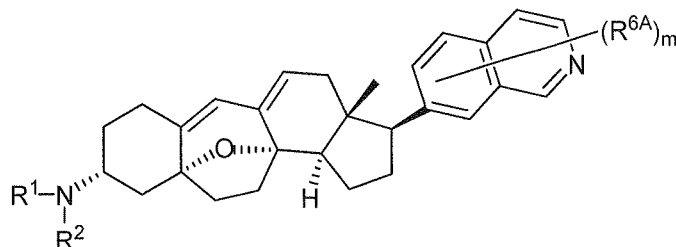


Claims

What is claimed is:

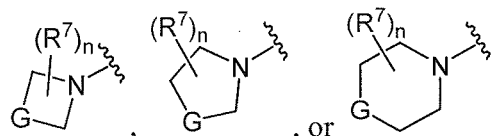
1. A compound of Formula:



or a pharmaceutically acceptable salt or quaternary amine salt thereof;

wherein:

m is 0, 1, 2, 3, or 4;

R¹ and R² are joined to form a ring of formula:  ;
n is 0, 1, or 2;

each instance of R^{6A} is independently halogen, -NO₂, -CN, -OR^{6C}, SR^{6C}, N(R^{6C})₂, -C(=O)R^{6C}, -C(=O)OR^{6C}, -C(=O)N(R^{6C})₂, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl;

wherein each instance of R^{6C} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen, optionally when attached to N the two R^{6C} groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring.

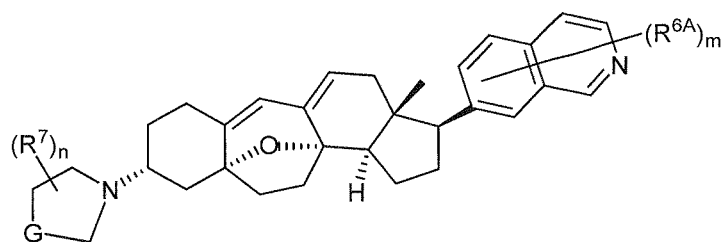
G is -NH-, -NR⁷-, -CH₂-, -CH(R⁷)-, or -C(R⁷)₂-;

each instance of R⁷ is independently amino, hydroxyl, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally

substituted heteroaryl, substituted amino, substituted hydroxyl, thiol, substituted thiol, carbonyl, sulfonyl, sulfinyl, or a nitrogen protecting group when attached to a nitrogen atom; and

optionally wherein two R^7 groups are joined to form an optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl ring, or an oxo (=O) group;

2. The compound of claim 1 of Formula:



or a pharmaceutically acceptable salt or quaternary amine salt thereof;

wherein:

n is 0, 1, or 2;

m is 0, 1, 2, 3, or 4;

G is -NH-, -NR⁷-, -CH₂-, -CH(R⁷)-, or -C(R⁷)₂-;

each instance of R^7 is independently amino, hydroxyl, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, substituted amino, substituted hydroxyl, thiol, substituted thiol, carbonyl, sulfonyl, sulfinyl, or a nitrogen protecting group when attached to a nitrogen atom;

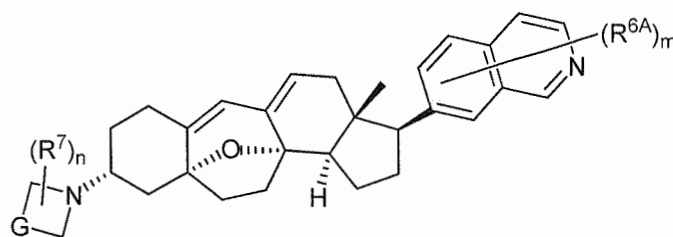
optionally wherein two R^7 groups are joined to form an optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl ring, or an oxo (=O) group;

each instance of R^{6A} is independently halogen, -NO₂, -CN, -OR^{6C}, SR^{6C}, N(R^{6C})₂, -C(=O)R^{6C}, -C(=O)OR^{6C}, -C(=O)N(R^{6C})₂, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl; and

wherein each instance of R^{6C} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl,

optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen, optionally when attached to N the two R^{6C} groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring.

3. The compound of claim 2, wherein m and n are independently 0, 1, or 2.
4. The compound of claim 3, wherein m is 0 and n is 1.
5. The compound of claim 4, wherein G is $-CH_2-$, $-CH(R^7)-$, or $-C(R^7)_2-$, and each instance of R^7 is independently hydroxyl, amino, or halogen.
6. The compound of claim 5, wherein G is $-CH(R^7)-$ and each instance of R^7 is hydroxyl.
7. The compound of claim 3 wherein m is 0 and n is 0.
8. The compound of claim 7, wherein G is $-CH(R^7)-$ and R^7 is amino.
9. The compound of claim 1 of Formula:



or a pharmaceutically acceptable salt or quaternary amine salt thereof;

wherein:

- n is 0, 1, or 2;
- m is 0, 1, 2, 3, or 4;
- G is $-O-$, $-S-$, $-NH-$, $-NR^7-$, $-CH_2-$, $-CH(R^7)-$, or $-C(R^7)_2-$;
- each instance of R^7 is independently amino, hydroxyl, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally

substituted heteroaryl, substituted amino, substituted hydroxyl, thiol, substituted thiol, carbonyl, sulfonyl, sulfinyl, or a nitrogen protecting group when attached to a nitrogen atom;

optionally wherein two R^7 groups are joined to form an optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl ring, or an oxo (=O) group;

each instance of R^{6A} is independently halogen, $-NO_2$, $-CN$, $-OR^{6C}$, SR^{6C} , $N(R^{6C})_2$, $-C(=O)R^{6C}$, $-C(=O)OR^{6C}$, $-C(=O)N(R^{6C})_2$, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl; and

wherein each instance of R^{6C} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen, optionally when attached to N the two R^{6C} groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring.

10. The compound of claim 9, wherein m and n are independently 0, 1, or 2.

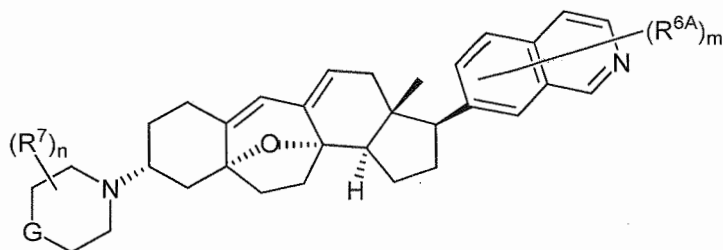
11. The compound of claim 10, wherein m and n are 0.

12. The compound of claim 11, wherein G is $-CH_2-$, $-CH(R^7)-$, or $-C(R^7)_2-$, and R^7 is hydroxyl, amino, or halogen.

13. The compound of claim 12, wherein G is $-CH(R^7)-$, and R^7 is hydroxyl.

14. The compound of claim 12, wherein G is $-CH(R^7)-$, and R^7 is amino.

15. The compound of claim 1 of Formula:



or a pharmaceutically acceptable salt or quaternary amine salt thereof;

wherein:

n is 0, 1, or 2;

m is 0, 1, 2, 3, or 4;

G is -O-, -S-, -NH-, -NR⁷-, -CH₂-, -CH(R⁷)-, or -C(R⁷)₂-;

each instance of R⁷ is independently amino, hydroxyl, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, substituted amino, substituted hydroxyl, thiol, substituted thiol, carbonyl, sulfonyl, sulfinyl, or a nitrogen protecting group when attached to a nitrogen atom;

optionally wherein two R⁷ groups are joined to form an optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl ring, or an oxo (=O) group;

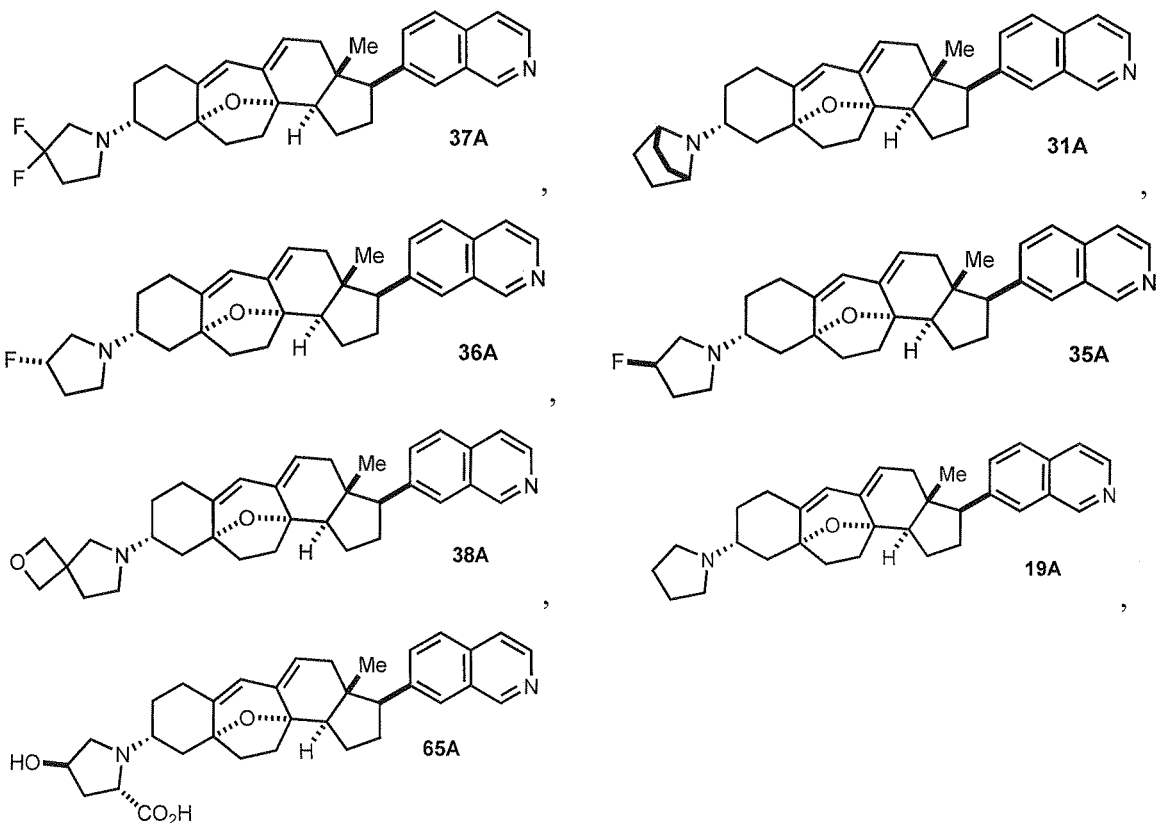
each instance of R^{6A} is independently halogen, -NO₂, -CN, -OR^{6C}, SR^{6C}, N(R^{6C})₂, -C(=O)R^{6C}, -C(=O)OR^{6C}, -C(=O)N(R^{6C})₂, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl; and

wherein each instance of R^{6C} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen, optionally when attached to N the two R^{6C} groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring.

