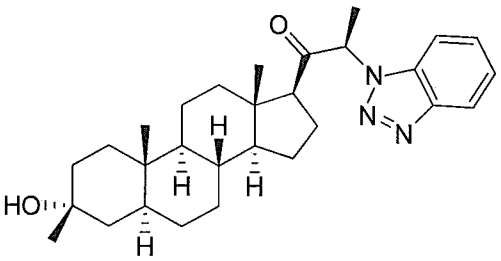
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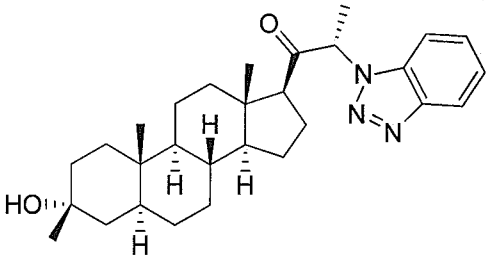
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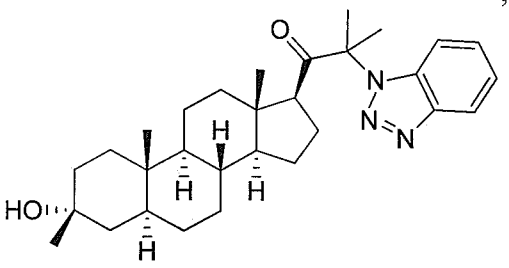
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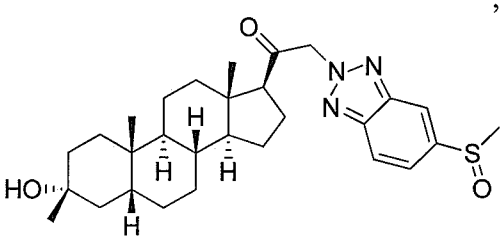
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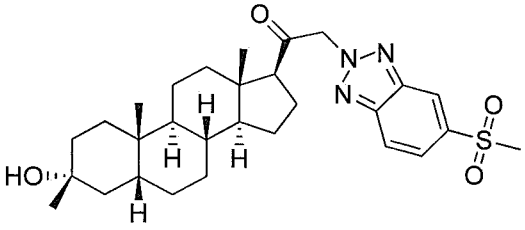
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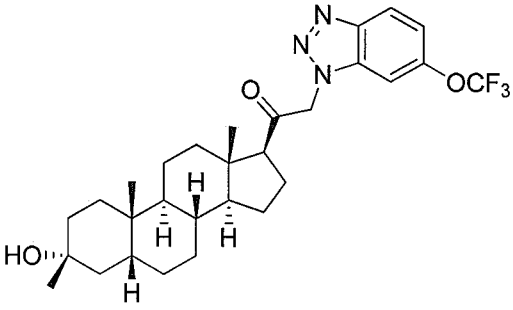
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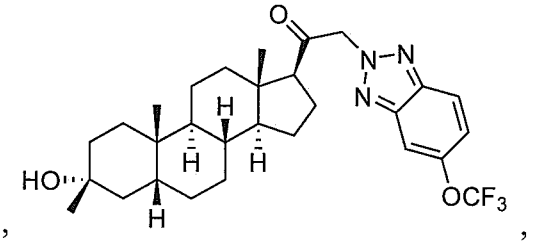

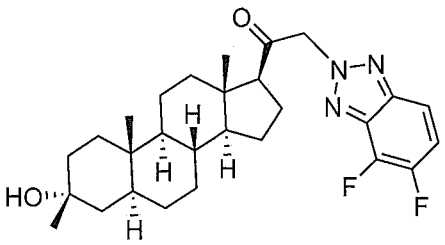
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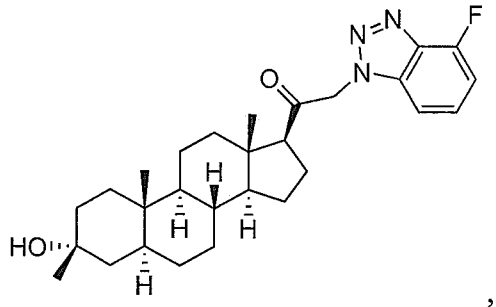
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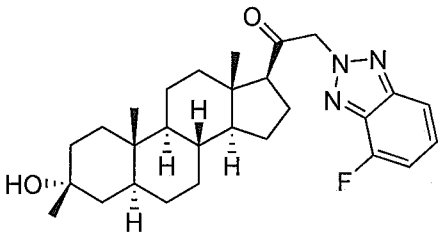
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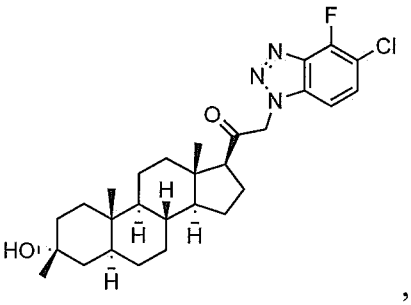
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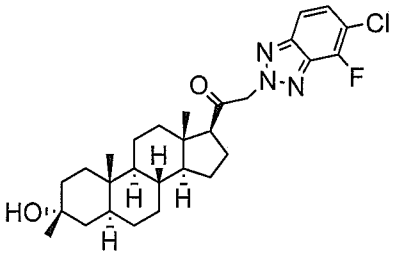
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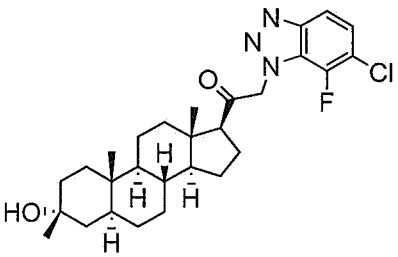
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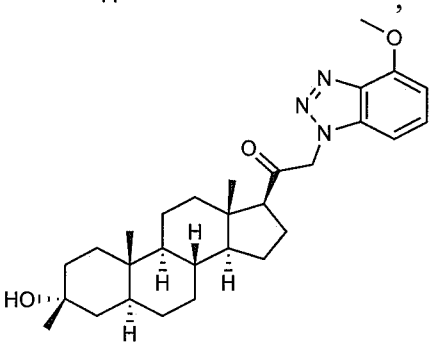
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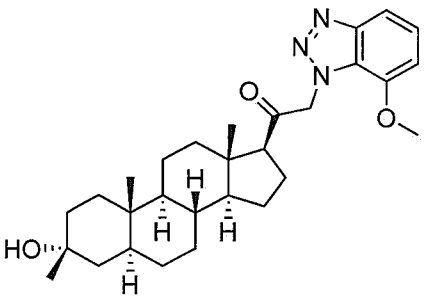
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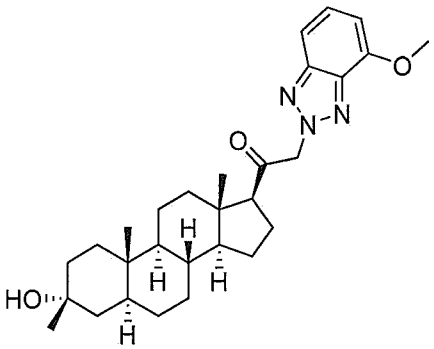
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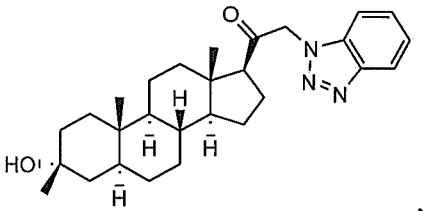
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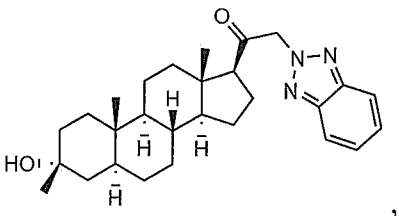
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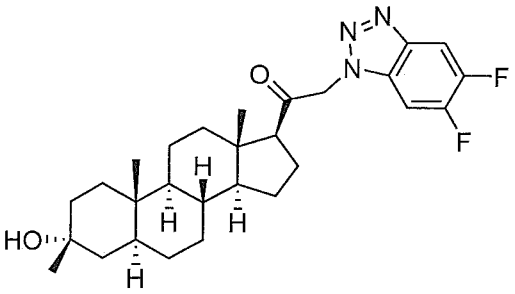
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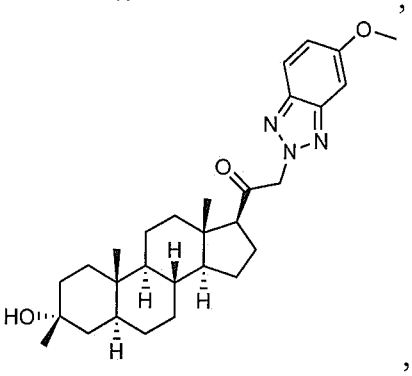
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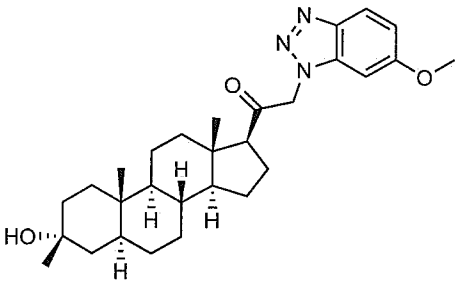
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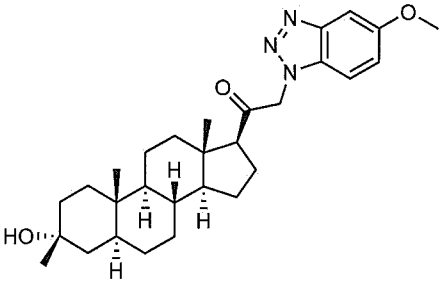
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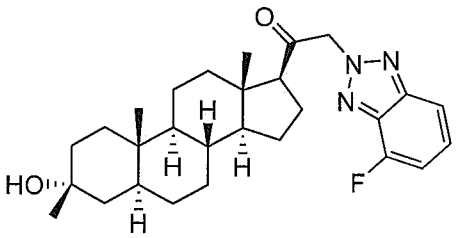
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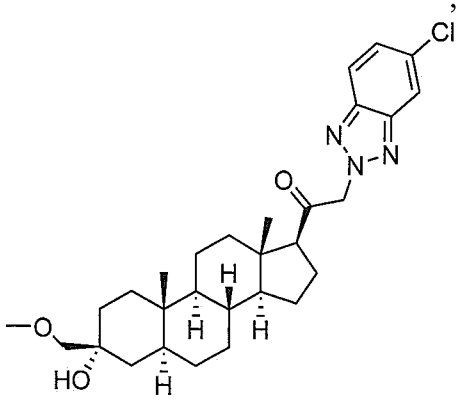
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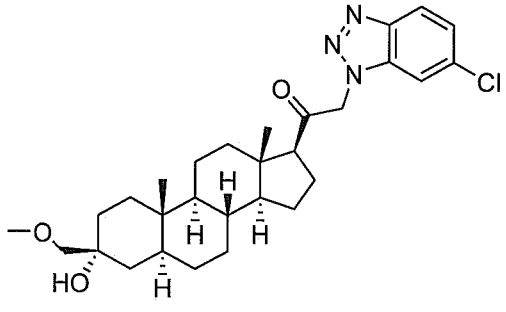

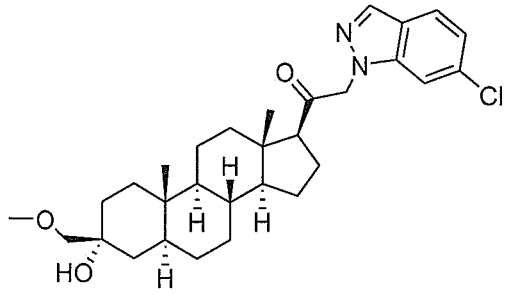
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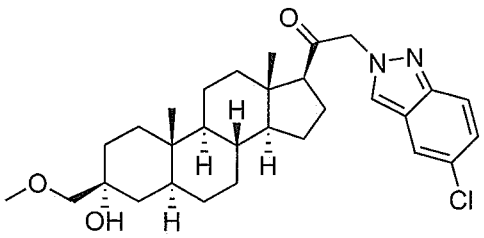
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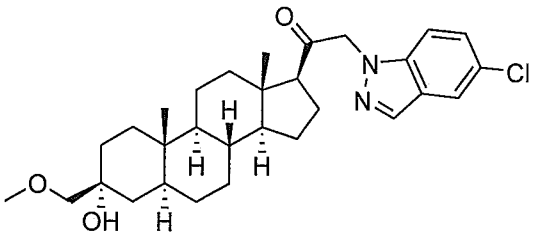
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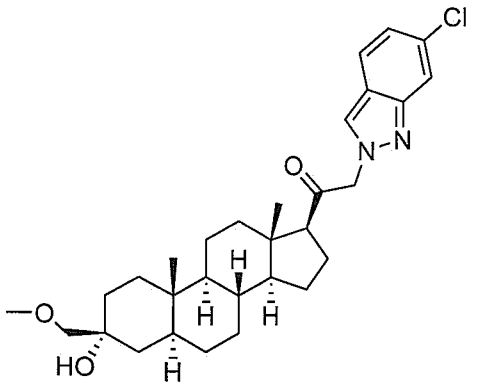
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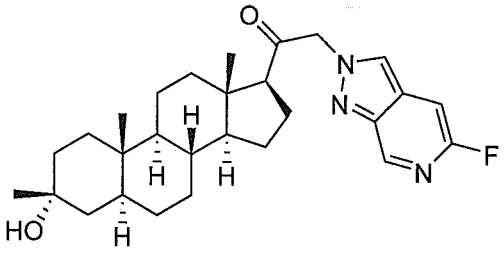
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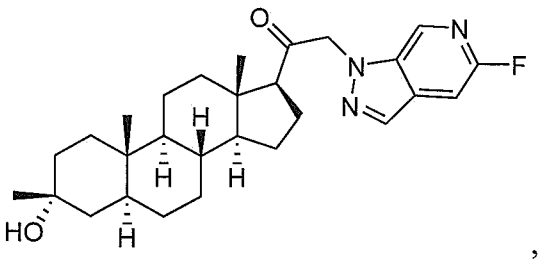
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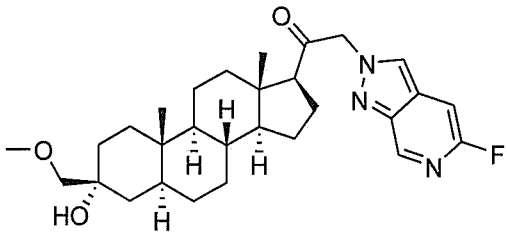
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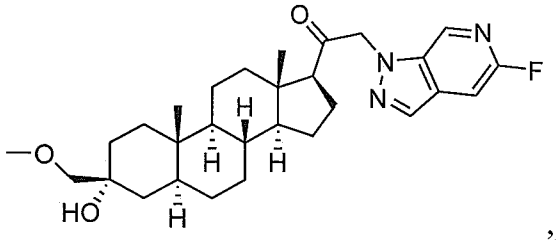
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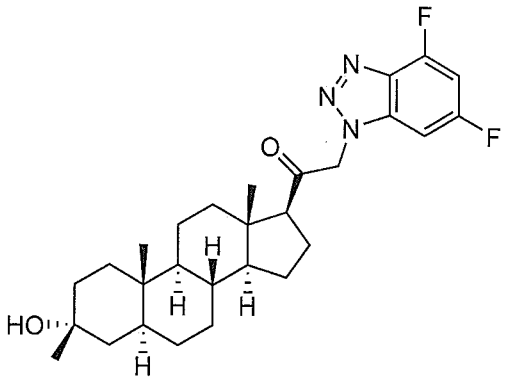
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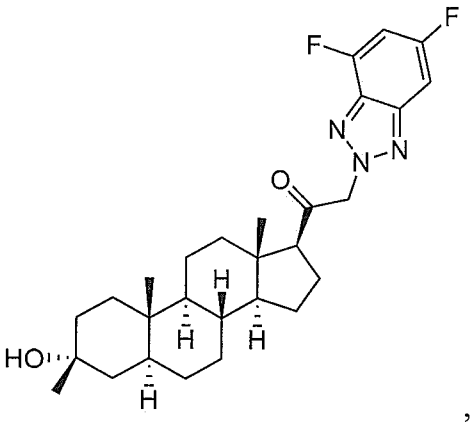
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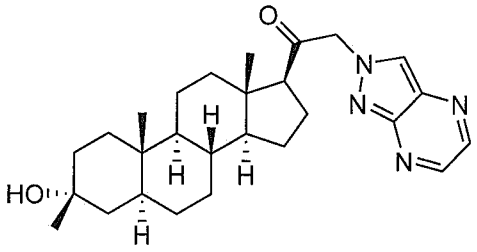
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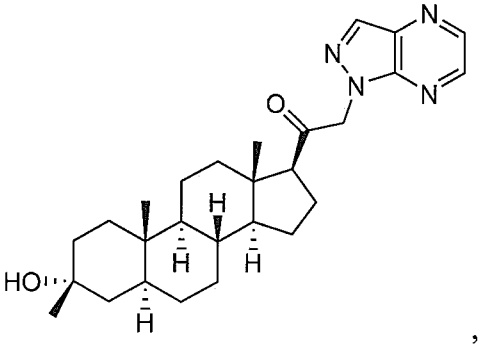
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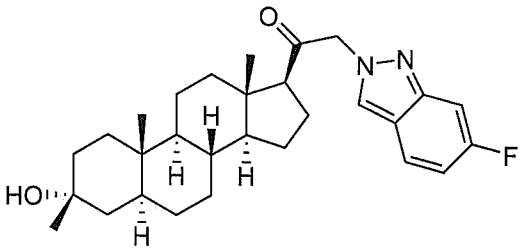
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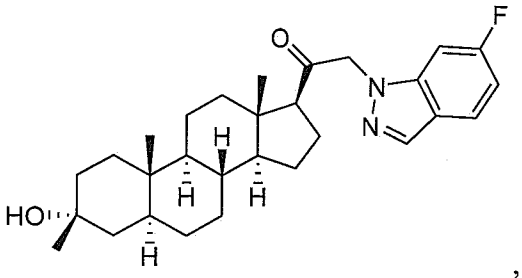
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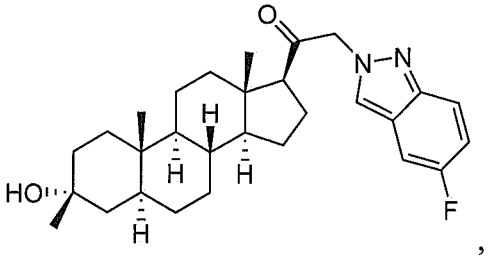
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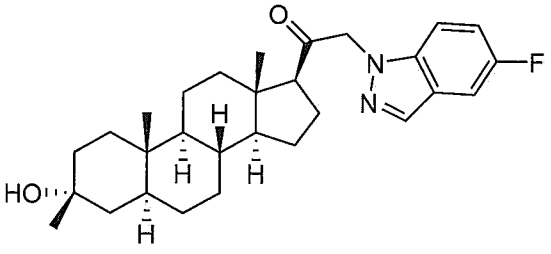
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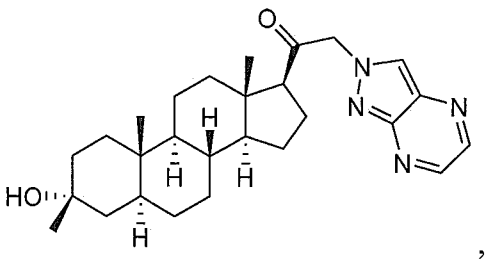
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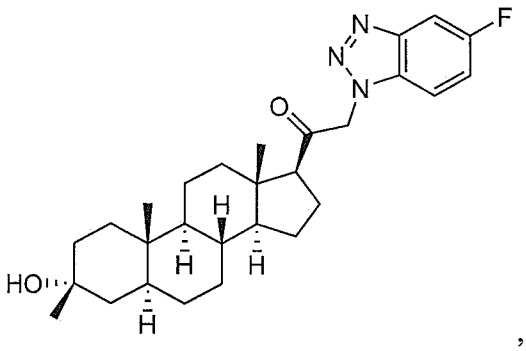
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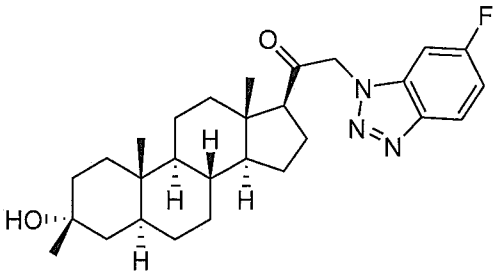
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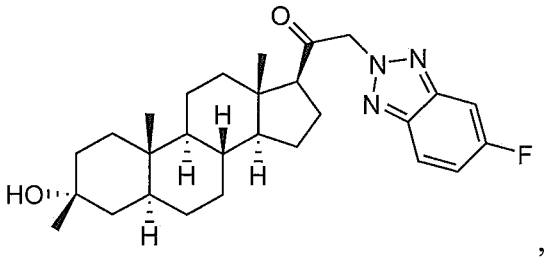
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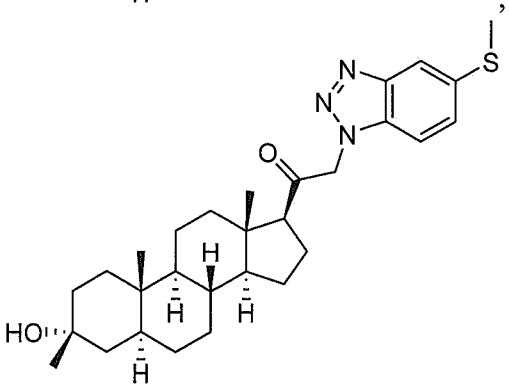
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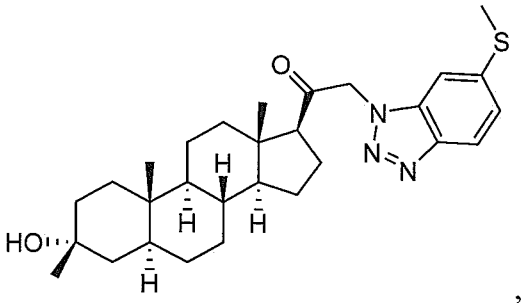
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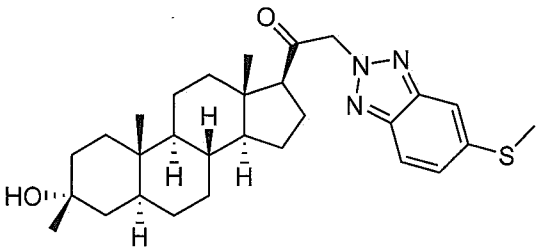
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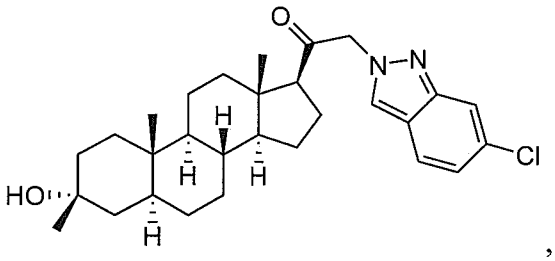
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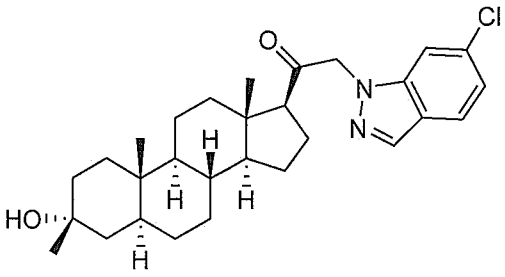
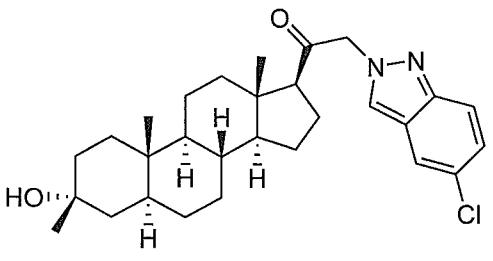
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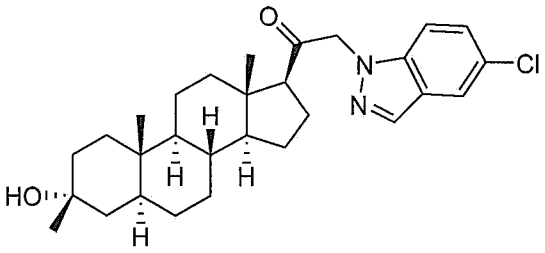
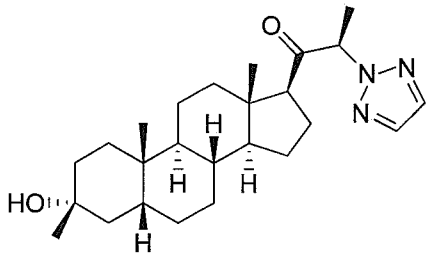
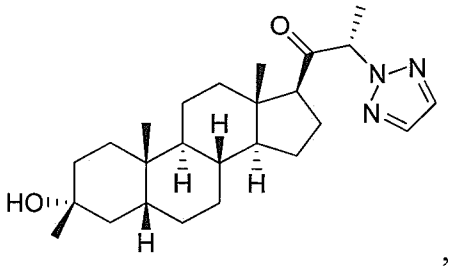
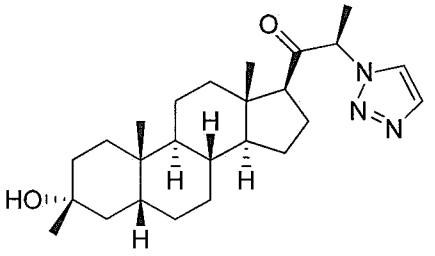
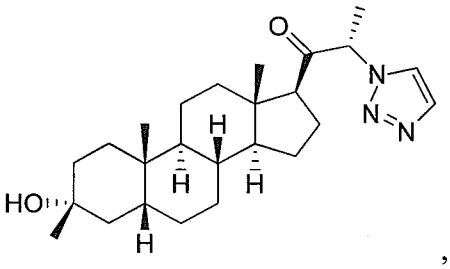
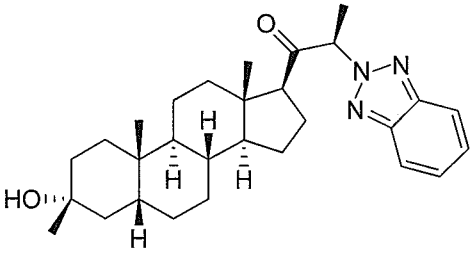
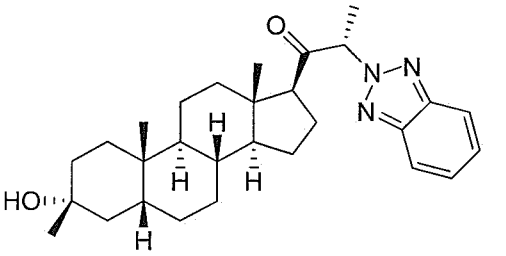
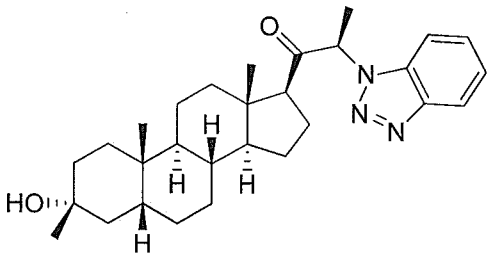


[017g] In another aspect of the present disclosure, there is provided a compound, wherein the compound is: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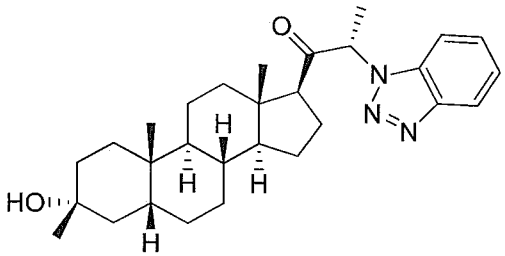
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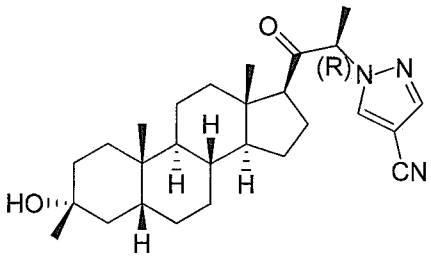
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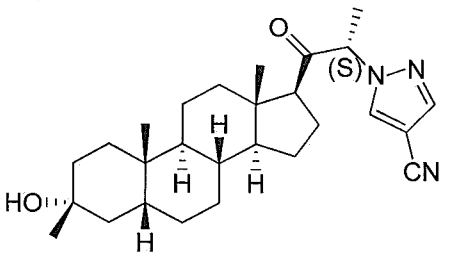
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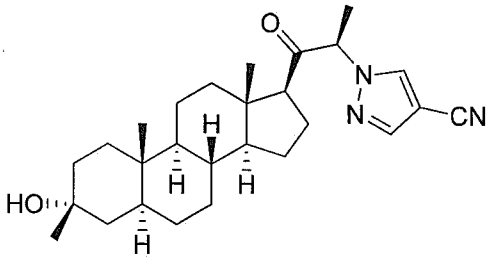
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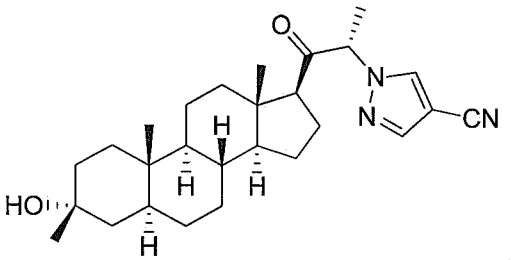
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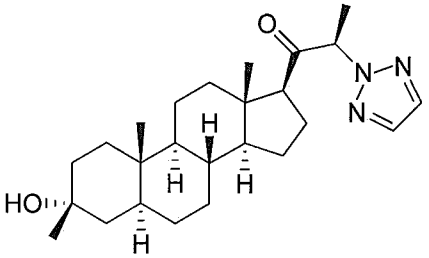
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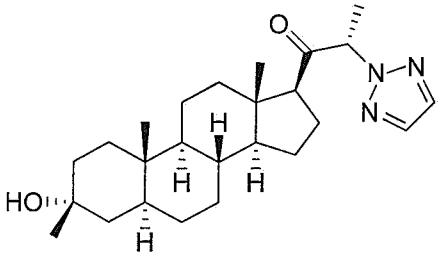
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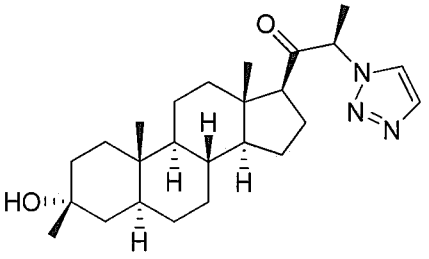
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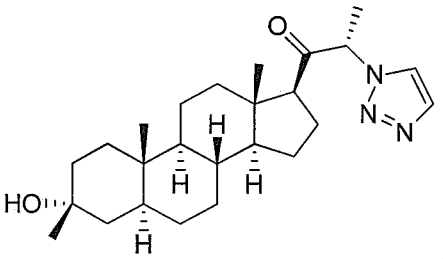
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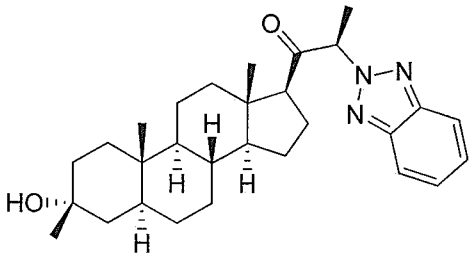
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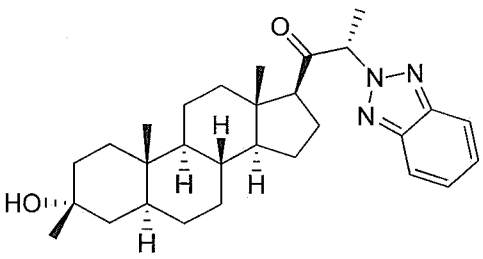
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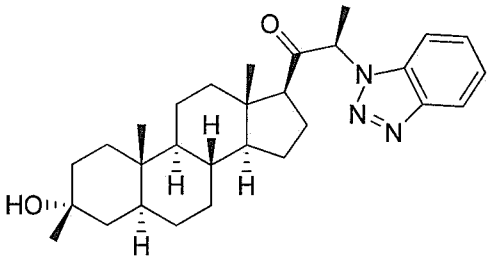
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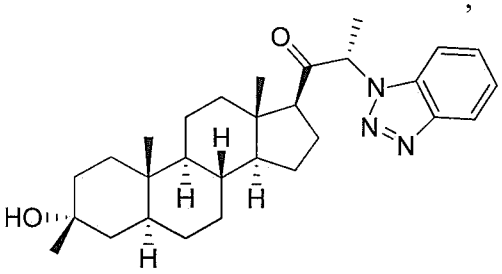
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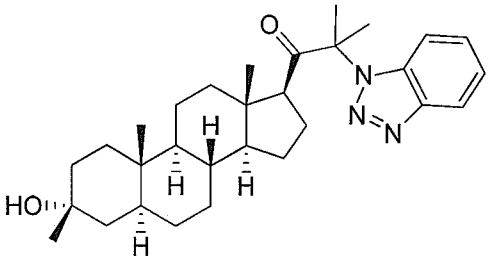
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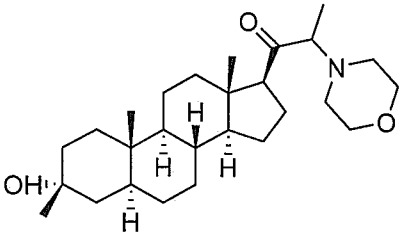
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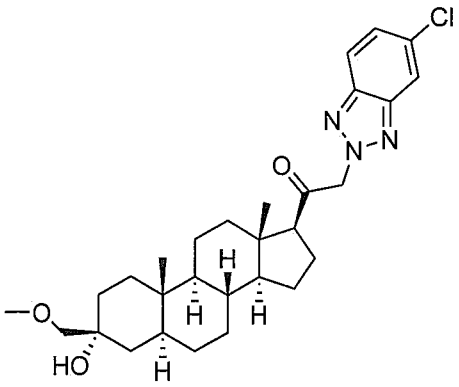
[017h] In a further aspect of the present disclosure, there is provided a compound, wherein the compound is: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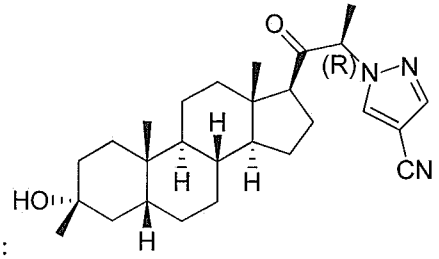
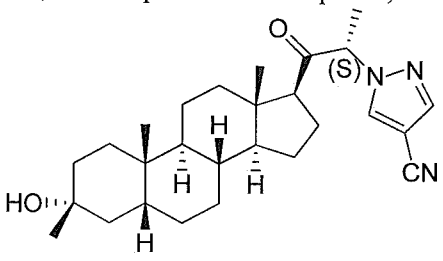
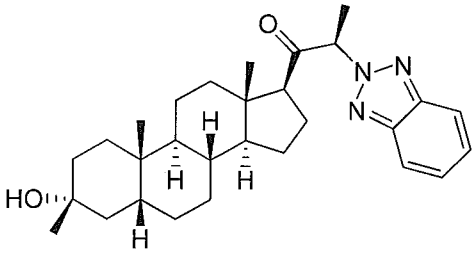
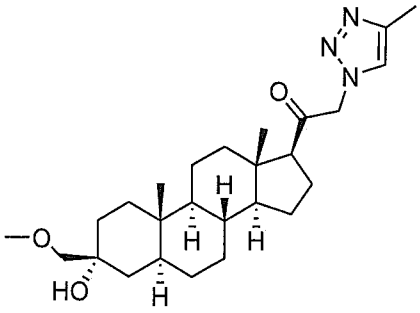
[017i] In another aspect of the present disclosure, there is provided a compound, wherein the compound is:  or 

[017j] In a further aspect of the present disclosure, there is provided a compound, wherein the compound is: 

[017k] In another aspect of the present disclosure, there is provided a compound, wherein the compound is: 

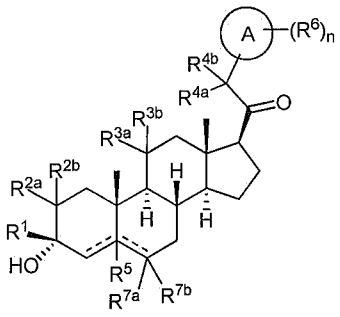
[18] Compounds of the present disclosure as described herein, act, in certain embodiments, as GABA modulators, *e.g.*, effecting the $GABA_A$ receptor in either a positive or negative manner. As modulators of the excitability of the central nervous system (CNS), as mediated by their ability to modulate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

[19] Thus, the present disclosure provides 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 embodiments, 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 embodiments, the compound is administered orally, subcutaneously, intravenously, or

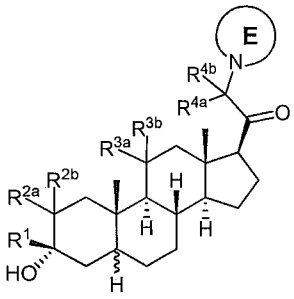
Claims

What is claimed is:

1. A compound of the Formula (**I-a**) or Formula (**II-b**):



(I-a)



(II-b)

or a pharmaceutically acceptable salt thereof;

wherein:

Ring E is heterocyclyl or heteroaryl;

Ring A is nitrogen linked heterocyclyl, or heteroaryl;

R^6 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} carbocylyl, C_{1-6} haloalkyl, halogen, cyano, nitro, OR^{A6}, $C(=O)R^{A6}$, $C(=O)OR^{A6}$, SR^{B6}, $S(=O)R^{B6}$, $S(=O)_2R^{B6}$, $N(R^{C6})(R^{D6})$, $C(=O)N(R^{C6})(R^{D6})$, $N(R^{C6})C(=O)R^{A6}$; and

n is 0, 1, 2, or 3;

wherein R^{A6} is hydrogen or C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} carbocylyl, or C_{1-6} haloalkyl; R^{B6} is C_{1-6} alkyl or C_{3-6} carbocylyl; and each of R^{C6} and R^{D6} is independently

hydrogen, C_{1-6} alkyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl, or R^{C6} and R^{D6} together with the nitrogen atom to which they are attached form a ring (e.g., a 3-6-membered ring (e.g., carbocycyl or heterocyclyl ring));

R^1 is methyl;

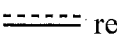
each of R^{2a} and R^{2b} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} carbocylyl, or $-OR^{A2}$, wherein R^{A2} is hydrogen or C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, or C_{3-6} carbocylyl;

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

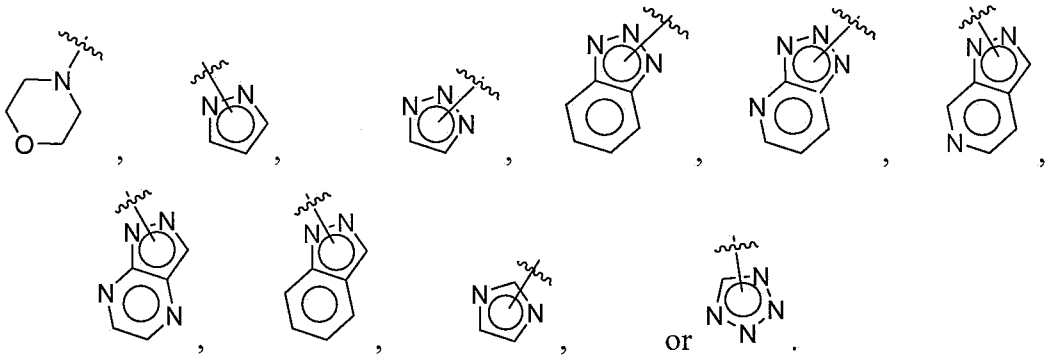
R^{4a} is hydrogen, C_{1-6} alkyl, or $-OR^{A4}$, wherein R^{A4} is hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, or C_{3-6} carbocylyl, and R^{4b} is hydrogen or C_{1-6} alkyl; or R^{4a} and R^{4b} are joined to form an oxo (=O) group; or R^{4a} and R^{4b} together with the carbon atom to which they are attached form a ring (e.g., a 3-6-membered ring (e.g., carbocycyl or heterocyclyl ring);

R^5 is absent or hydrogen;

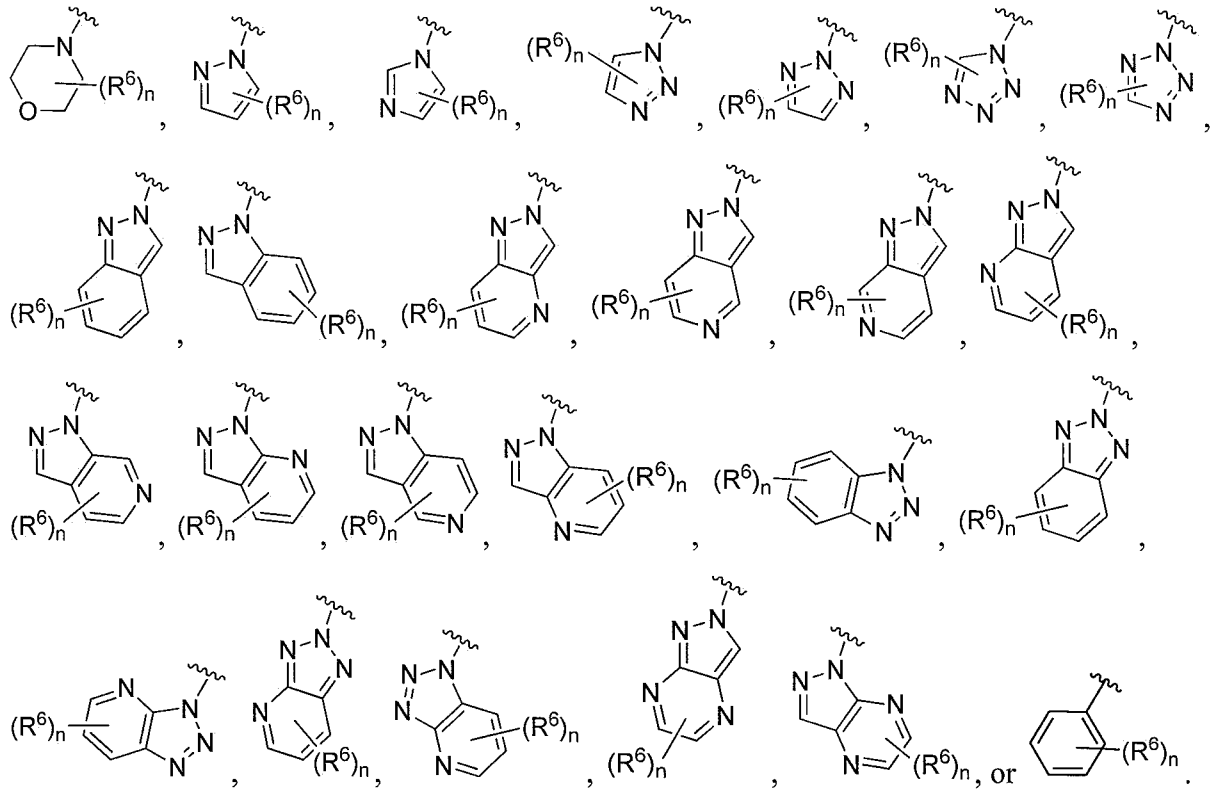
each of R^{7a} and R^{7b} is independently hydrogen or halogen;

 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.