16. The compound of claim 15, wherein m and n are independently 0, 1, or 2.

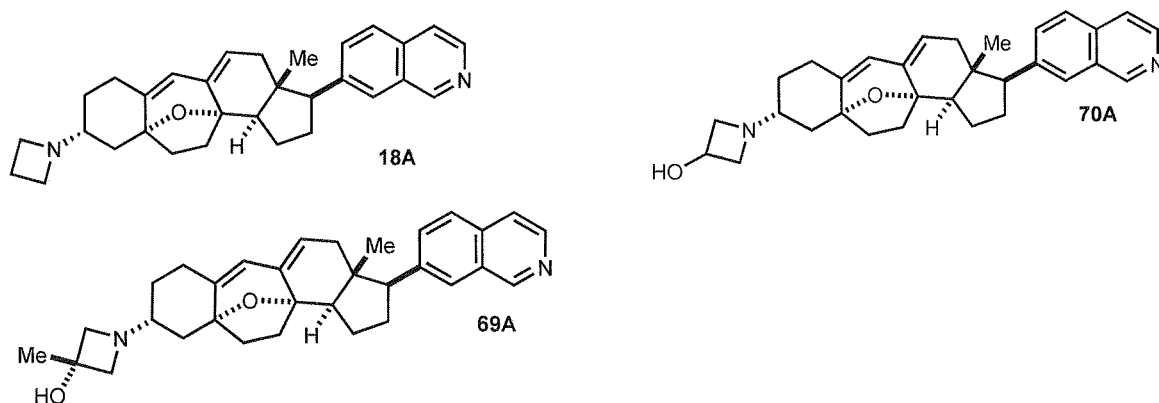
17. The compound of claim 16, wherein G is -O-, -CH₂-, -CH(R⁷)-, or -C(R⁷)₂-, and each instance of R⁷ is independently hydroxyl, amino, or halogen.

18. The compound of claim 2, wherein the compound is selected from the group consisting of:



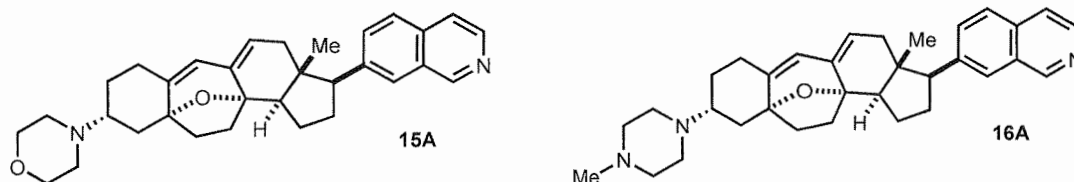
and pharmaceutically acceptable salts thereof.

19. The compound of claim 9, wherein the compound is selected from the group consisting of:



and pharmaceutically acceptable salts thereof.

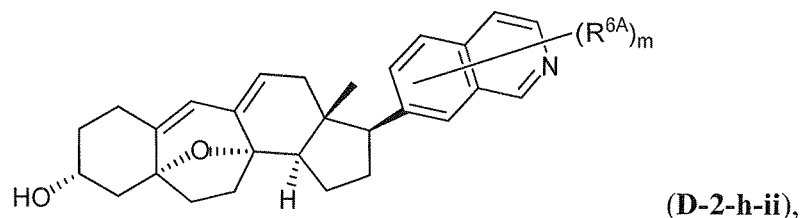
20. The compound of claim 15, wherein the compound is selected from the group consisting of:



and pharmaceutically acceptable salts thereof.

21. A pharmaceutical composition comprising a compound according to any one of claims 1 to 20, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable excipient.
22. Use of a compound according to any one claims 1 to 20, or a pharmaceutically acceptable salt, in the manufacture of a medicament for the treatment of a medical condition by inhibiting CDK8 and/or CDK19 kinase activity in a subject.
23. The use of claim 22, wherein the condition is a diabetic condition, an inflammatory condition, macular degeneration, obesity, atherosclerosis, a condition associated with angiogenesis, or a proliferative disorder.
24. The use of claim 23, wherein the condition is a proliferative disorder and the proliferative disorder is primary myelofibrosis (PMF).
25. The use of claim 22, wherein the condition is a cancer.
26. The use of claim 25, wherein the cancer is a solid tumor or a hematopoietic cancer.
27. The use of claim 26, wherein the cancer is a hematopoietic cancer, and the hematopoietic cancer is selected from multiple myeloma, lymphoma, and acute myelocytic leukemia (AML).
28. The use of any one of claims 22 to 27, wherein the subject is a human.

29. A compound of formula:



or a pharmaceutically acceptable salt thereof;

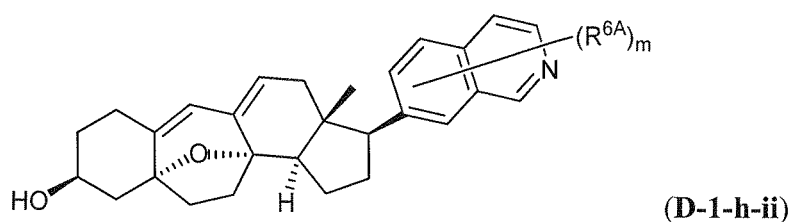
wherein:

m is 0, 1, 2, 3, or 4;

each instance of R^{6A} is independently halogen, $-NO_2$, $-CN$, $-OR^{6C}$, SR^{6C} , $N(R^{6C})_2$, $-C(=O)R^{6C}$, $-C(=O)OR^{6C}$, $-C(=O)N(R^{6C})_2$, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl; and

wherein each instance of R^{6C} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen, optionally when attached to N the two R^{6C} groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring.

30. A compound of formula:



or a pharmaceutically acceptable salt thereof;

wherein:

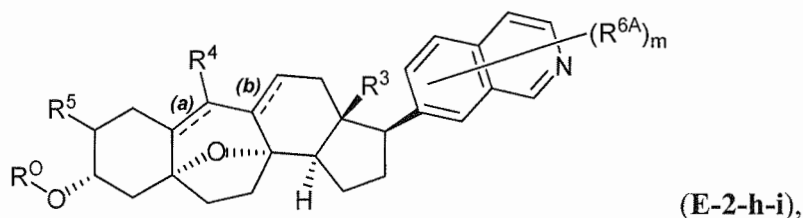
m is 0, 1, 2, 3, or 4;

each instance of R^{6A} is independently halogen, $-NO_2$, $-CN$, $-OR^{6C}$, SR^{6C} , $N(R^{6C})_2$, $-C(=O)R^{6C}$, $-C(=O)OR^{6C}$, $-C(=O)N(R^{6C})_2$, optionally substituted alkyl, optionally substituted

alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl; and

wherein each instance of R^{6C} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen, optionally when attached to N the two R^{6C} groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring.

31. A compound of formula:



or a pharmaceutically acceptable salt thereof;

wherein:

m is 0, 1, 2, 3, or 4;

R^4 is hydrogen, halogen, optionally substituted alkyl, or $-\text{Si}(R^A)_3$;

R^5 is hydrogen, halogen, or optionally substituted alkyl;

each instance of --- , designated as **(a)** and **(b)** represents a single or double bond;

R^O is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $-\text{C}(=\text{O})R^A$, $-\text{C}(=\text{O})\text{OR}^A$, $-\text{C}(=\text{O})\text{N}(R^A)_2$, or an oxygen protecting group.

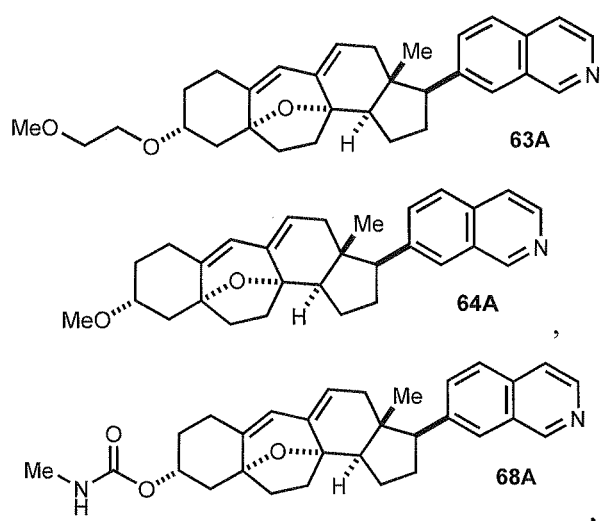
each instance of R^A is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, carbonyl, silyl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen; optionally when

attached to N the two R^A groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring;

each instance of R^{6A} is independently halogen, $-\text{NO}_2$, $-\text{CN}$, $-\text{OR}^{6C}$, SR^{6C} , $\text{N}(\text{R}^{6C})_2$, $-\text{C}(=\text{O})\text{R}^{6C}$, $-\text{C}(=\text{O})\text{OR}^{6C}$, $-\text{C}(=\text{O})\text{N}(\text{R}^{6C})_2$, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl; and

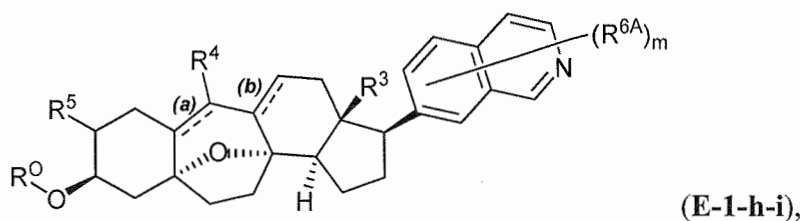
wherein each instance of R^{6C} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen, optionally when attached to N the two R^{6C} groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring.

32. The compound of claim 31, wherein the compound is selected from the group consisting of:



and pharmaceutically acceptable salts thereof.

33. A compound of formula:



or a pharmaceutically acceptable salt thereof;

wherein:

m is 0, 1, 2, 3, or 4;

R^4 is hydrogen, halogen, optionally substituted alkyl, or $-\text{Si}(R^A)_3$;

R^5 is hydrogen, halogen, or optionally substituted alkyl;

each instance of --- , designated as (a) and (b) represents a single or double bond;

R^O is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $-\text{C}(=\text{O})R^A$, $-\text{C}(=\text{O})\text{OR}^A$, $-\text{C}(=\text{O})\text{N}(R^A)_2$, or an oxygen protecting group.