2. The compound of claim 1, wherein E is selected from:



3. The compound of any one of the preceding claims, wherein A is:



4. The compound of any one of claims 1-2, wherein E is a ring comprising at least two nitrogen atoms.

5. The compound of claim 4, wherein 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.

6. The compound of any one of claims 1-5, wherein E is a ring comprising at least three nitrogen atoms.

7. The compound of any one of claims 1-6, wherein E is a ring comprising four nitrogen atoms.

8. The compound of claim 7, wherein at least one of R^2, R^{3a}, R^{4a} or R^{4b} is not hydrogen.

9. The compound of any one of claims 1-8, wherein E is a ring comprising 2, 3 or 4 nitrogen atoms.

10. The compound of any one of claims 1-9, wherein E is a ring selected from pyrazole, triazole, tetrazole, indazole, benzotriazole, triazolopyridine, triazolopyrazine, pyrazolopyrazine, or morpholine.

11. The compound of any one of claims 1-2, wherein A is a 6-membered heterocyclyl ring (e.g., a 6-membered heterocyclyl ring comprising at least two heteroatoms).

12. The compound of any one of claims 1-2, wherein A is a 5-6-membered heterocyclyl ring, and n is 1 or 2.

13. The compound of claim 1, wherein E is morpholine.

14. The compound of any one of the preceding claims, wherein R^2 is hydrogen, $-OR^{A2}$, wherein R^{A2} is hydrogen, or substituted or unsubstituted C_{1-6} alkyl (e.g., methyl, ethyl).

15. The compound of any one of the preceding claims, wherein R^{3a} is $-OR^{A3}$, wherein R^{A3} is hydrogen, or substituted or unsubstituted C_{1-6} alkyl (e.g., methyl).

16. The compound of claim 1, wherein R^{3a} and R^{3a} are joined to form an oxo (=O) group.

17. The compound of any one of the preceding claims, wherein R^{4a} is hydrogen, substituted C_{1-6} alkyl, or unsubstituted C_{1-6} alkyl (e.g., methyl).

18. The compound of any one of the preceding claims, wherein R^{4b} is hydrogen, or substituted C_{1-6} alkyl, or unsubstituted C_{1-6} alkyl (e.g., methyl).

19. The compound of claim 1, wherein R^{4a} is hydrogen, and R^{4b} is substituted C_{1-6} alkyl or unsubstituted C_{1-6} alkyl (e.g., methyl).

20. The compound of any one of the preceding claims, wherein each of R^{4a} and R^{4a} is independently unsubstituted C_{1-6} alkyl (e.g., methyl).

21. The compound of any one of the preceding claims, wherein each of R^{4a} and R^{4a} is independently hydrogen.

22. The compound of any one of the preceding claims, wherein R^5 is hydrogen.

23. The compound of any one of the preceding claims, wherein n is 0.

24. The compound of any one of the preceding claims, wherein 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.

25. The compound of any one of the preceding claims, wherein n is 1 and R^6 is halogen (e.g., -F, -Br, -Cl) or cyano.

26. The compound of any one of the preceding claims, wherein n is 1 and R^6 is substituted or unsubstituted C_{1-6} alkyl (e.g., methyl).

27. The compound of any one of the preceding claims, wherein 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., $-CF_3$).

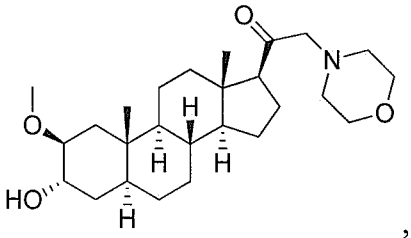
28. The compound of any one of the preceding claims, wherein n is 1 and R^6 is SR^{B6}, $-S(=O)R^{B6}$, or $S(=O)_2R^{B6}$, wherein R^{B6} is substituted or unsubstituted C_{1-6} alkyl (e.g., methyl).

29. The compound of any one of the preceding claims, wherein 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.

30. The compound of any one of the preceding claims, wherein n is 2 and R^6 is independently selected from halogen (e.g., -F, -Br, -Cl).