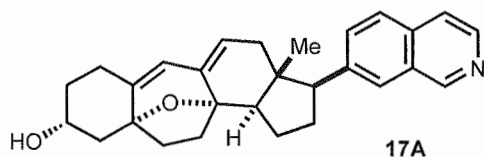
each instance of R^A is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, carbonyl, silyl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen; optionally when attached to N the two R^A groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring;

each instance of R^{6A} is independently halogen, $-\text{NO}_2$, $-\text{CN}$, $-\text{OR}^{6C}$, SR^{6C} , $\text{N}(R^{6C})_2$, $-\text{C}(=\text{O})R^{6C}$, $-\text{C}(=\text{O})\text{OR}^{6C}$, $-\text{C}(=\text{O})\text{N}(R^{6C})_2$, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl; and

wherein each instance of R^{6C} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen, optionally when attached to N

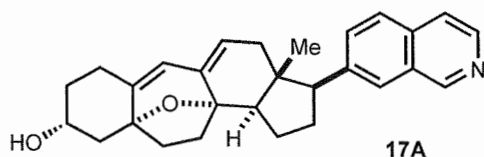
the two R^{6C} groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring.

34. A compound of Formula:



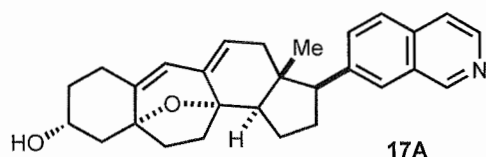
or a pharmaceutically acceptable salt thereof.

35. A pharmaceutical composition comprising compound:



or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

36. Use of a compound:



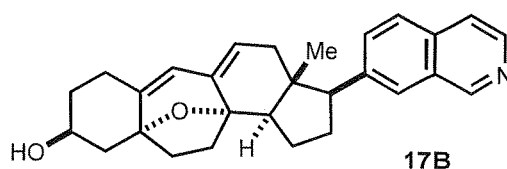
or a pharmaceutically acceptable salt optionally in a pharmaceutical composition thereof for the manufacture of a medicament for the treatment of a medical condition by inhibiting CDK8 and/or CDK19 kinase activity in a subject.

37. The use of claim 36, wherein the condition is a diabetic condition, an inflammatory condition, macular degeneration, obesity, atherosclerosis, a condition associated with angiogenesis, or a proliferative disorder.

38. The use of claim 37, wherein the condition is a proliferative disorder and the proliferative disorder is primary myelofibrosis (PMF).

39. The use of claim 36, wherein the condition is a cancer.

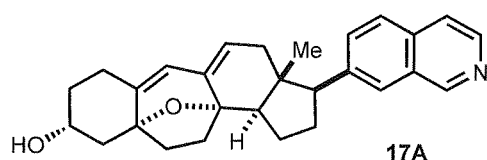
40. The use of claim 39, wherein the cancer is a solid tumor or a hematopoietic cancer.
41. The use of claim 40, wherein the cancer is a hematopoietic cancer, and the hematopoietic cancer is selected from multiple myeloma, lymphoma, and acute myelocytic leukemia (AML).
42. The use of any one of claims 36 to 41, wherein the subject is a human.
43. The compound of claim 30, wherein the compound is:



or a pharmaceutically acceptable salt thereof.

44. A compound according to any one claims 1 to 20, or a pharmaceutically acceptable salt, optionally in a pharmaceutical composition, for use in therapy.

45. A compound:

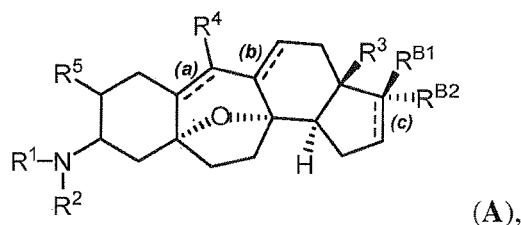


or a pharmaceutically acceptable salt optionally in a pharmaceutical composition thereof for use in therapy.

Claims

What is claimed is:

1. A compound of Formula (A):



or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof;
wherein:

R^1 is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $-OR^A$, $-SR^A$, $-N(R^A)_2$, $-C(=O)R^A$, $-C(=O)OR^A$, $-C(=O)N(R^A)_2$, $-S(=O)_2R^A$, or a nitrogen protecting group;

R^2 is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $-C(=O)R^A$, $-C(=O)OR^A$, $-C(=O)N(R^A)_2$, $-S(=O)_2R^A$, or a nitrogen protecting group;

or R^1 and R^2 are joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl;

R^3 is hydrogen or optionally substituted alkyl;

R^4 is hydrogen, halogen, optionally substituted alkyl, or $-Si(R^A)_3$;

R^5 is hydrogen, halogen, or optionally substituted alkyl;

each instance of $---$, designated as (a), (b), and (c), represents a single or double bond, provided that when $---$ designated as (c) represents a double bond, then one of R^{B1} and R^{B2} is absent, and provided that when $---$ designated as (c) represents a single bond, then both R^{B1} and R^{B2} are present;

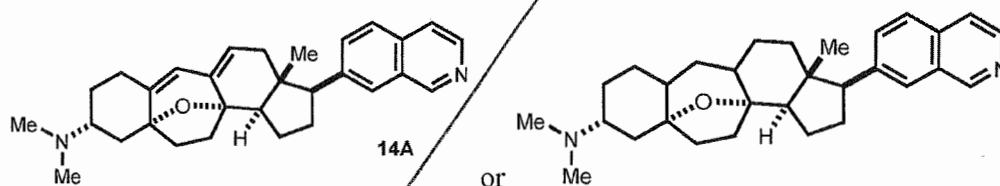
each instance of R^{B1} and R^{B2} is, independently, hydrogen, $-L_1-R^{B3}$, or $-X^AR^A$ wherein X^A is $-O-$, $-S-$, or $-N(R^A)-$; or R^{B1} and R^{B2} are joined to form an oxo group, provided that at least one of R^{B1} and R^{B2} is not hydrogen;

L_1 is a bond, $-C(=O)-$, $-C(=O)O-$, $-C(=O)S-$, $-C(=O)N(R^L)-$, or $-N(R^L)-(C(R^{LL})_2)_p-$, wherein R^L is hydrogen, optionally substituted alkyl, or a nitrogen protecting group, each

instance of R^{LL} is independently hydrogen, halogen, or optionally substituted alkyl, and p is 0, 1, or 2;

R^{B3} is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, provided that when L_1 is a bond, then R^{B3} is not hydrogen; and

each instance of R^A is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, carbonyl, silyl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen; optionally when attached to N the two R^A groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring; and optionally when R^{B1} and R^{B2} are each $-X^A R^A$ then two R^A groups may be joined to form an optionally substituted heterocyclyl ring; provided the compound is not:



or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein each instance of R^1 and R^2 is hydrogen.
3. The compound of claim 1, wherein R^1 is hydrogen, and R^2 is optionally substituted alkyl.
4. The compound of claim 3, wherein R^1 is hydrogen, and R^2 is $-CH_3$.
5. The compound of claim 1, wherein each instance of R^1 and R^2 is independently optionally substituted alkyl.

6. The compound of claim 1, wherein at least one of R^1 and R^2 is alkyl substituted with one or more amino, substituted amino, hydroxyl, substituted hydroxyl, thiol, substituted thiol, or sulfonyl substituents.

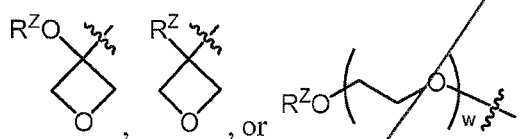
7. The compound of claim 6, wherein at least one of R^1 and R^2 is a group of formula:



wherein:

p is 1, 2, 3, 4, 5, or 6; and

Z is $-\text{CH}_2\text{X}^Z$, $-\text{CH}(\text{X}^Z)_2$, $-\text{C}(\text{X}^Z)_3$, $-\text{OR}^Z$, $-\text{SR}^Z$, $-\text{N}(\text{R}^Z)_2$, $-\text{S}(\text{O})_2\text{N}(\text{R}^Z)_2$,



wherein each instance of R^Z is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $-\text{C}(=\text{O})\text{R}^Z$, $-\text{C}(=\text{O})\text{OR}^Z$, $-\text{C}(=\text{O})\text{N}(\text{R}^Z)_2$, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen, optionally when attached to N the two R^Z groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring;

each instance of X^Z is independently fluoro, chloro, bromo, or iodo; and

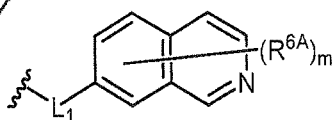
w is an integer between 1 and 10, inclusive.

8. The compound of claim 1, wherein R^1 is $-\text{S}(=\text{O})_2\text{R}^A$ and R^2 is optionally substituted alkyl.

9. The compound of claim 1, wherein R^1 and R^2 are joined to form an optionally substituted heterocyclyl.

10. The compound of claim 9, wherein R^1 and R^2 are joined to form an optionally substituted aziridinyl, optionally substituted azetidiny, optionally substituted pyrrolidinyl, optionally substituted imidazolidine-2,4-dione, optionally substituted piperidinyl, or optionally substituted morpholinyl.

11. The compound of any one of claims 1 to 10, wherein R^3 is optionally substituted alkyl.
12. The compound of claim 11, wherein R^3 is $-\text{CH}_3$.
13. The compound of any one of claims 1 to 12, wherein R^4 is hydrogen.
14. The compound of any one of claims 1 to 13, wherein R^5 is hydrogen.
15. The compound of any one of claims 1 to 14, wherein each instance of --- designated as (a), and (b) is a double bond.
16. The compound of any one of claims 1 to 15, wherein --- designated as (c) represents a single bond.
17. The compound of any one of claims 1 to 16, wherein R^{B1} is L_1-R^{B3} and R^{B2} is hydrogen.
18. The compound of claim 17, wherein L_1 is a bond.
19. The compound of claim 17 or 18, wherein $-L_1-R^{B3}$ is:



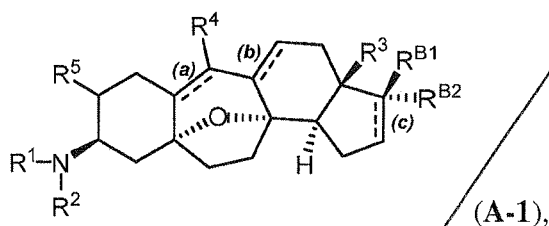
wherein:

each instance of R^{6A} is independently halogen, $-\text{NO}_2$, $-\text{CN}$, $-\text{OR}^{6C}$, SR^{6C} , $\text{N}(\text{R}^{6C})_2$, $-\text{C}(=\text{O})\text{R}^{6C}$, $-\text{C}(=\text{O})\text{OR}^{6C}$, $-\text{C}(=\text{O})\text{N}(\text{R}^{6C})_2$, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl;

wherein each instance of R^{6C} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to oxygen, a sulfur

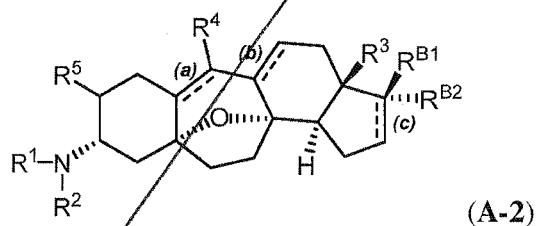
protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen, optionally when attached to N the two R^{6C} groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring; and
 m is 0 or an integer between 1 and 4, inclusive.