31. The compound of any one of the preceding claims, wherein n is 2 and one of R^6 is fluorine.

32. A compound wherein the compound is: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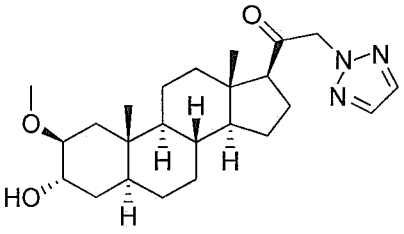
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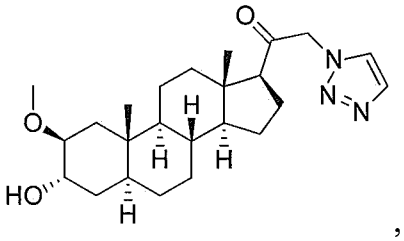
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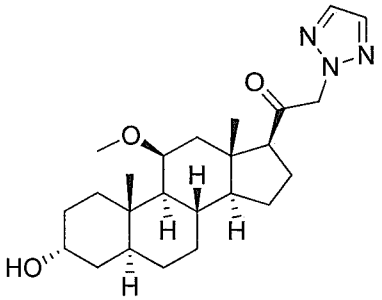
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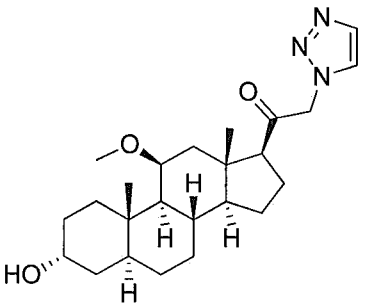
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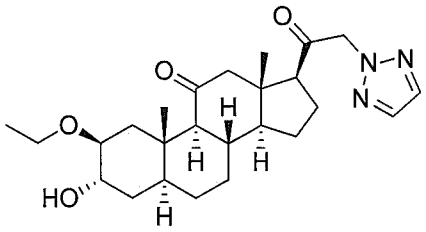
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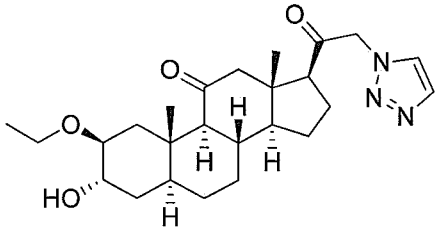
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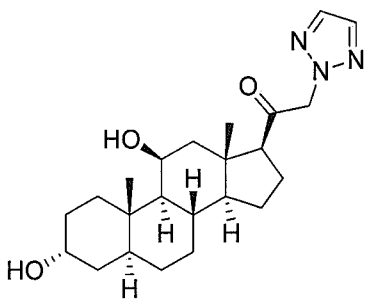
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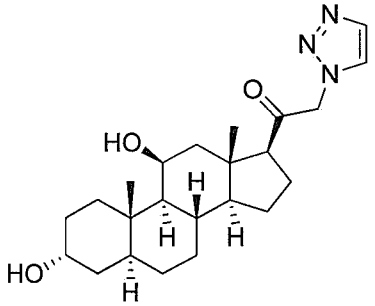
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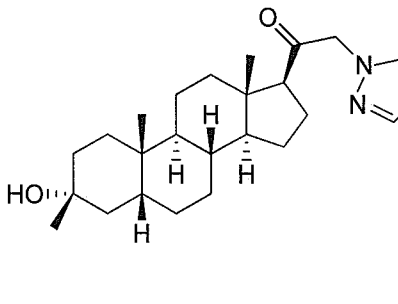
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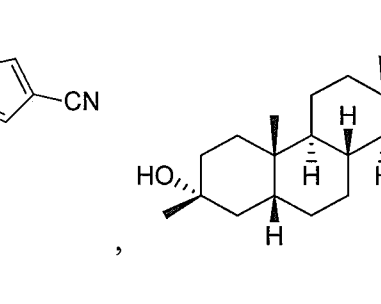
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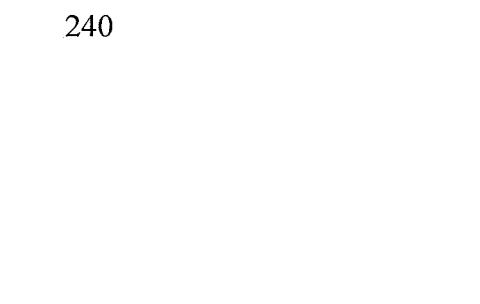
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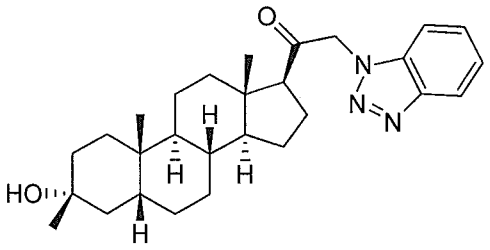
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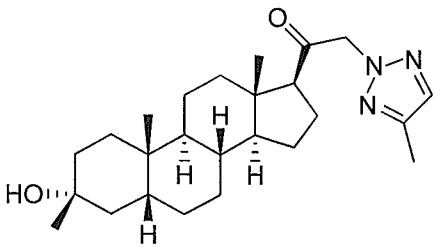
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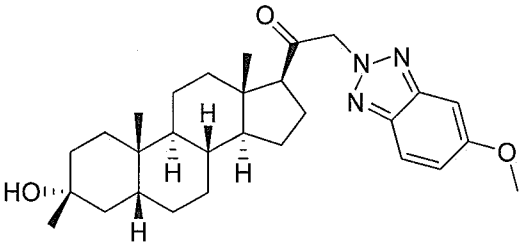
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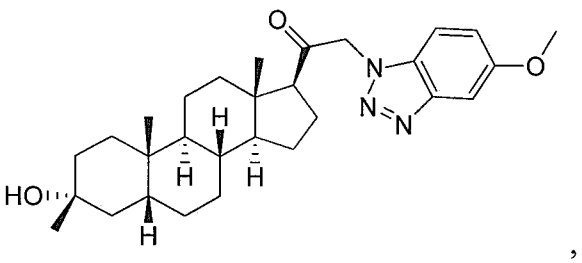
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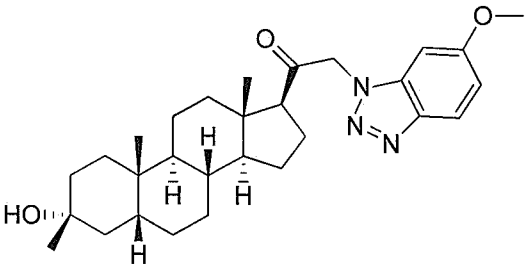
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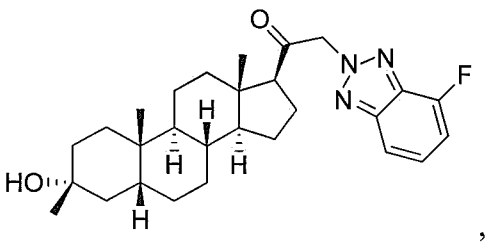
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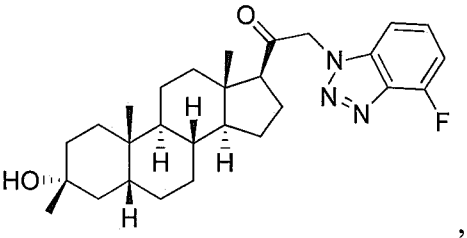
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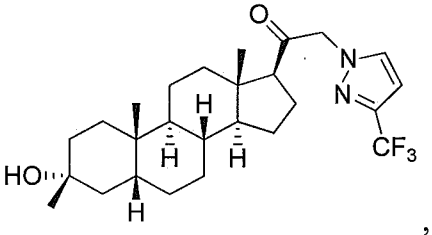
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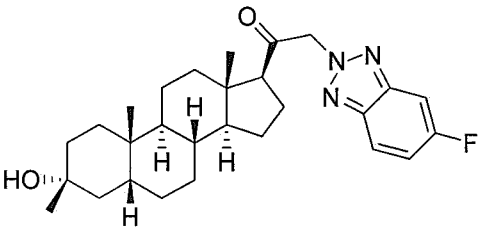
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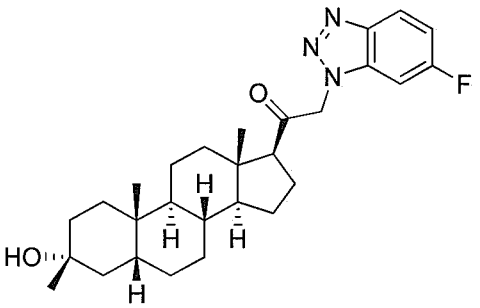
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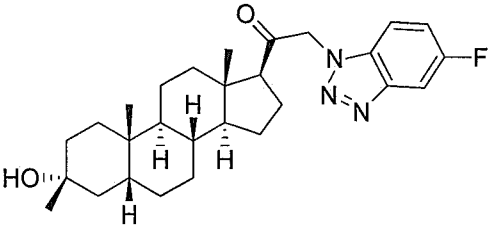
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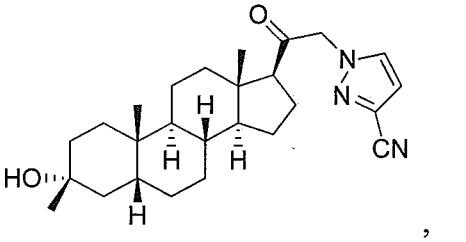
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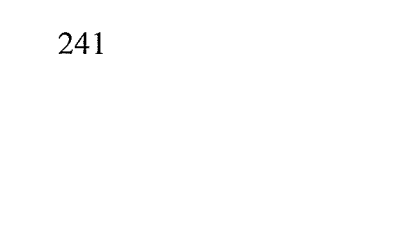
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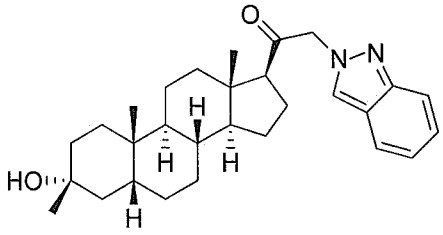
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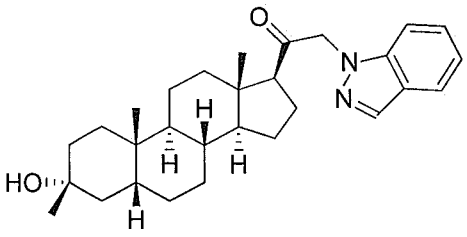
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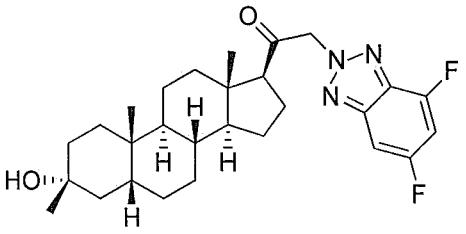
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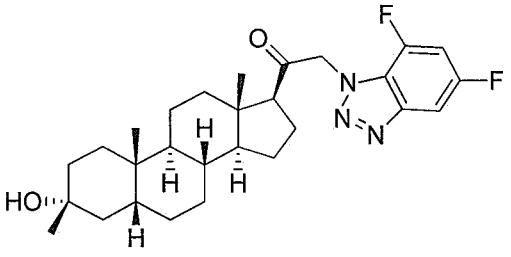
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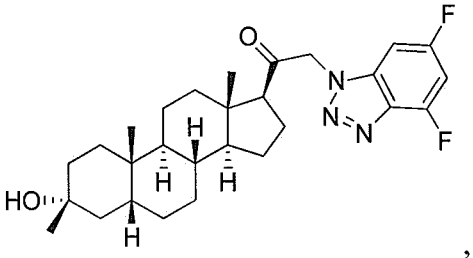
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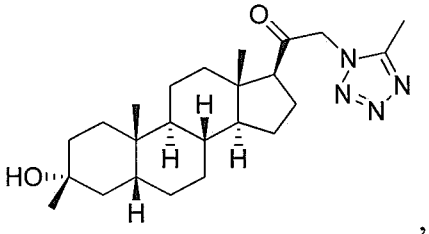
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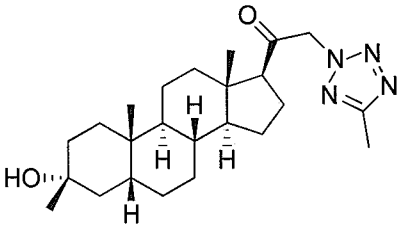
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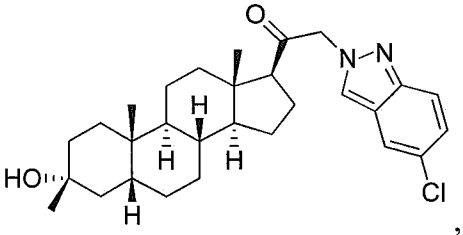
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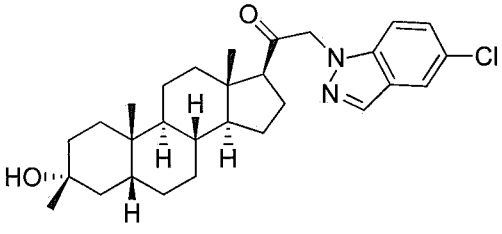
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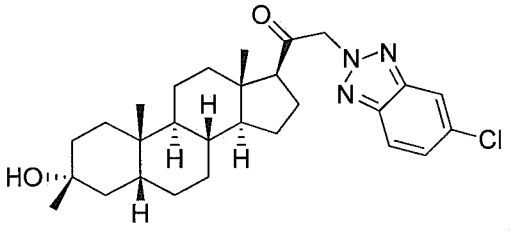
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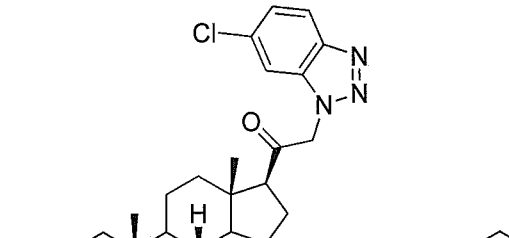
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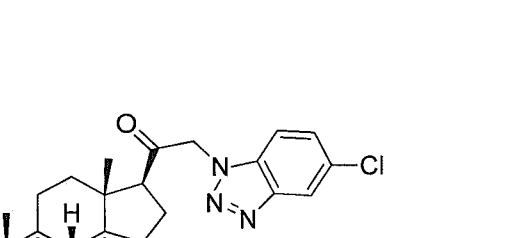
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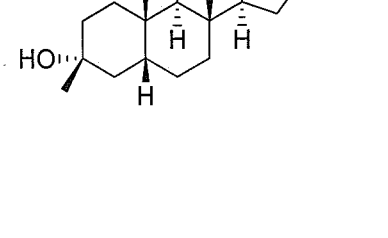
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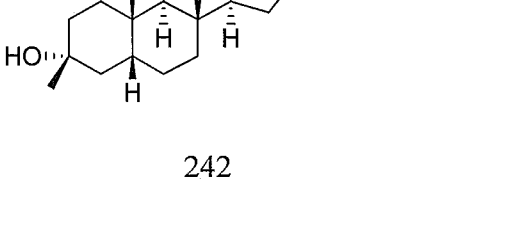
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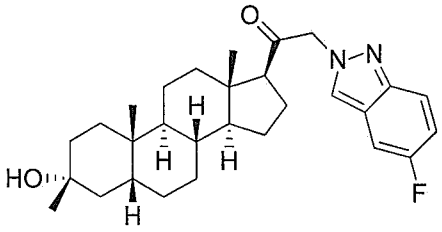
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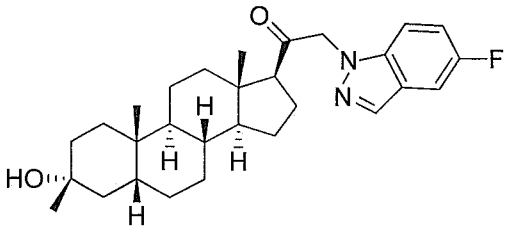
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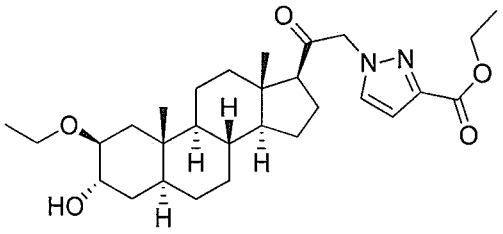
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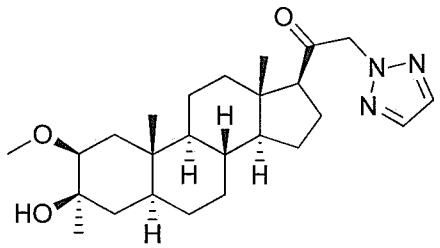
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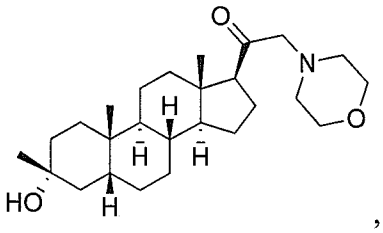
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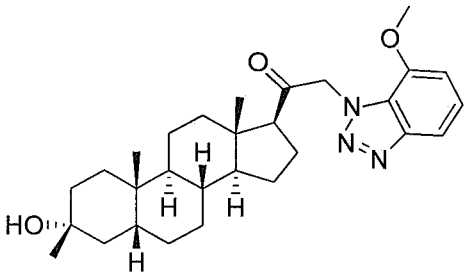
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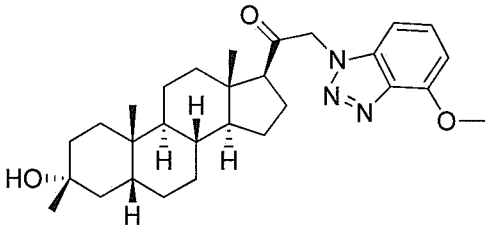
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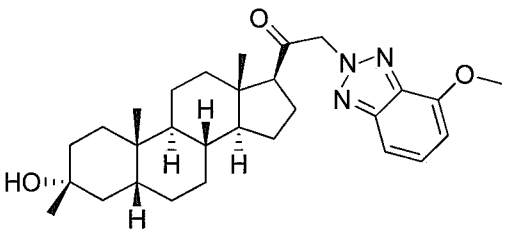
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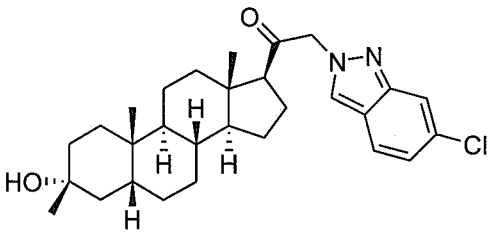
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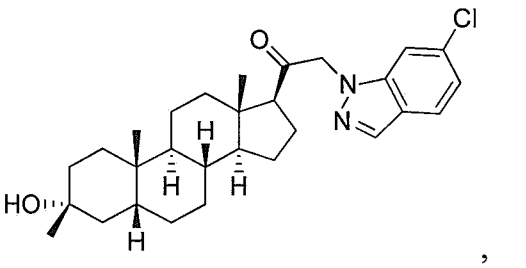
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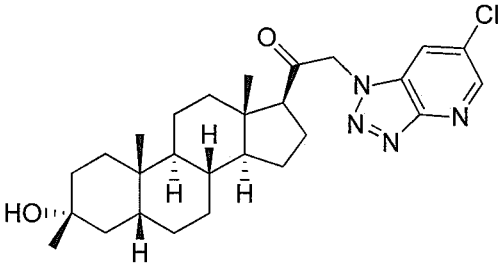
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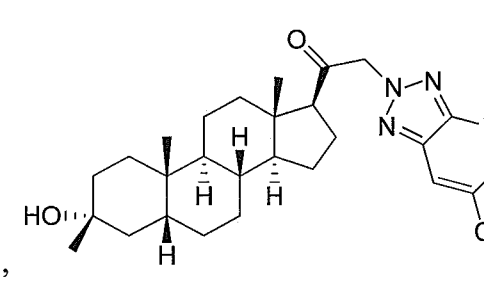
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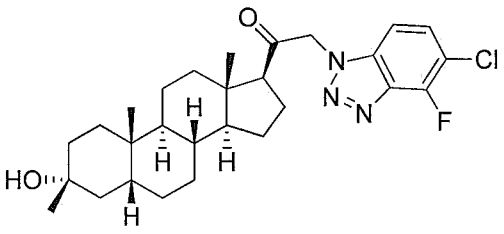
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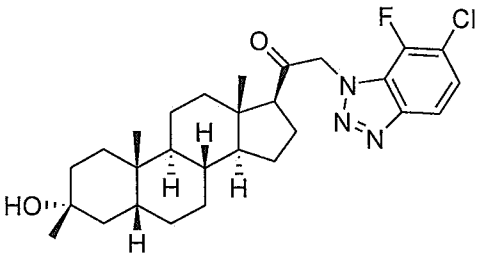
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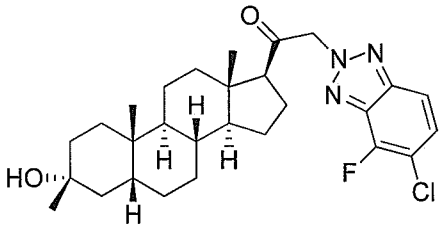
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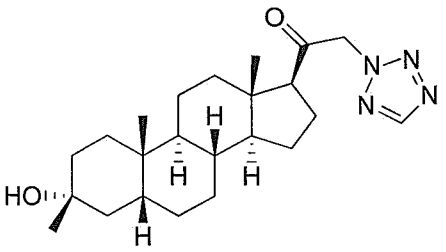
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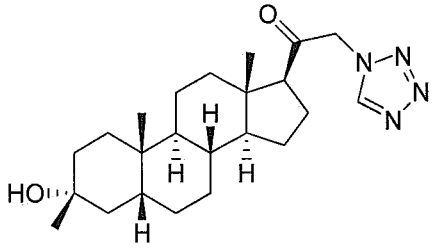
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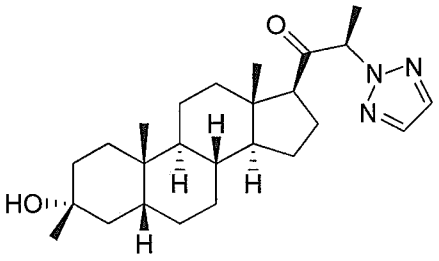
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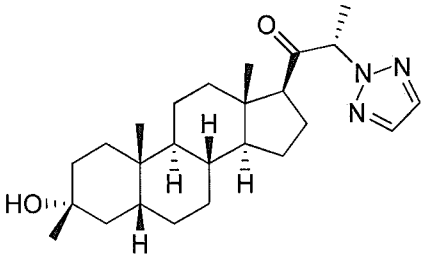
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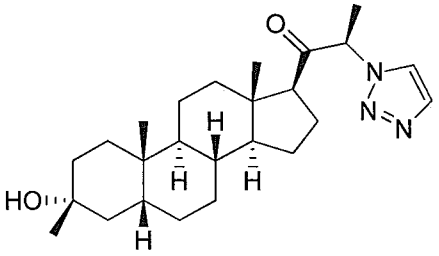
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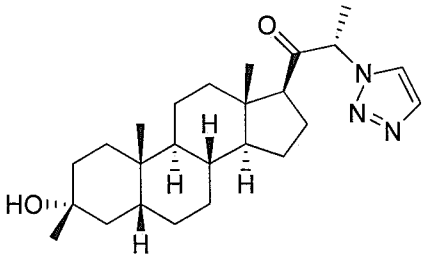
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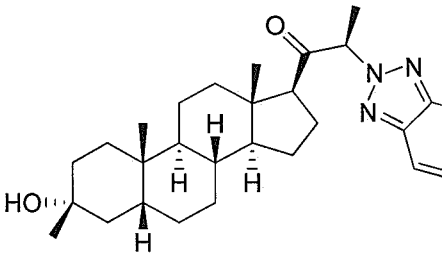
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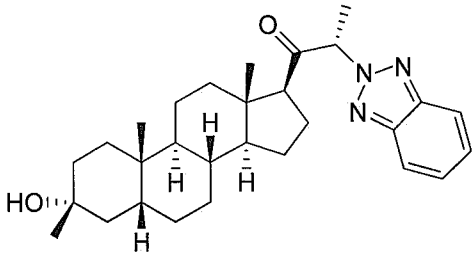
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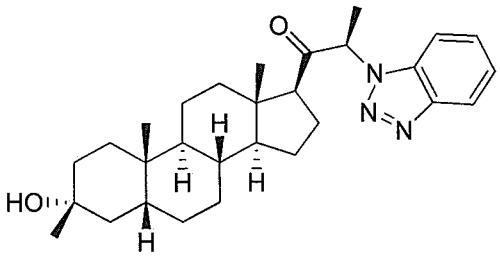
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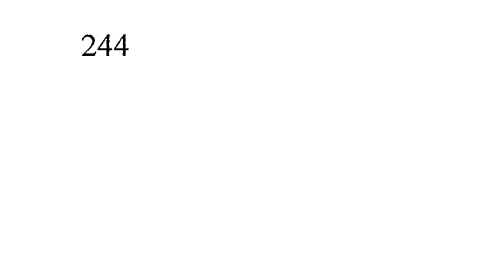
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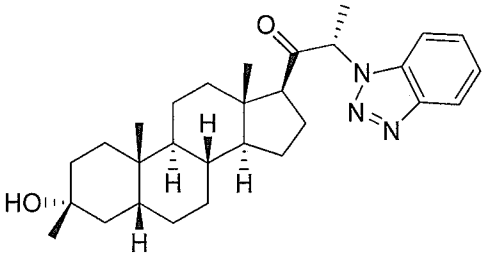
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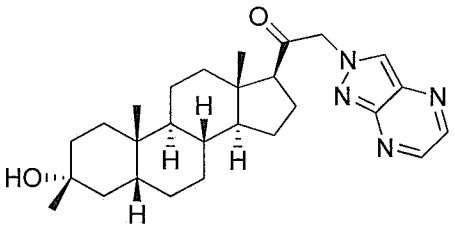
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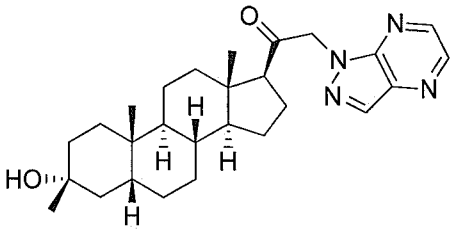
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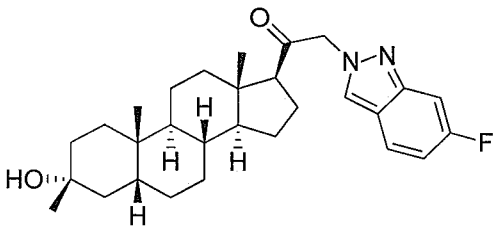
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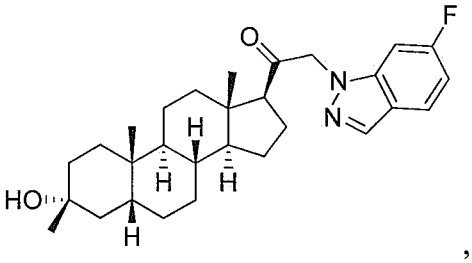
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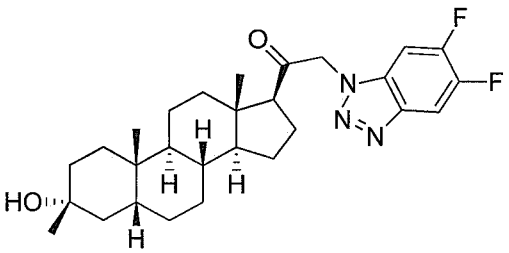
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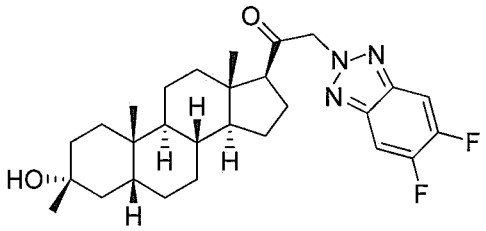
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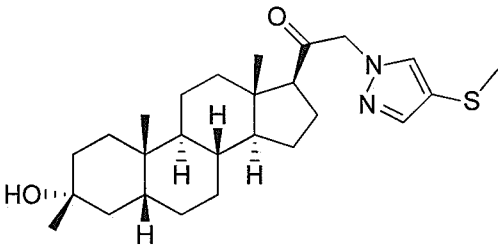
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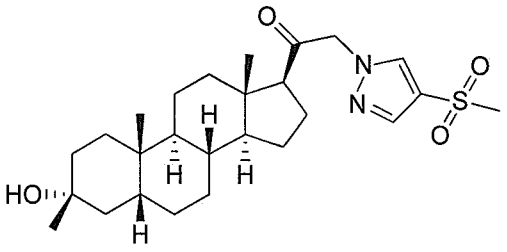
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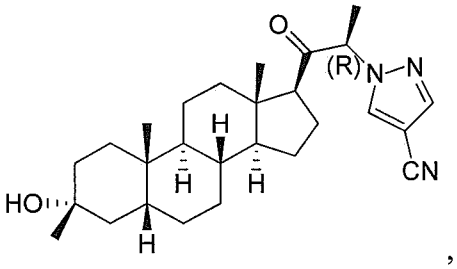
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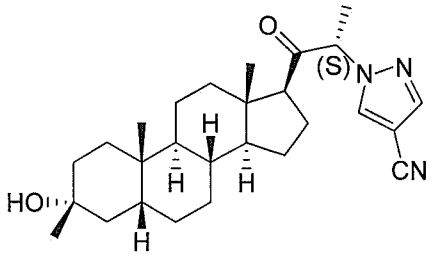
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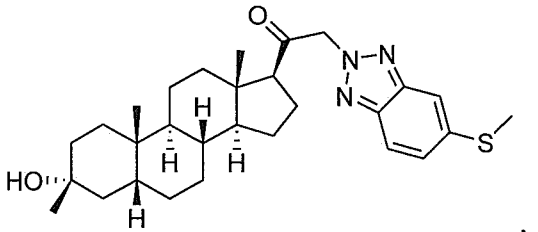
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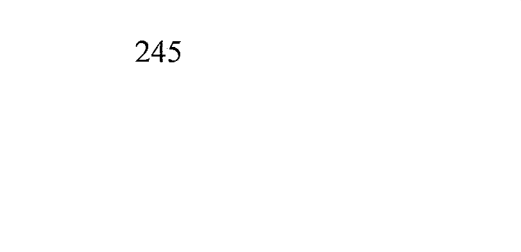
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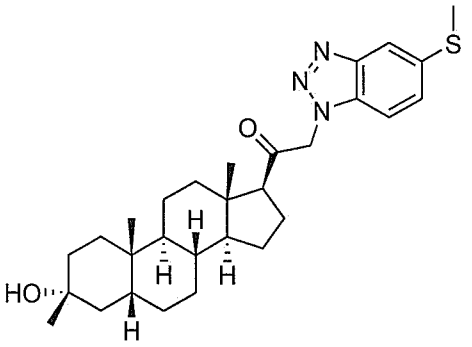
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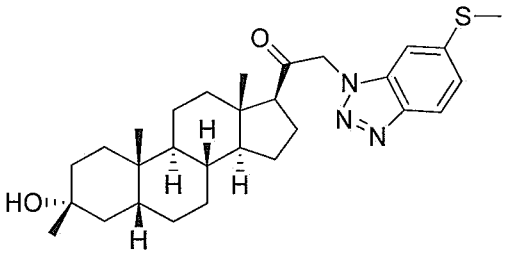
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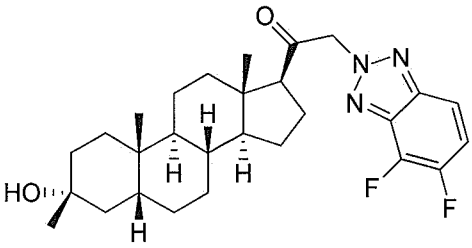
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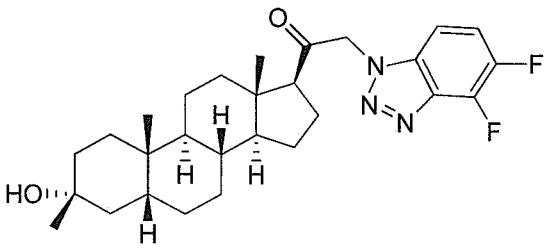
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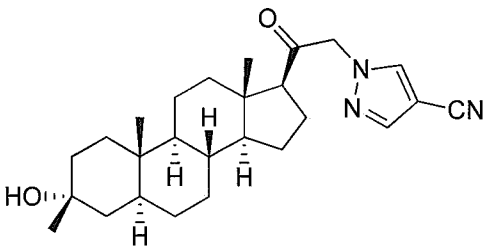
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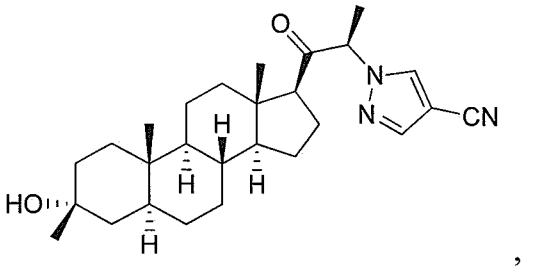
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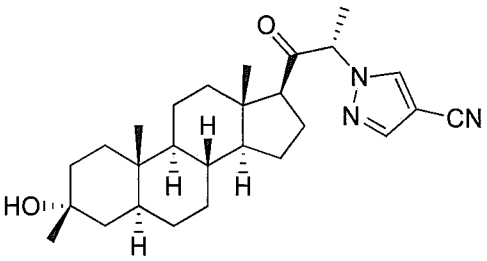
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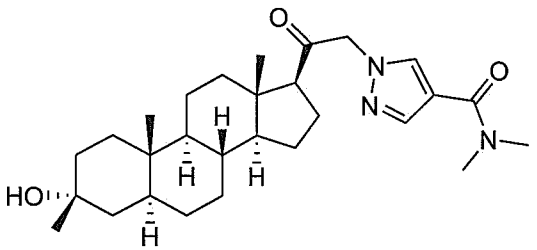
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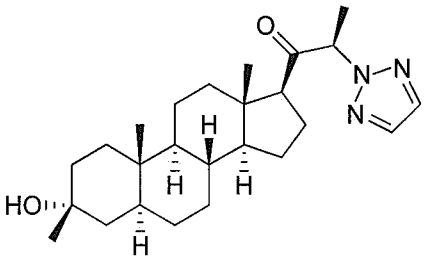
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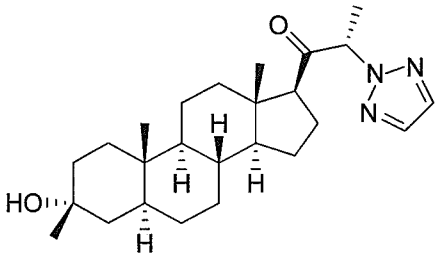
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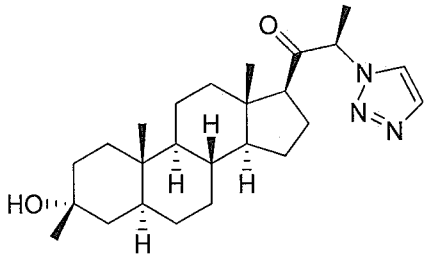
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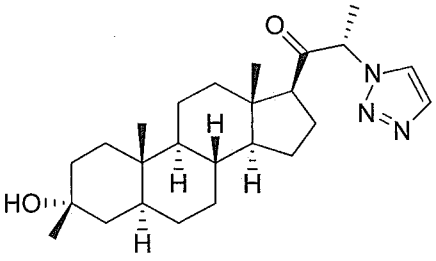
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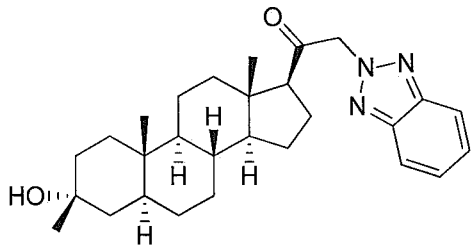
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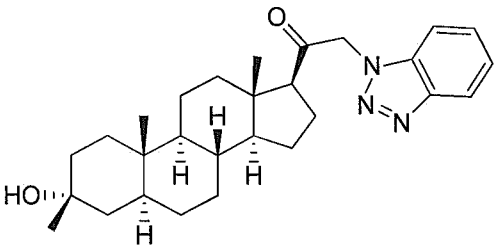
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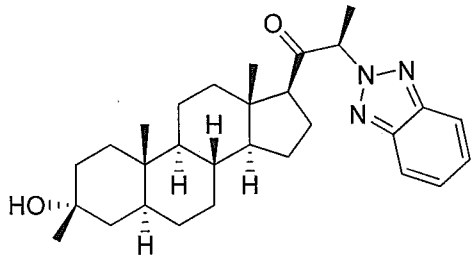
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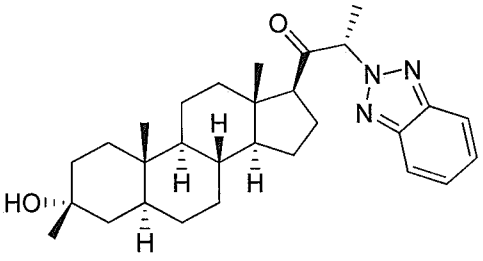
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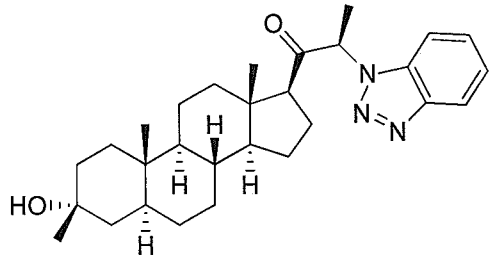
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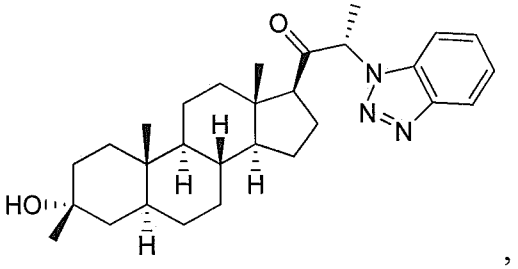
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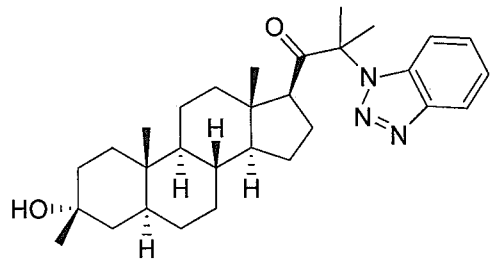
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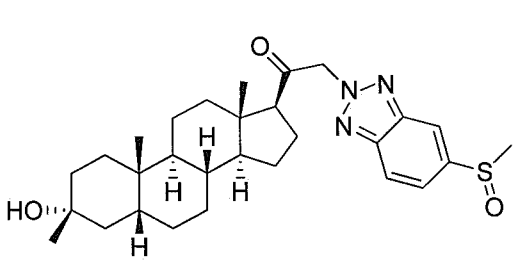
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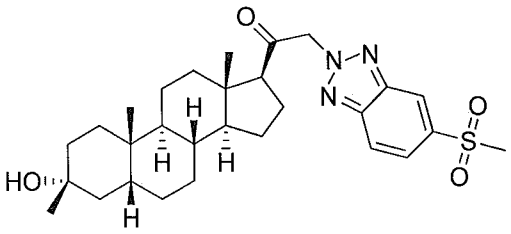
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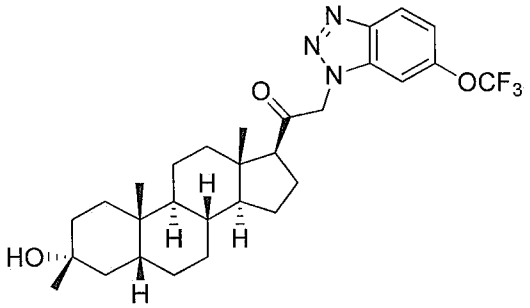
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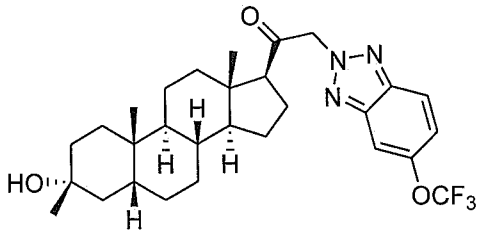
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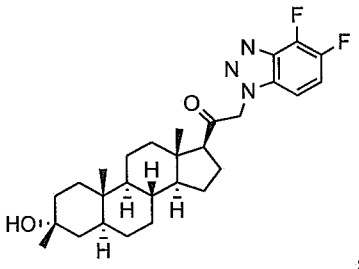
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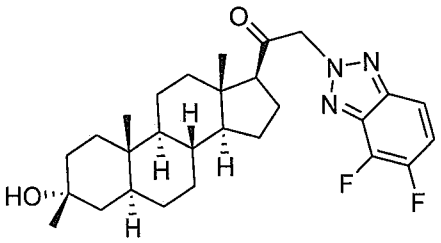
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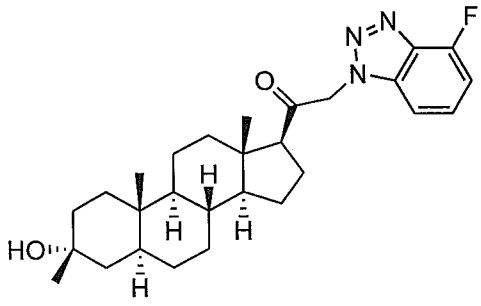
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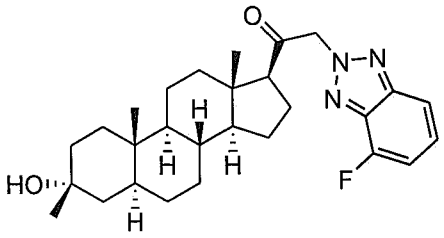
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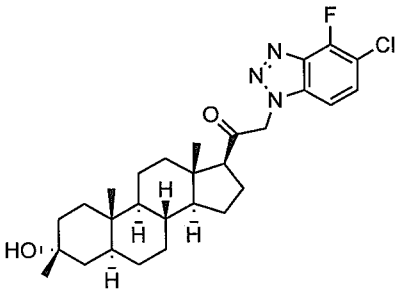
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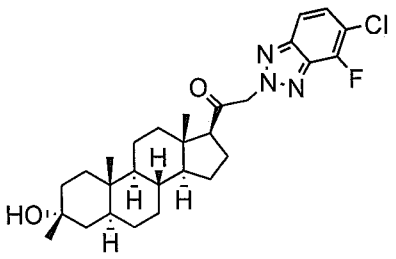
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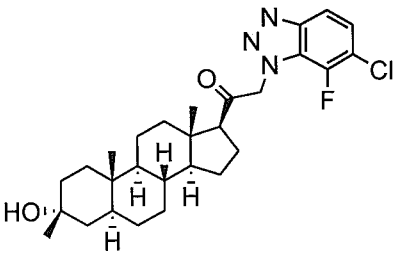
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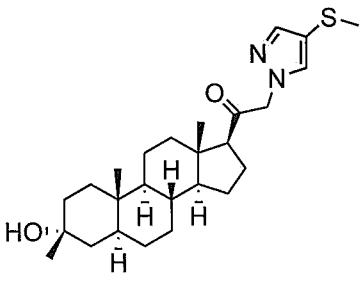
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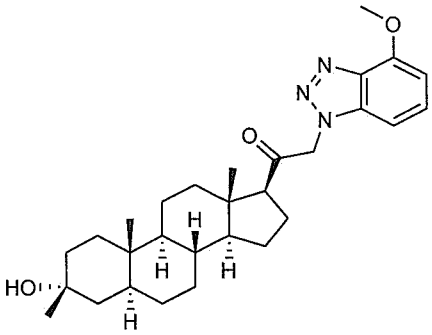
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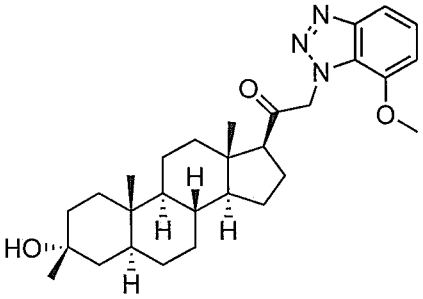
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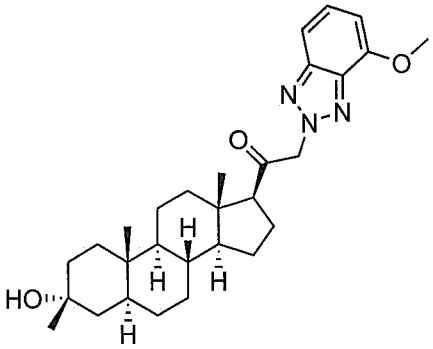
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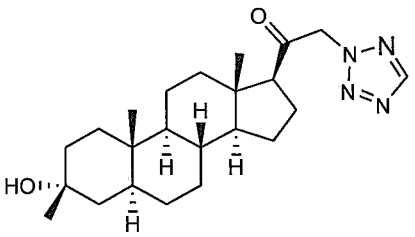
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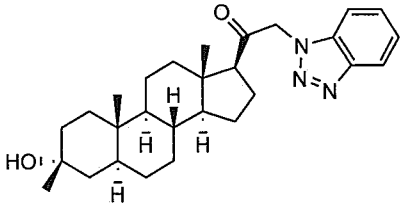
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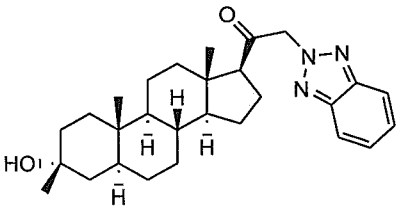
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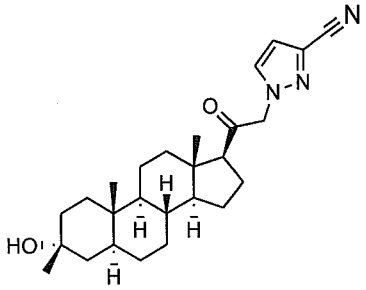
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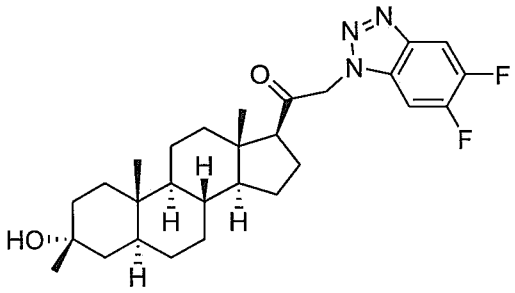
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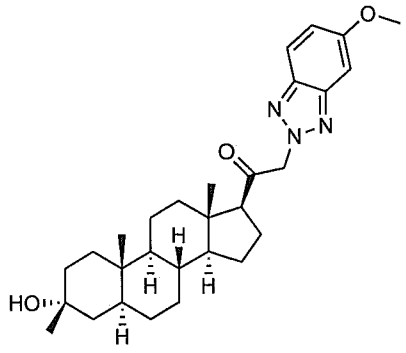
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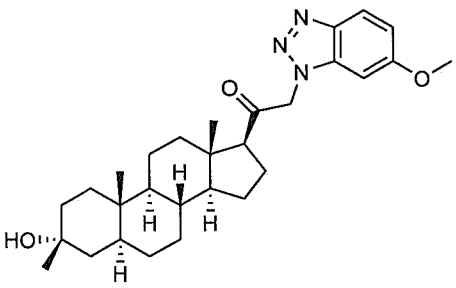
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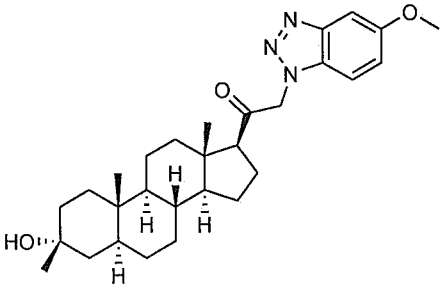
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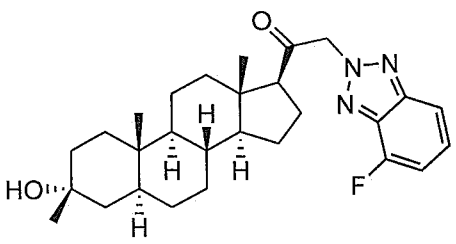
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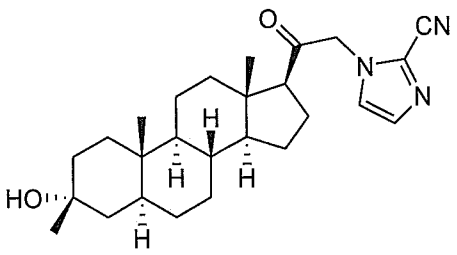
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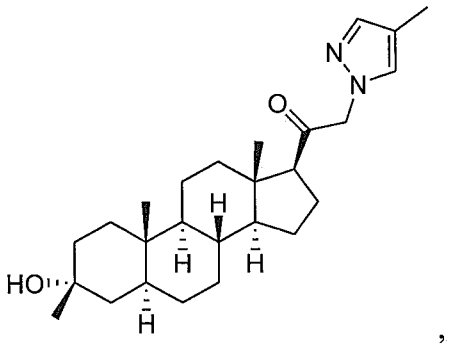
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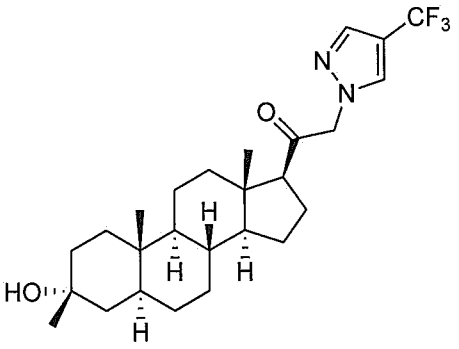
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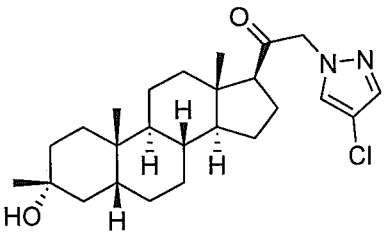
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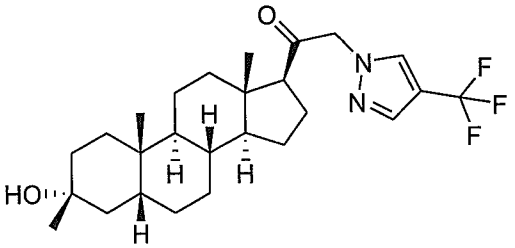
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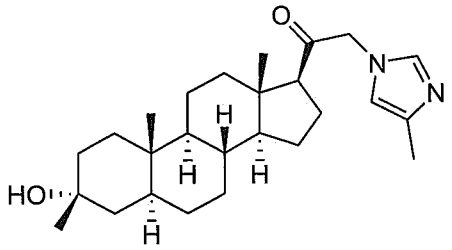
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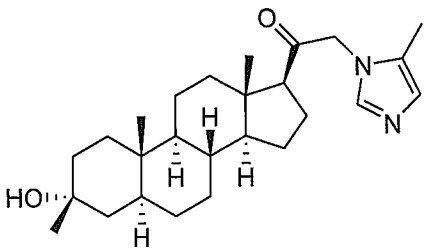
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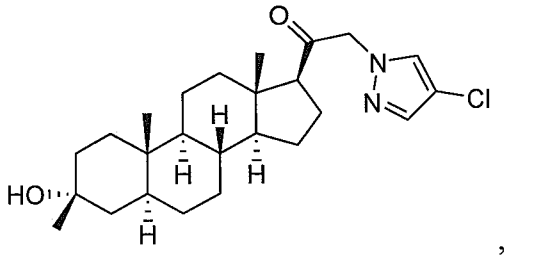
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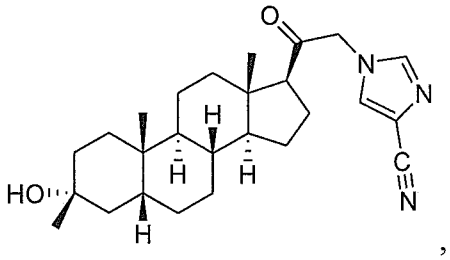
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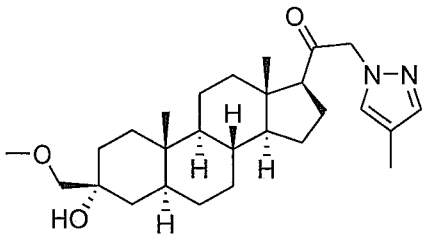
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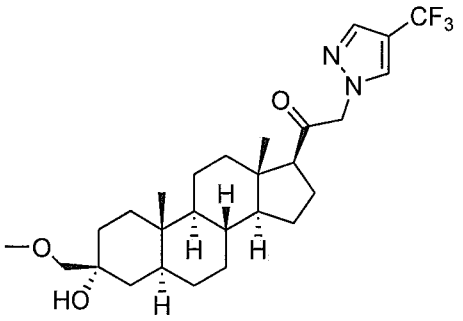
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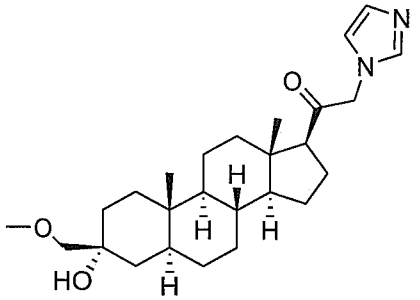
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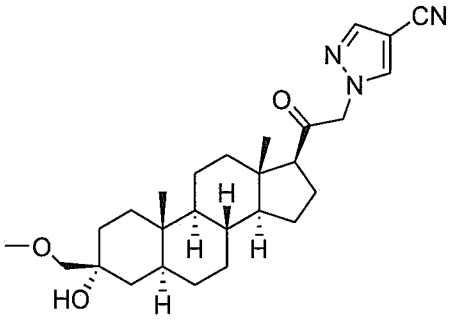
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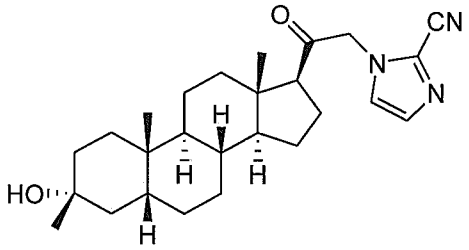
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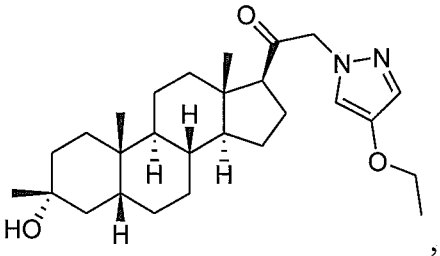
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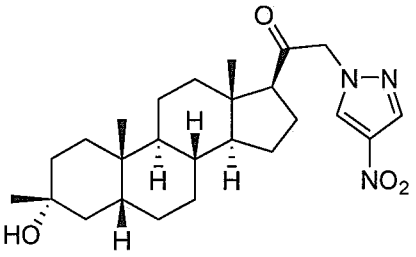
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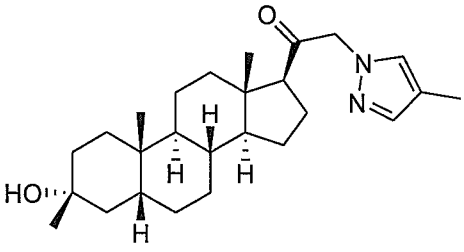
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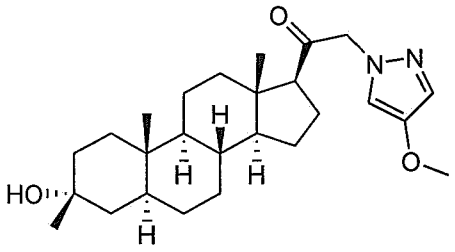
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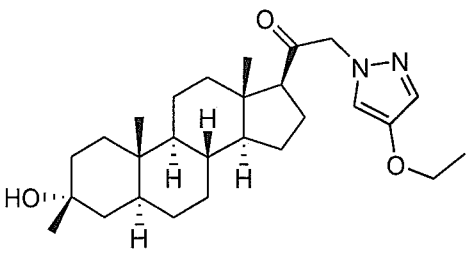
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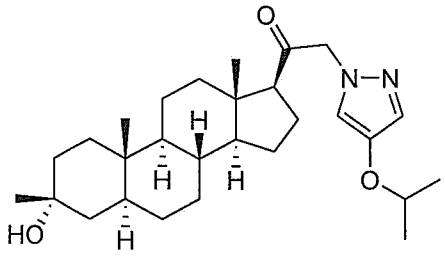
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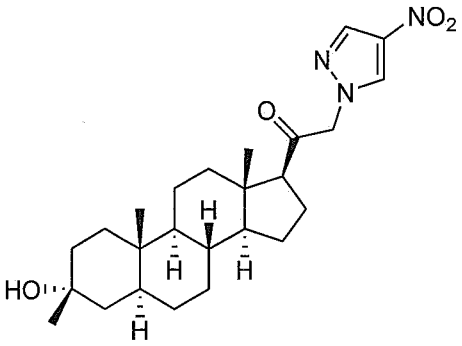
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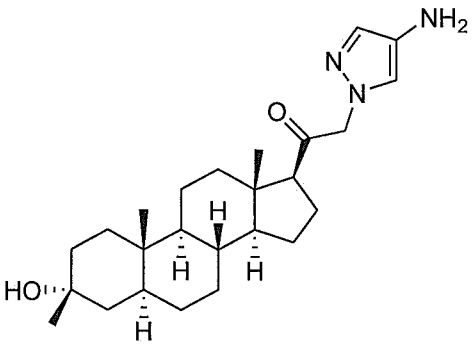
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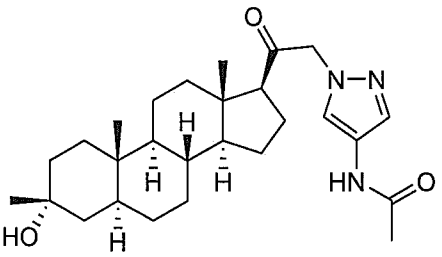
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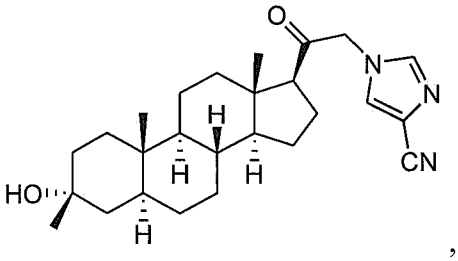
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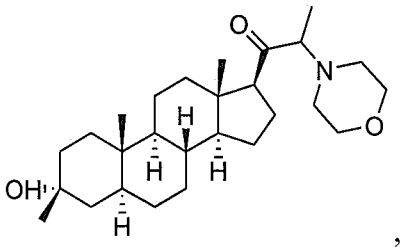
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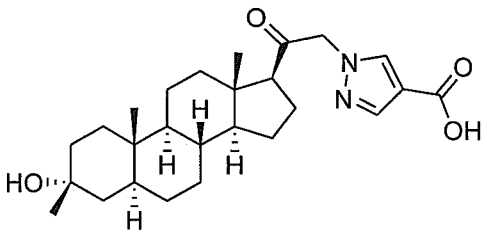
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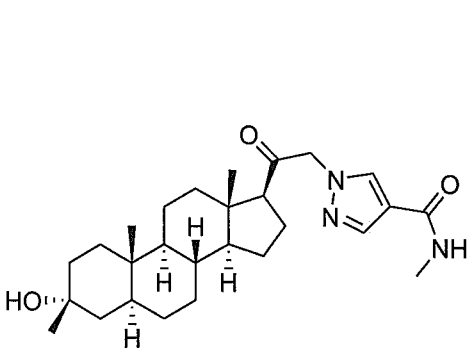
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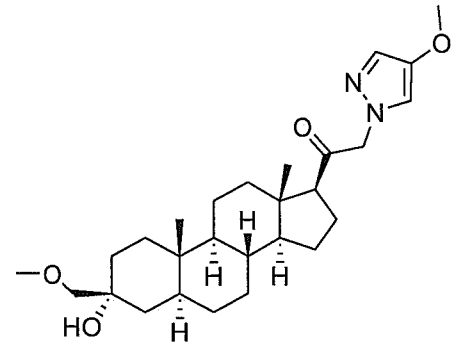
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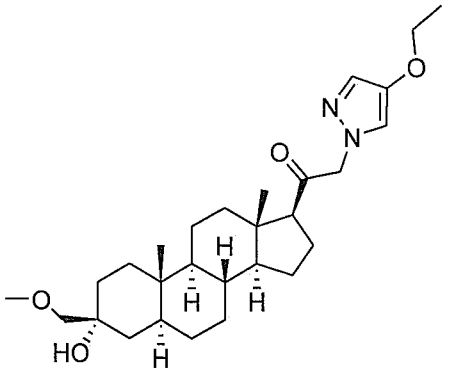
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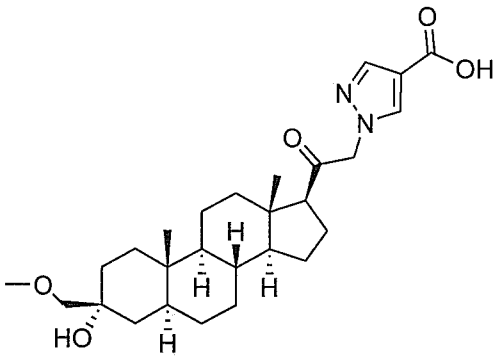
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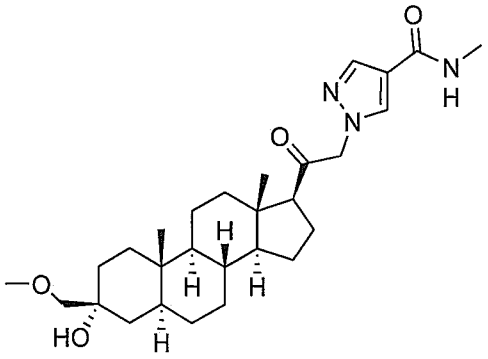
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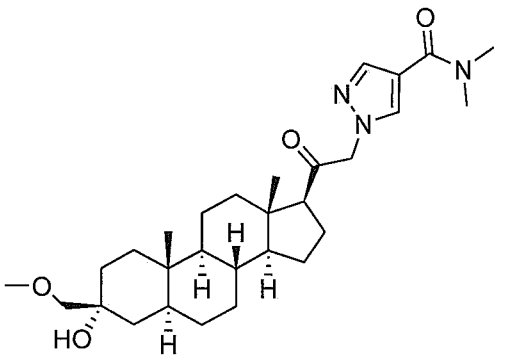
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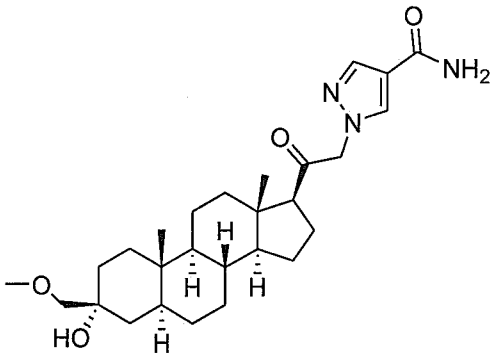
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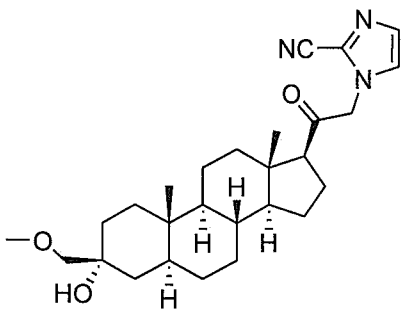
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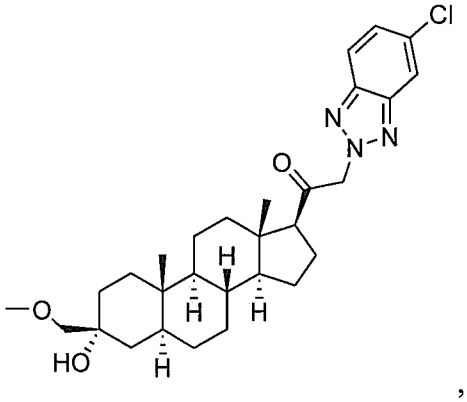
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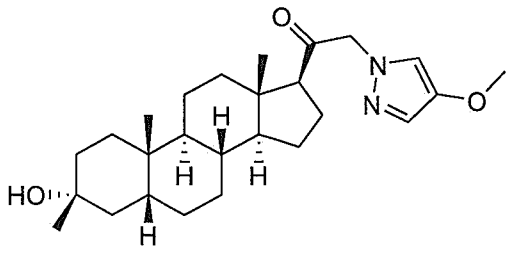
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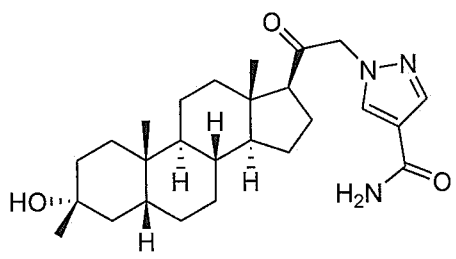
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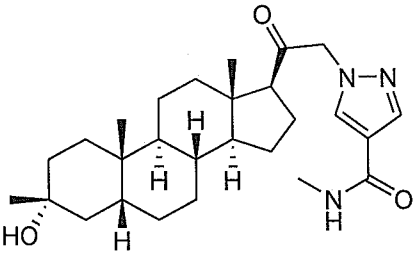
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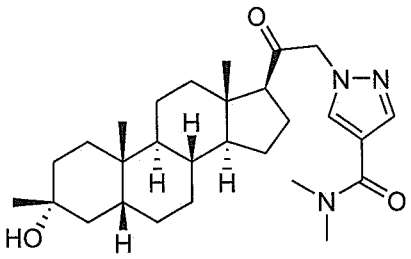
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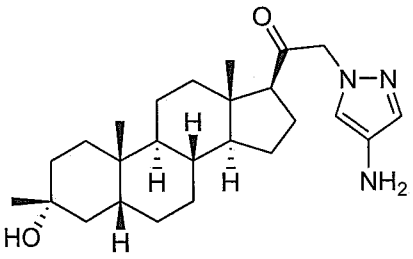
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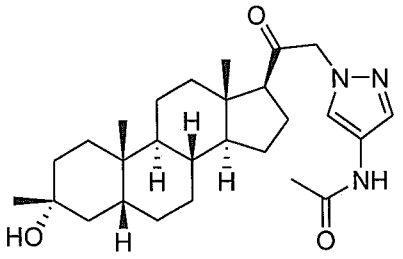
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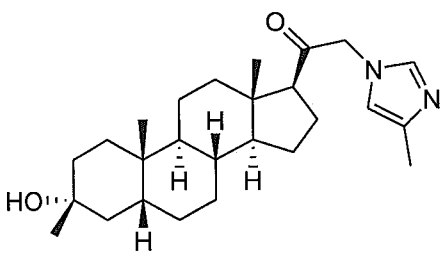
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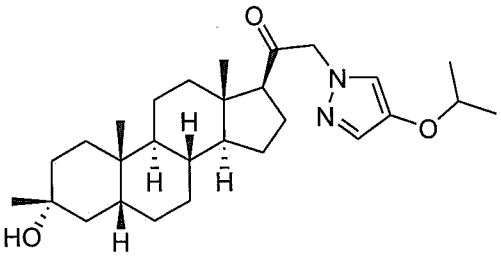
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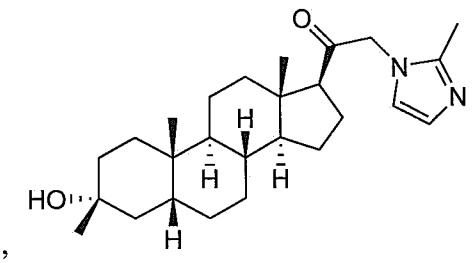
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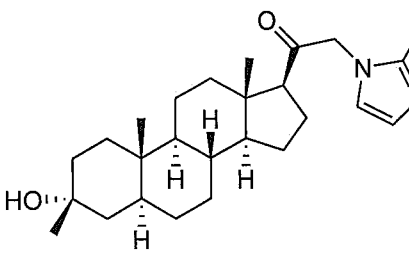
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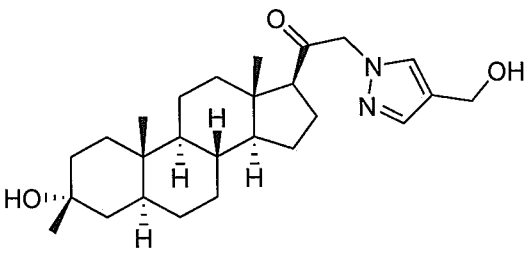
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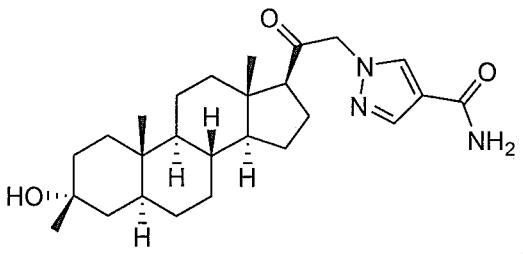
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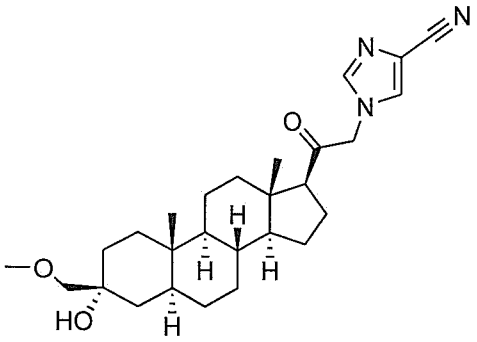
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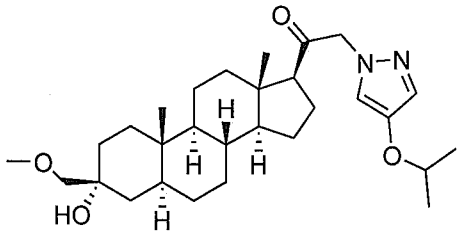
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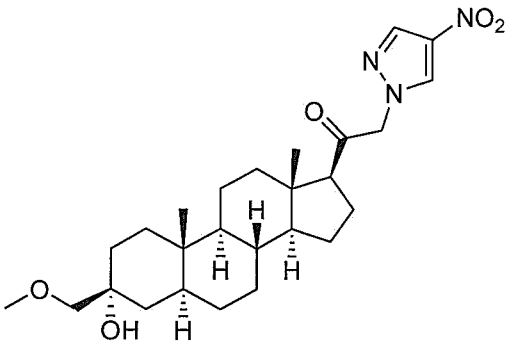
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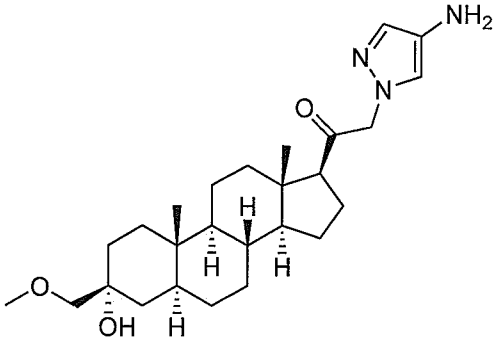
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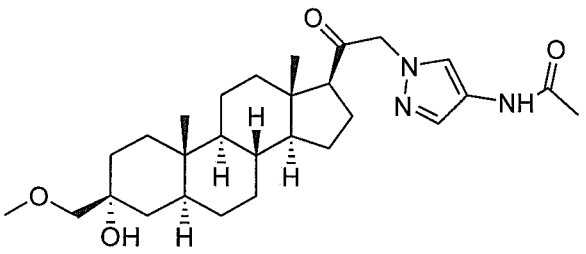
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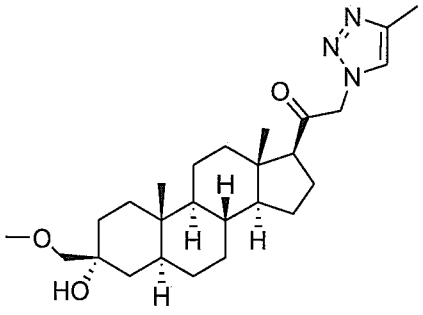
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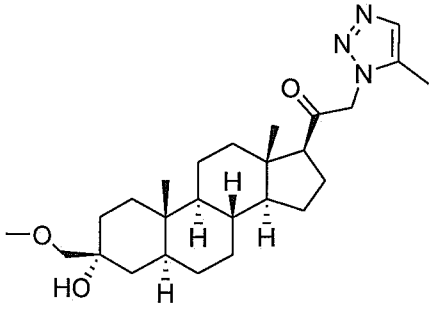
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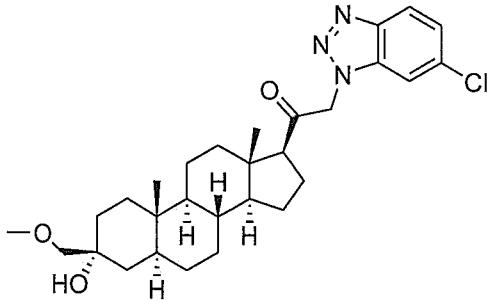
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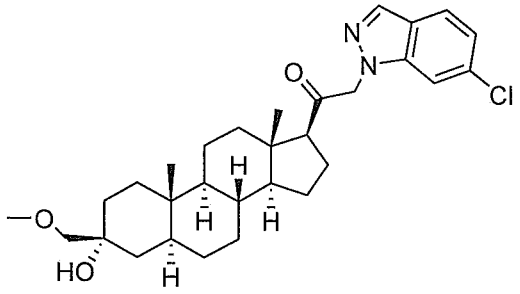
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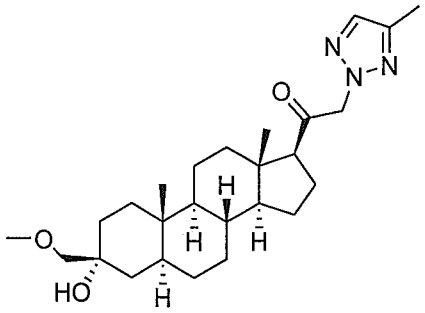
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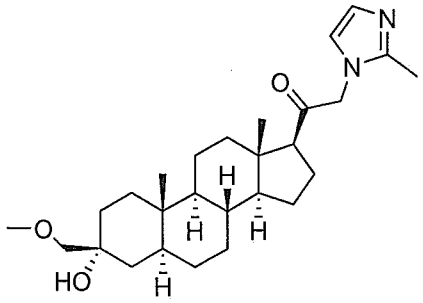
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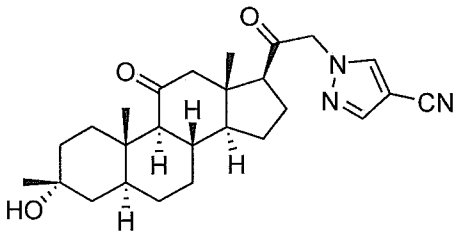
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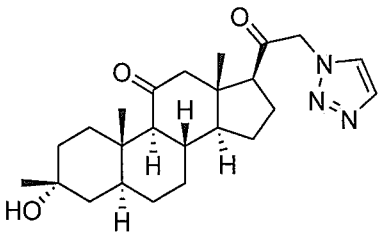
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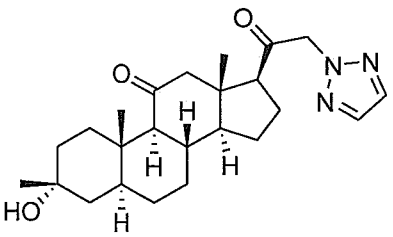
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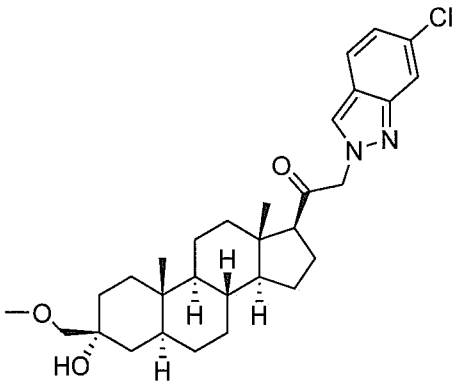
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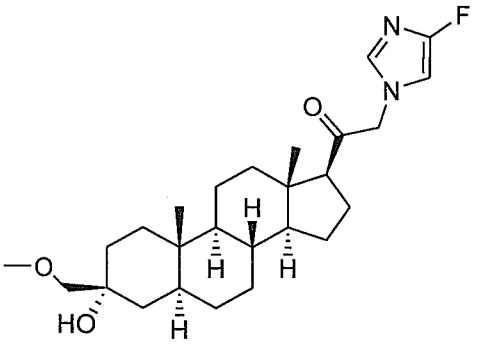
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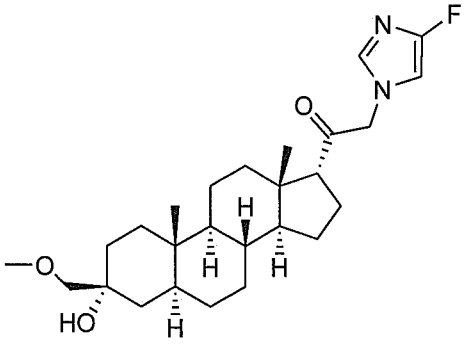
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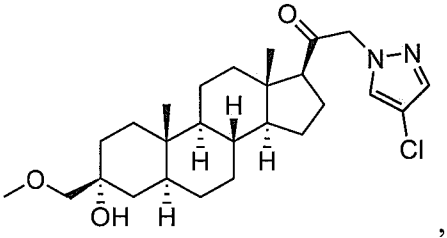
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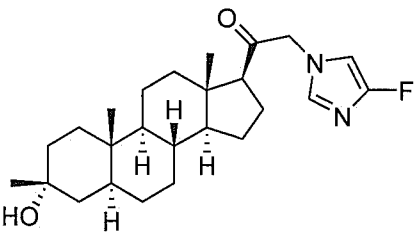
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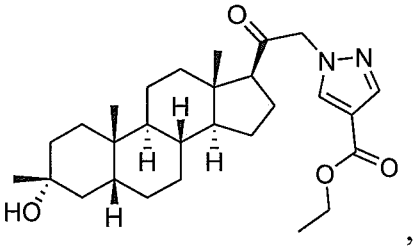
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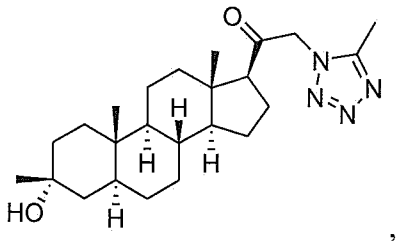
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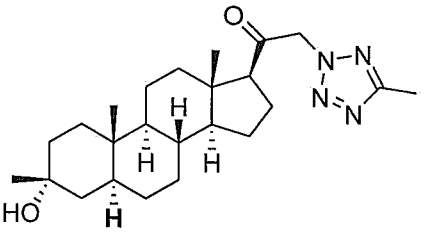
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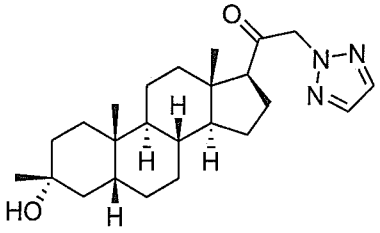
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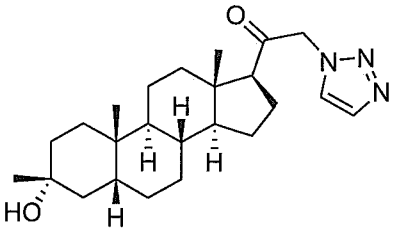
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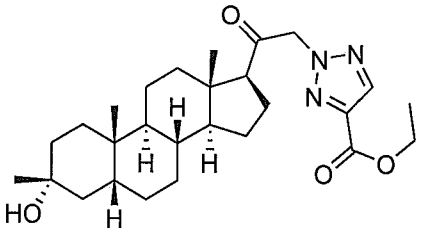
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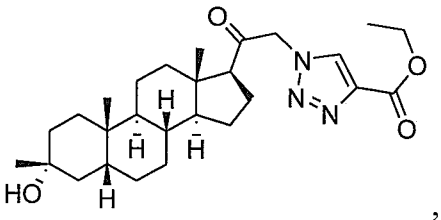
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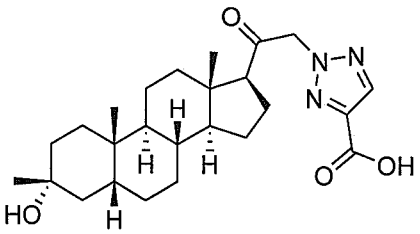
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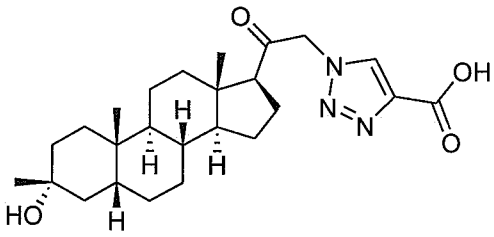
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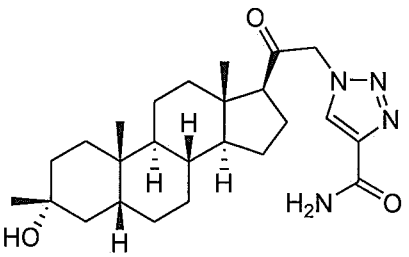
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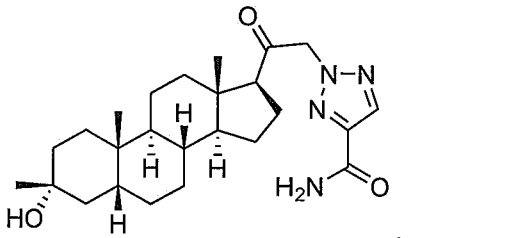
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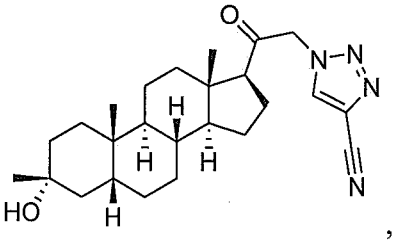
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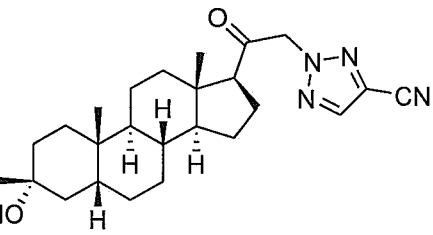
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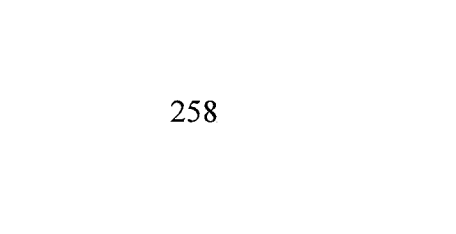
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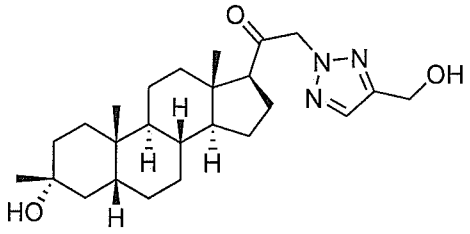
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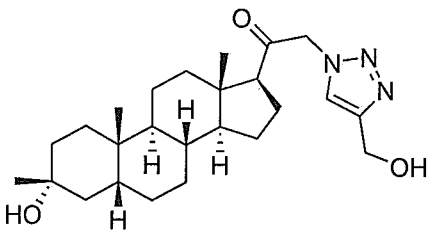
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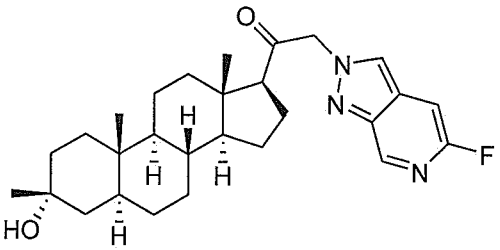
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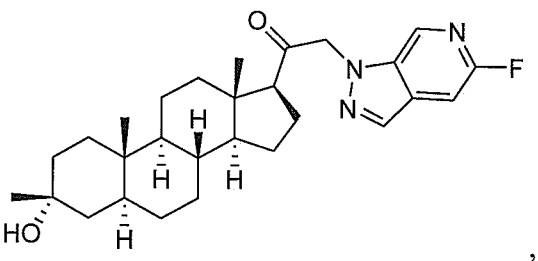
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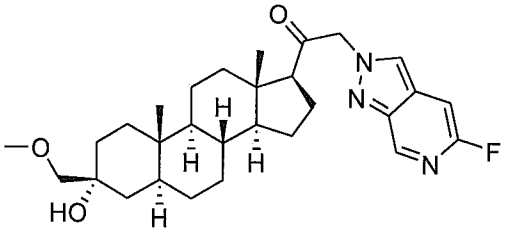
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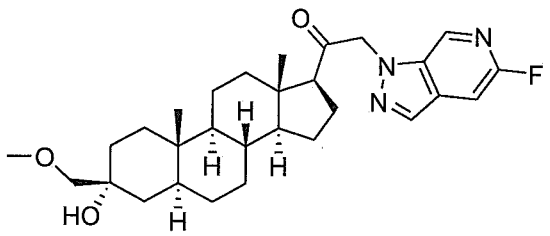
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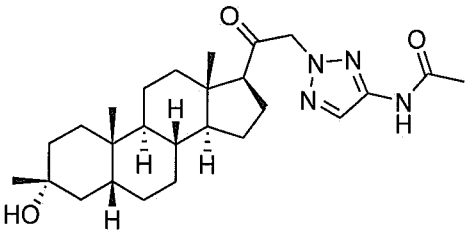
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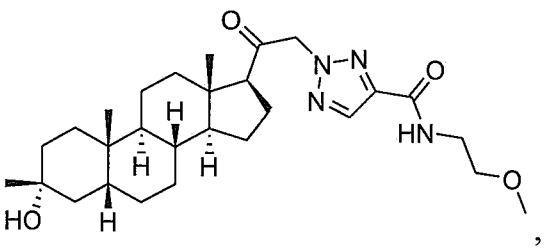
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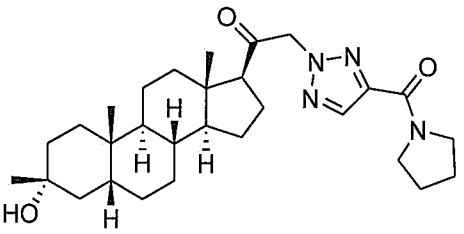
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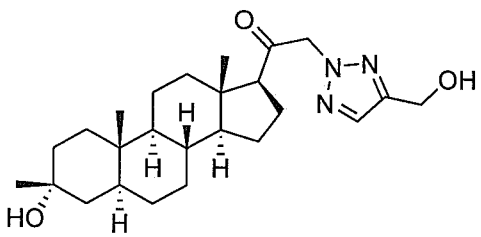
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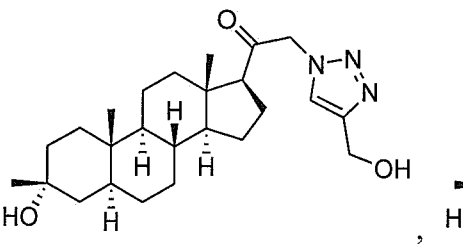
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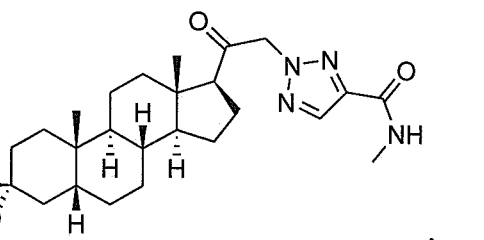
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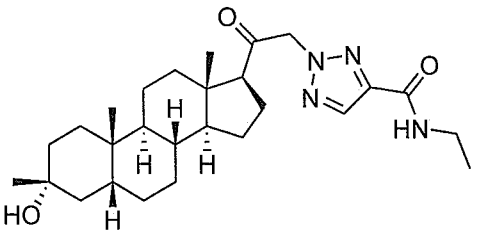
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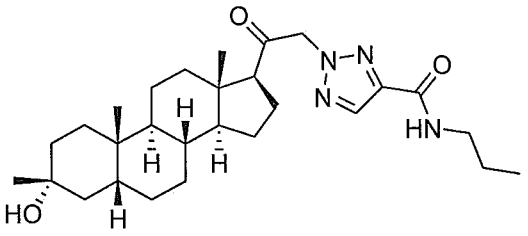
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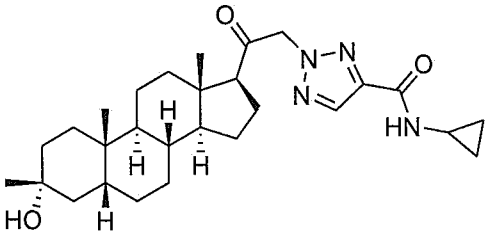
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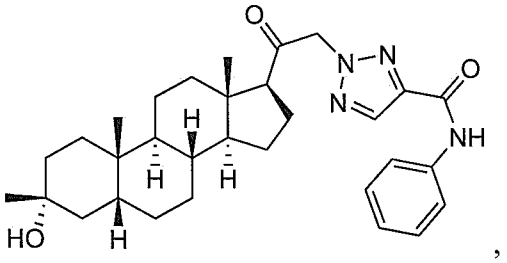
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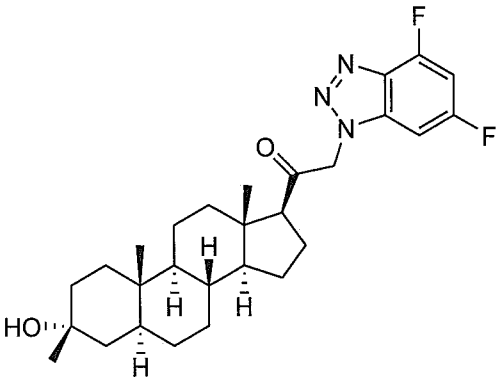
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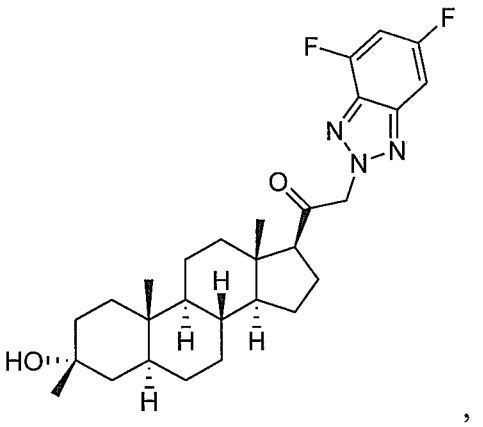
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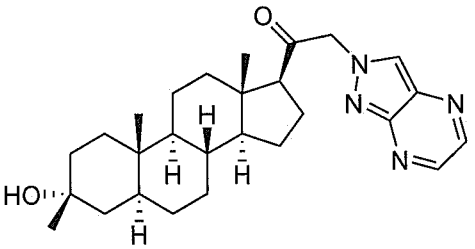
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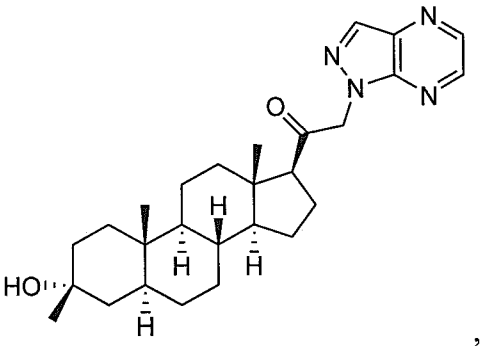
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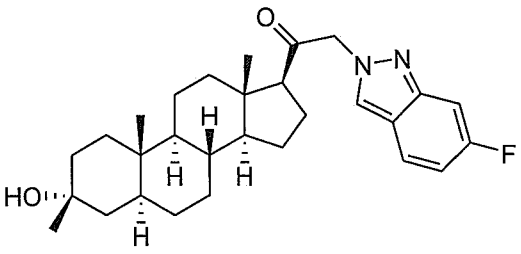
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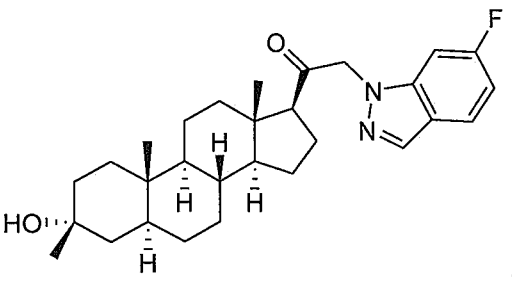
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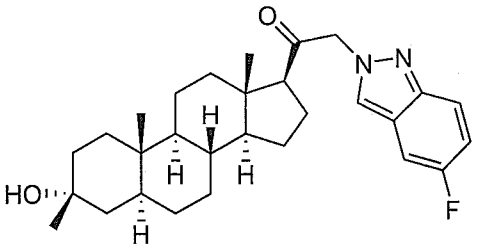
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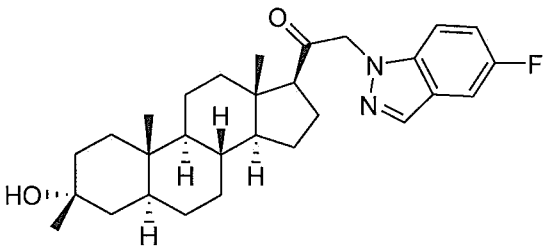
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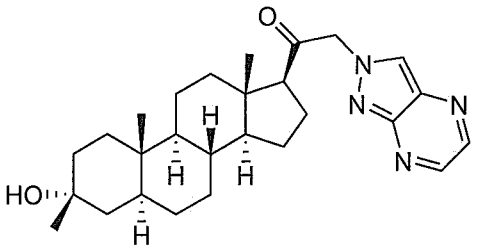
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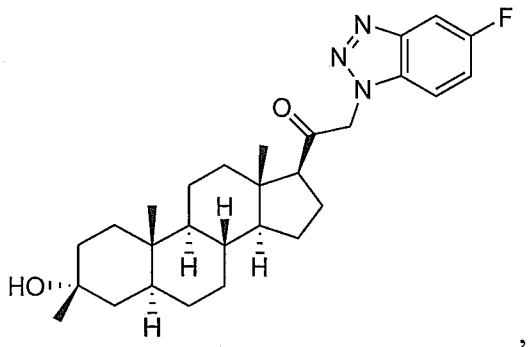
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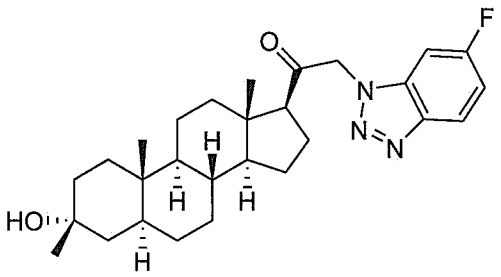
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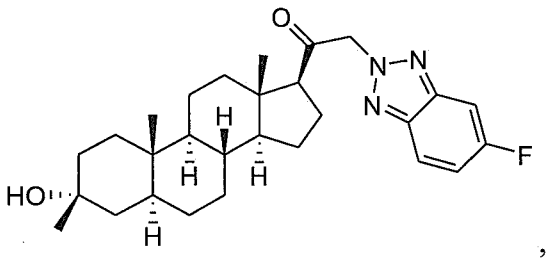
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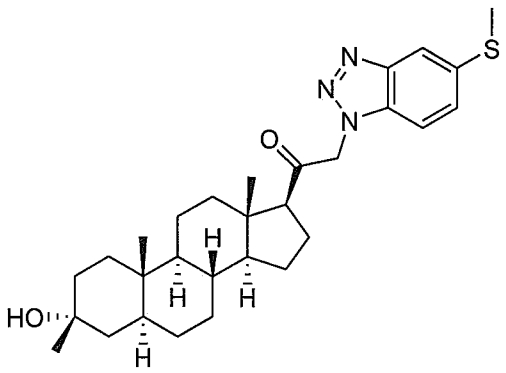
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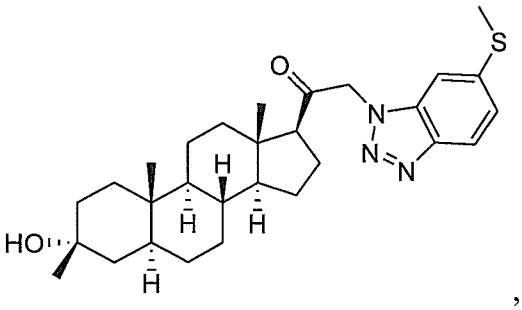
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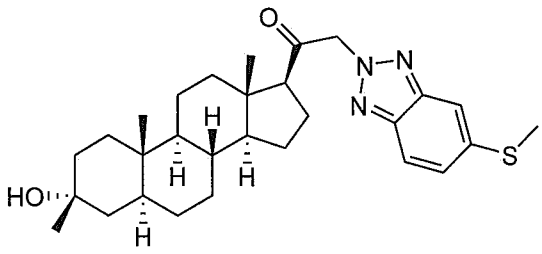
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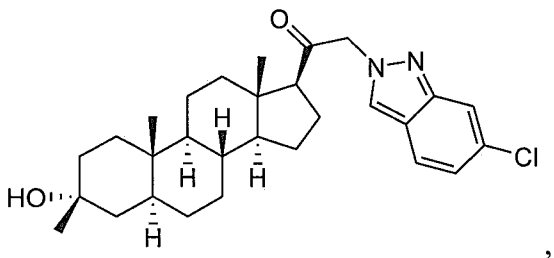
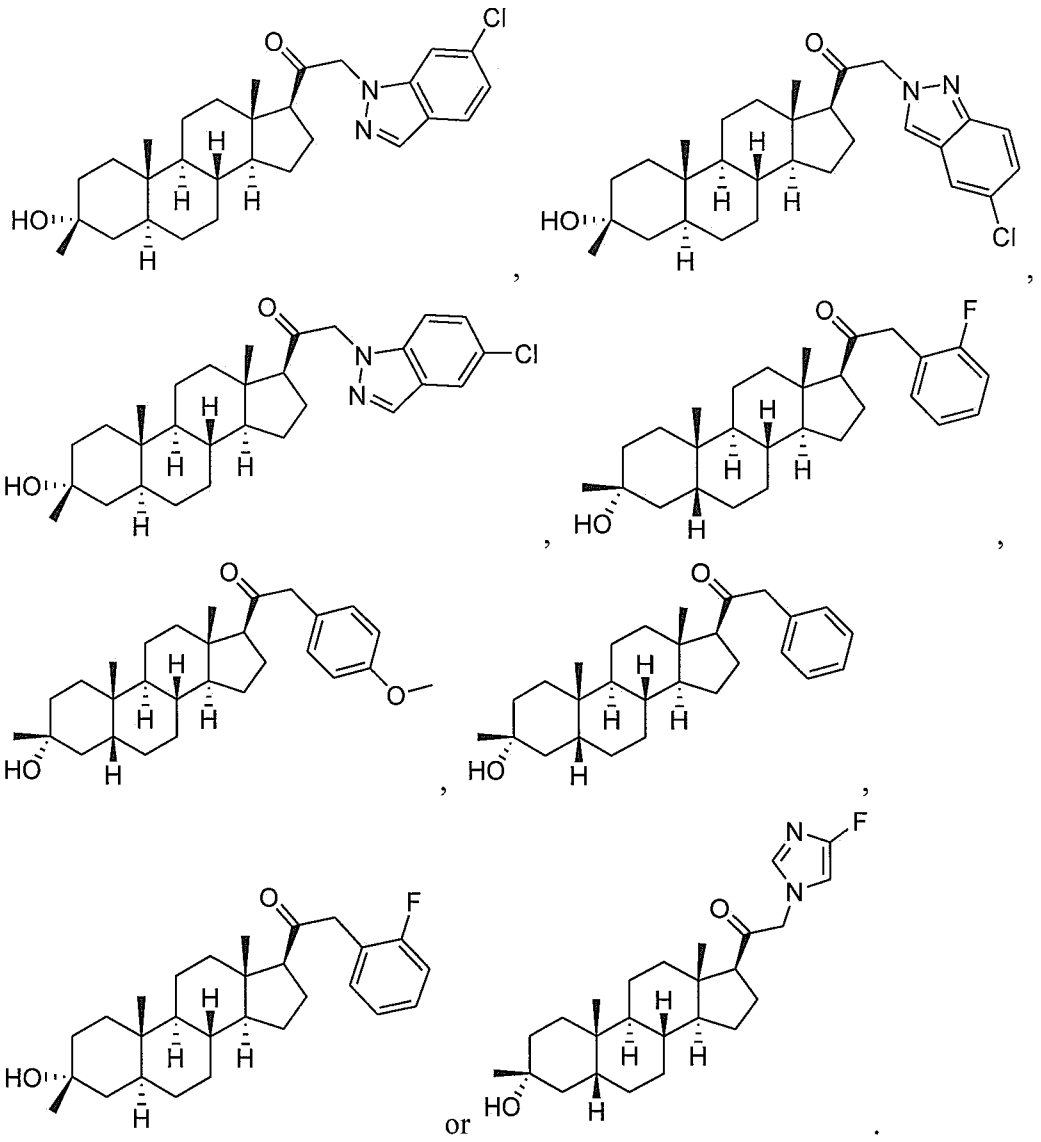