20. The compound of any one of claims 1 to 19, wherein the compound of Formula (A) is of Formula (A-1):



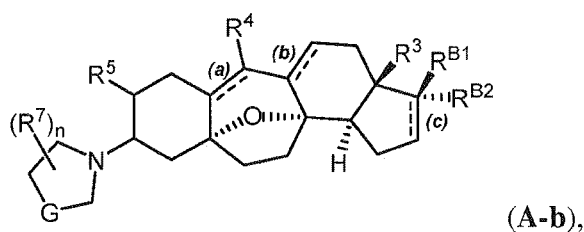
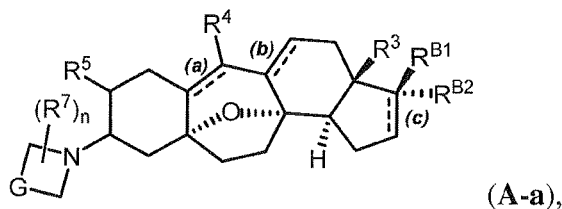
or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof.

21. The compound of any one of claims 1 to 19, wherein the compound of Formula (A) is of Formula (A-2):

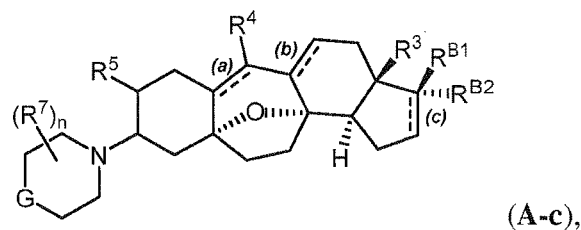


or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof.

22. The compound of any one of claims 1 to 19, wherein the compound is of Formula (A-a), (A-b), or (A-c):



or



or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof;

wherein:

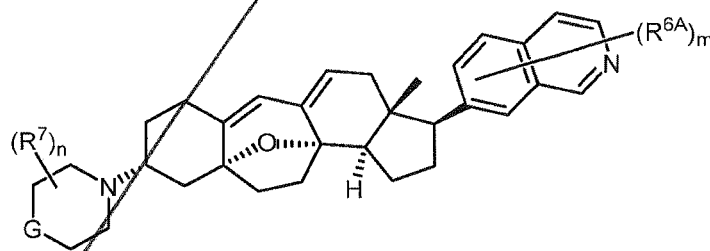
G is -O-, -S-, -NH-, -NR⁷-, -CH₂-, -CH(R⁷)-, or -C(R⁷)₂-;

each instance of R⁷ is independently halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, amino, substituted amino, hydroxyl, substituted hydroxyl, thiol, substituted thiol, carbonyl, sulfonyl, sulfinyl, or a nitrogen protecting group when attached to a nitrogen atom;

optionally wherein two R⁷ groups are joined to form an optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl ring, or an oxo (=O) group, and

n is 0, 1, 2, 3, or 4.

23. The compound of claim 22, wherein the compound is:



or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof;

wherein:

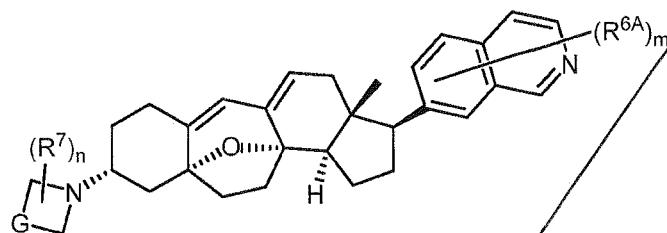
each instance of R^{6A} is independently halogen, -NO₂, -CN, -OR^{6C}, SR^{6C}, N(R^{6C})₂, -C(=O)R^{6C}, -C(=O)OR^{6C}, -C(=O)N(R^{6C})₂, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl;

wherein each instance of R^{6C} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally

substituted heteroaryl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen, optionally when attached to N the two R^{6C} groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring; and

m is 0 or an integer between 1 and 4, inclusive.

24. The compound of claim 22, wherein the compound is:



or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof;

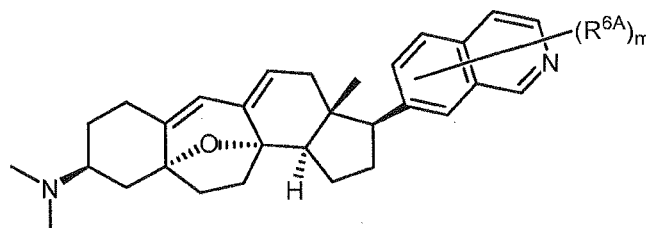
wherein:

each instance of R^{6A} is independently halogen, $-NO_2$, $-CN$, $-OR^{6C}$, SR^{6C} , $N(R^{6C})_2$, $-C(=O)R^{6C}$, $-C(=O)OR^{6C}$, $-C(=O)N(R^{6C})_2$, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl;

wherein each instance of R^{6C} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen, optionally when attached to N the two R^{6C} groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring; and

m is 0 or an integer between 1 and 4, inclusive.

25. The compound of claim 1, wherein the compound is:



or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof;

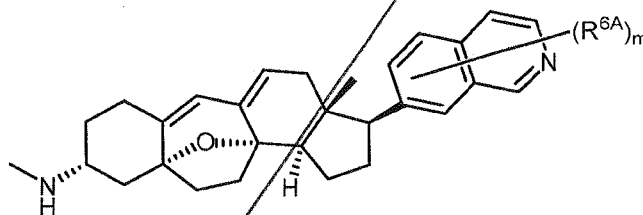
wherein:

each instance of R^{6A} is independently halogen, $-NO_2$, $-CN$, $-OR^{6C}$, SR^{6C} , $N(R^{6C})_2$, $-C(=O)R^{6C}$, $-C(=O)OR^{6C}$, $-C(=O)N(R^{6C})_2$, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl;

wherein each instance of R^{6C} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen, optionally when attached to N the two R^{6C} groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring; and

m is 0 or an integer between 1 and 4, inclusive.

26. The compound of claim 1, wherein the compound is:



or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof;

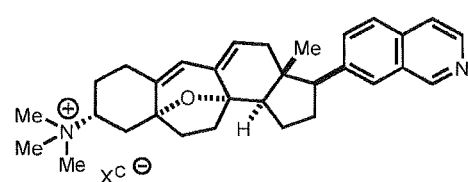
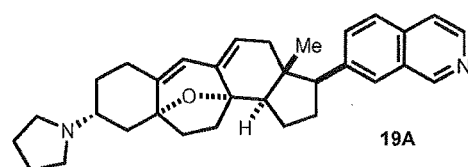
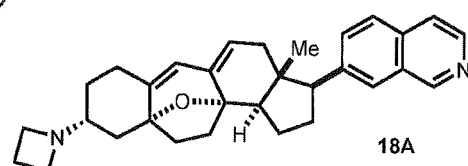
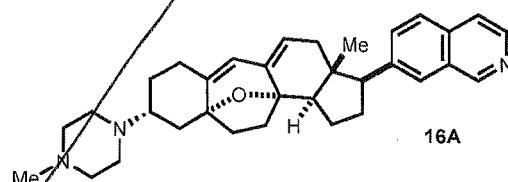
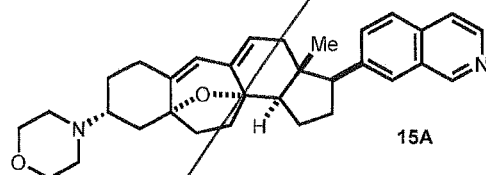
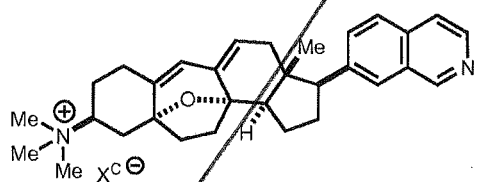
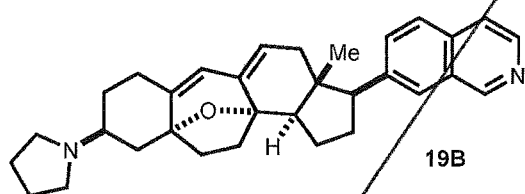
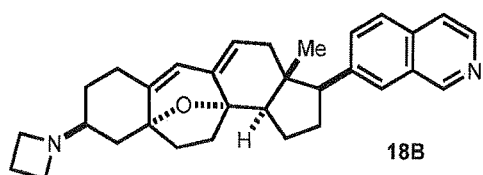
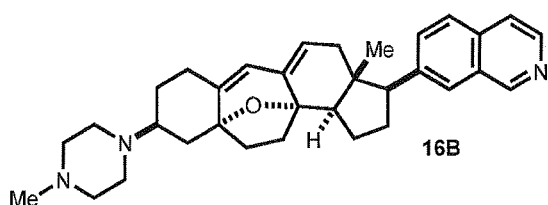
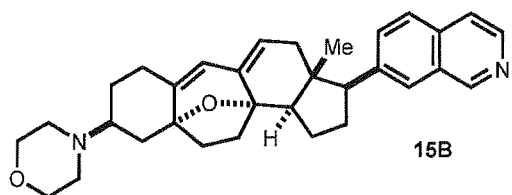
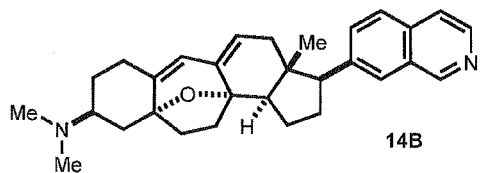
wherein:

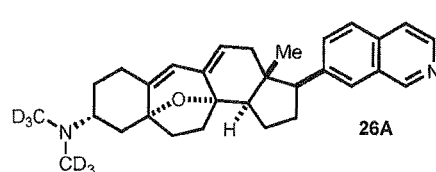
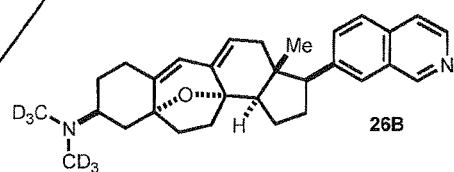
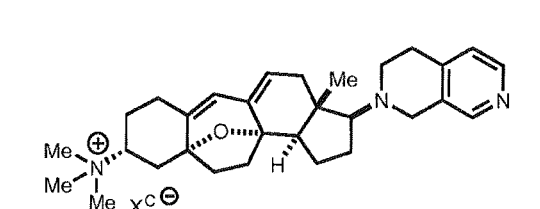
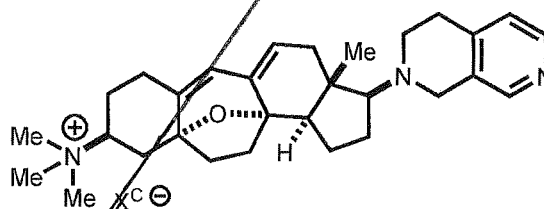
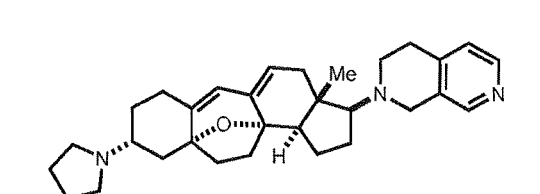
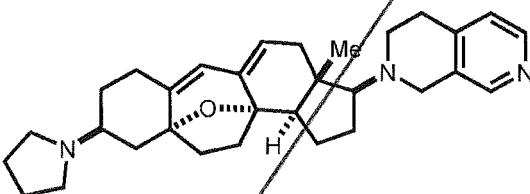
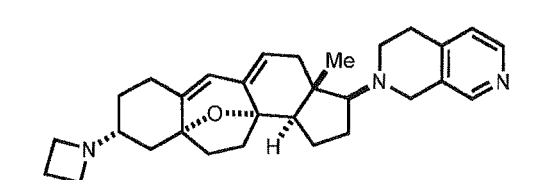
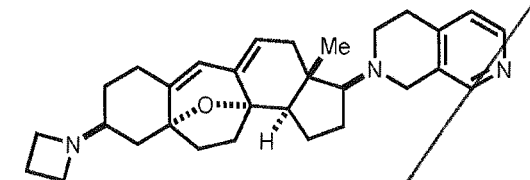
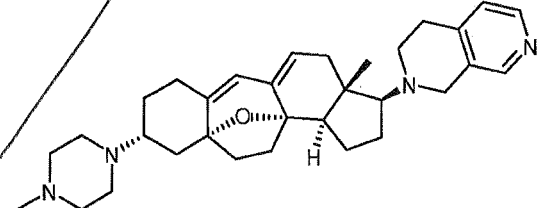
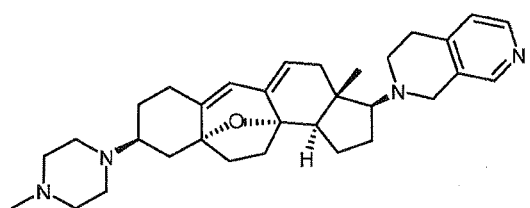
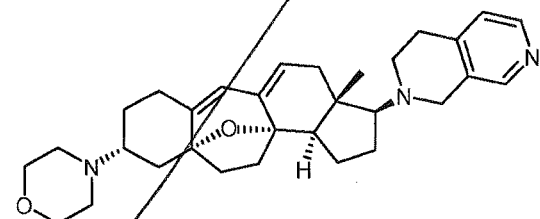
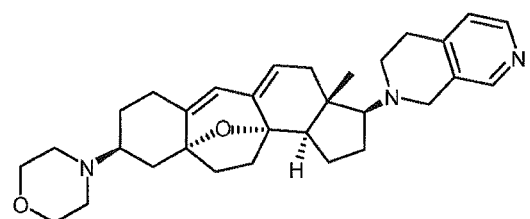
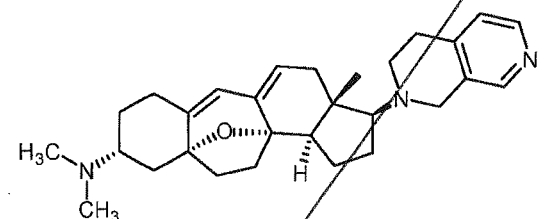
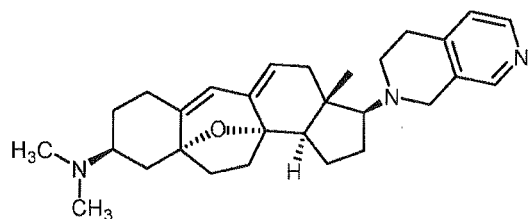
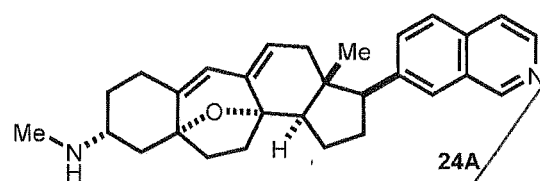
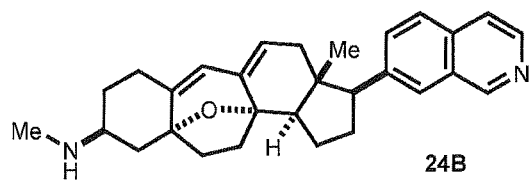
each instance of R^{6A} is independently halogen, $-NO_2$, $-CN$, $-OR^{6C}$, SR^{6C} , $N(R^{6C})_2$, $-C(=O)R^{6C}$, $-C(=O)OR^{6C}$, $-C(=O)N(R^{6C})_2$, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl;

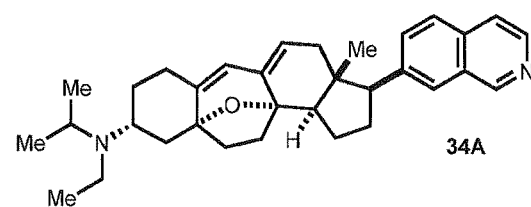
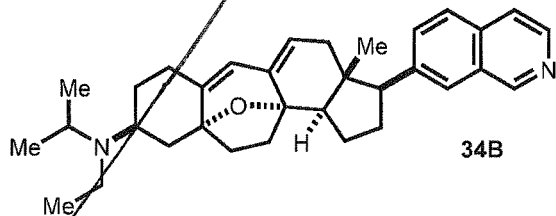
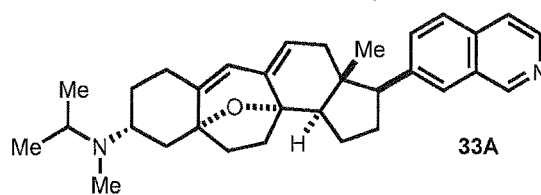
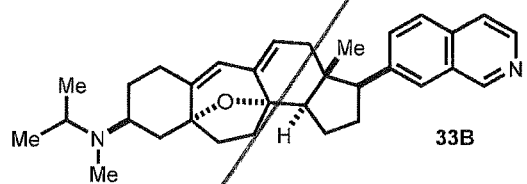
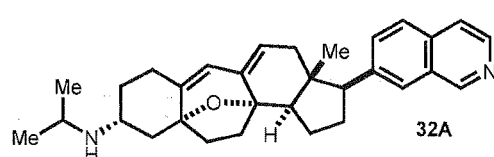
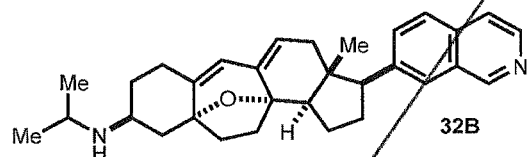
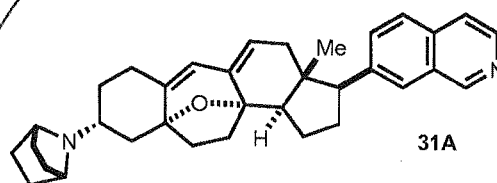
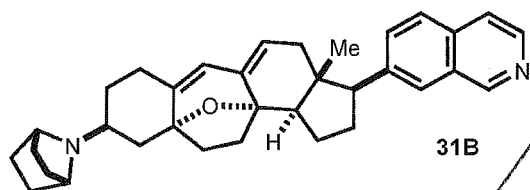
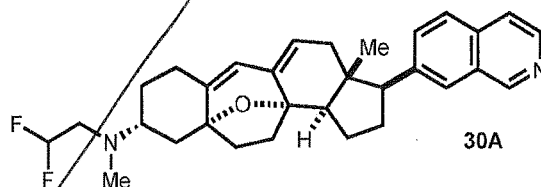
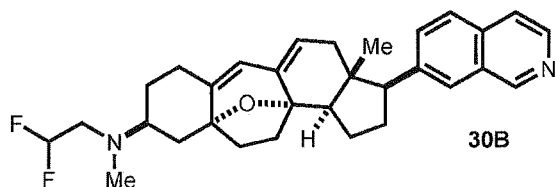
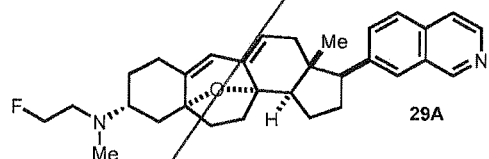
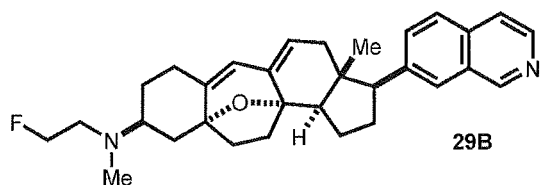
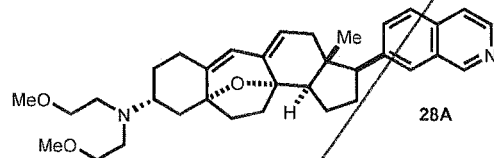
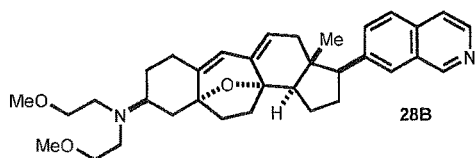
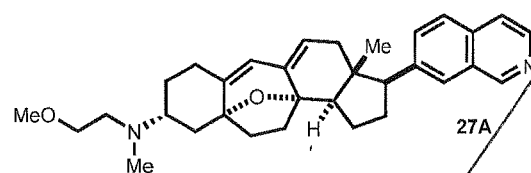
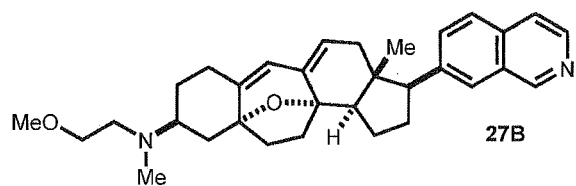
wherein each instance of R^{6C} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen, optionally when attached to N the two R^{6C} groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring; and