33. A pharmaceutical composition comprising a compound of any one of the preceding claims and a pharmaceutically acceptable excipient.

34. Use of a compound of claim 1 in the manufacture of a medicament for inducing sedation and/or anesthesia in a subject.

35. Use of a compound, a pharmaceutically acceptable salt thereof, or pharmaceutical composition of a compound of claim 1, in the manufacture of a medicament for a method of administration to a subject in need thereof, wherein the subject experiences sedation and/or anesthesia within two hours of administration.

36. The use of claim 35, wherein the subject experiences sedation and/or anesthesia within one hour of administration.

37. The use of claim 35, wherein the subject experiences sedation and/or anesthesia instantaneously.

38. The use of claim 35, wherein the compound is to be administered by intravenous administration.

39. The use of claim 35, wherein the compound is to be administered chronically.

40. The use of claim 35, wherein the subject is a mammal.

41. The use of claim 40, wherein the subject is a human.

42. The use of claim 35, wherein the compound is to be administered in combination with another therapeutic agent.

43. Use of a compound of claim 1 in the manufacture of a medicament for treating seizure in a subject.

44. Use of a compound of claim 1 in the manufacture of a medicament for treating epilepsy or status or status epilepticus in a subject.

45. The use of claim 44, wherein 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).

46. Use of of a compound, a pharmaceutically acceptable salt thereof, or pharmaceutical composition of one of a compound of claim 1, in the manufacture of a medicament for treating disorders related to GABA function in a subject in need thereof.

47. Use of a compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a CNS-related disorder in a subject in need thereof.

48. The use of claim 47, wherein the CNS-related disorder is 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, pain, traumatic brain injury, a vascular disease, a substance abuse disorder and/or withdrawal syndrome, or tinnitus.

49. The use of claim 47, wherein the compound is to be administered orally.

50. The use of claim 47, wherein the compound is to be administered intramuscularly.

51. The use of claim 47, wherein the subject is a subject with Rett syndrome, Fragile X syndrome, or Angelman syndrome.

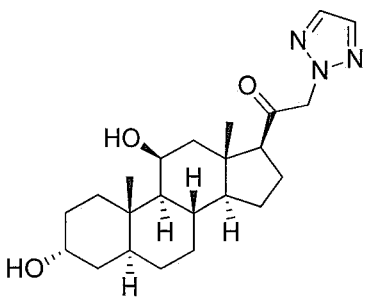
52. The use of claim 47, wherein the CNS–related disorder is a sleep disorder, an eating disorder, a mood disorder, a schizophrenia spectrum disorder, a convulsive disorder, a disorder of memory and/or cognition, a movement disorder, a personality disorder, autism spectrum disorder, pain, traumatic brain injury, a vascular disease, a substance abuse disorder and/or withdrawal syndrome, or tinnitus.

53. The use of claim 47, wherein the CNS-related disorder is depression (e.g., post-partum depression).

54. The use of claim 47, wherein the CNS-related disorder is tremor (e.g., essential tremor).

55. The use of claim 47, wherein the CNS-related disorder is an eating disorder (e.g., anorexia nervosa, bulimia nervosa, binge-eating disorder, cachexia).

56. A compound, wherein the compound is: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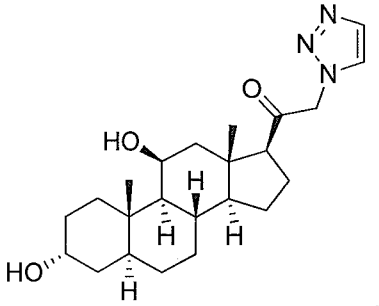
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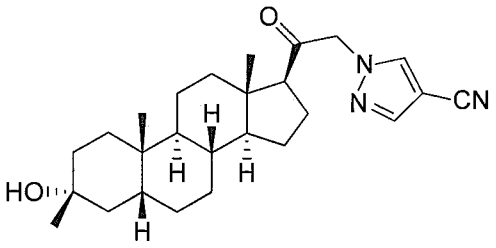
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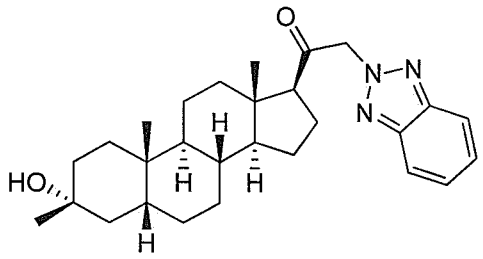
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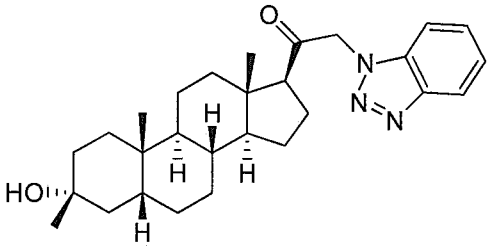
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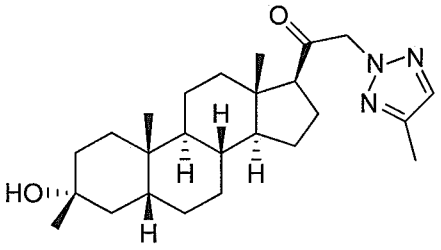
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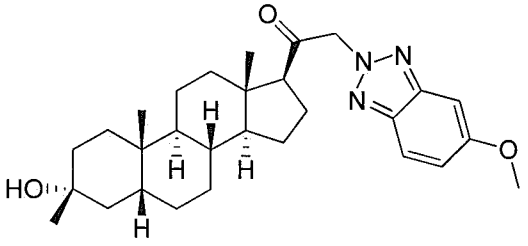
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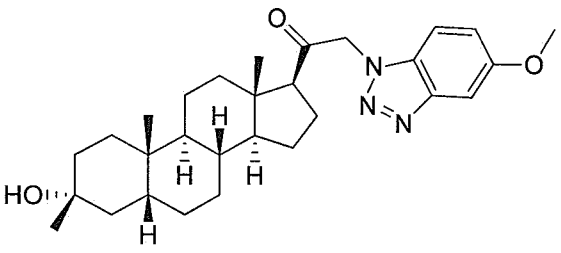
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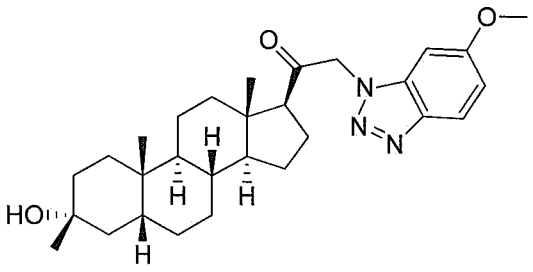
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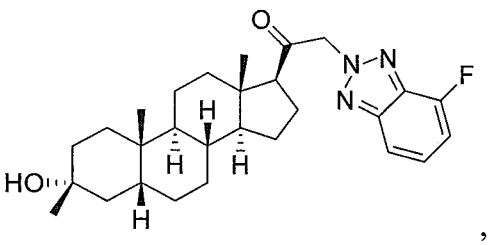
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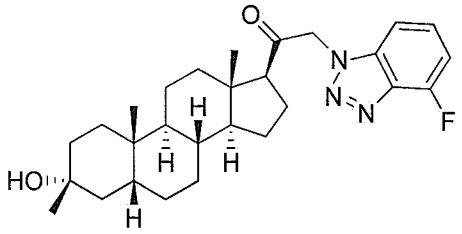
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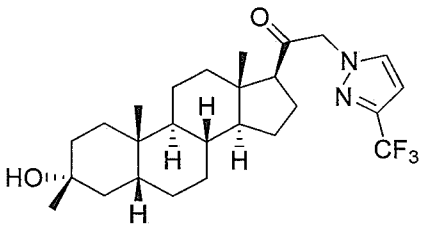
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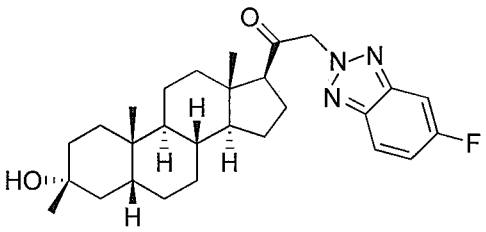
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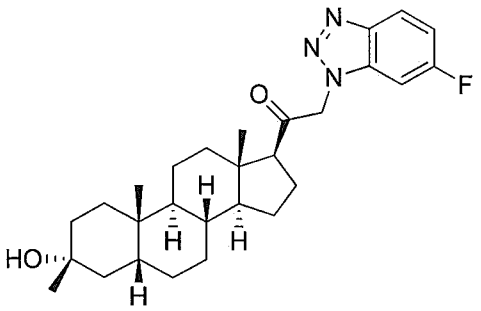
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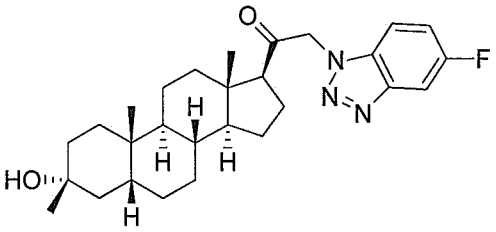
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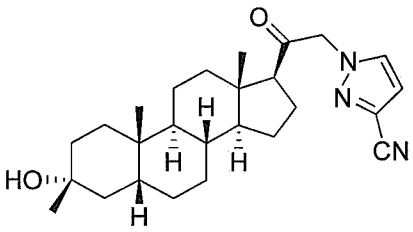
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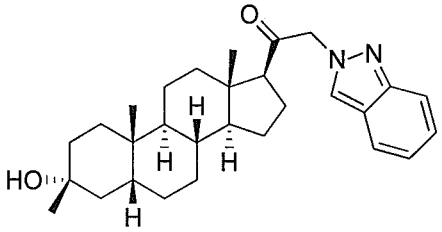
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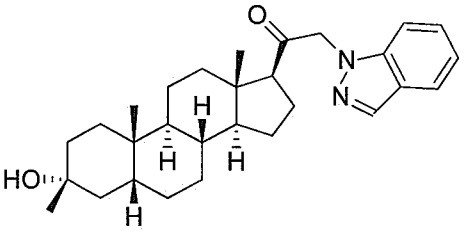
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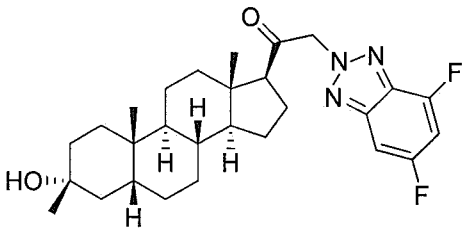
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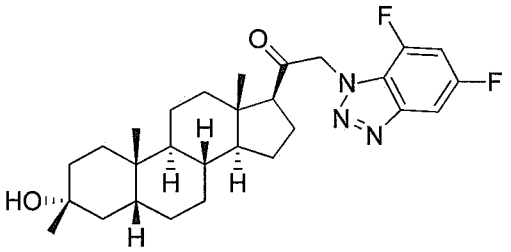
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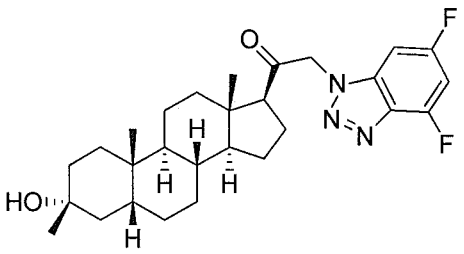
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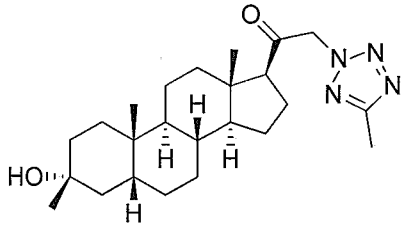
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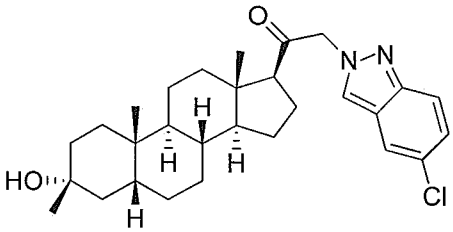
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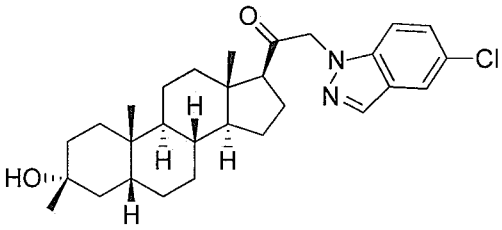
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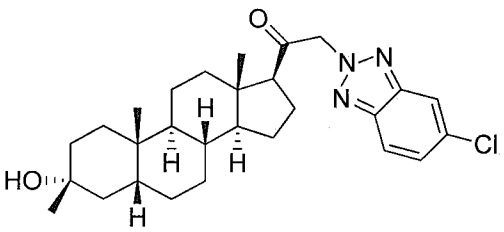
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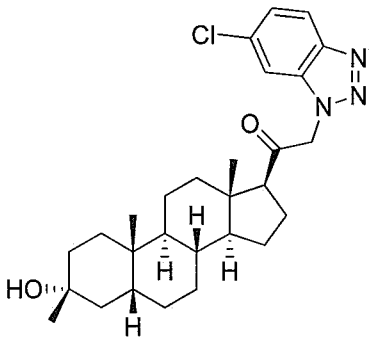
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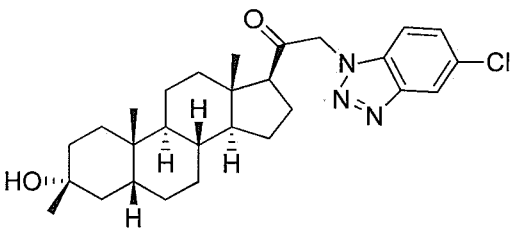
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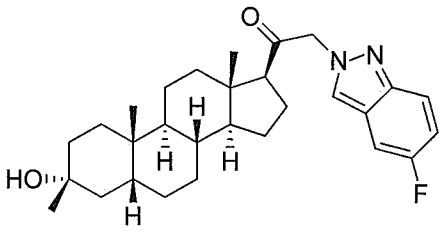
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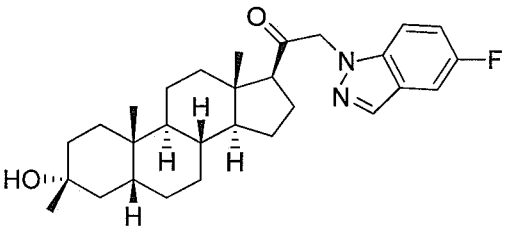
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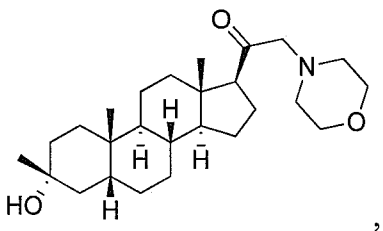
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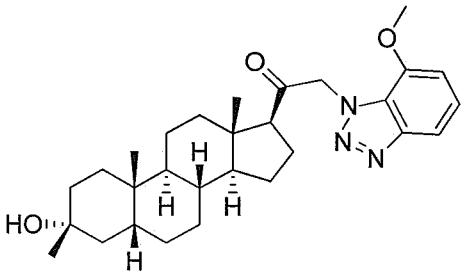
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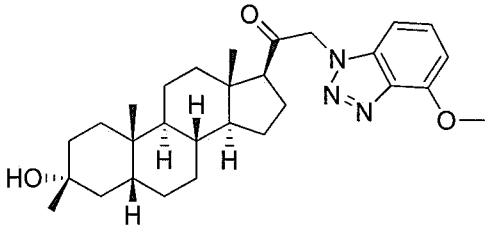
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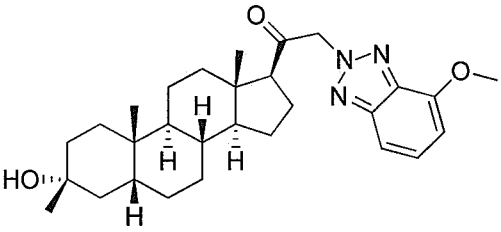

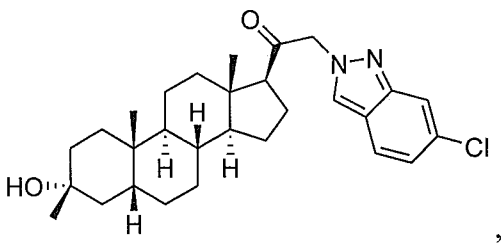
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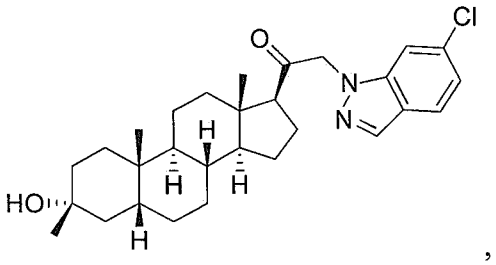
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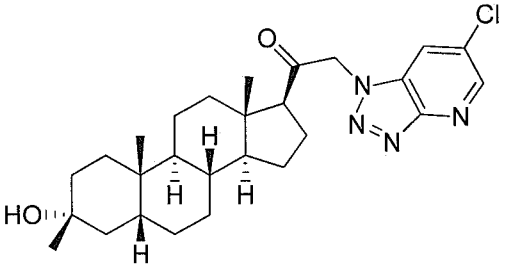
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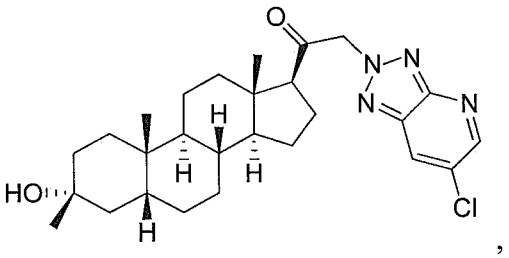
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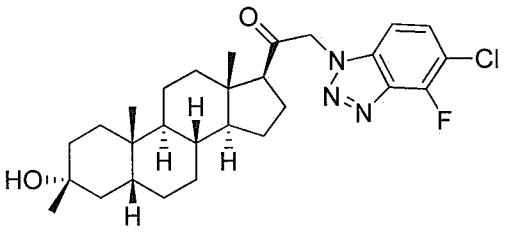
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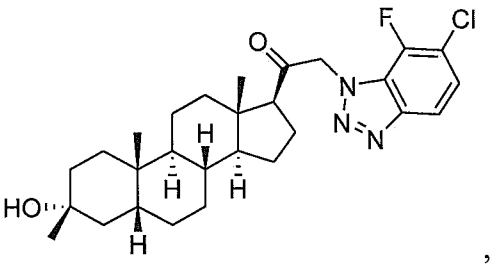
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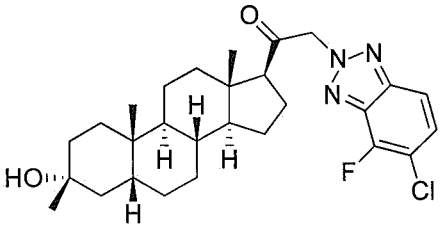
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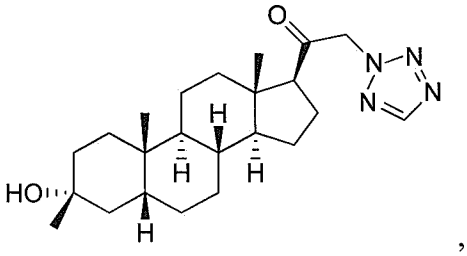
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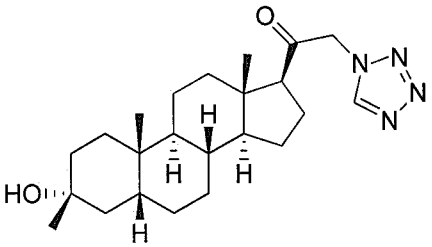
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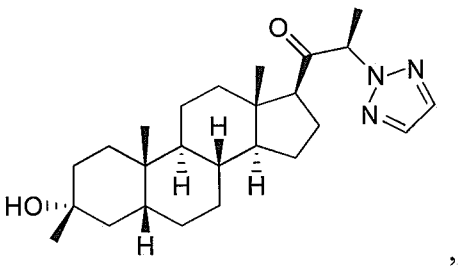
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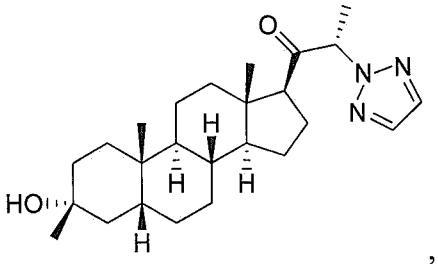
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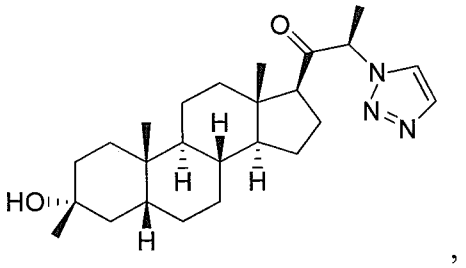
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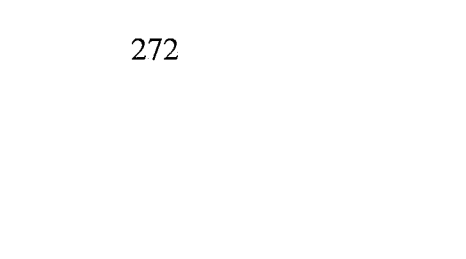
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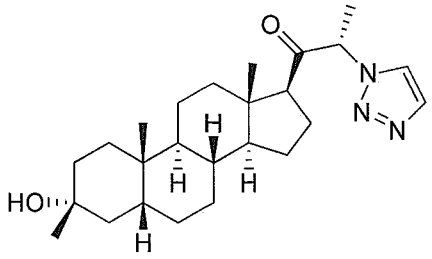
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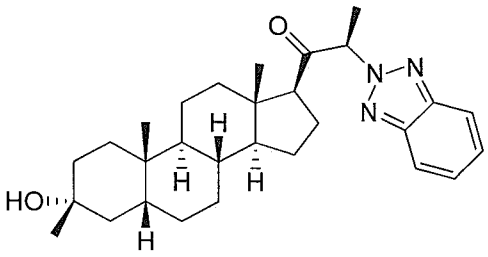
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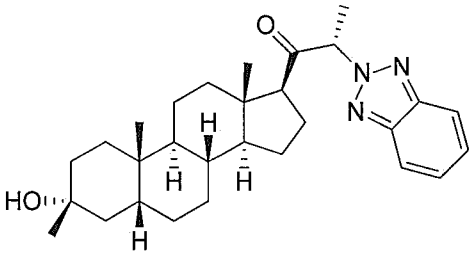
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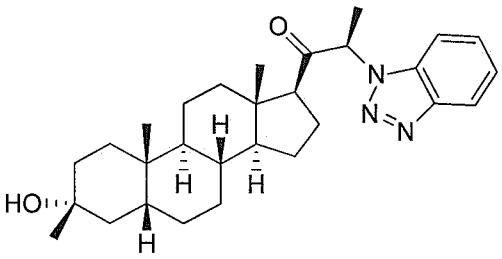
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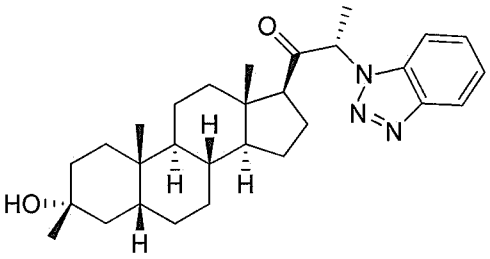
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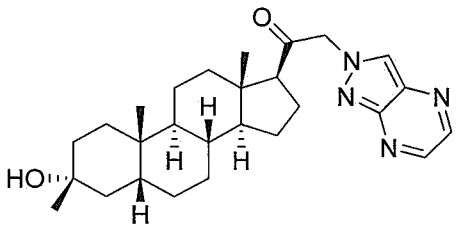
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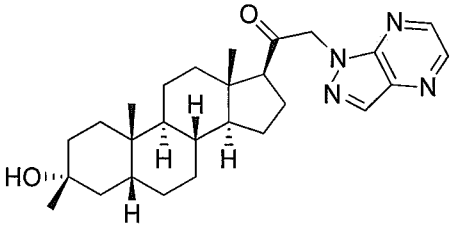
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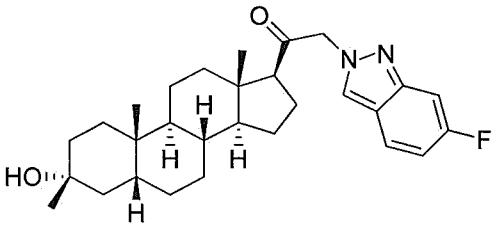
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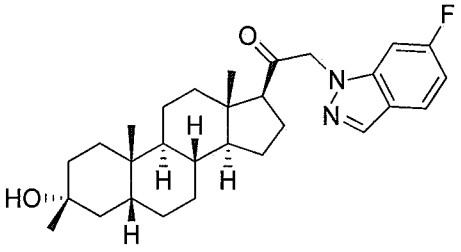
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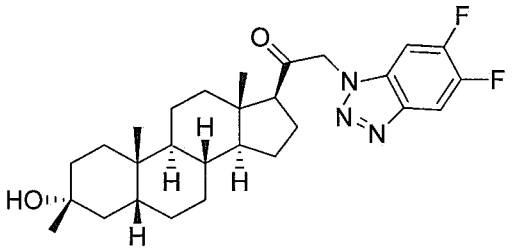
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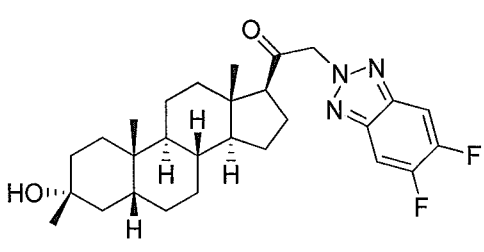
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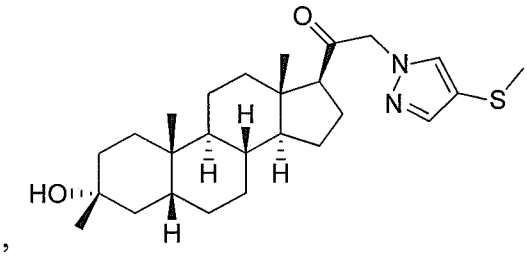
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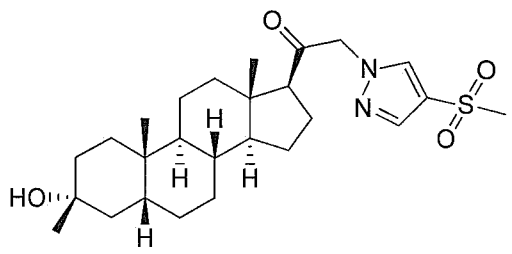
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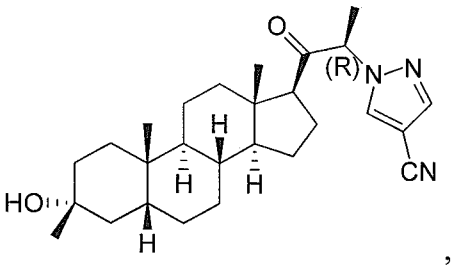
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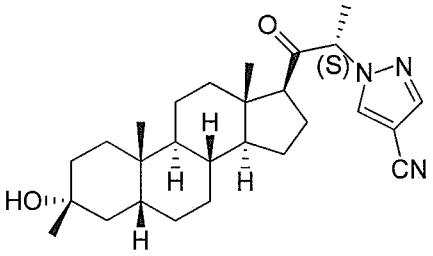
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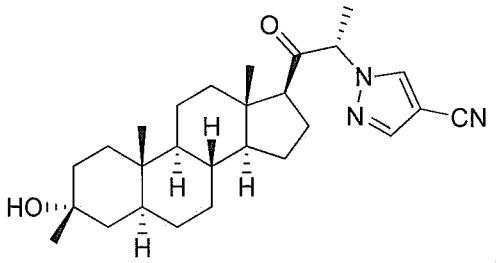
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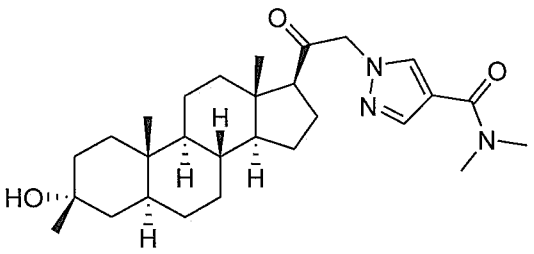
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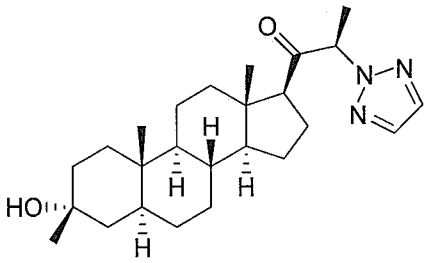
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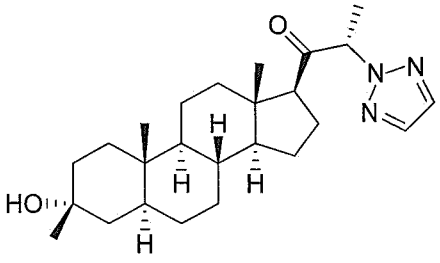
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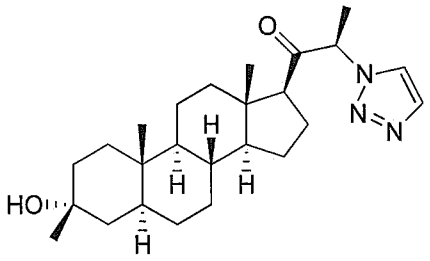
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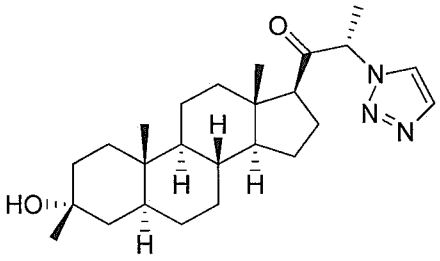
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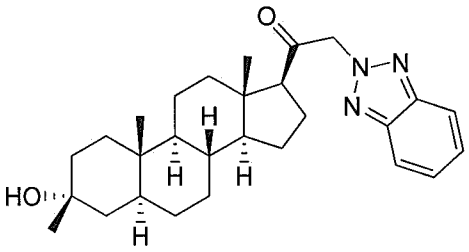
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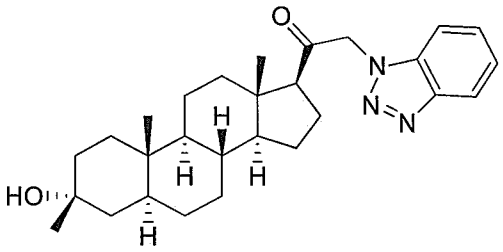
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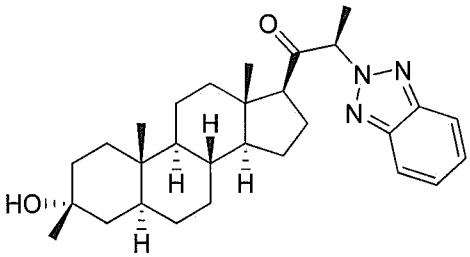
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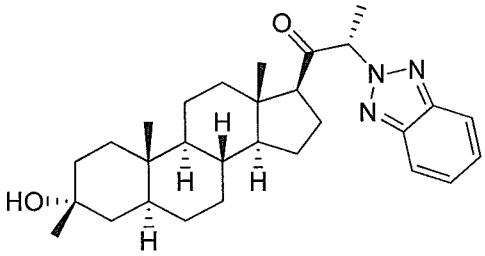
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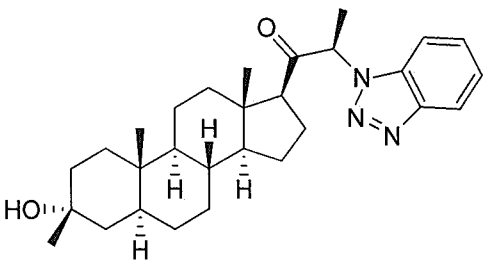
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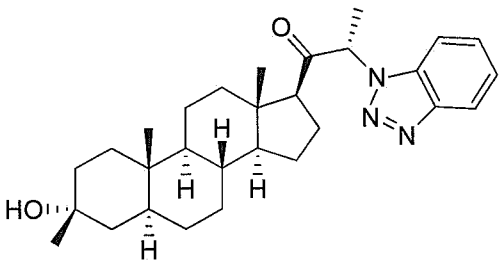
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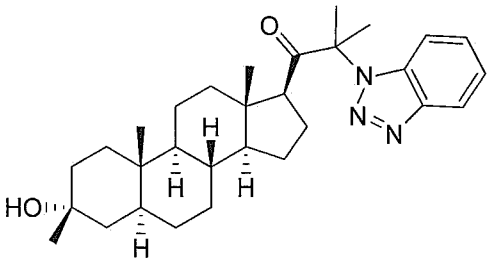
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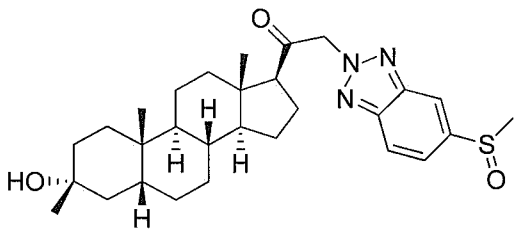
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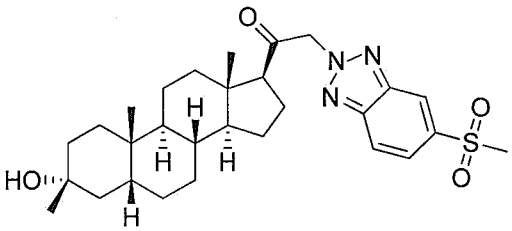
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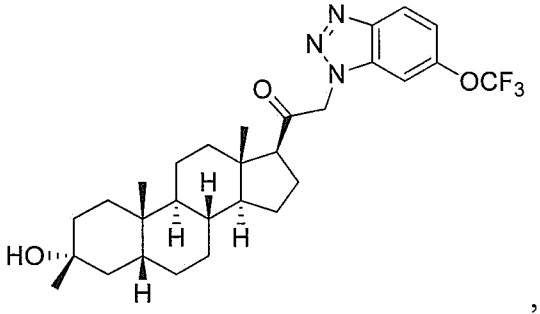
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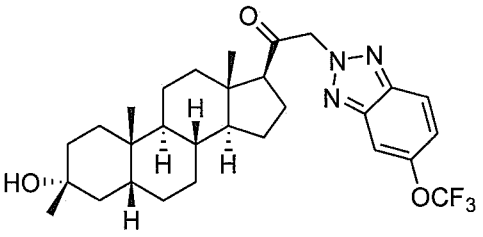
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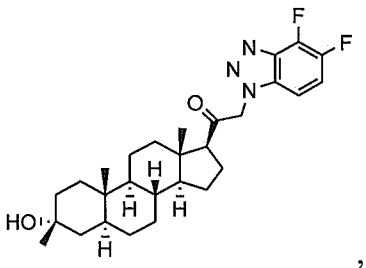
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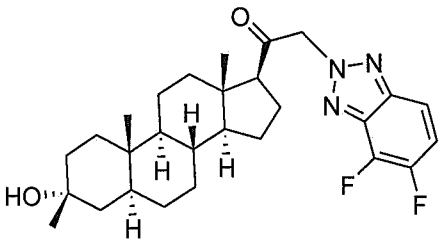
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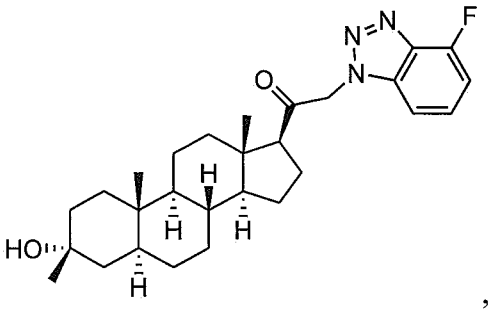
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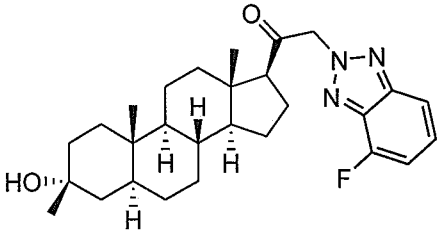
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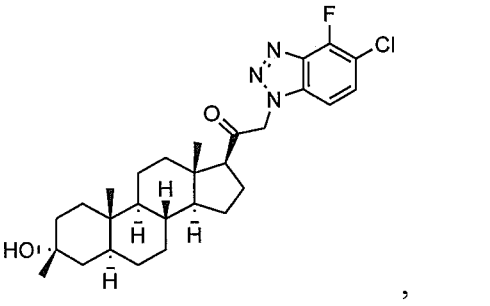
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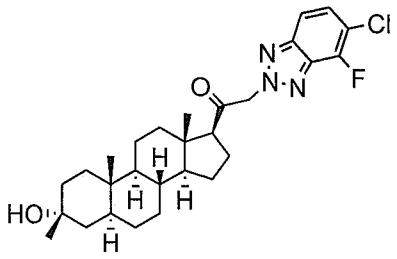
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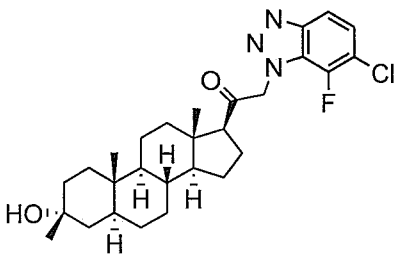
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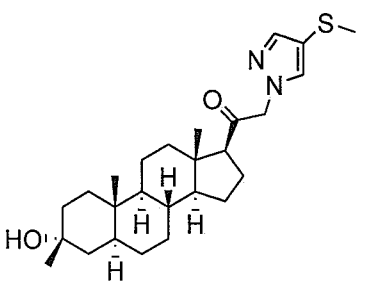
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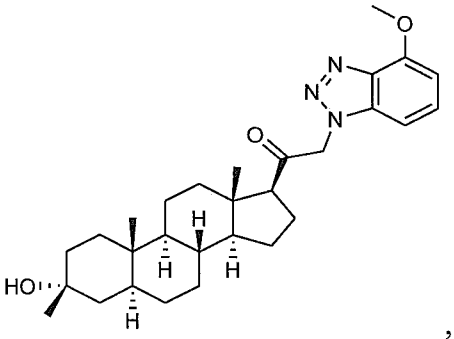
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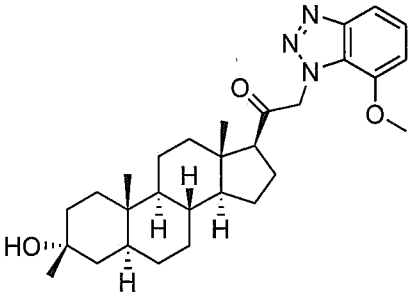
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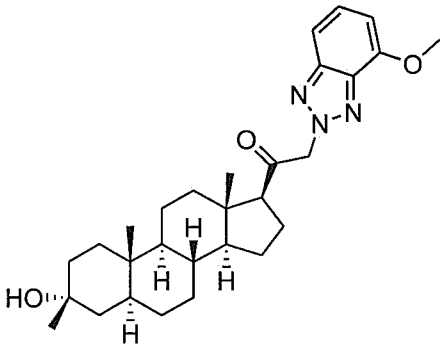
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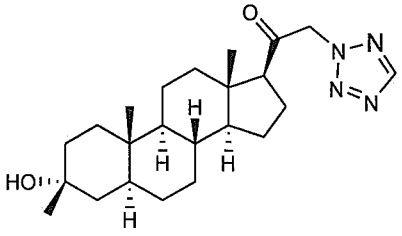
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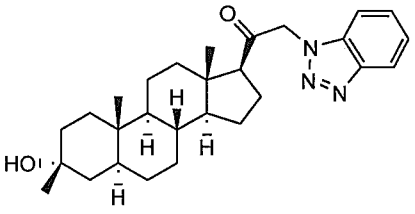
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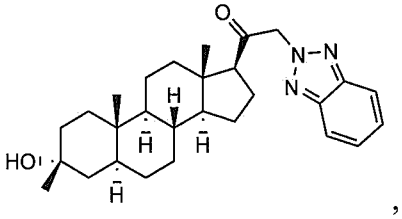
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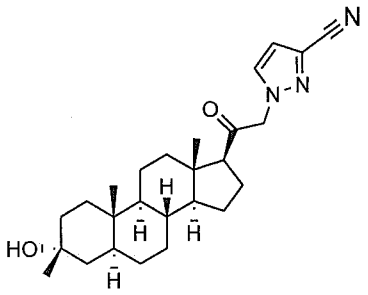
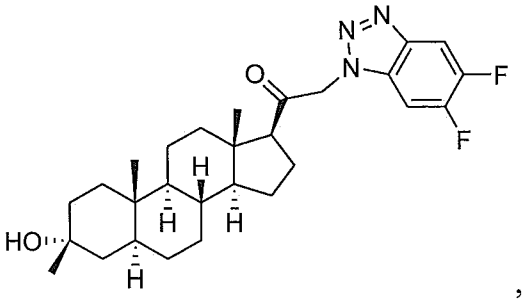
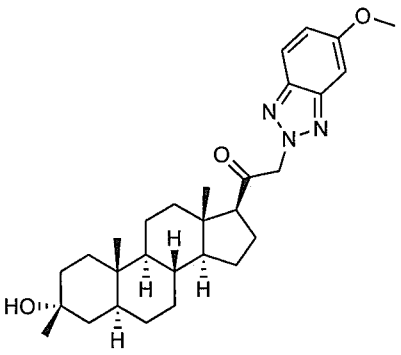
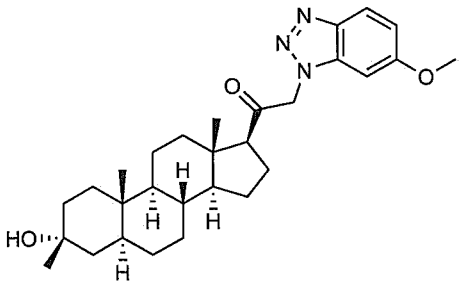
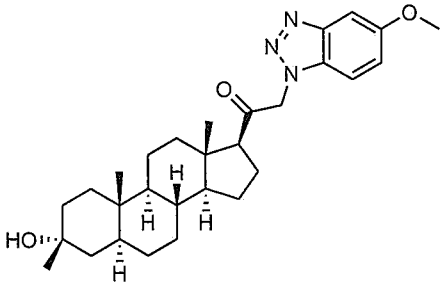
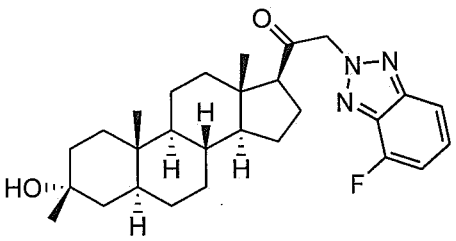
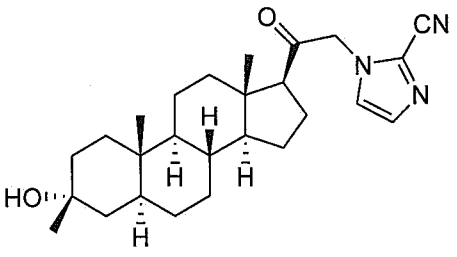
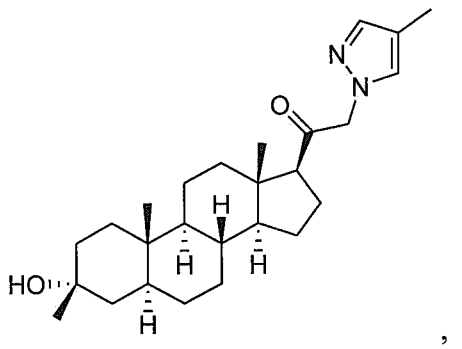

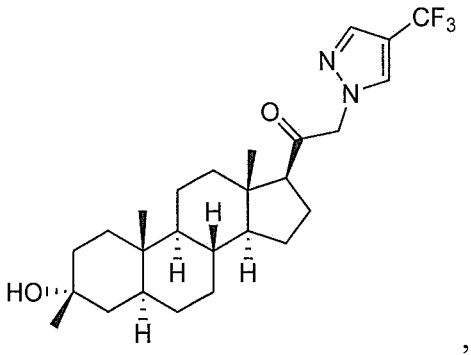
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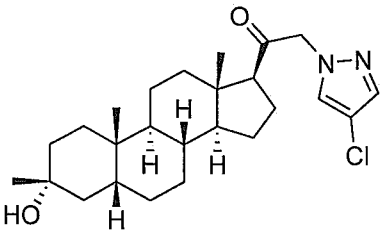
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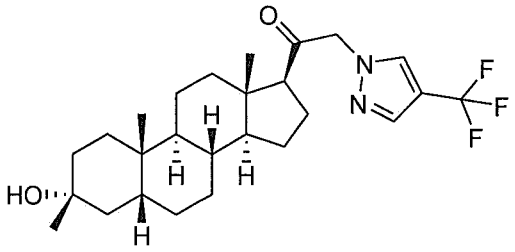
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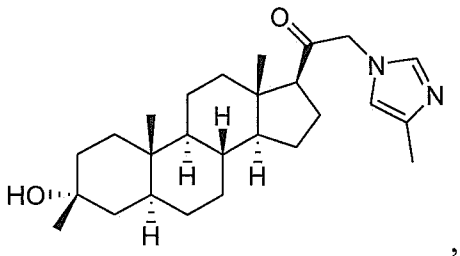
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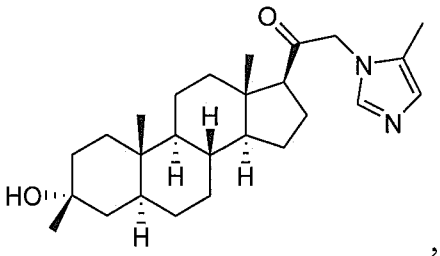
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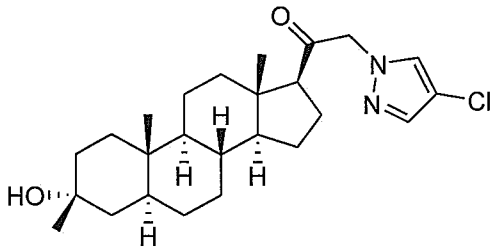
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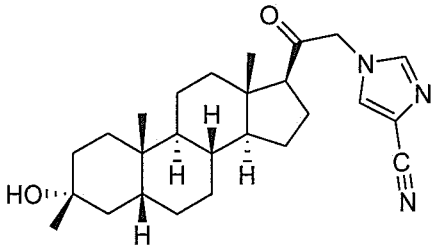
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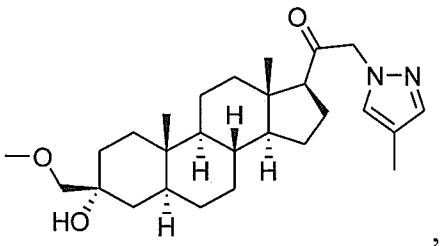
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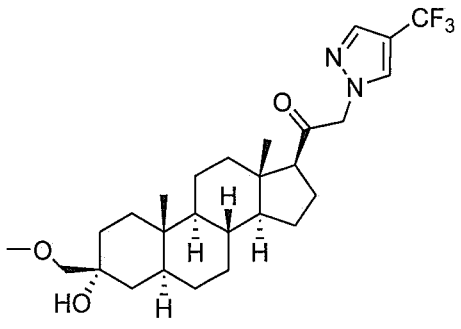
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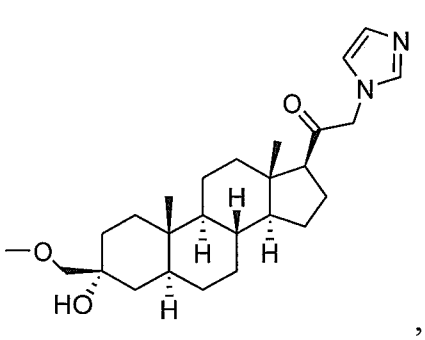

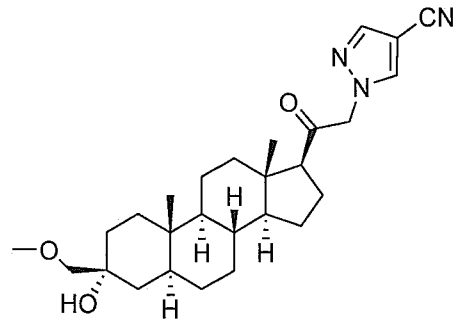
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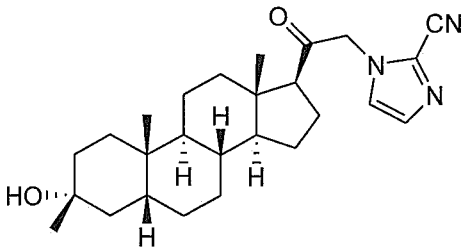
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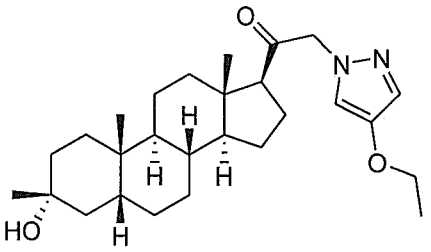
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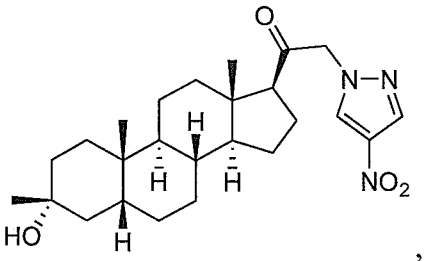
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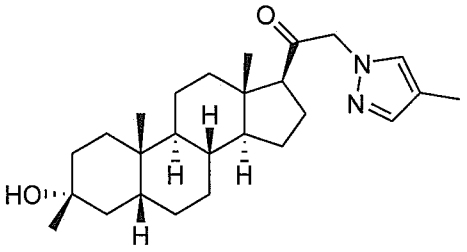
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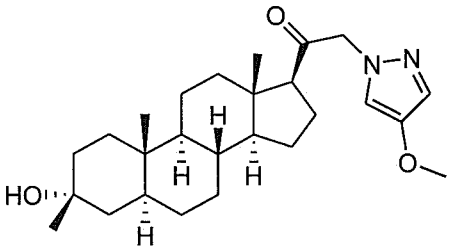
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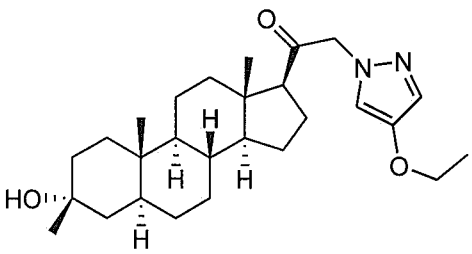
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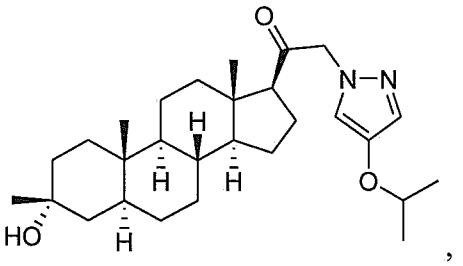
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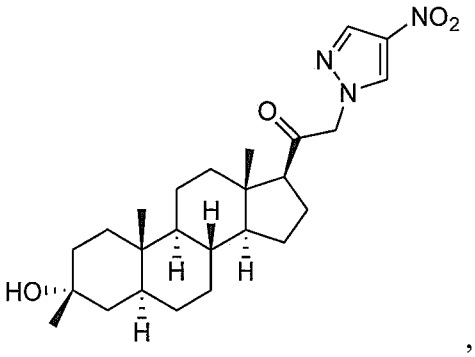
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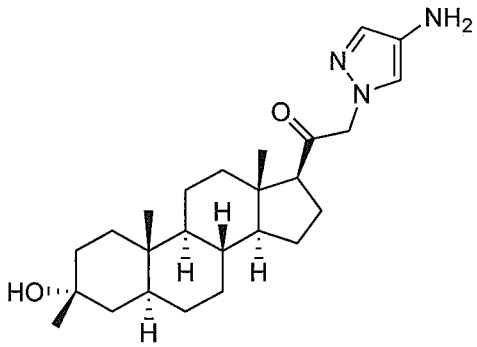
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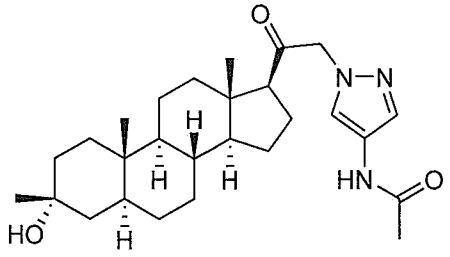
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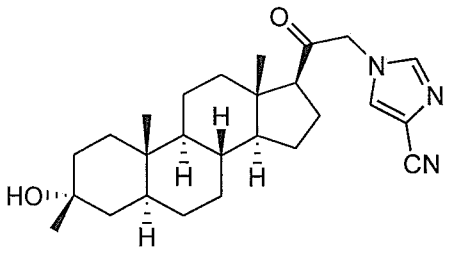
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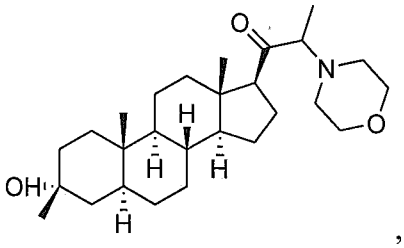
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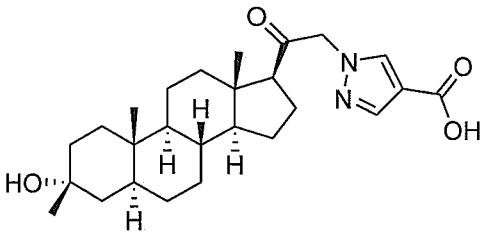
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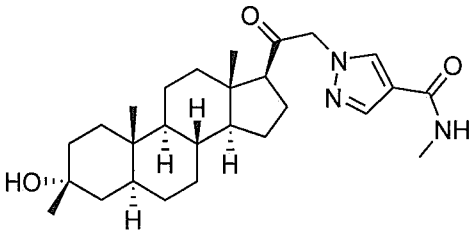
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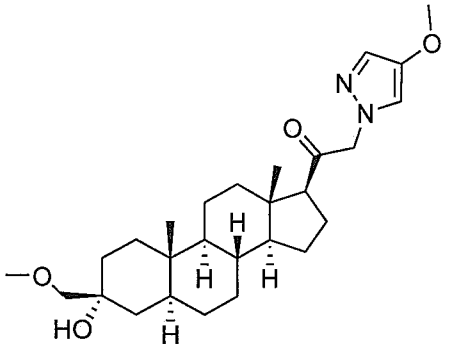
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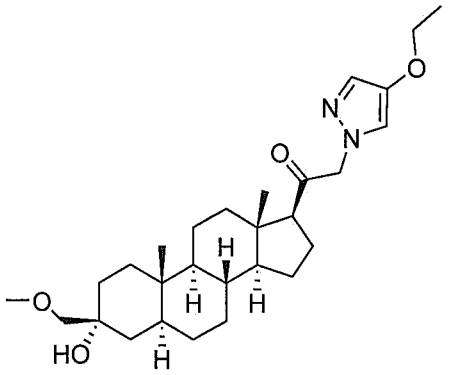
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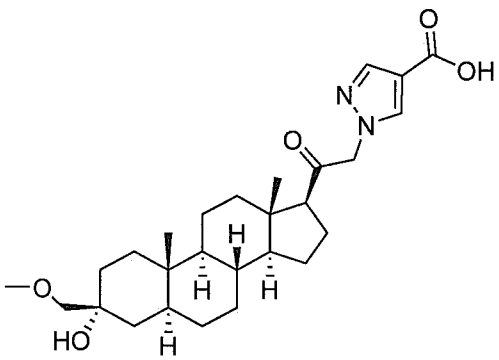
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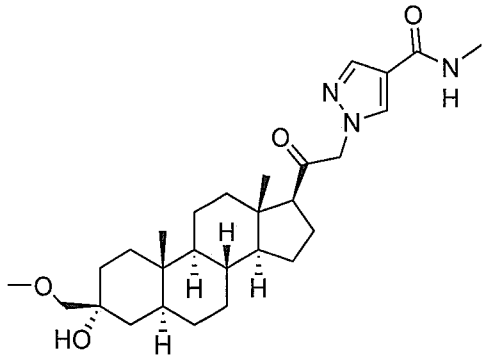
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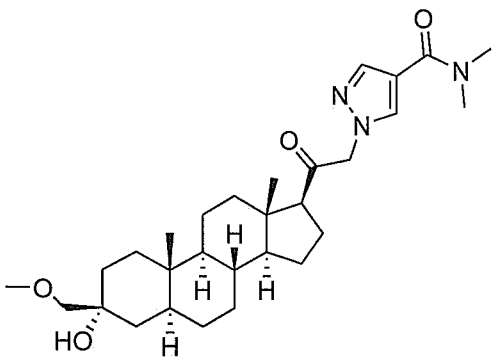
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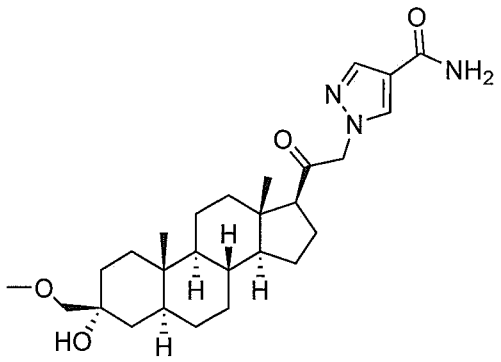
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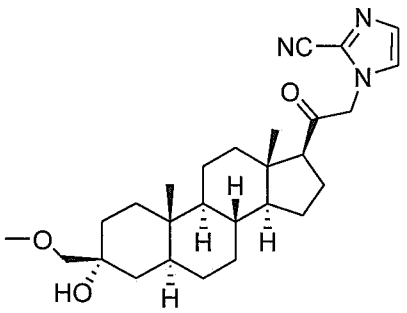
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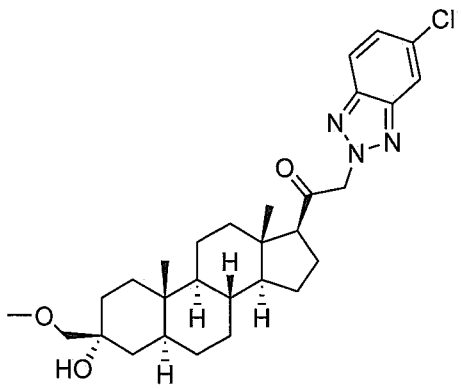
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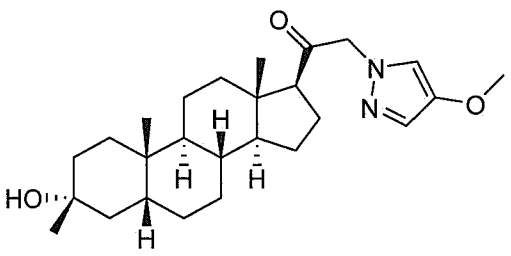
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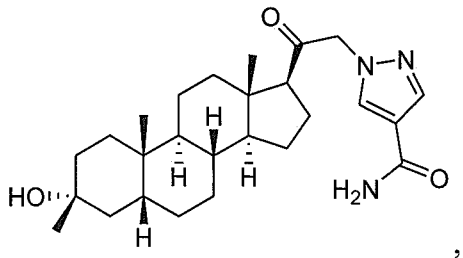
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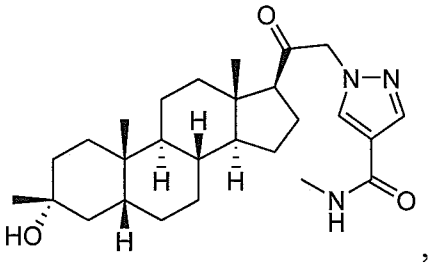
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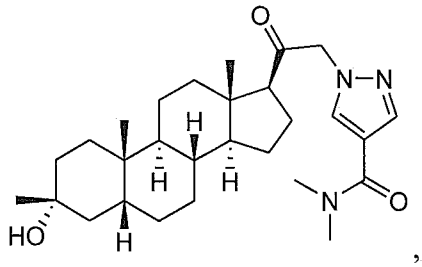
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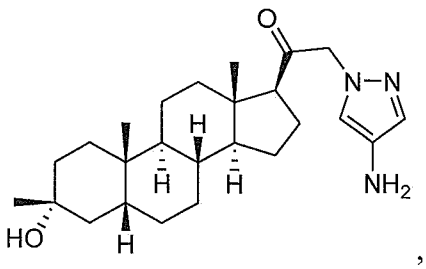
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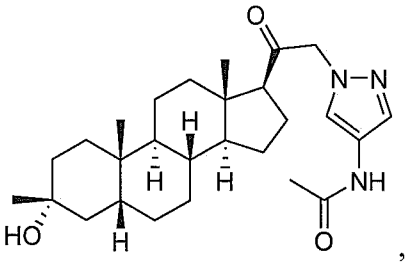
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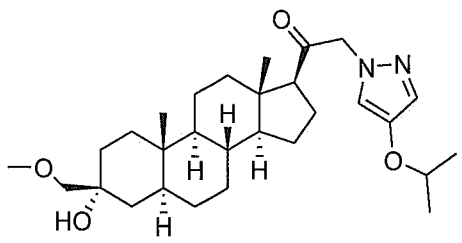
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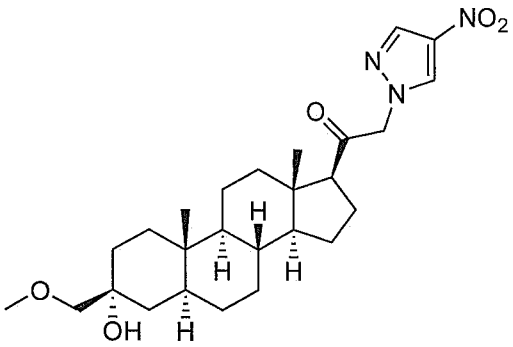
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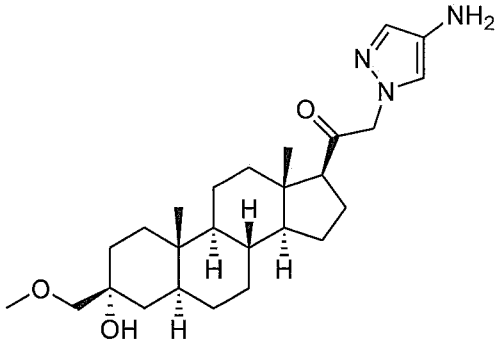
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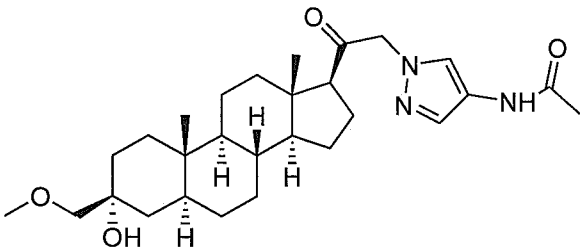
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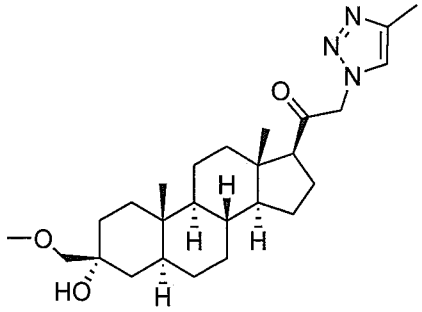
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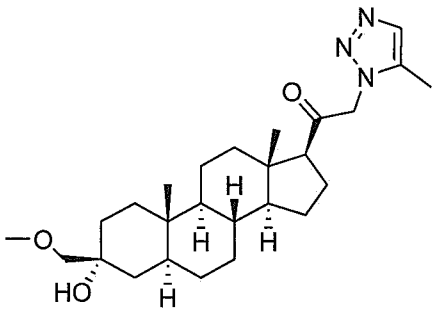
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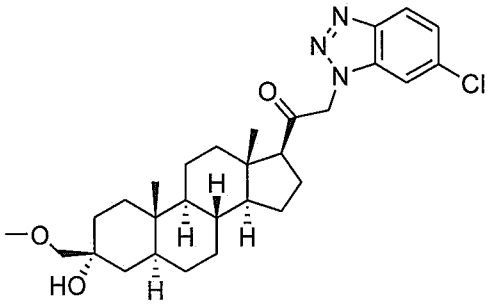
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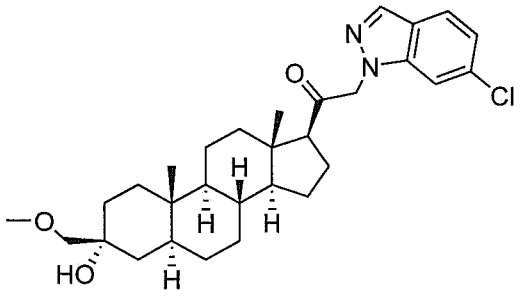
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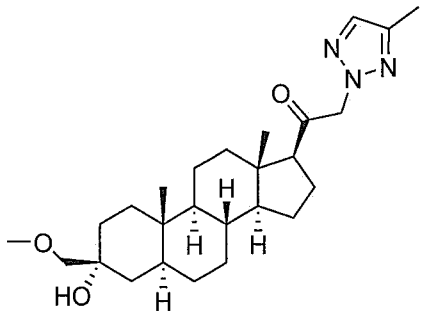
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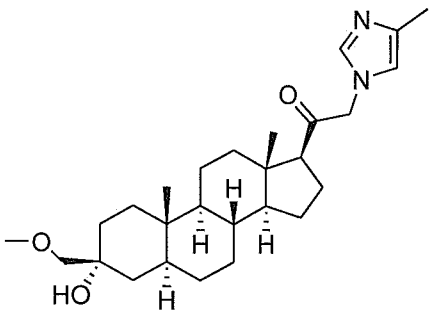
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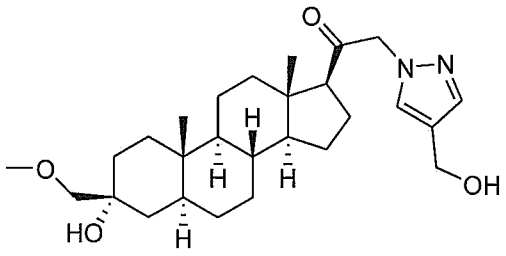
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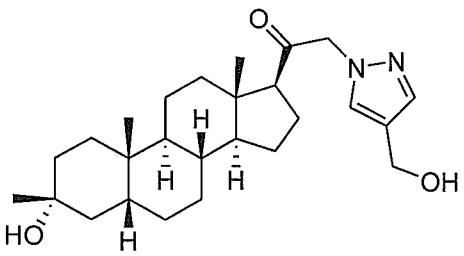
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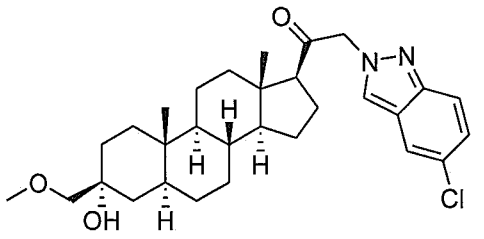
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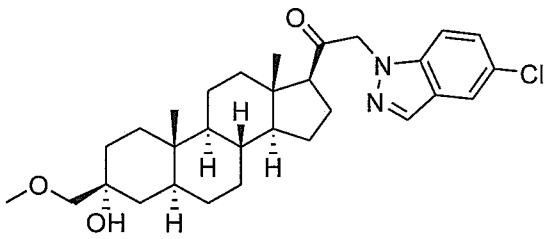
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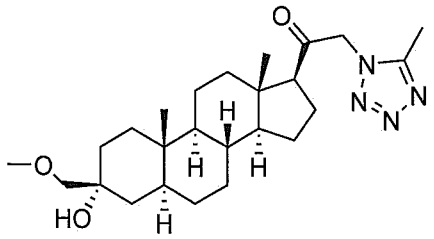
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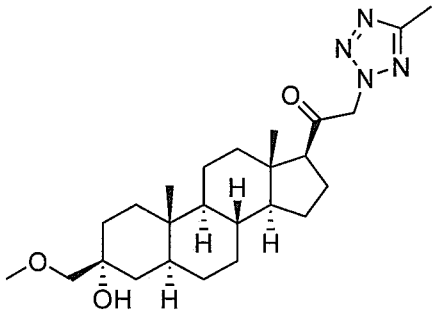
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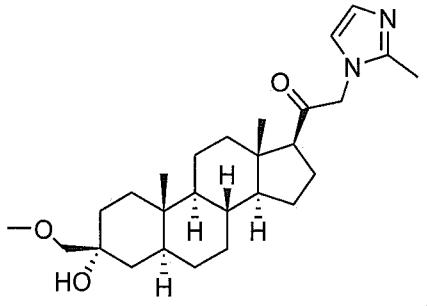
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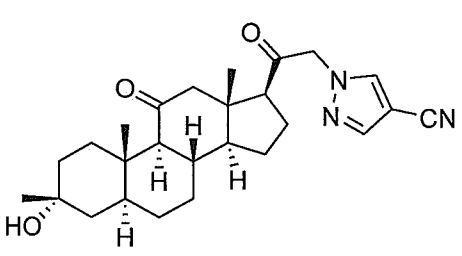