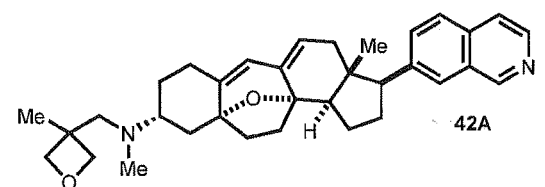
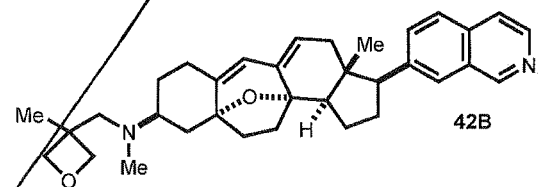
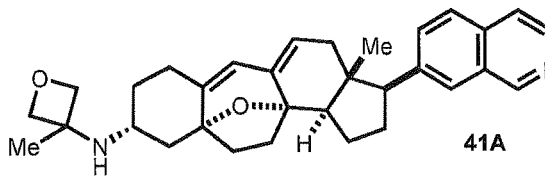
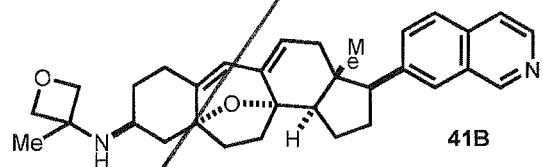
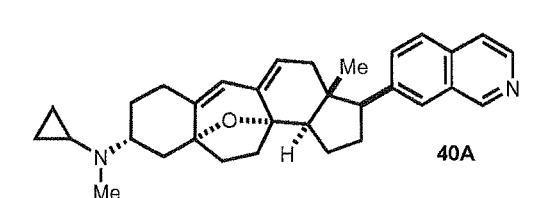
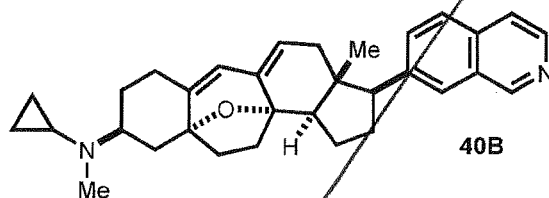
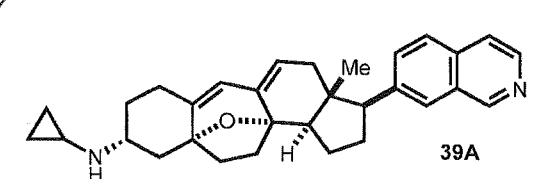
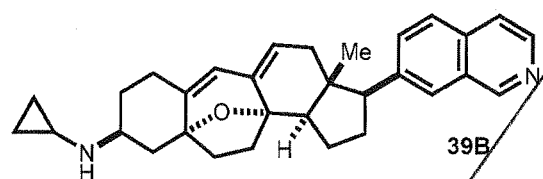
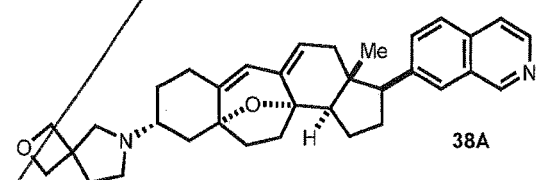
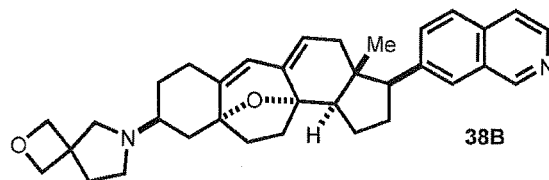
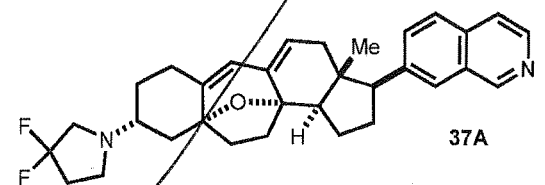
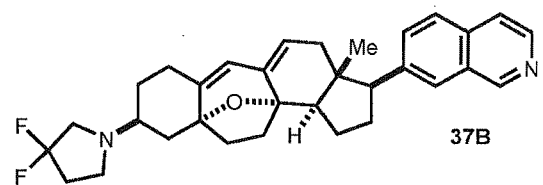
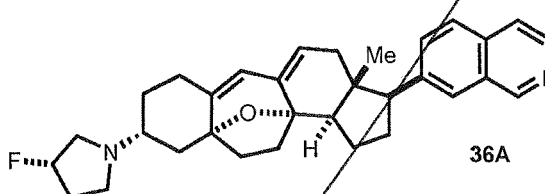
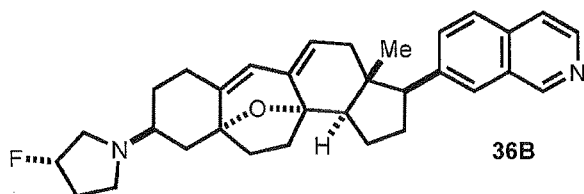
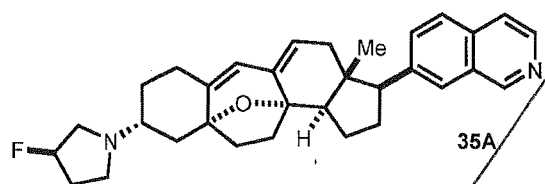
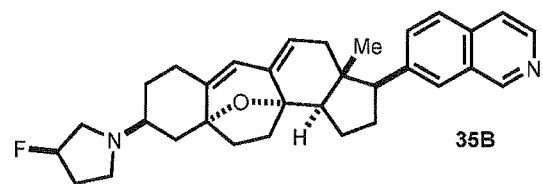
m is 0 or an integer between 1 and 4, inclusive.

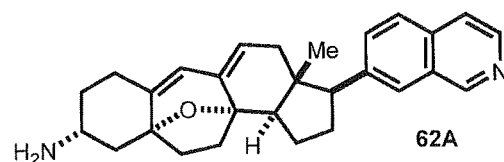
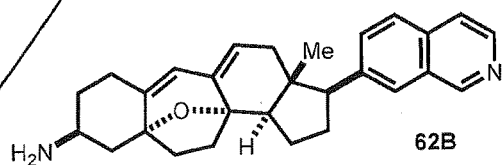
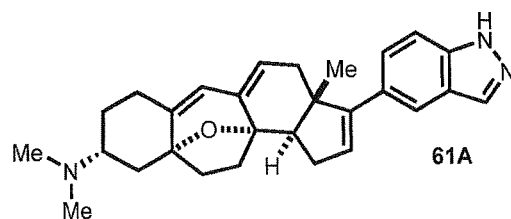
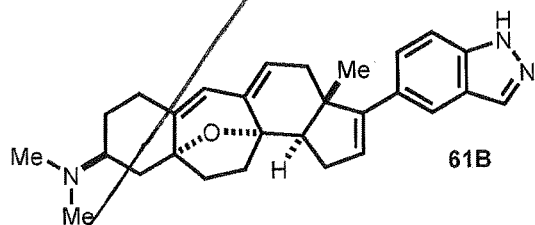
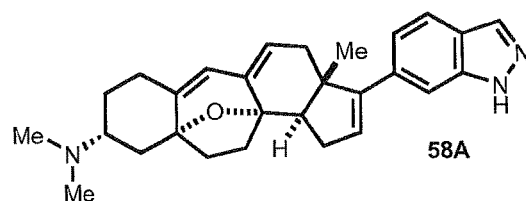
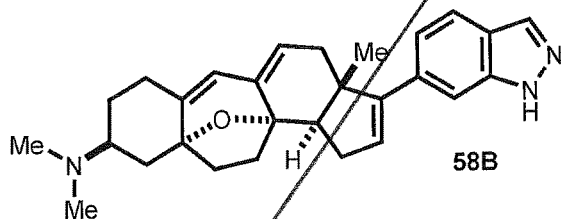
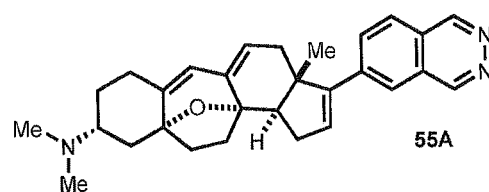
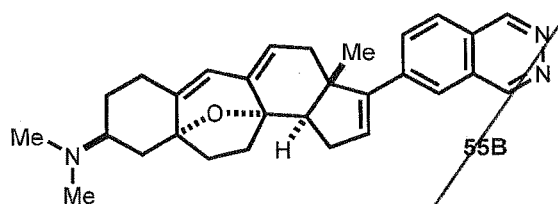
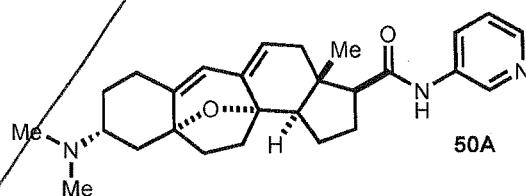
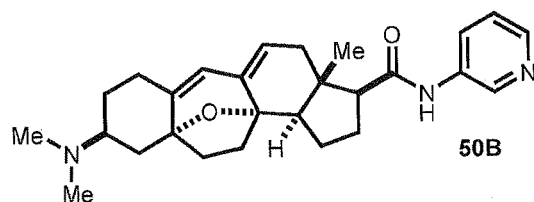
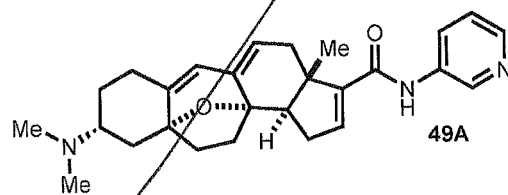
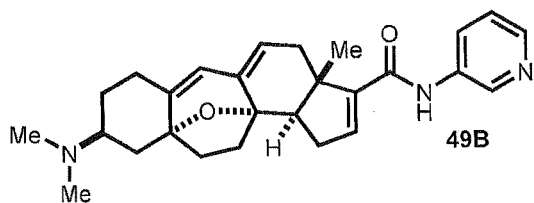
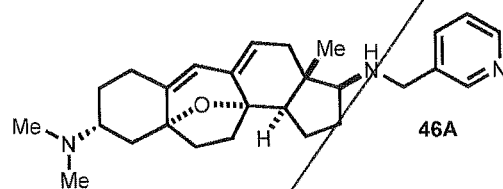
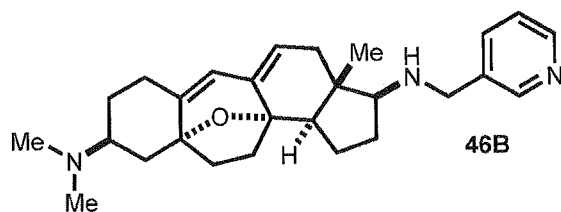
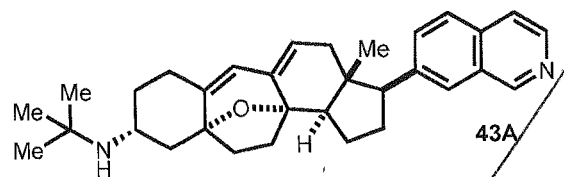
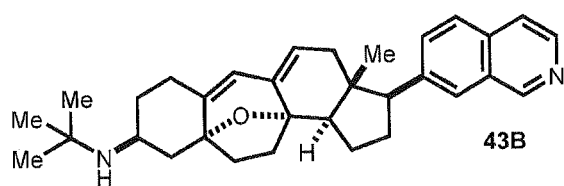
27. The compound of claim 1, wherein the compound is selected from the group consisting of:

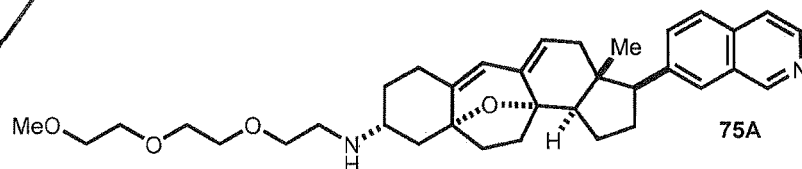
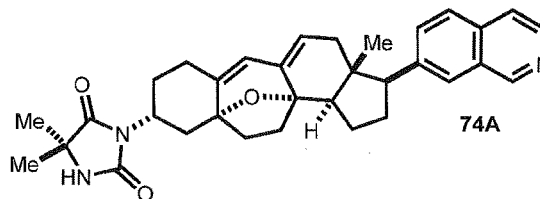
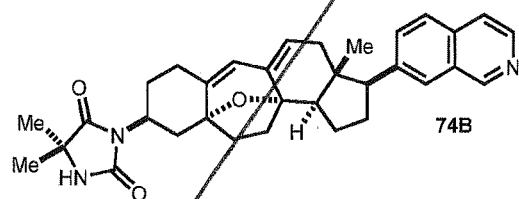
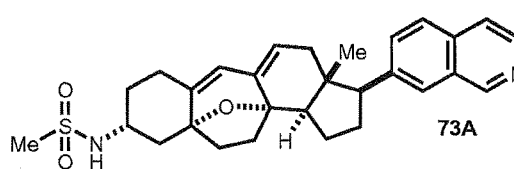
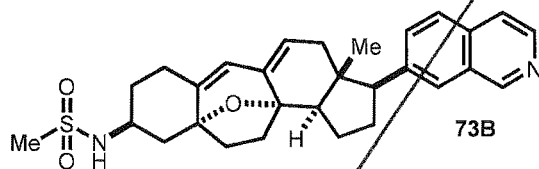
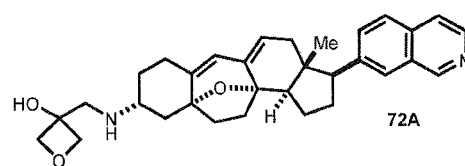
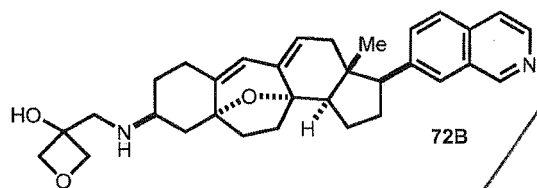
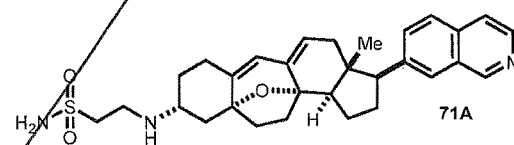
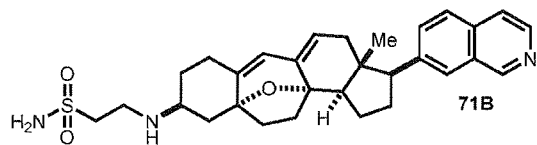
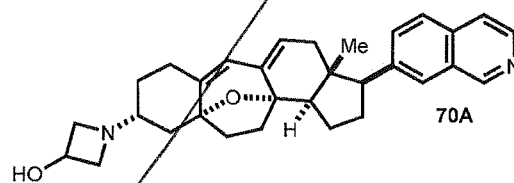
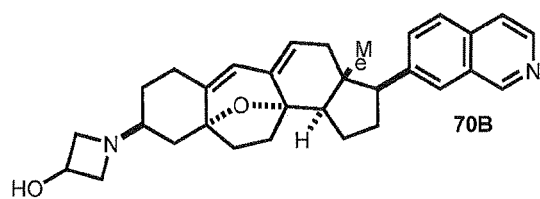
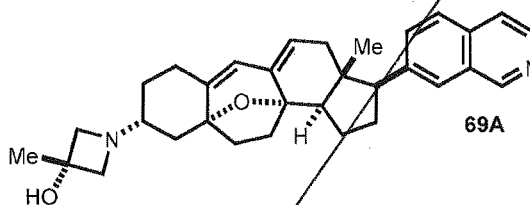
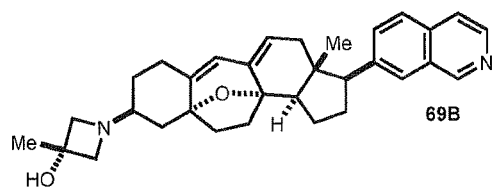
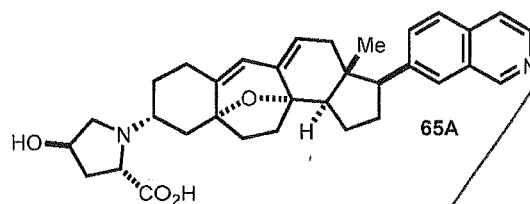
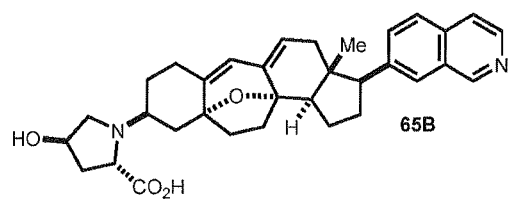


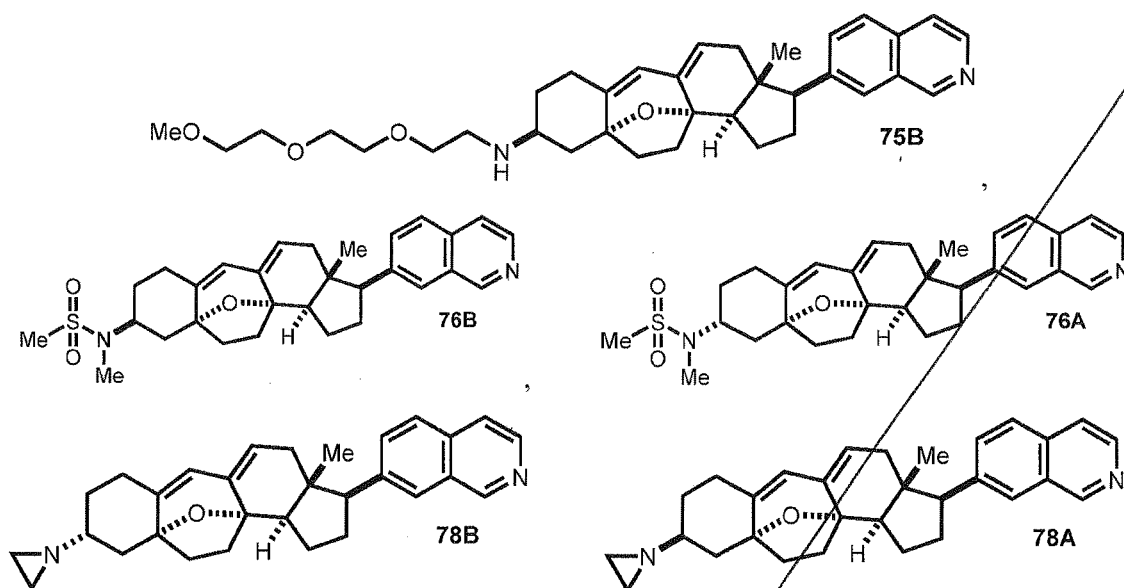






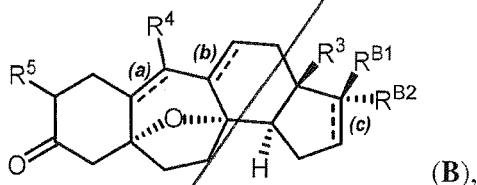






and pharmaceutically acceptable salts thereof.

28. A compound of Formula (B):



or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof;
wherein:

R^3 is hydrogen or optionally substituted alkyl;

R^4 is hydrogen, halogen, optionally substituted alkyl, or $-\text{Si}(\text{R}^A)_3$;

R^5 is hydrogen, halogen, or optionally substituted alkyl;

each instance of $---$, designated as (a), (b), and (c), represents a single or double bond, provided that when $---$ designated as (c) represents a double bond, then one of R^{B1} and R^{B2} is absent, and provided that when $---$ designated as (c) represents a single bond, then both R^{B1} and R^{B2} are present;

each instance of R^{B1} and R^{B2} is, independently, hydrogen, $-\text{L}_1-\text{R}^{B3}$, or $-\text{X}^A\text{R}^A$ wherein X^A is $-\text{O}-$, $-\text{S}-$, or $-\text{N}(\text{R}^A)-$; or R^{B1} and R^{B2} are joined to form an oxo group, provided that at least one of R^{B1} and R^{B2} is not hydrogen;

L_1 is a bond, $-\text{C}(=\text{O})-$, $-\text{C}(=\text{O})\text{O}-$, $-\text{C}(=\text{O})\text{S}-$, $-\text{C}(=\text{O})\text{N}(\text{R}^L)-$, or $-\text{N}(\text{R}^L)-(\text{C}(\text{R}^{\text{IL}})_2)_p-$, wherein R^L is hydrogen, optionally substituted alkyl, or a nitrogen protecting group, each

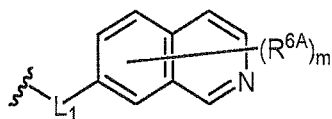
instance of R^{LL} is independently hydrogen, halogen, or optionally substituted alkyl, and p is 0, 1, or 2;

R^{B3} is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, provided that when L_1 is a bond, then R^{B3} is not hydrogen; and

each instance of R^A is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, carbonyl, silyl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen; optionally when attached to N the two R^A groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring; and optionally when R^{B1} and R^{B2} are each $-X^A R^A$ then two R^A groups may be joined to form an optionally substituted heterocyclyl ring.