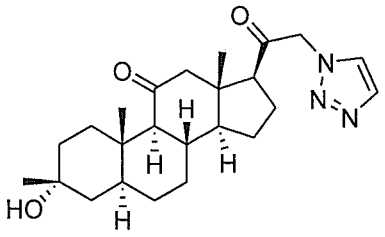
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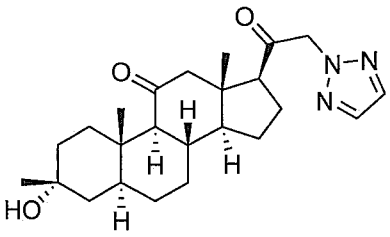
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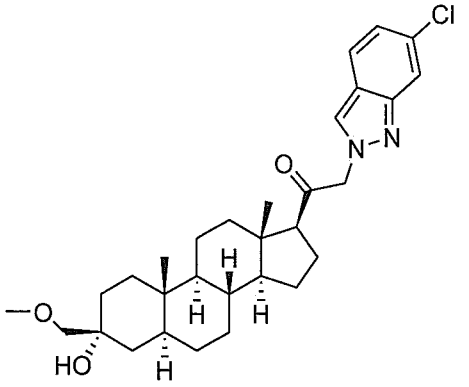
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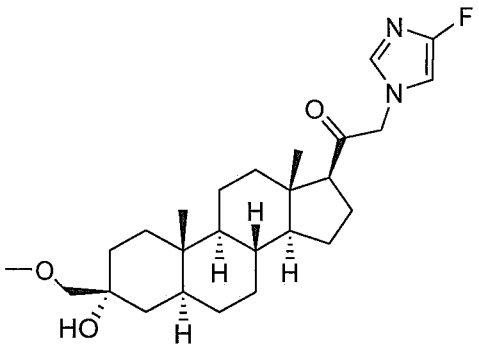
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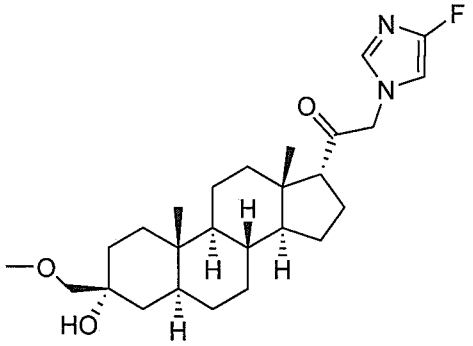
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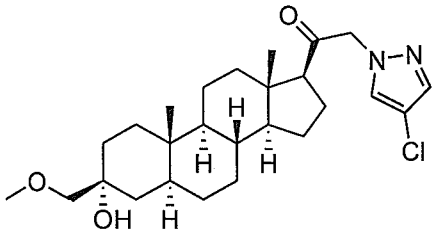
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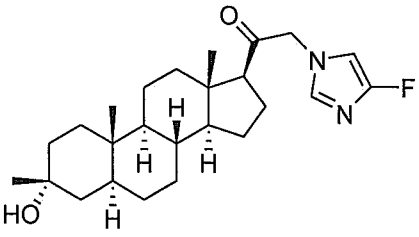
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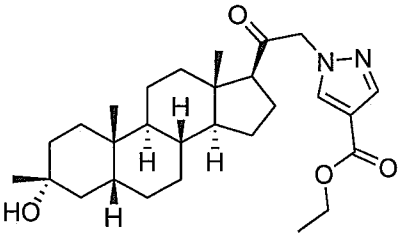
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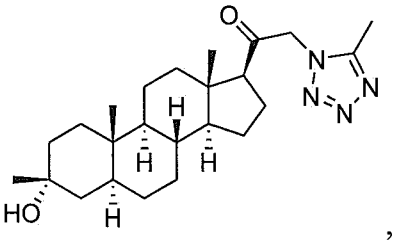
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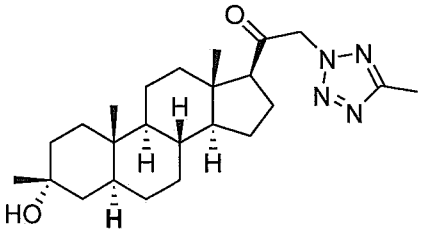

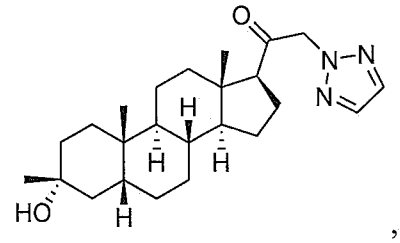
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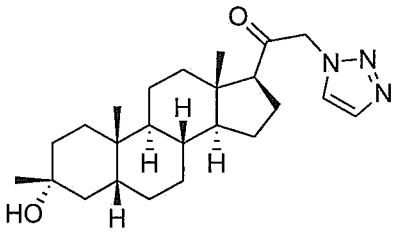
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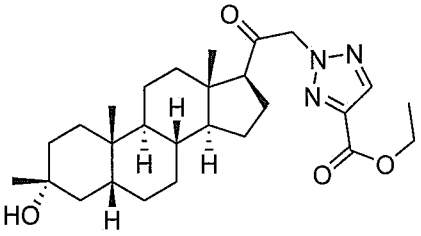
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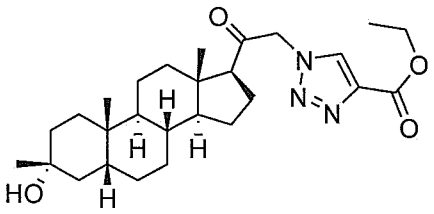
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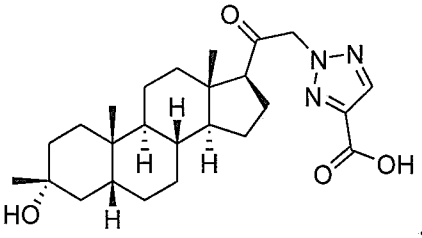
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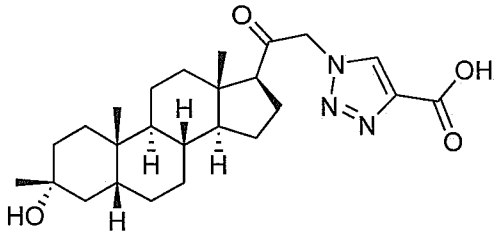
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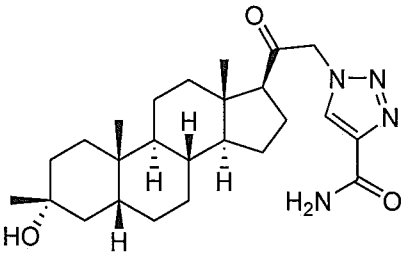
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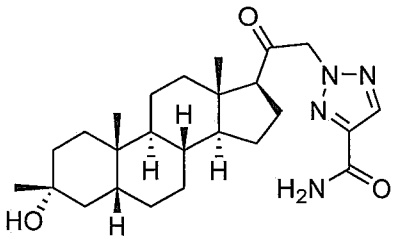
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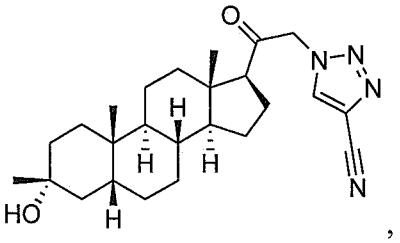
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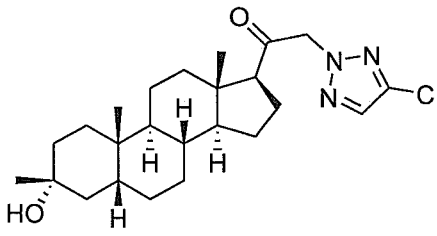
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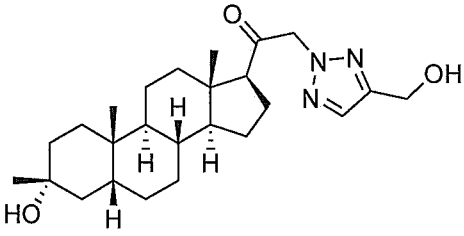
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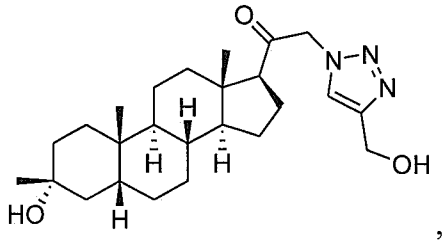
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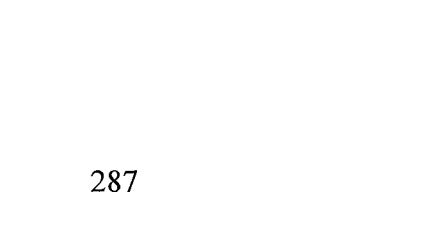
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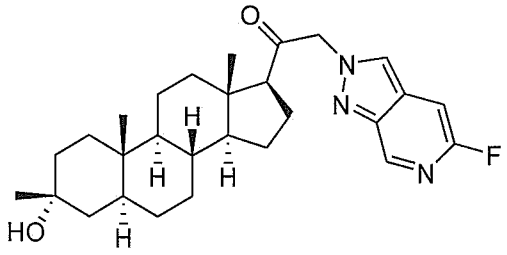
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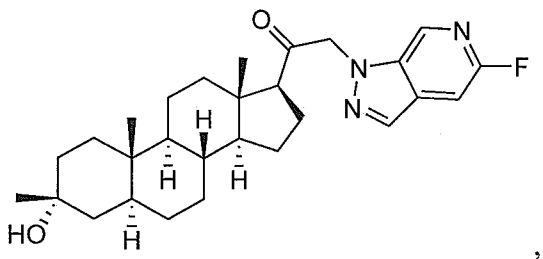
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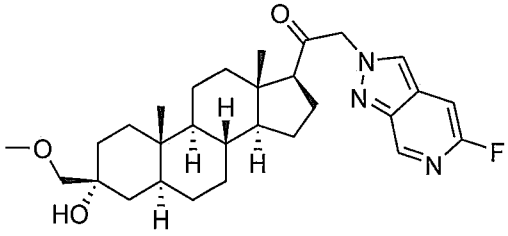
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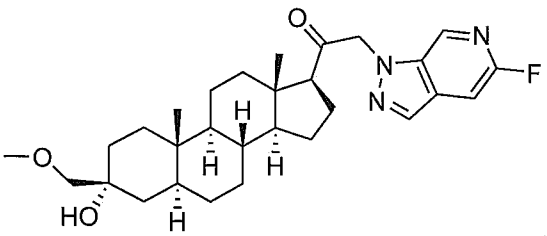
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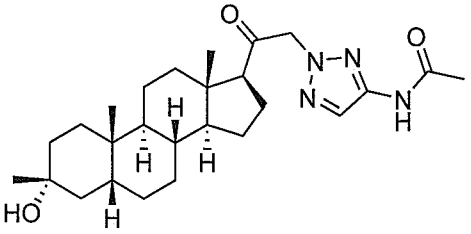
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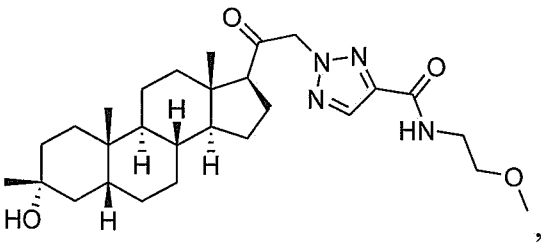
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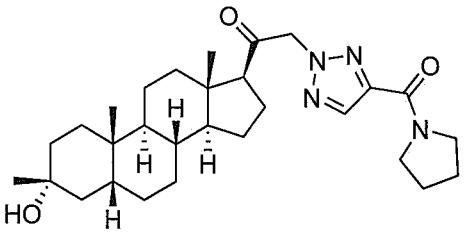
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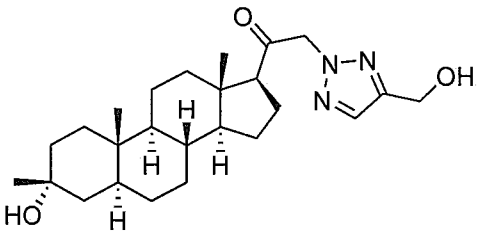
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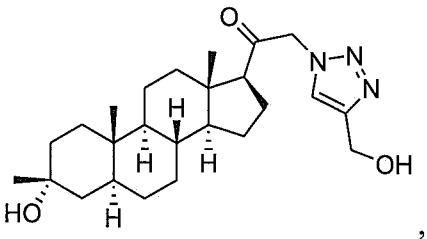
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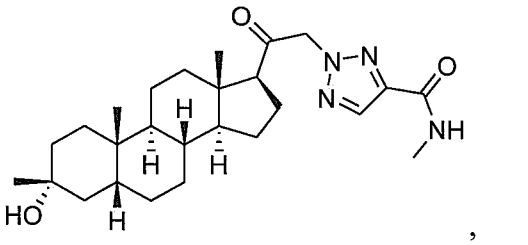
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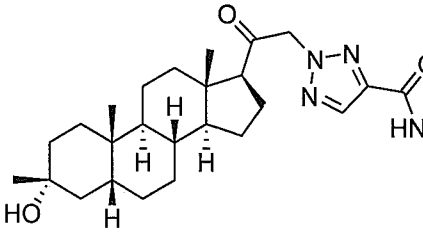
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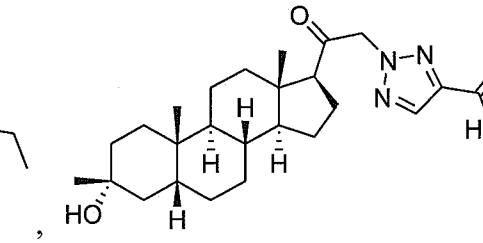
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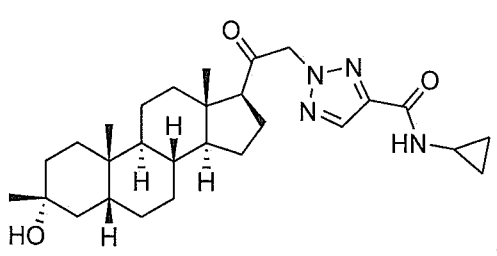
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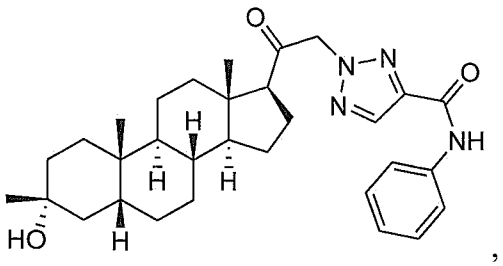
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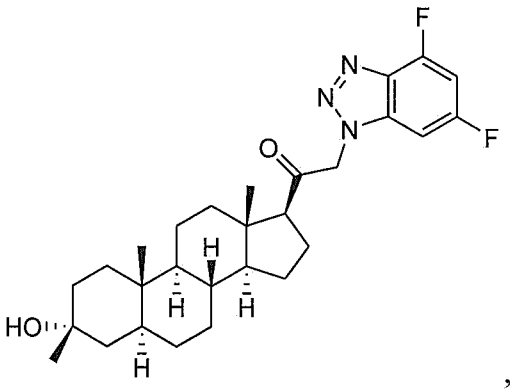
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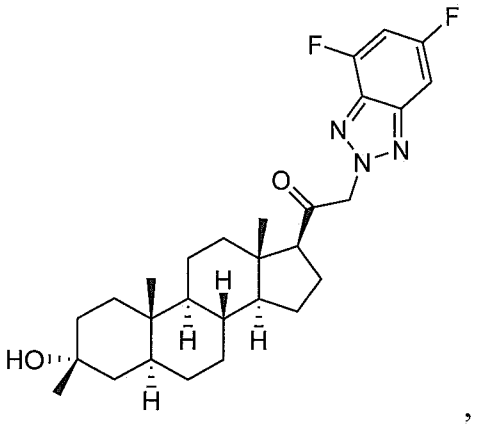
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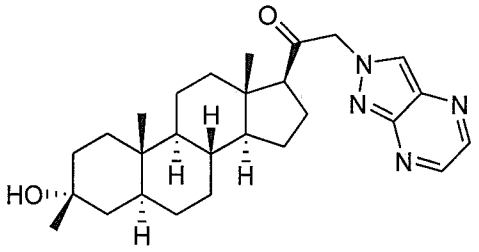
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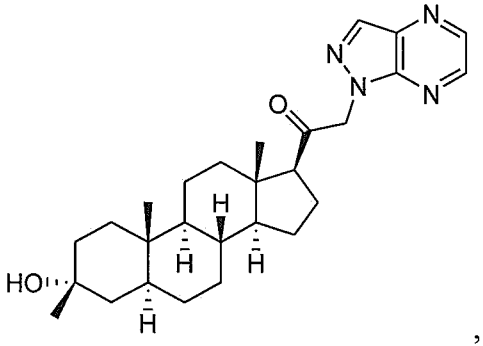
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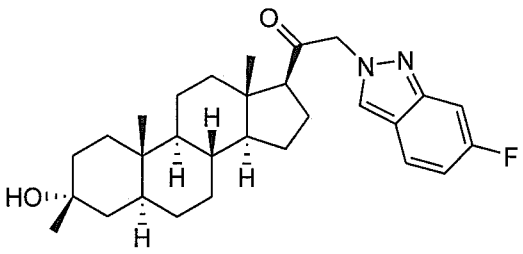
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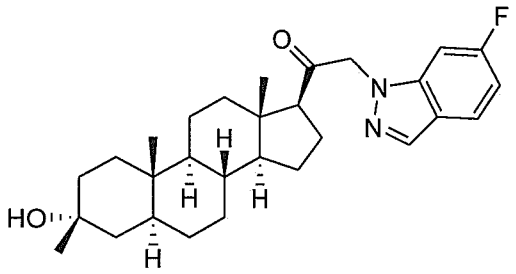
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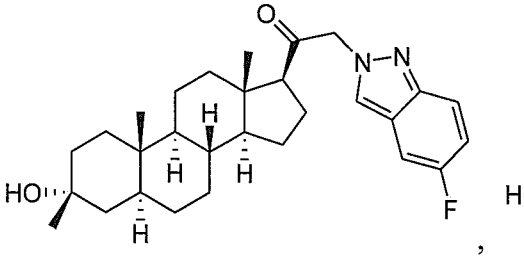
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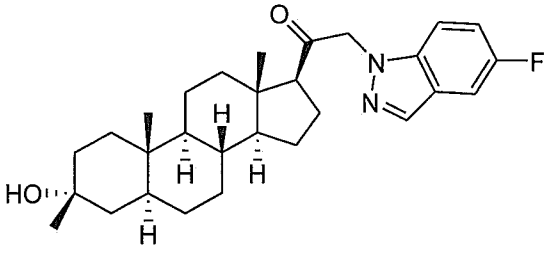
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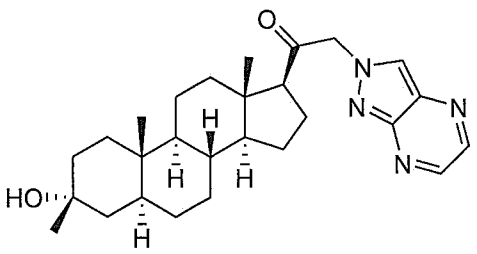
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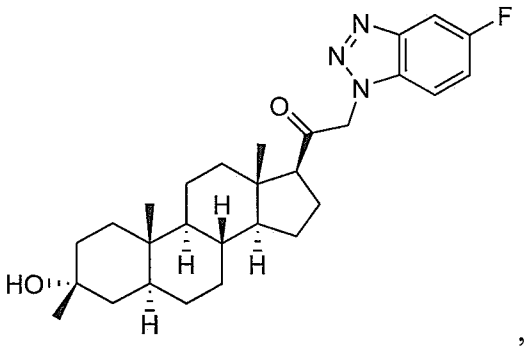
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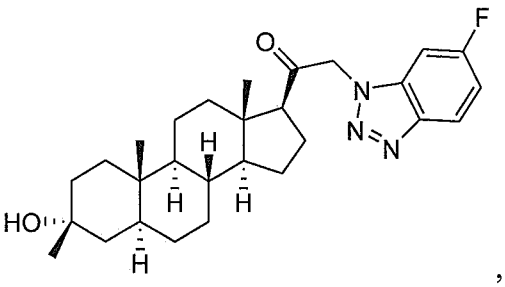
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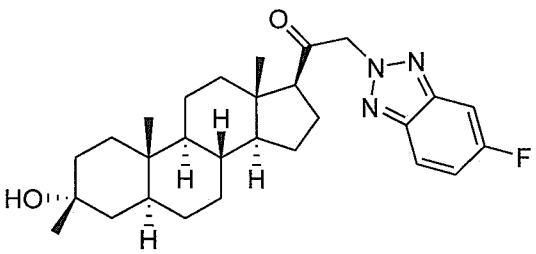
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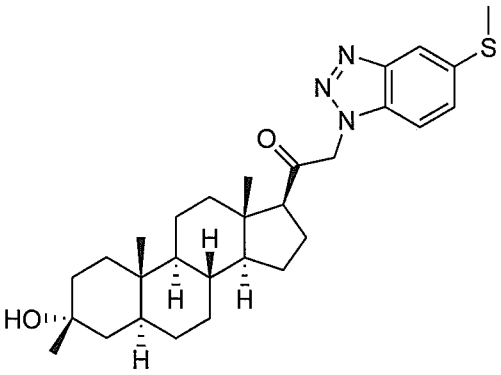
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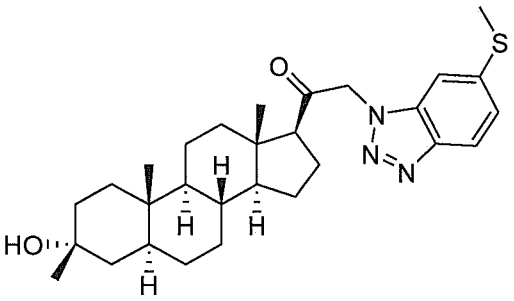
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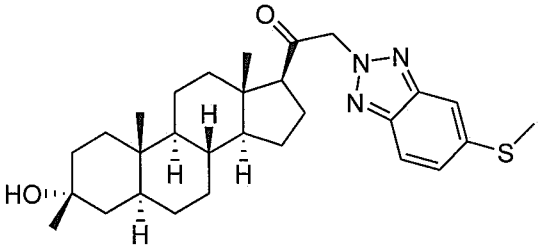
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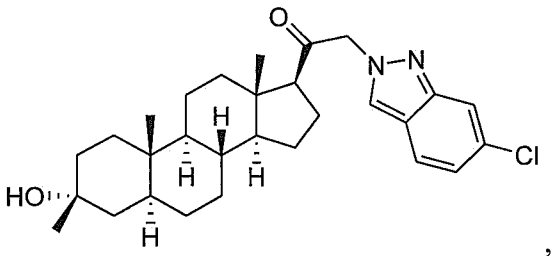
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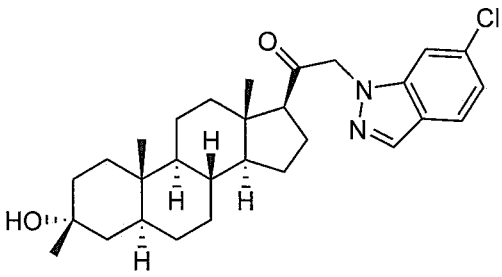
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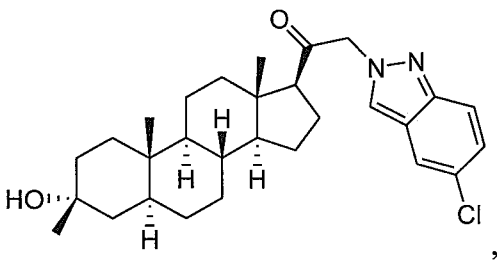
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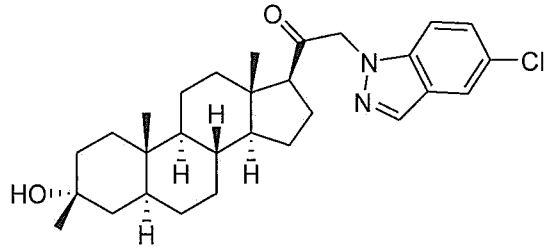
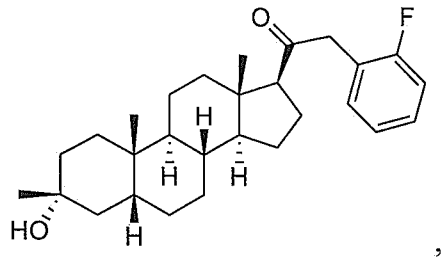
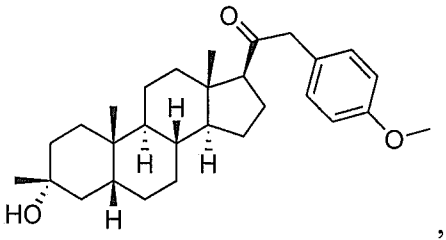
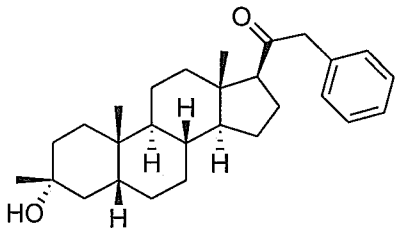
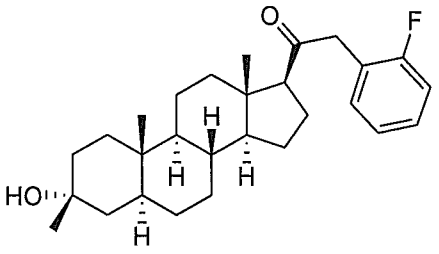
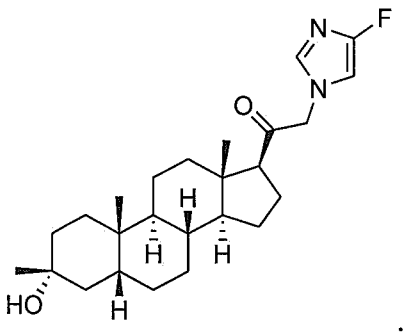
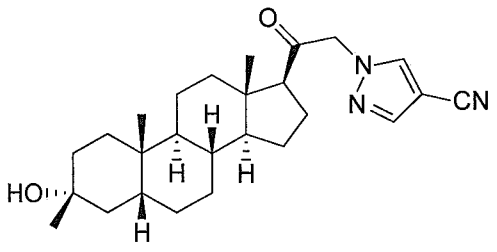
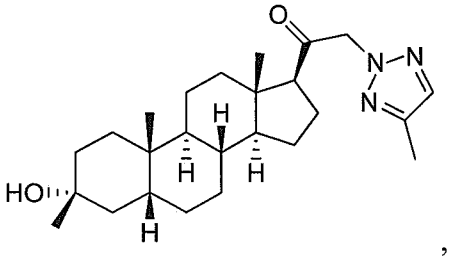
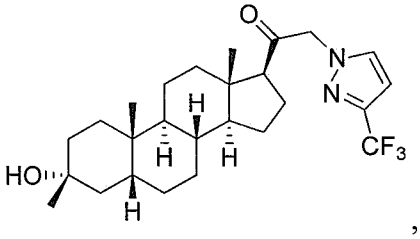
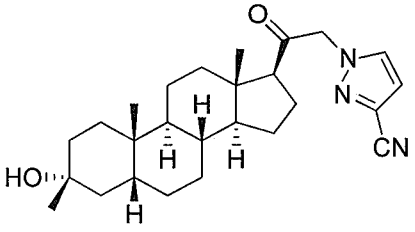
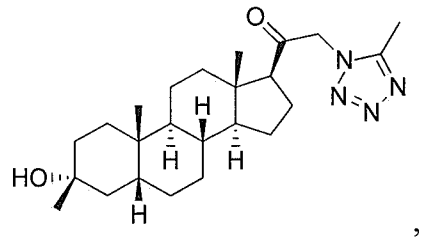







57. A pharmaceutical composition comprising a compound of any one of the preceding claims and a pharmaceutically acceptable excipient.

58. A compound, wherein the compound is: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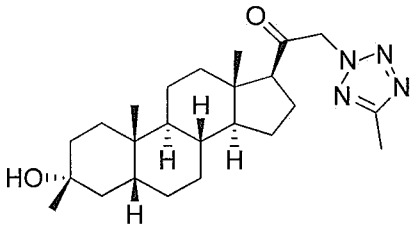
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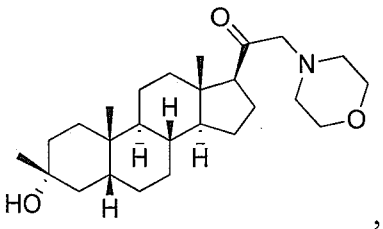
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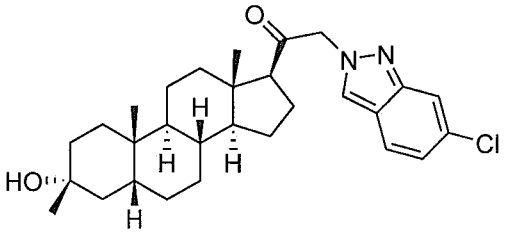
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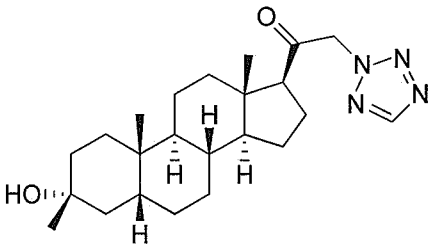
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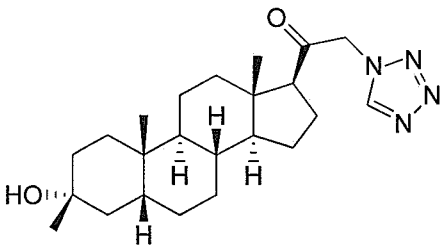
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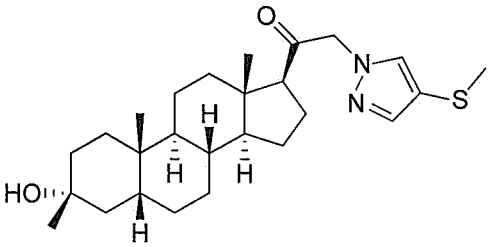
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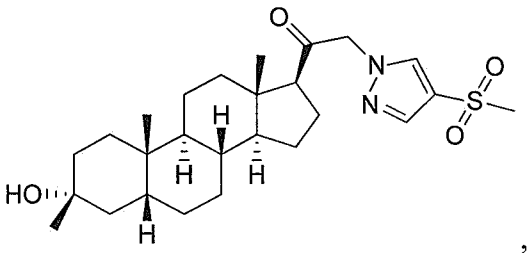
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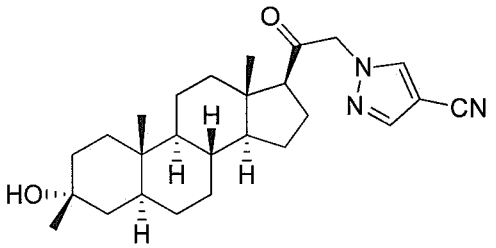
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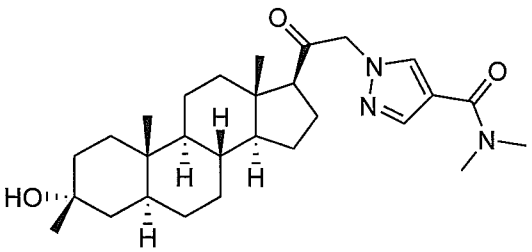
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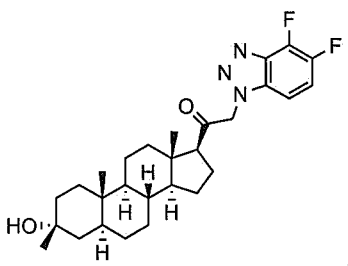
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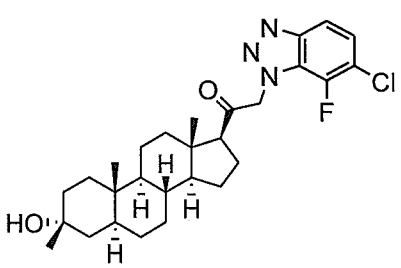
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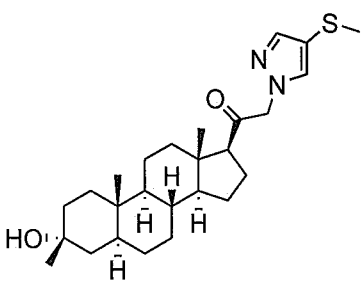
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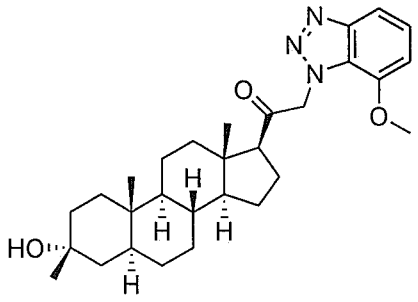
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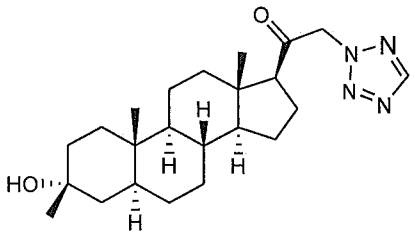
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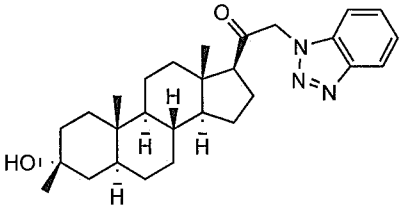
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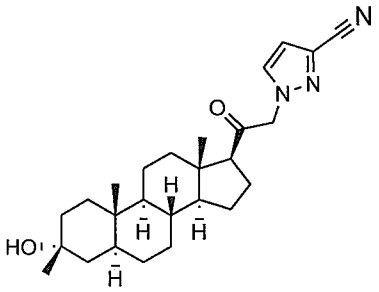
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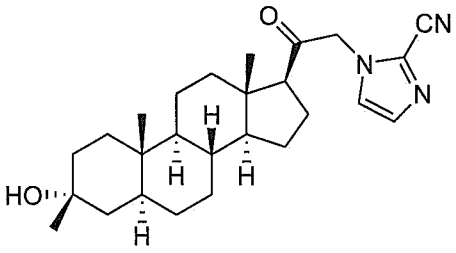
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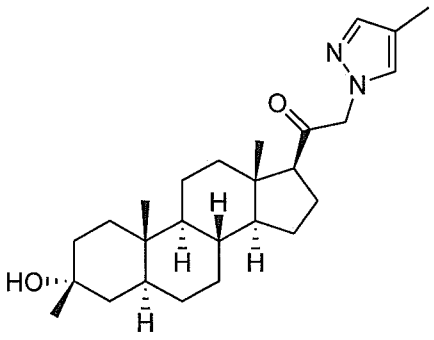
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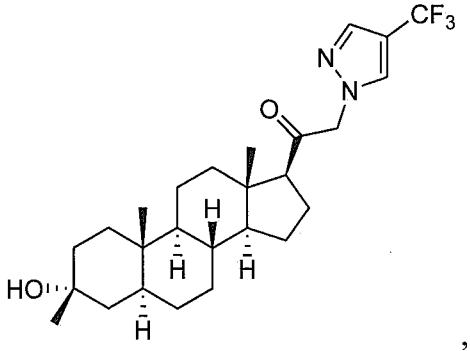
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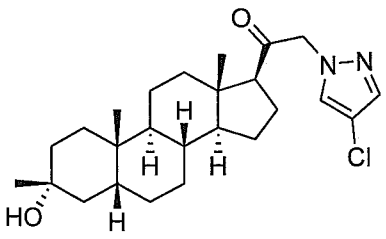
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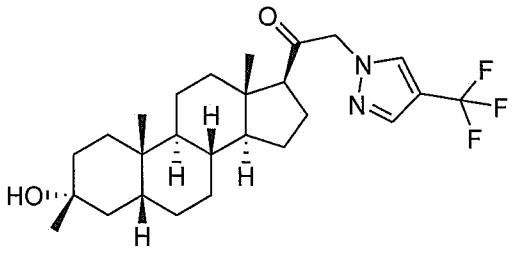
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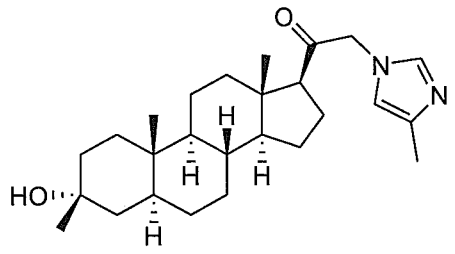
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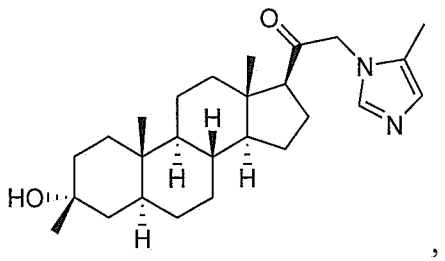
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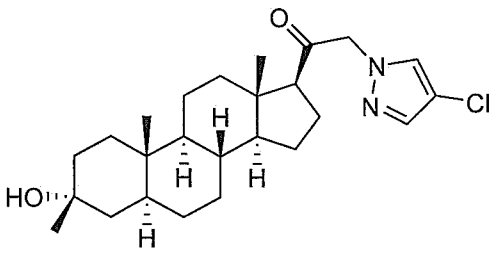
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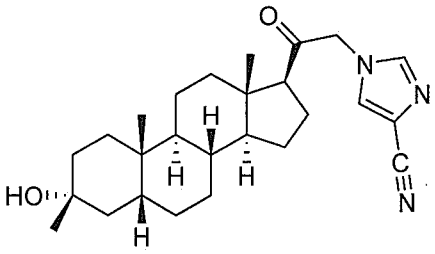
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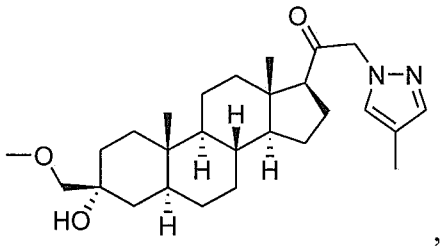
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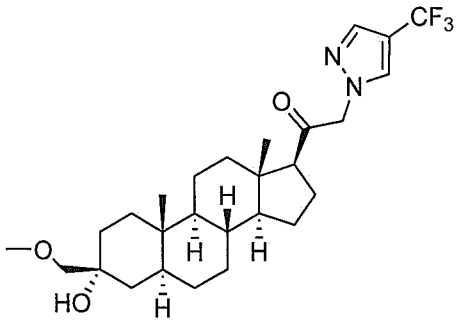
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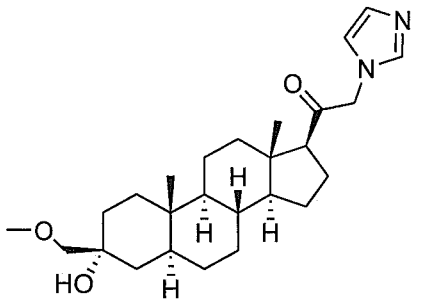
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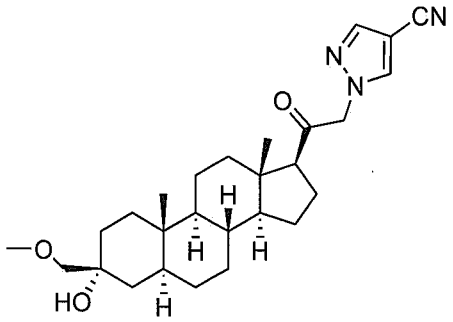
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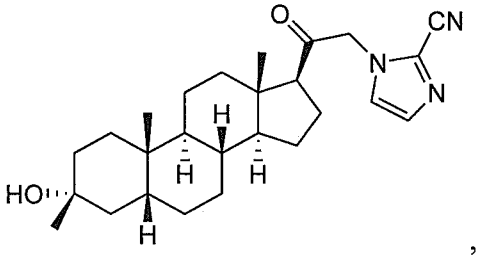
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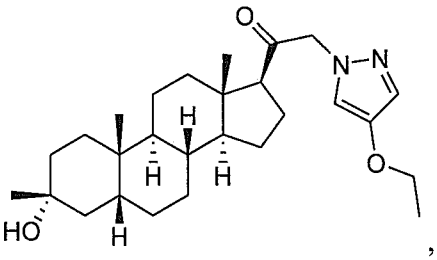
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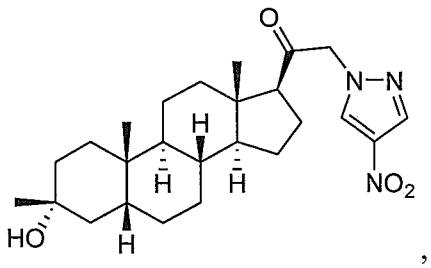
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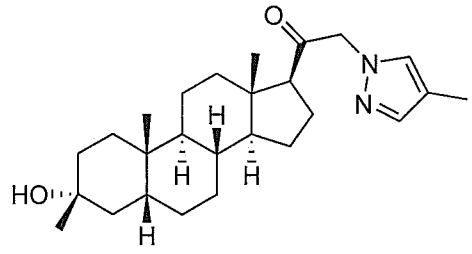
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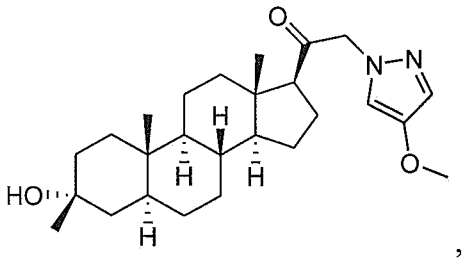
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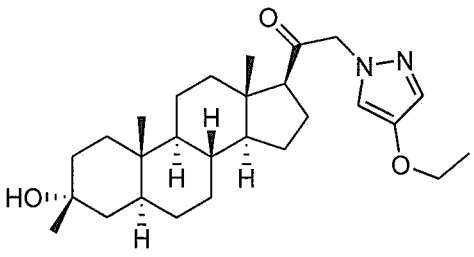
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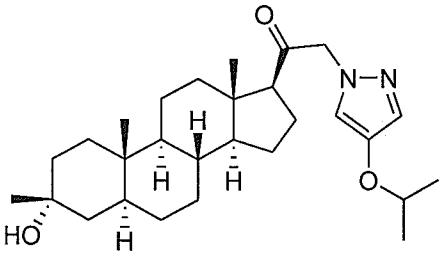
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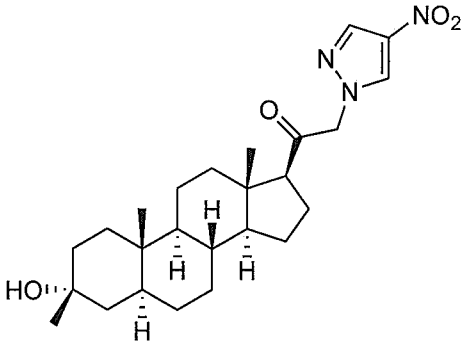
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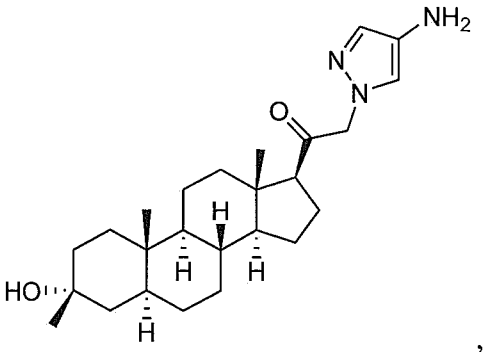
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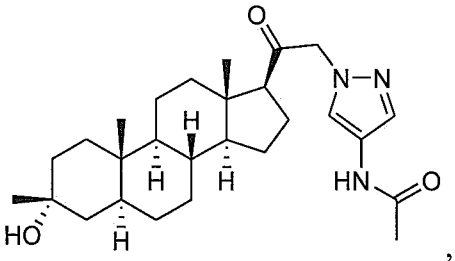
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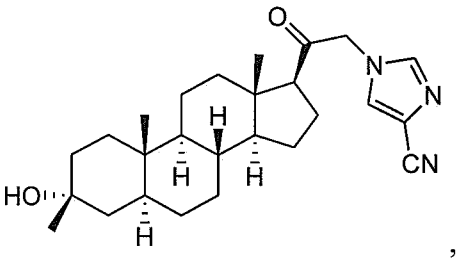
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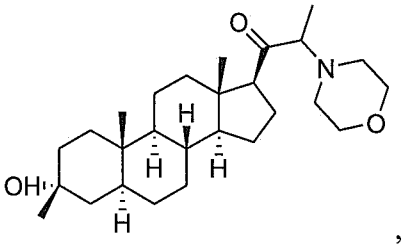
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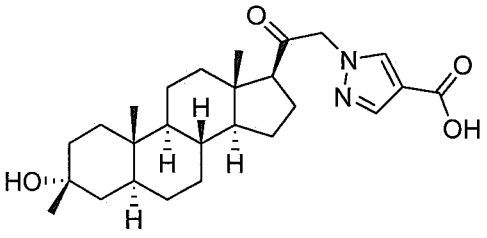
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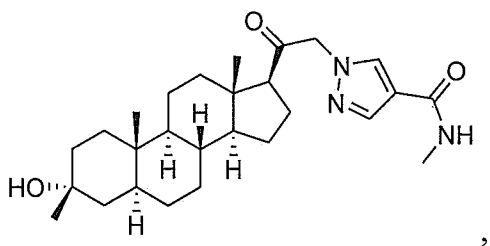
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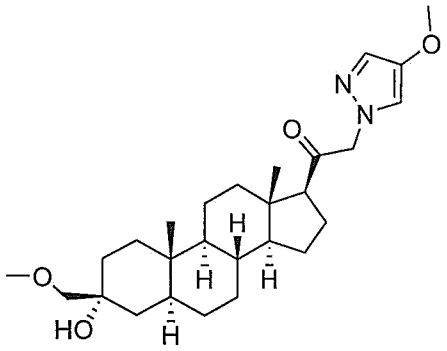
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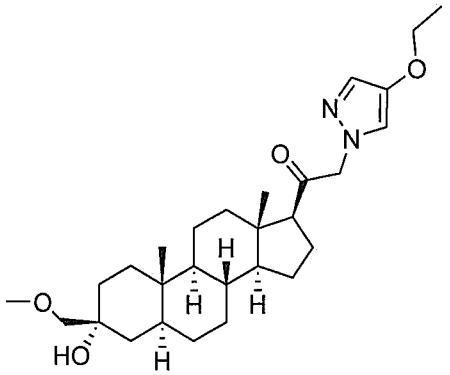
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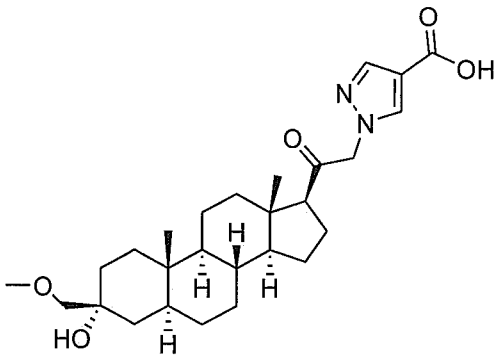
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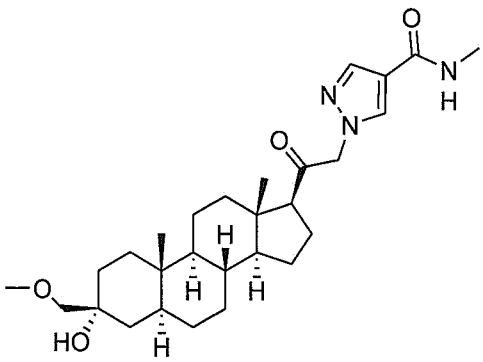
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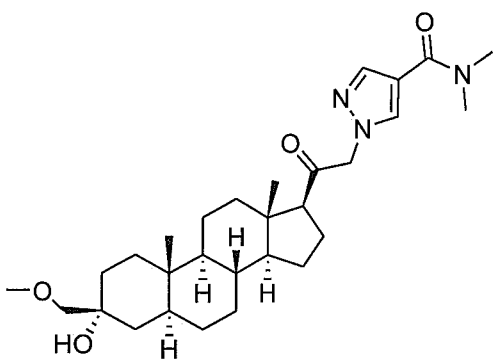
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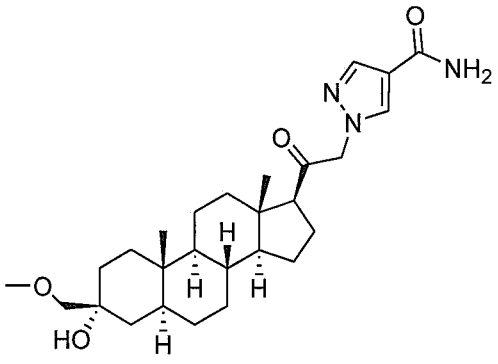
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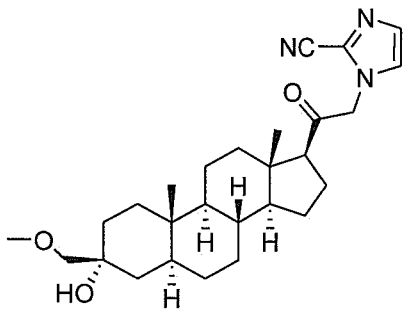
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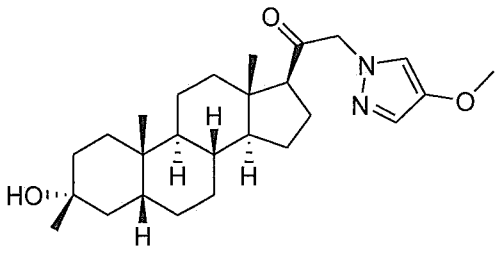
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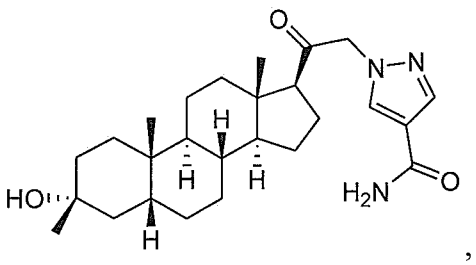
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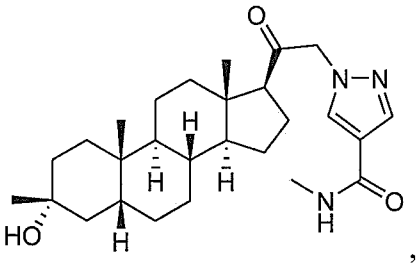
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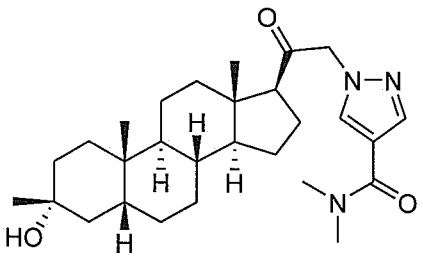
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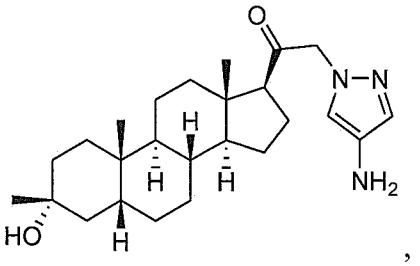
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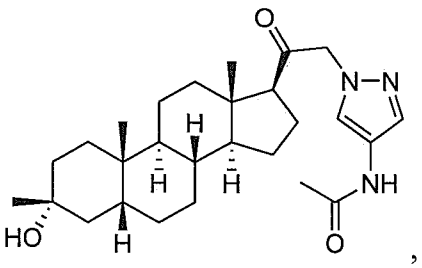
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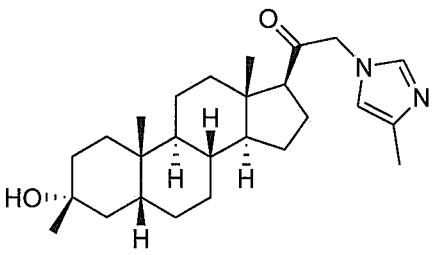
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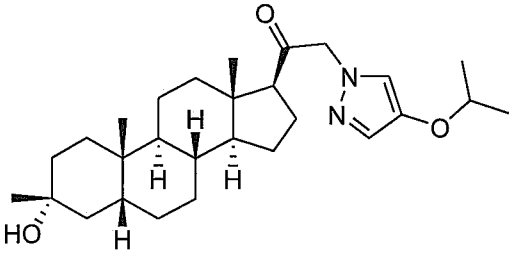
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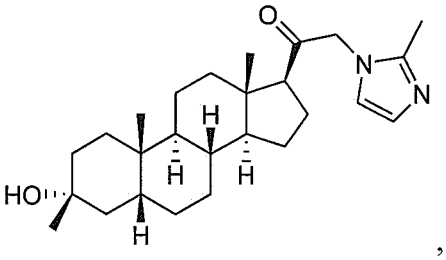
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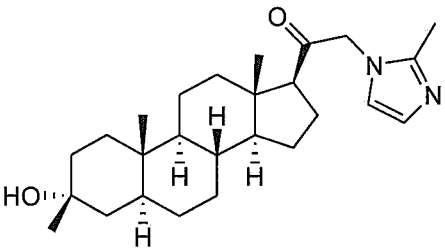
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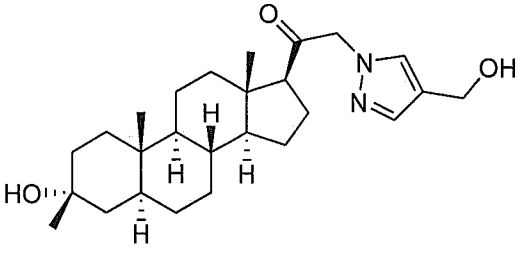
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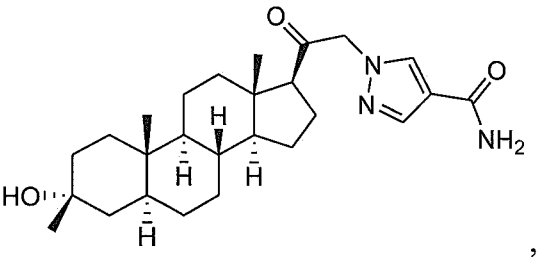
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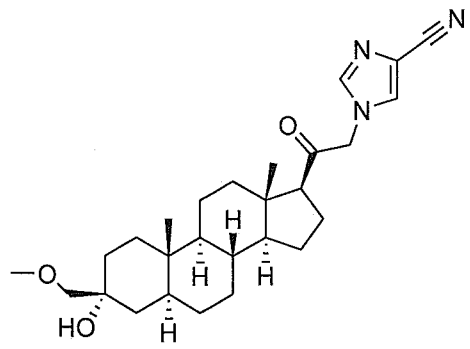
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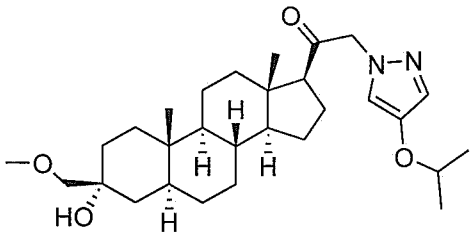
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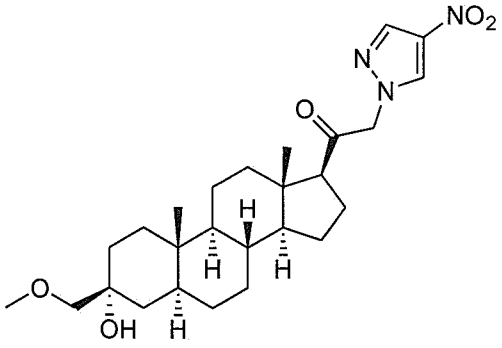
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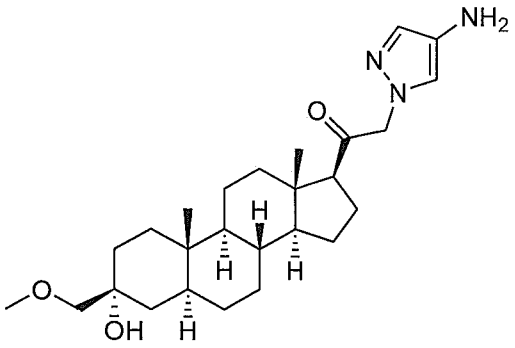
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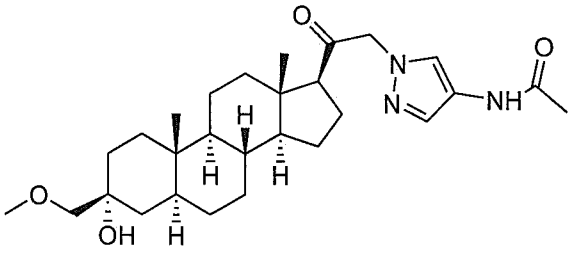
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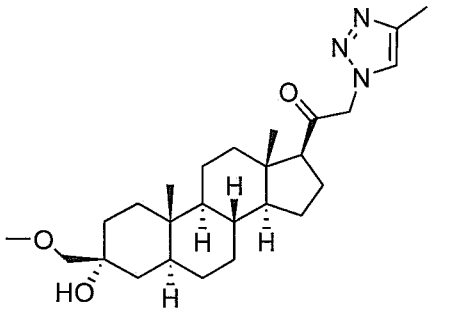
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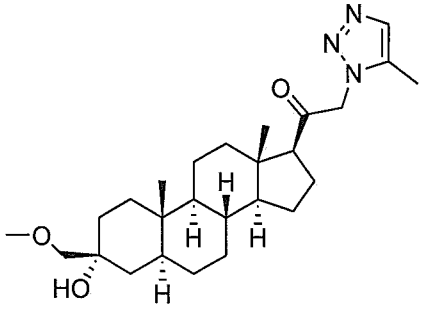
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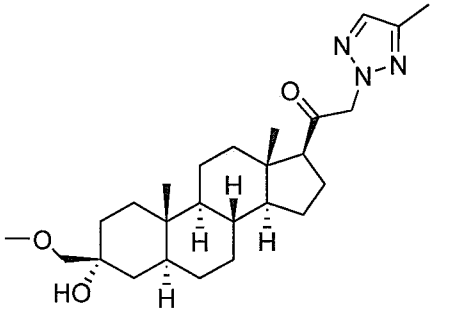
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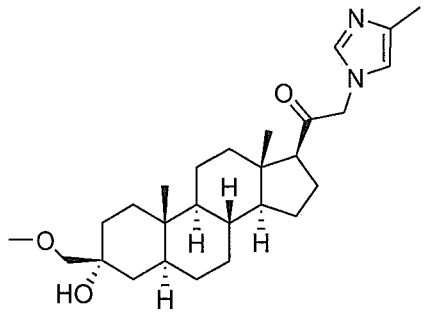
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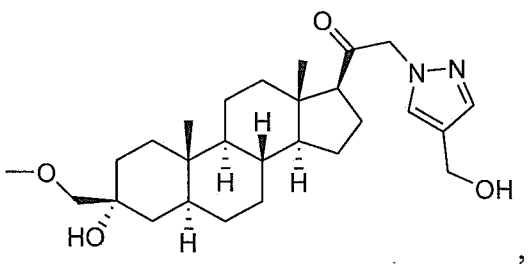
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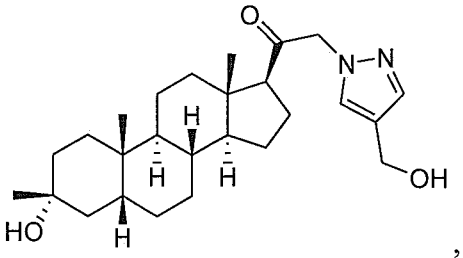
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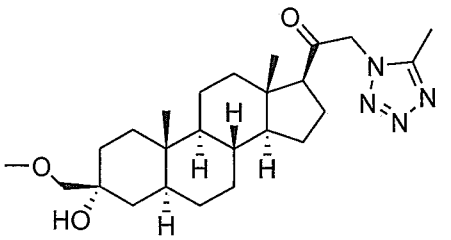
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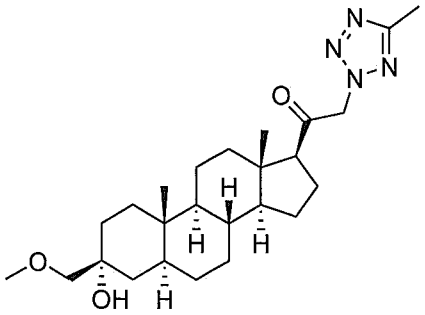
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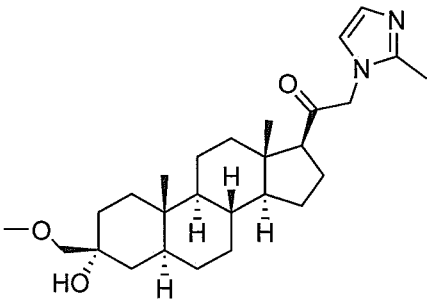
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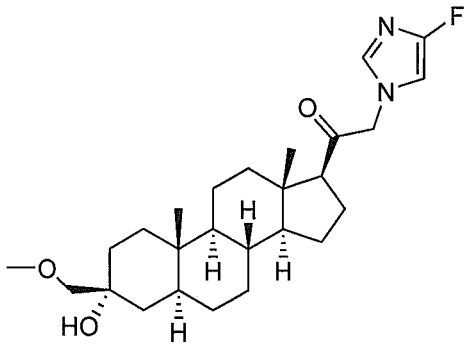
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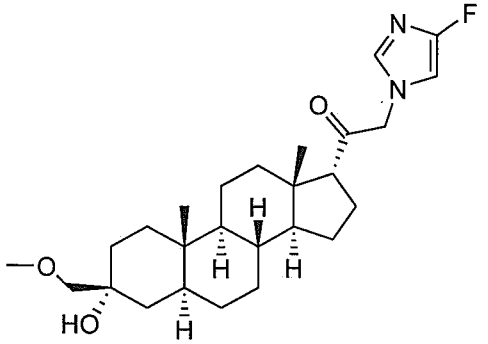
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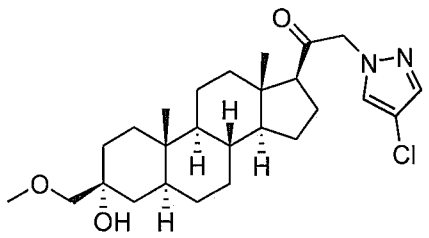
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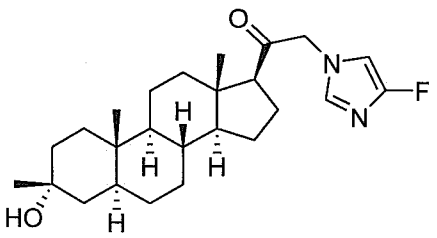
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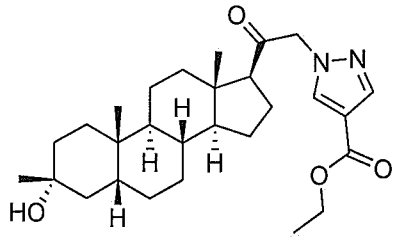
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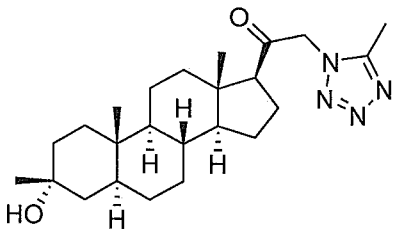
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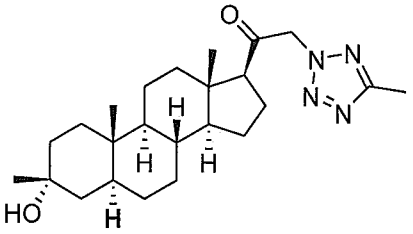
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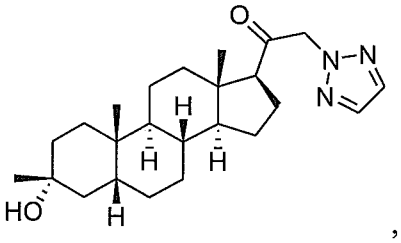
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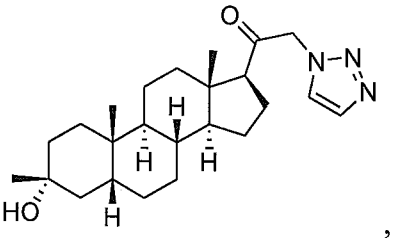
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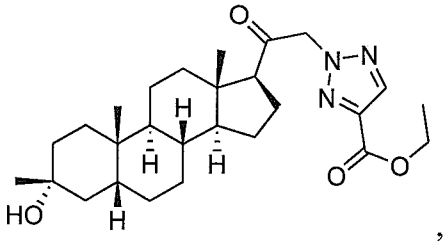
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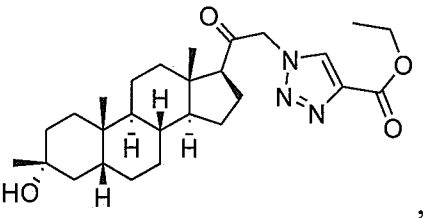
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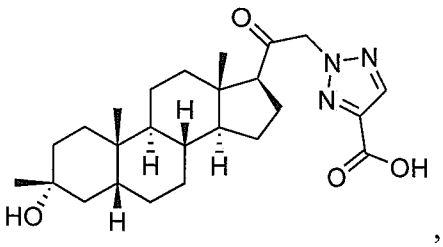
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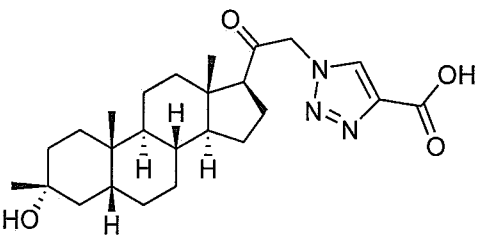
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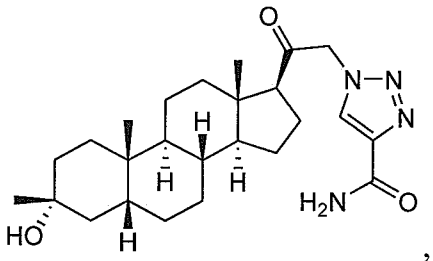
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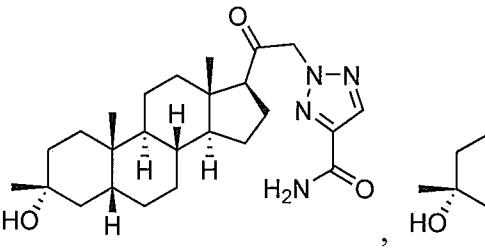
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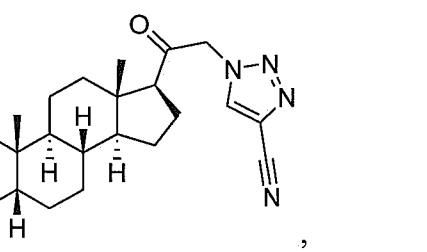
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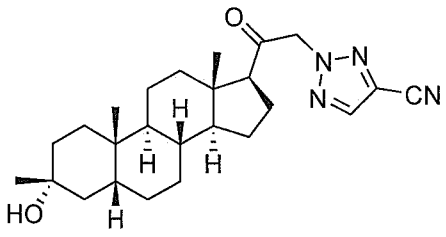
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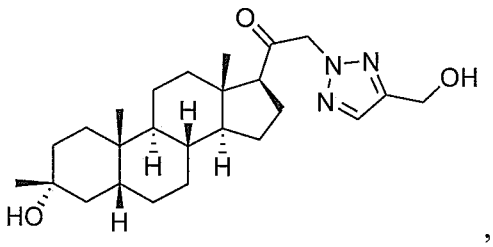
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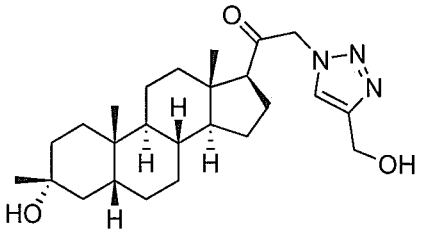
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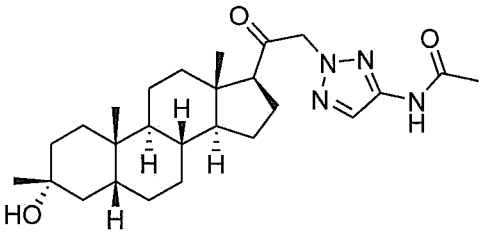
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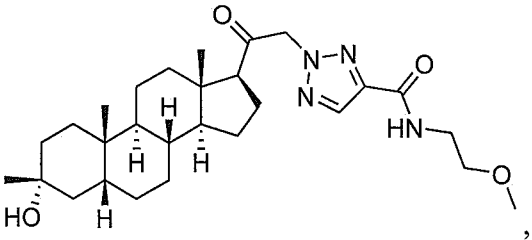
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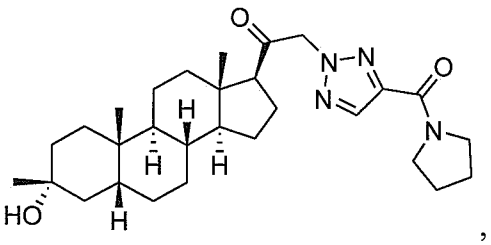
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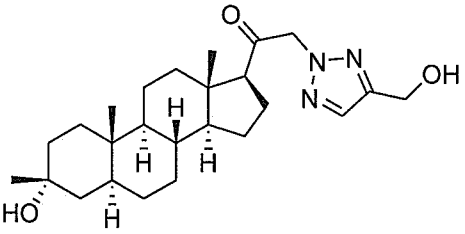
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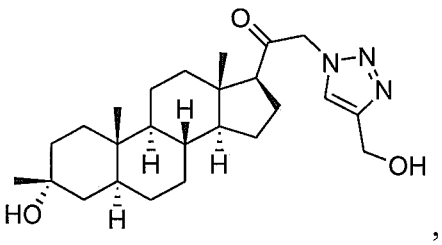
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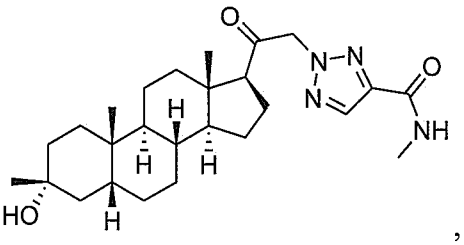
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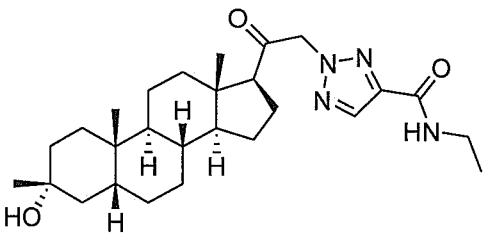
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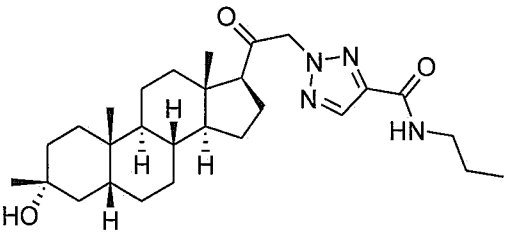
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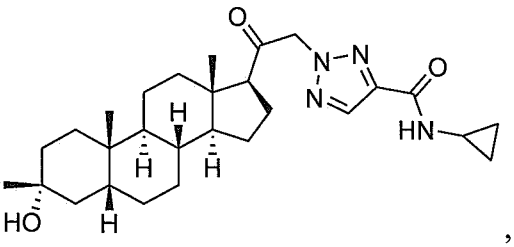
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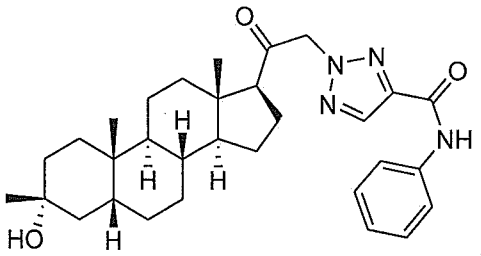
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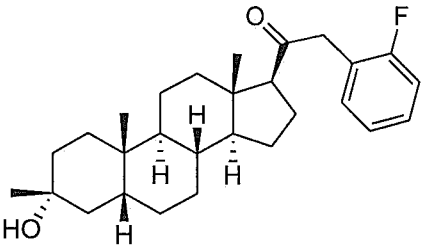
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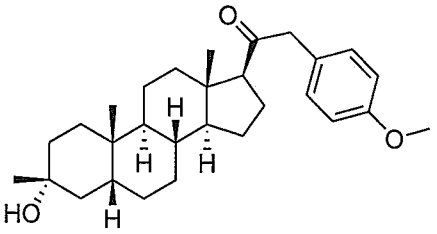
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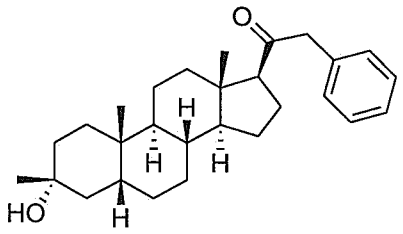
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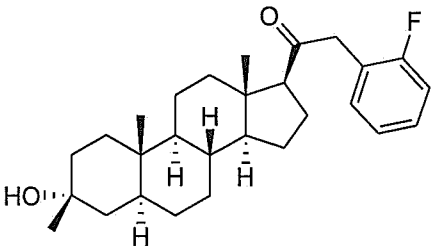
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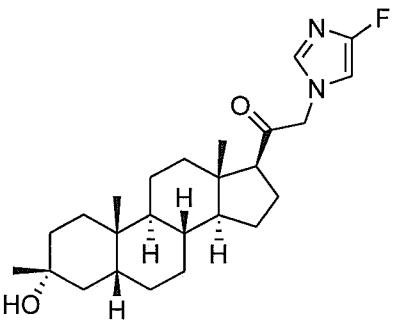
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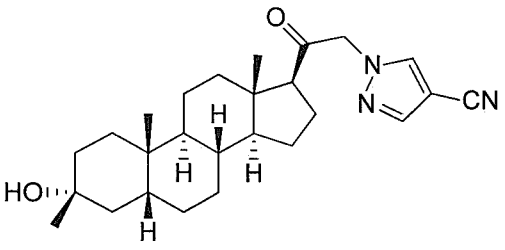
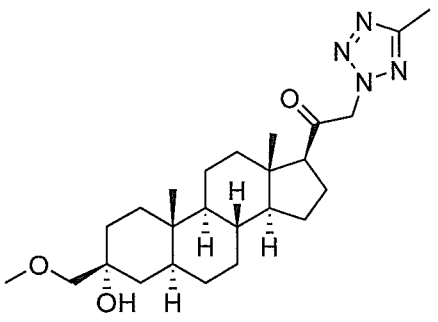
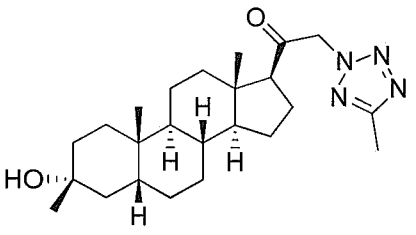
59. A compound, wherein the compound is:  .

60. A compound, wherein the compound is:  .

61. A compound, wherein the compound is:  .

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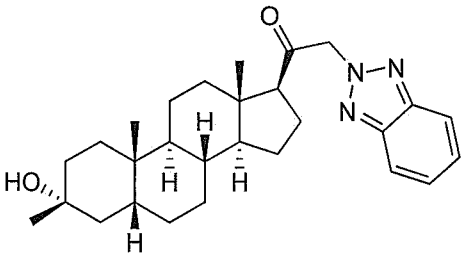
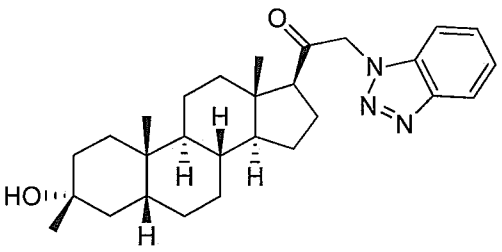
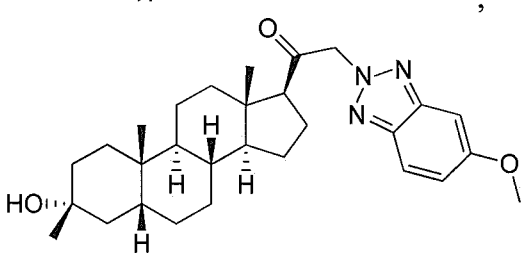
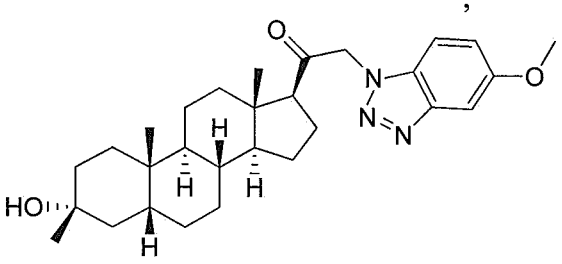
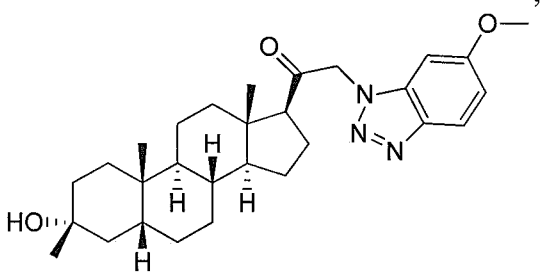
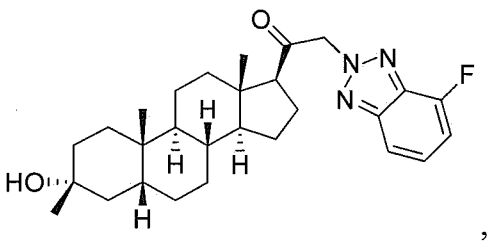
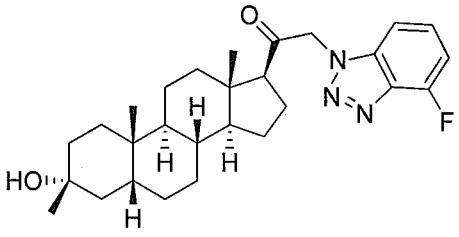
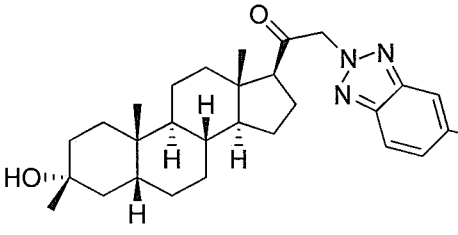
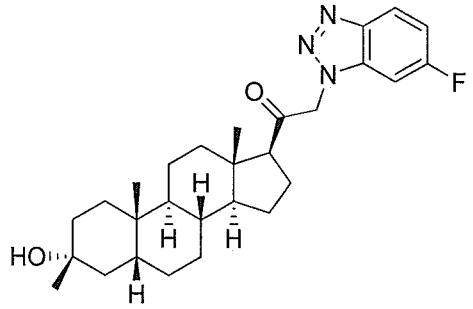
 ,
 ,
 ,
 ,
 ,
 ,
 ,
 .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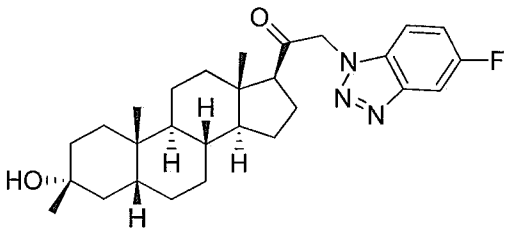
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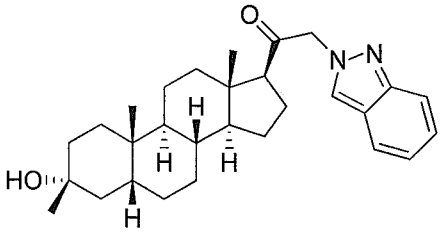
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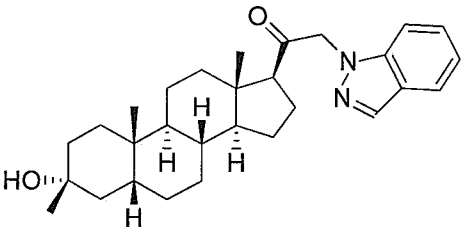
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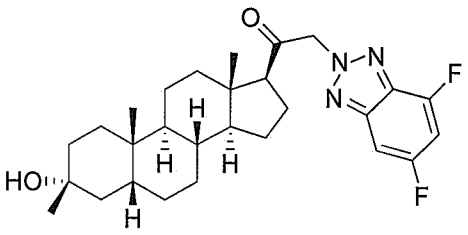
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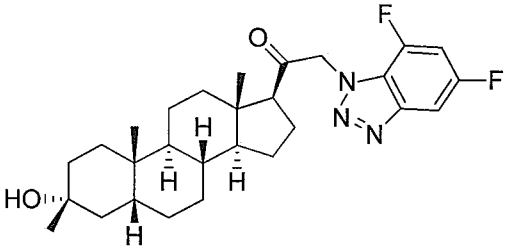
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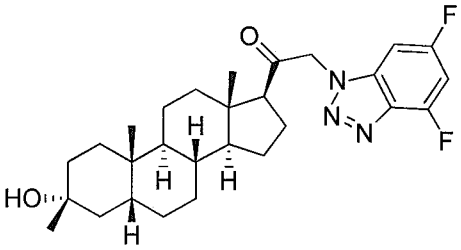
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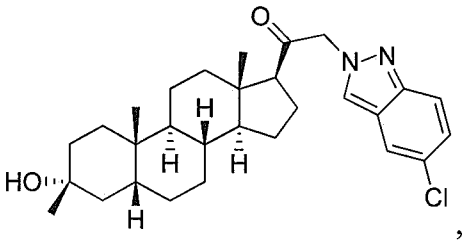
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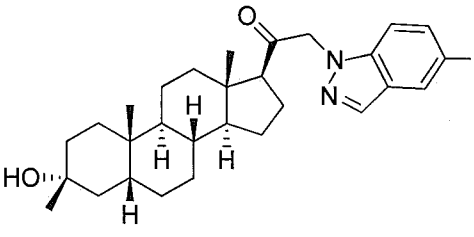
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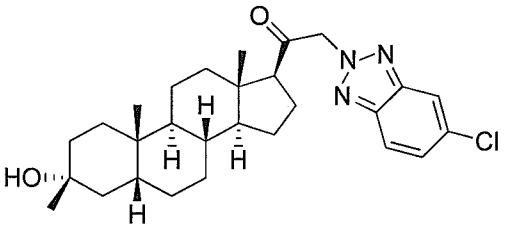
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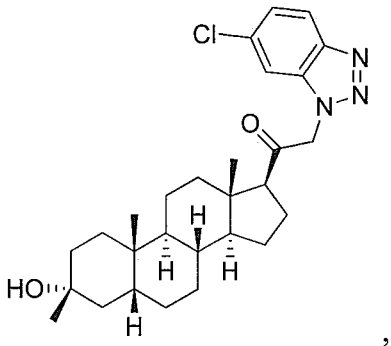
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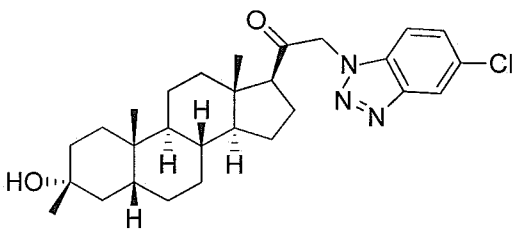
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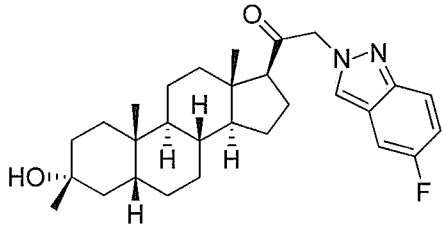
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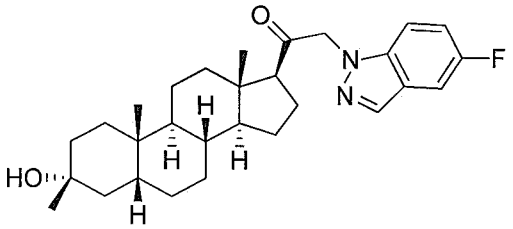
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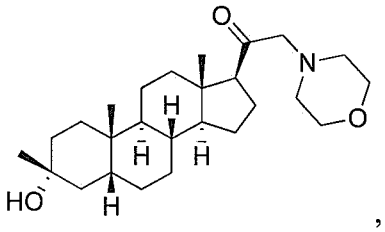
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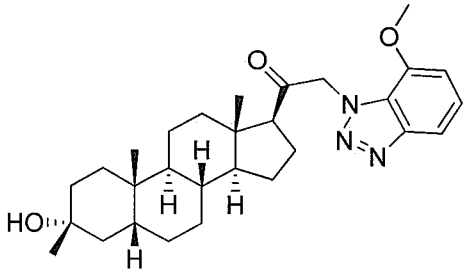
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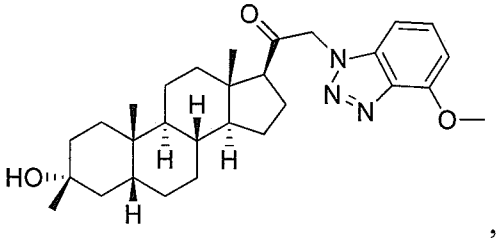
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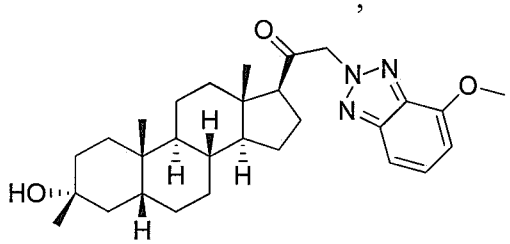
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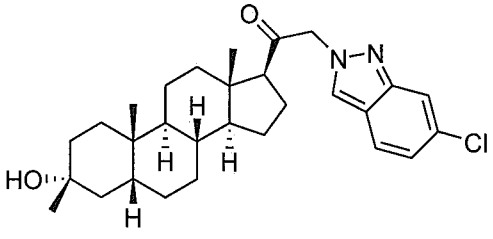
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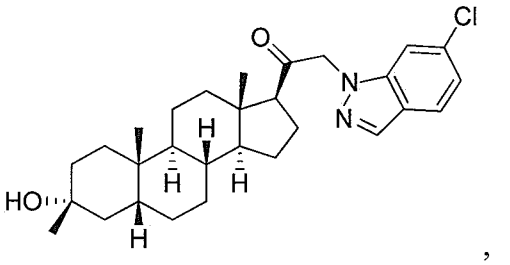
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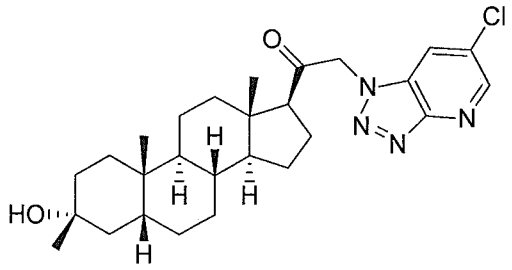
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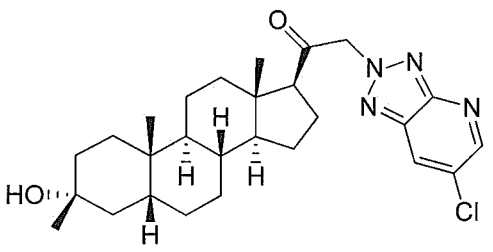
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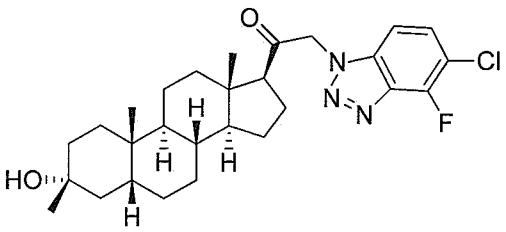
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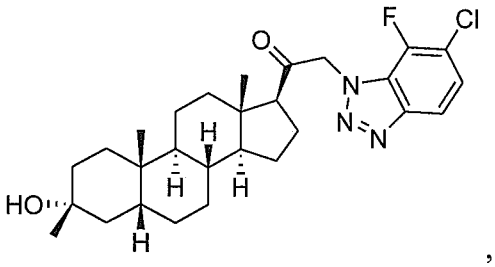
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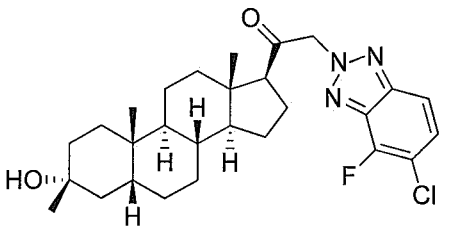
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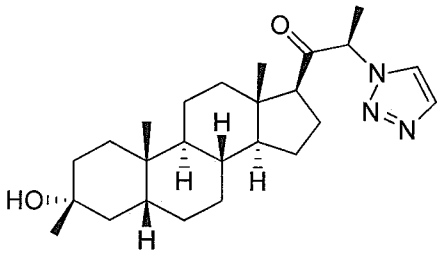
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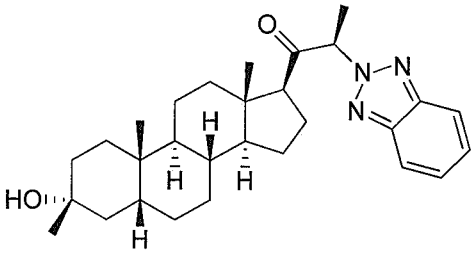
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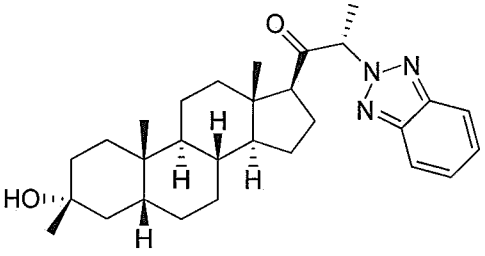
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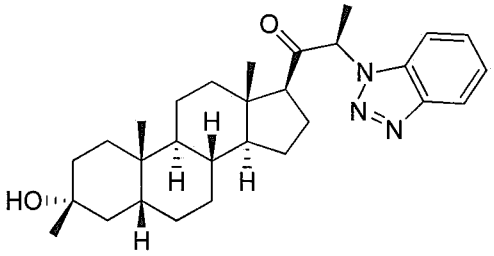
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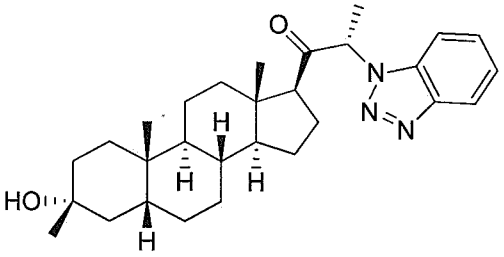
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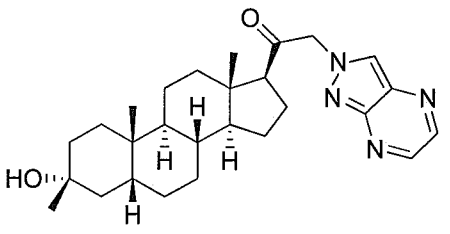
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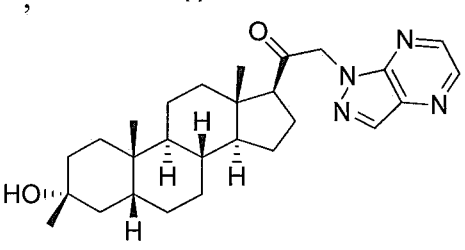
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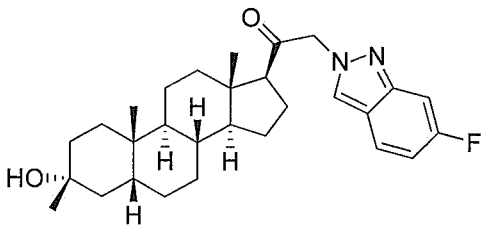
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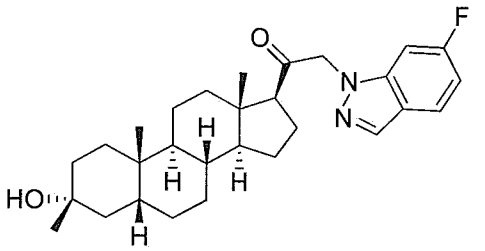
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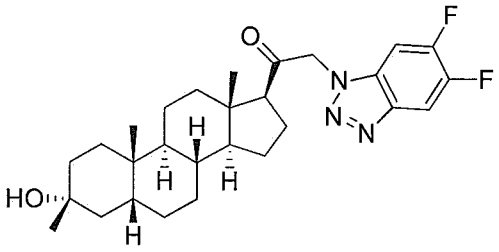
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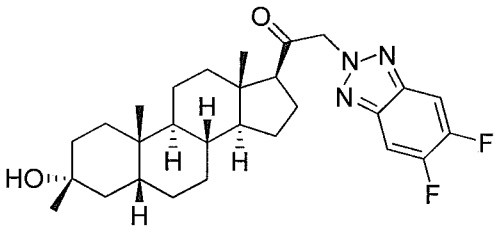
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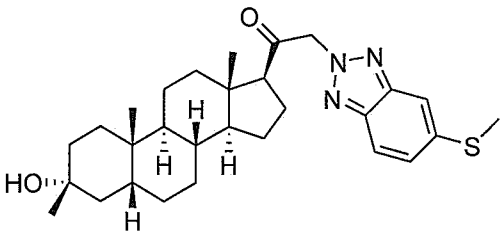
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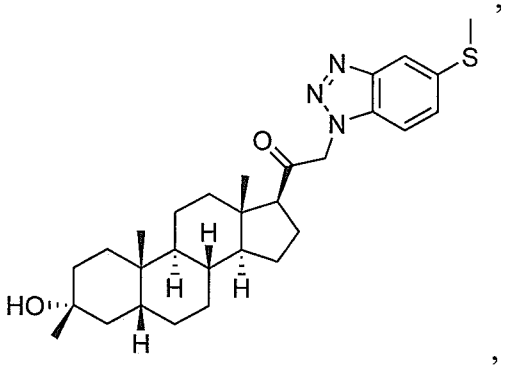
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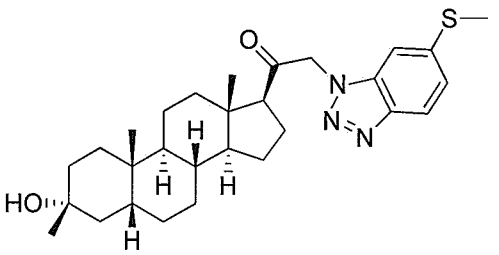
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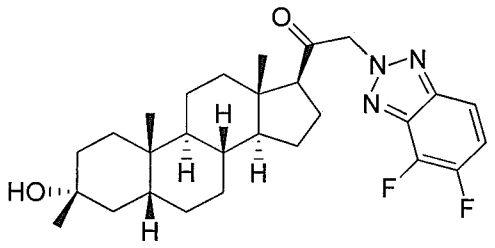
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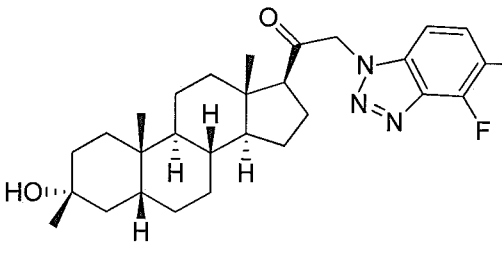
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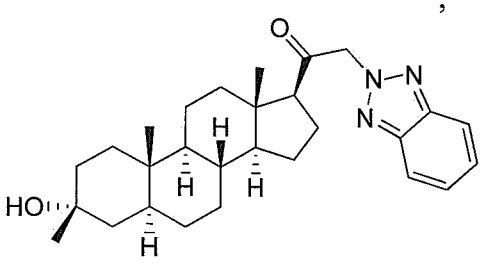
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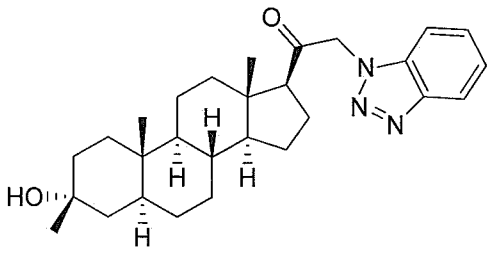
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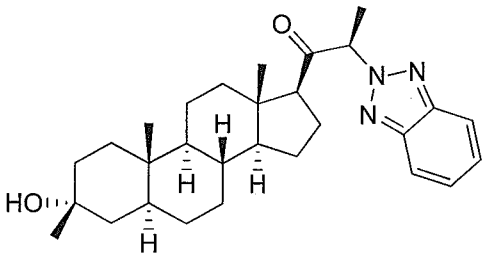
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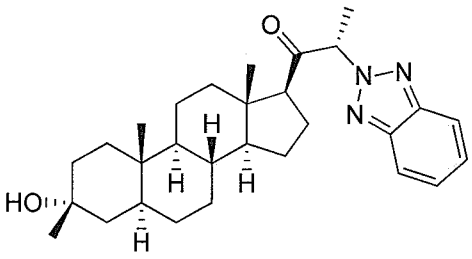
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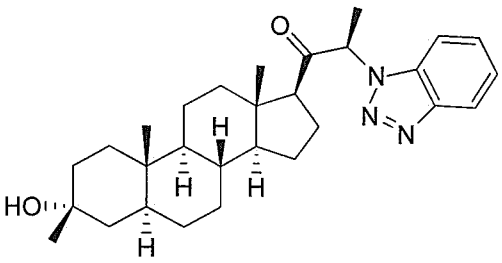
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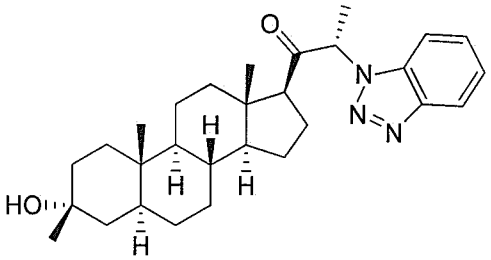
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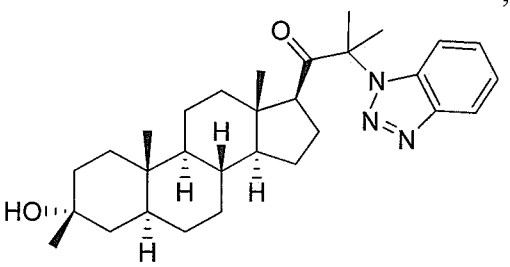
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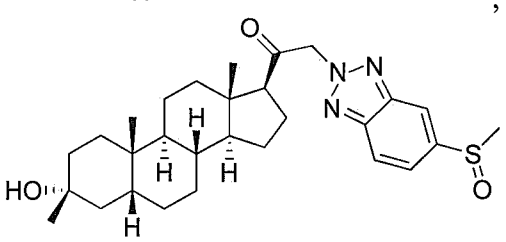
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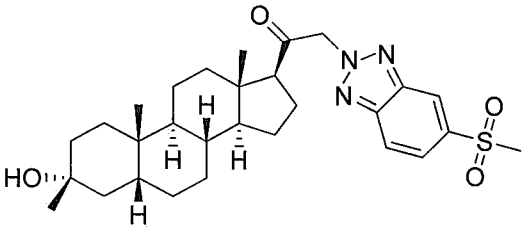
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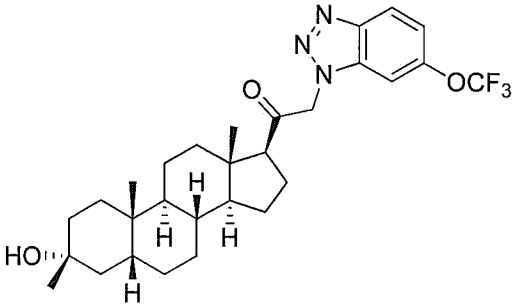
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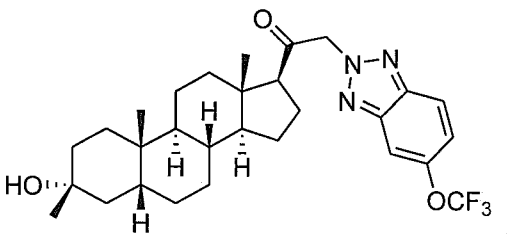

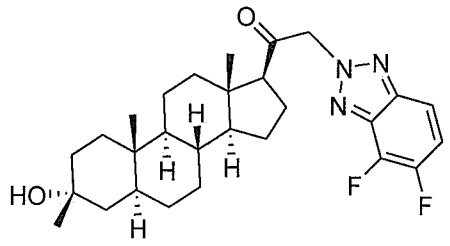
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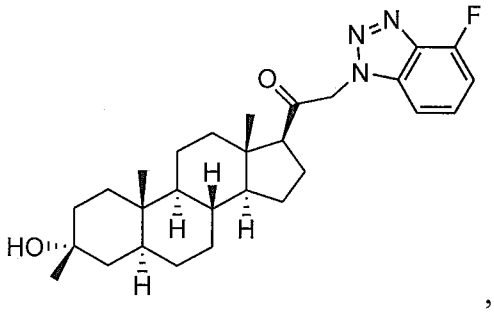
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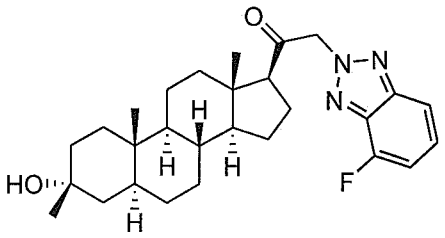
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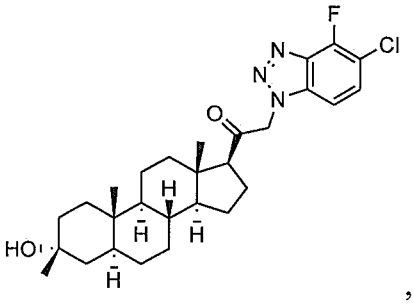
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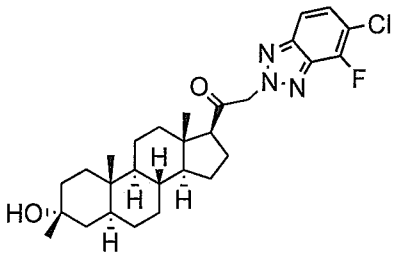
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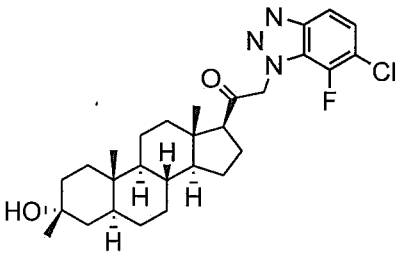
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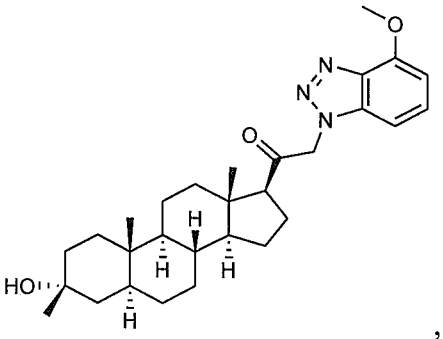
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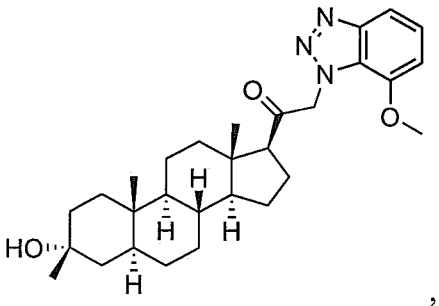
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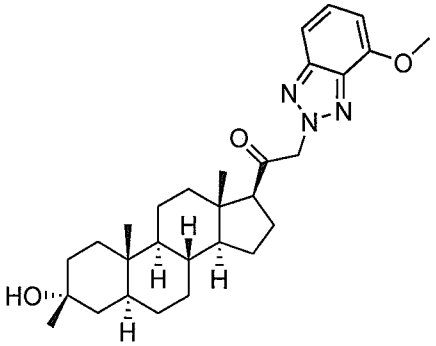
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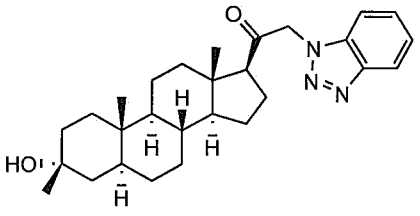
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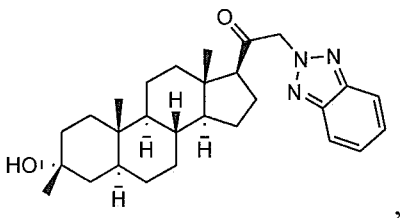
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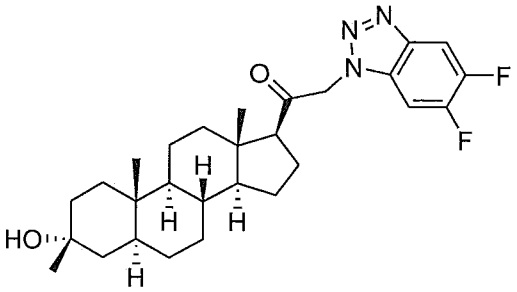
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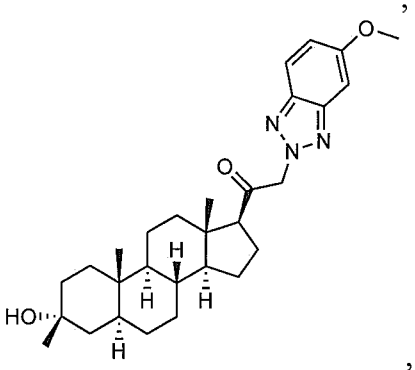
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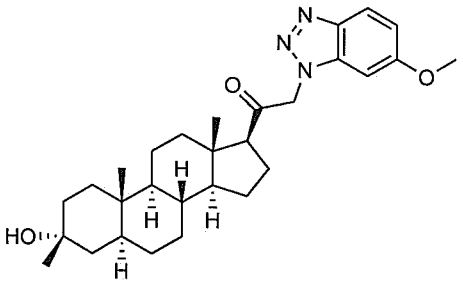
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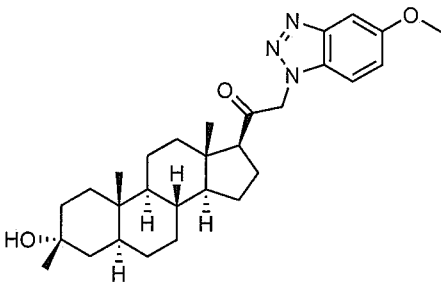
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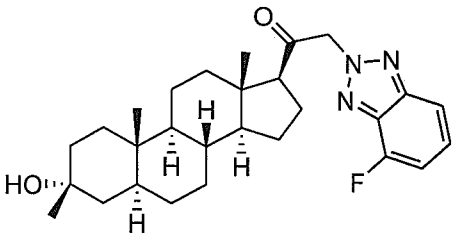
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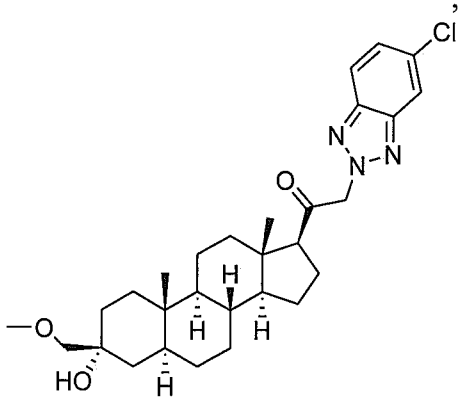
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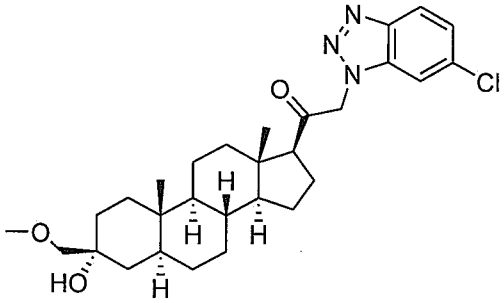
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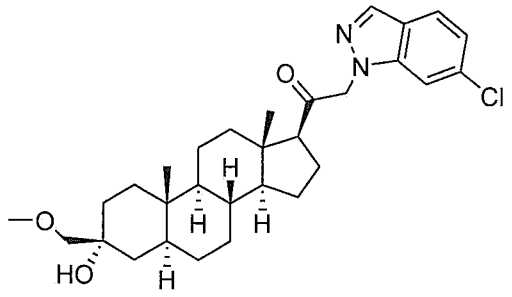
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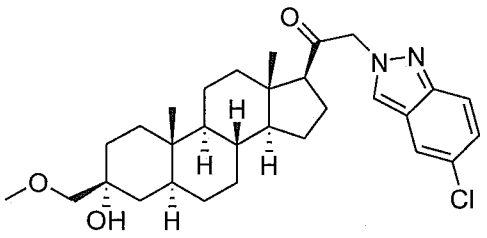
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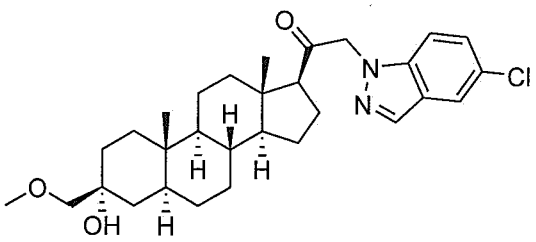
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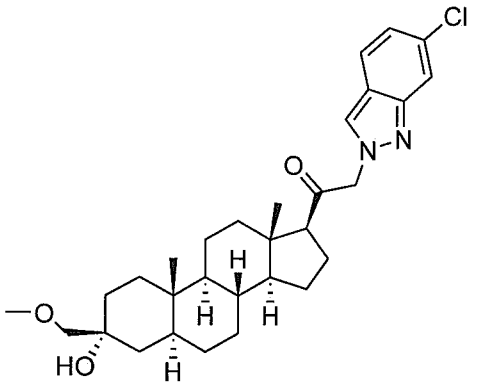
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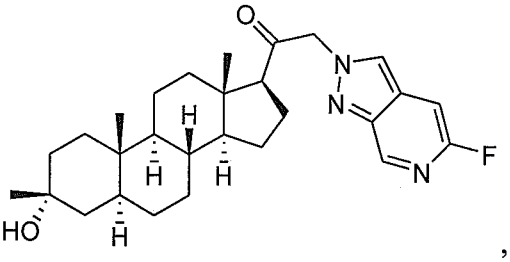
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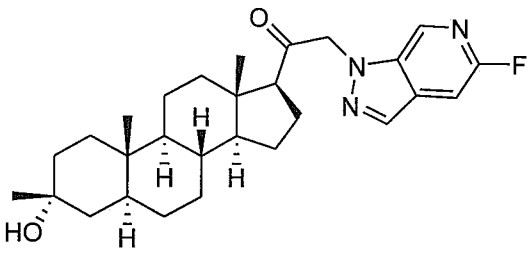
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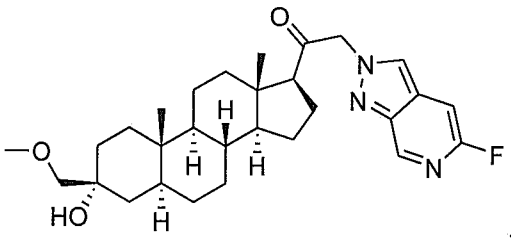
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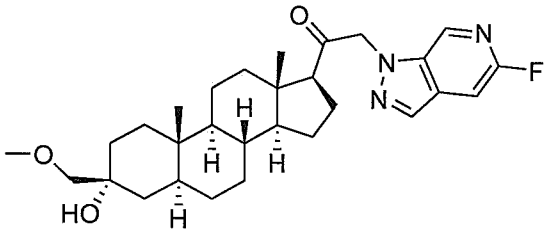
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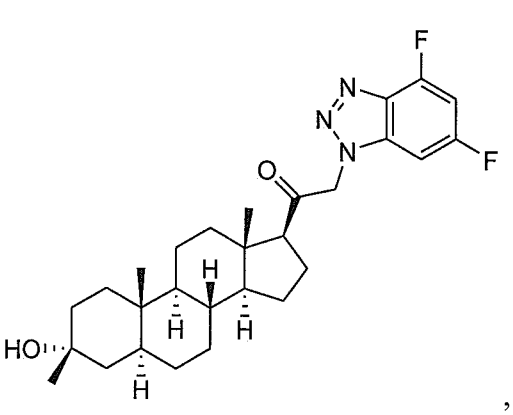
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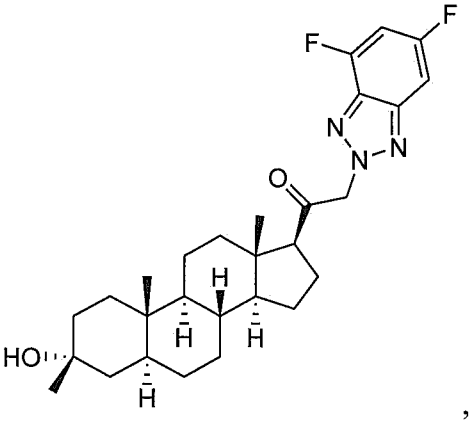
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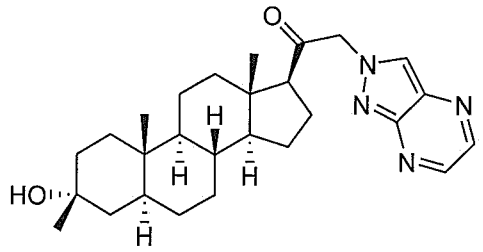
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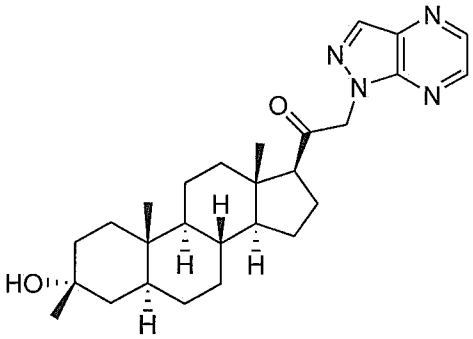
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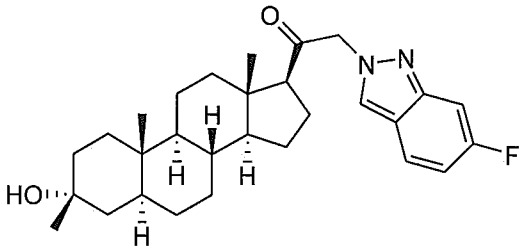
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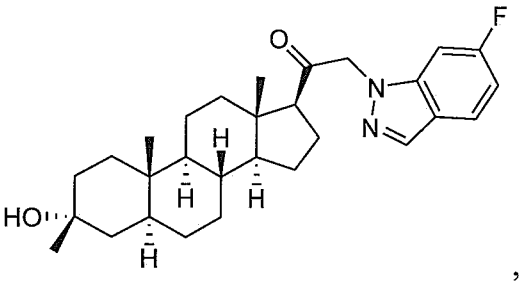
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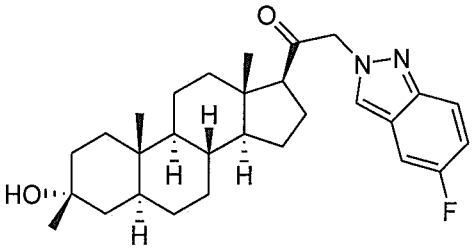
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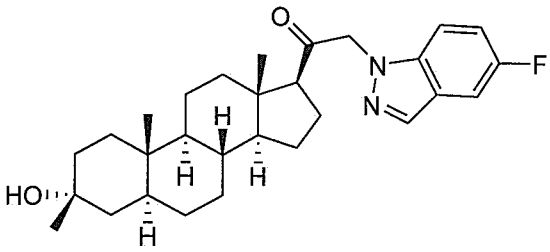
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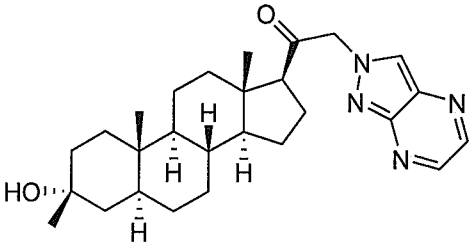
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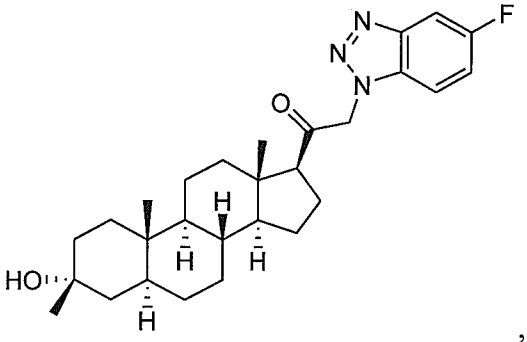
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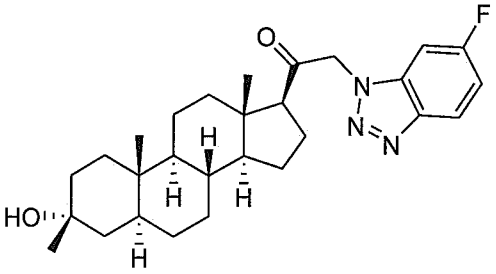
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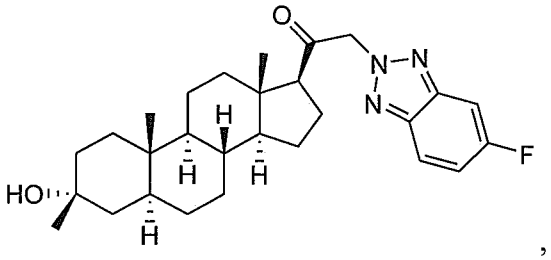

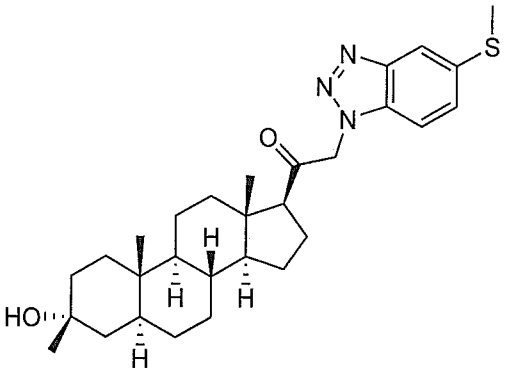
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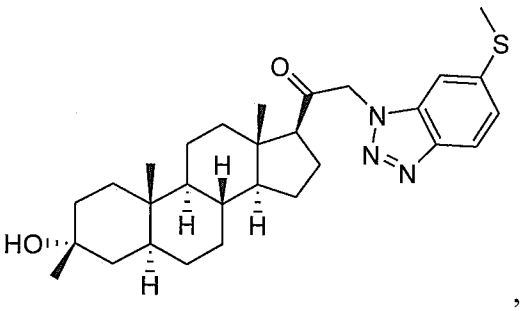
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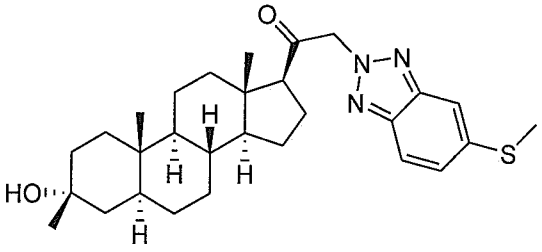
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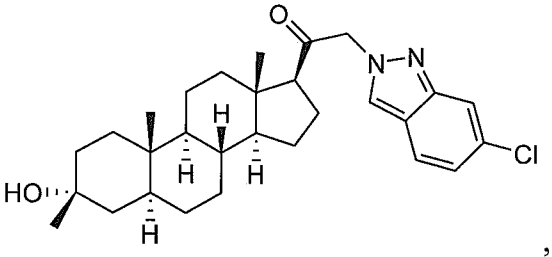
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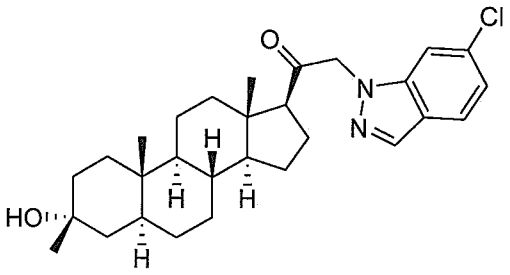
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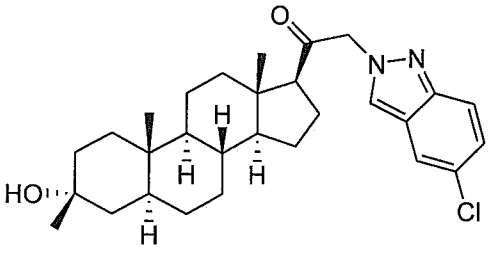
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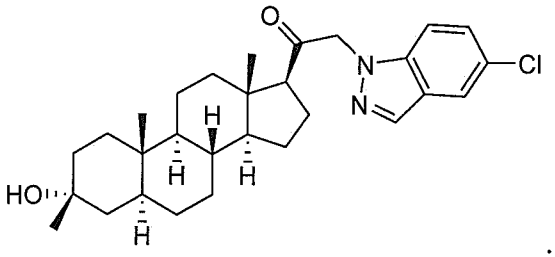
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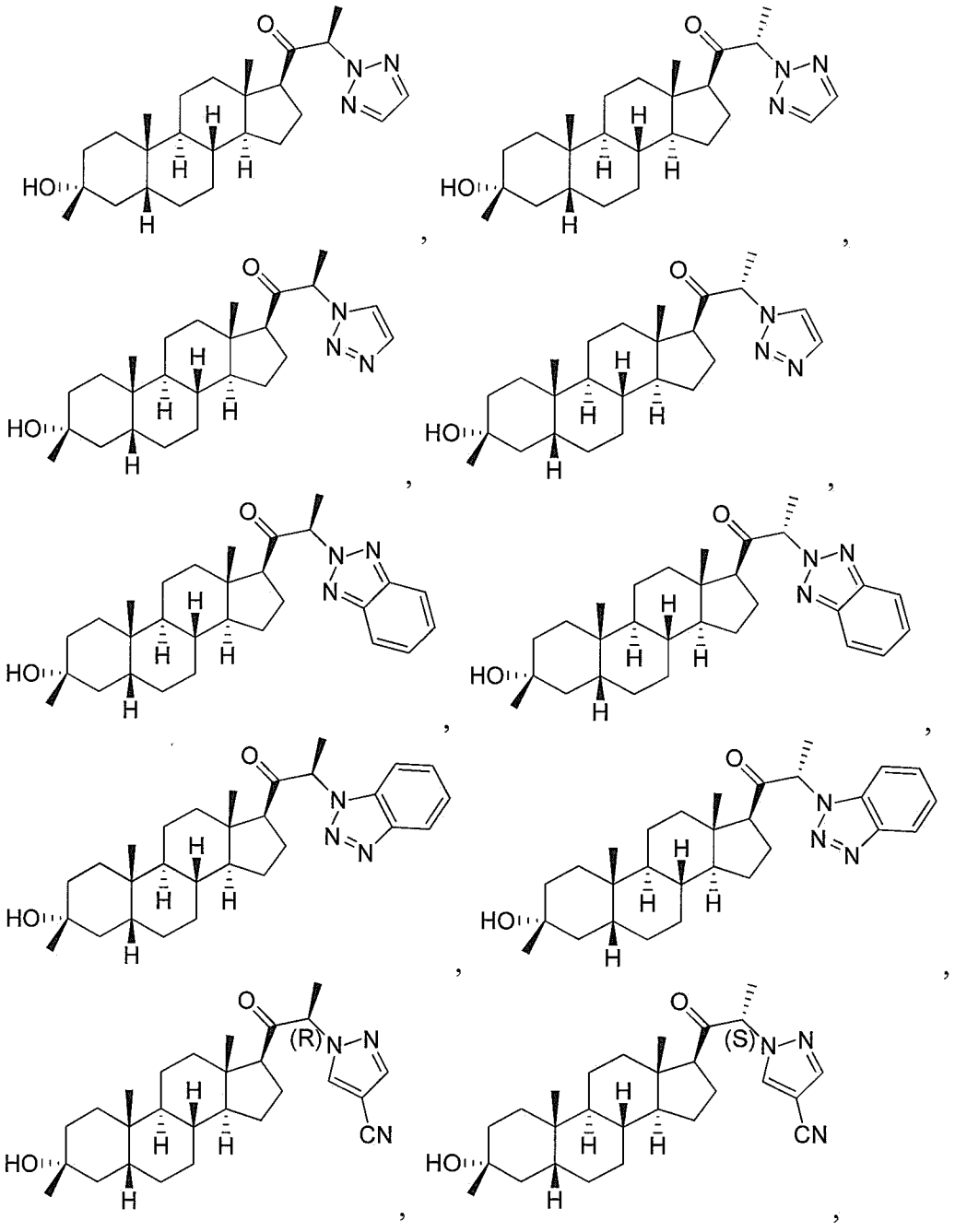

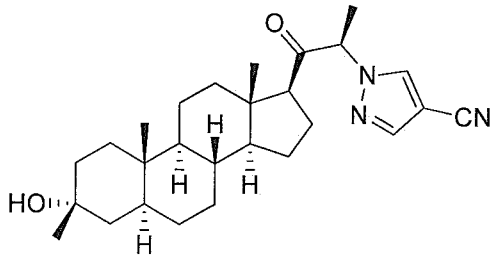
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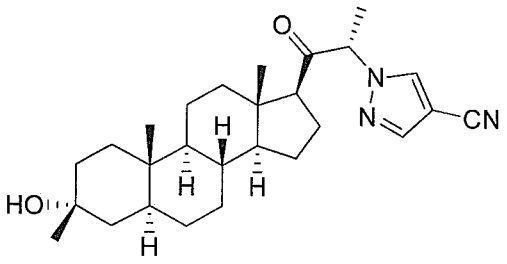
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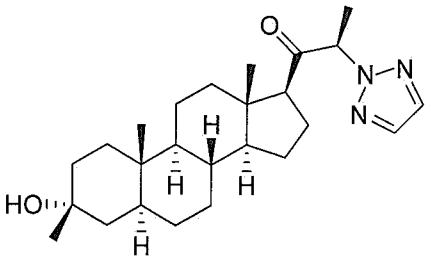
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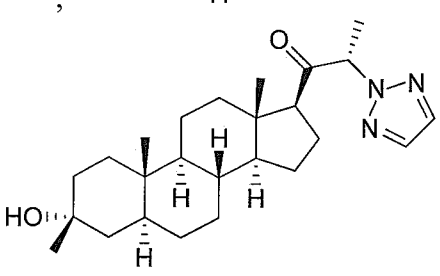
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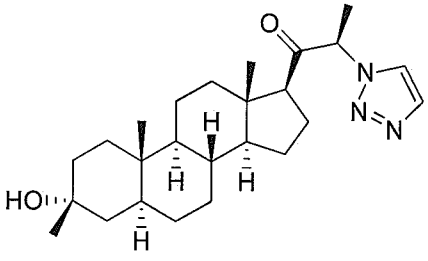
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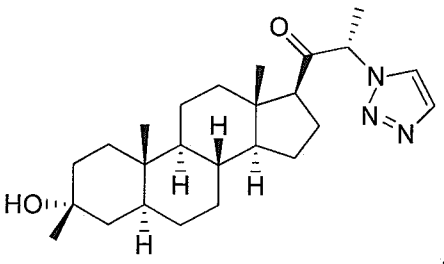
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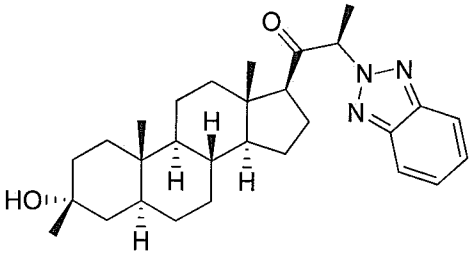
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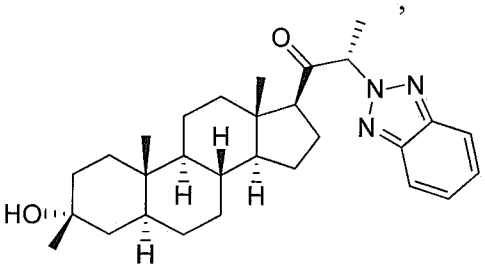
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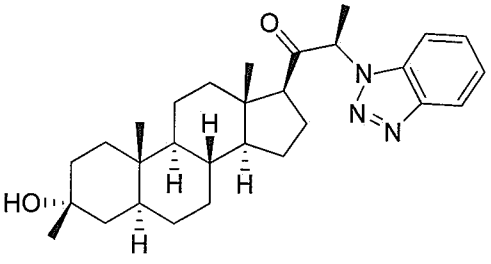
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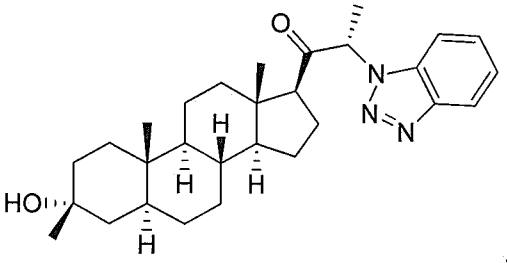
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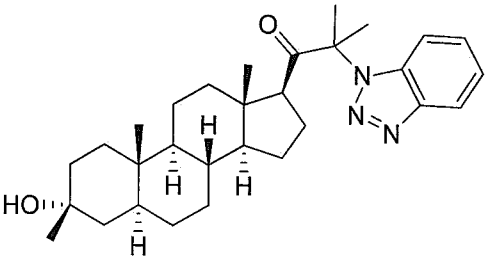
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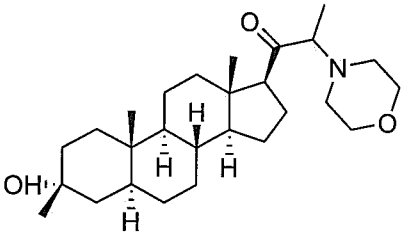
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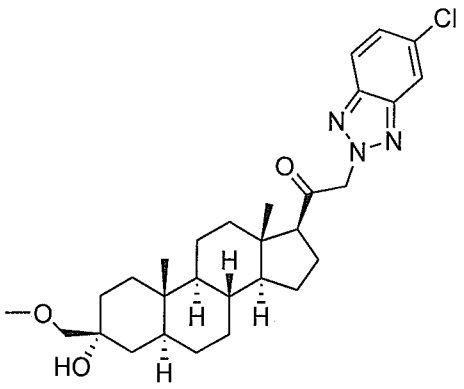
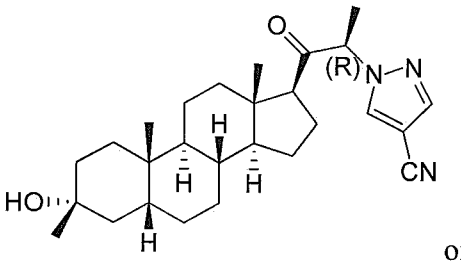


65. A compound, wherein the compound is:



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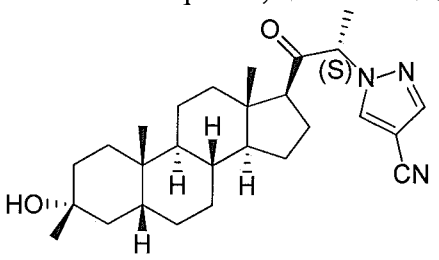
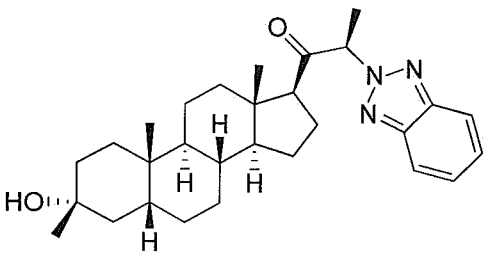


66. A compound, wherein the compound is:



67. A compound, wherein the compound is: 