29. The compound of claim 28, wherein R^3 is optionally substituted alkyl.
30. The compound of claim 29, wherein R^3 is $-\text{CH}_3$.
31. The compound of any one of claims 29 and 30, wherein R^4 is hydrogen.
32. The compound of any one of claims 29 to 31, wherein R^5 is hydrogen.
33. The compound of any one of claims 29 to 32, wherein each instance of --- designated as (a), and (b) is a double bond.
34. The compound of any one of claims 29 to 33, wherein --- designated as (c) represents a single bond.
35. The compound of any one of claims 29 to 34, wherein R^{B1} is L_1-R^{B3} and R^{B2} is hydrogen.
36. The compound of claim 35, wherein L_1 is a bond.

37. The compound of claim 35 or 36, wherein $-L_1-R^{B3}$ is:



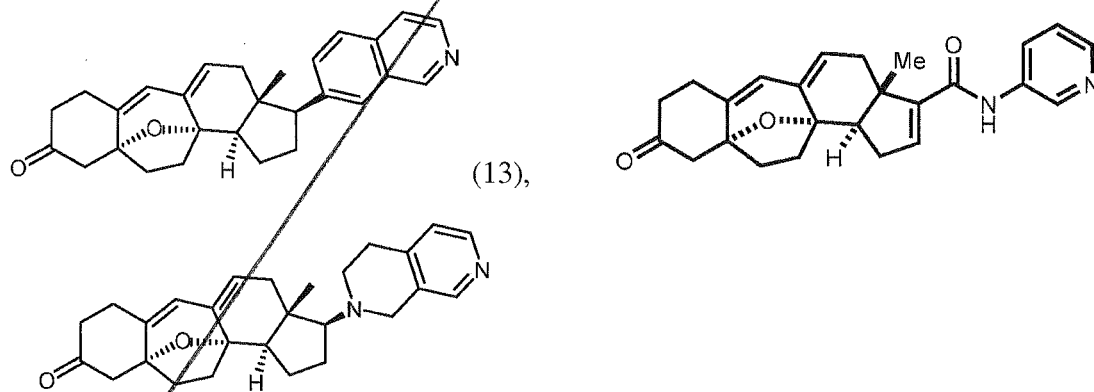
wherein:

each instance of R^{6A} is independently halogen, $-NO_2$, $-CN$, $-OR^{6C}$, SR^{6C} , $N(R^{6C})_2$, $-C(=O)R^{6C}$, $-C(=O)OR^{6C}$, $-C(=O)N(R^{6C})_2$, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl;

wherein each instance of R^{6C} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen, optionally when attached to N the two R^{6C} groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring; and

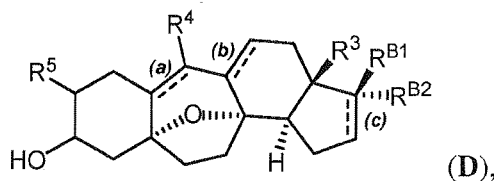
m is 0 or an integer between 1 and 4, inclusive.

38. The compound of claim 28, wherein the compound is selected from the group consisting of:



and pharmaceutically acceptable salts, quaternary amine salts, or N-oxides thereof.

39. A compound of Formula (D):



or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof;

wherein:

R^3 is hydrogen or optionally substituted alkyl;

R^4 is hydrogen, halogen, optionally substituted alkyl, or $-\text{Si}(R^A)_3$;

R^5 is hydrogen, halogen, or optionally substituted alkyl;

each instance of --- , designated as (a), (b), and (c), represents a single or double bond, provided that when --- designated as (c) represents a double bond, then one of R^{B1} and R^{B2} is absent, and provided that when --- designated as (c) represents a single bond, then both R^{B1} and R^{B2} are present;

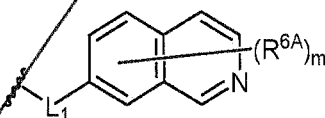
each instance of R^{B1} and R^{B2} is, independently, hydrogen, $-\text{L}_1-\text{R}^{B3}$, or $-\text{X}^A\text{R}^A$ wherein X^A is $-\text{O}-$, $-\text{S}-$, or $-\text{N}(R^A)-$; or R^{B1} and R^{B2} are joined to form an oxo group, provided that at least one of R^{B1} and R^{B2} is not hydrogen;

L_1 is a bond, $-\text{C}(=\text{O})-$, $-\text{C}(=\text{O})\text{O}-$, $-\text{C}(=\text{O})\text{S}-$, $-\text{C}(=\text{O})\text{N}(R^L)-$, or $-\text{N}(R^L)-(\text{C}(R^{LL})_2)_p-$, wherein R^L is hydrogen, optionally substituted alkyl, or a nitrogen protecting group, each instance of R^{LL} is independently hydrogen, halogen, or optionally substituted alkyl, and p is 0, 1, or 2;

R^{B3} is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, provided that when L_1 is a bond, then R^{B3} is not hydrogen; and

each instance of R^A is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, carbonyl, silyl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen; optionally when attached to N the two R^A groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring; and optionally when R^{B1} and R^{B2} are each $-\text{X}^A\text{R}^A$ then two R^A groups may be joined to form an optionally substituted heterocyclyl ring.

40. The compound of claim 39, wherein R^3 is optionally substituted alkyl.
41. The compound of claim 40, wherein R^3 is $-\text{CH}_3$.
42. The compound of any one of claims 39 to 41, wherein R^4 is hydrogen.
43. The compound of any one of claims 39 to 42, wherein R^5 is hydrogen.
44. The compound of any one of claims 39 to 43, wherein each instance of ~~----~~ designated as (a), and (b) is a double bond.
45. The compound of any one of claims 39 to 44, wherein ~~----~~ designated as (c) represents a single bond.
46. The compound of any one of claims 39 to 45, wherein R^{B1} is L_1-R^{B3} and R^{B2} is hydrogen.
47. The compound of claim 46, wherein L_1 is a bond.
48. The compound of claim 45 or 46, wherein $-L_1-R^{B3}$ is:



wherein:

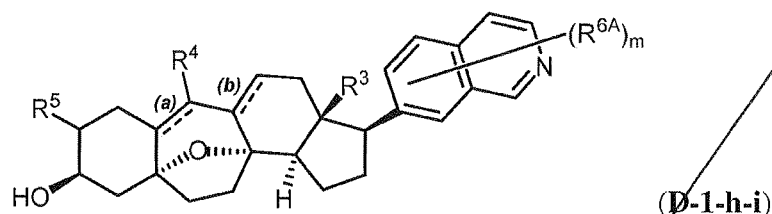
each instance of R^{6A} is independently halogen, $-\text{NO}_2$, $-\text{CN}$, $-\text{OR}^{6C}$, SR^{6C} , $\text{N}(\text{R}^{6C})_2$, $-\text{C}(=\text{O})\text{R}^{6C}$, $-\text{C}(=\text{O})\text{OR}^{6C}$, $-\text{C}(=\text{O})\text{N}(\text{R}^{6C})_2$, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl;

wherein each instance of R^{6C} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to

nitrogen, optionally when attached to N the two R^{6C} groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring; and

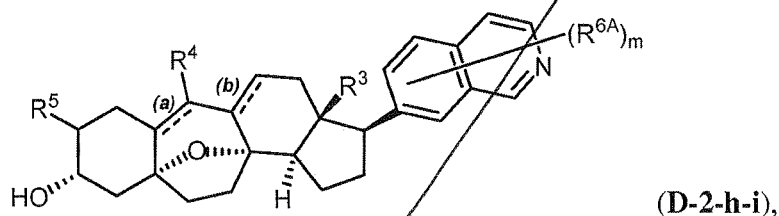
m is 0 or an integer between 1 and 4, inclusive.

49. The compound of claim 48, wherein the compound is:



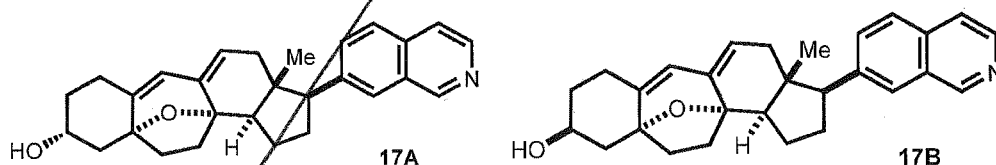
or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof.

50. The compound of claim 48, wherein the compound is:



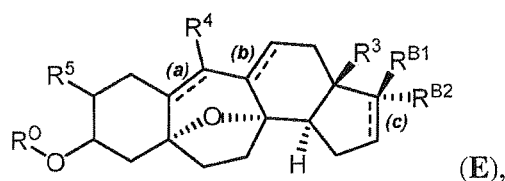
or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof.

51. The compound of claim 39, wherein the compound is selected from the group consisting of:



and pharmaceutically acceptable salts thereof.

52. A compound of Formula (E):



or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof;

wherein:

R^3 is hydrogen or optionally substituted alkyl;

R^4 is hydrogen, halogen, optionally substituted alkyl, or $-\text{Si}(R^A)_3$;

R^5 is hydrogen, halogen, or optionally substituted alkyl;

each instance of $----$, designated as (a), (b), and (c), represents a single or double bond, provided that when $----$ designated as (c) represents a double bond, then one of R^{B1} and R^{B2} is absent, and provided that when $----$ designated as (c) represents a single bond, then both R^{B1} and R^{B2} are present;

each instance of R^{B1} and R^{B2} is, independently, hydrogen, $-\text{L}_1-\text{R}^{B3}$, or $-\text{X}^A\text{R}^A$ wherein X^A is $-\text{O}-$, $-\text{S}-$, or $-\text{N}(\text{R}^A)-$; or R^{B1} and R^{B2} are joined to form an oxo group, provided that at least one of R^{B1} and R^{B2} is not hydrogen;

L_1 is a bond, $-\text{C}(=\text{O})-$, $-\text{C}(=\text{O})\text{O}-$, $-\text{C}(=\text{O})\text{S}-$, $-\text{C}(=\text{O})\text{N}(\text{R}^L)-$, or $-\text{N}(\text{R}^L)-(\text{C}(\text{R}^{\text{LL}})_2)_p-$, wherein R^L is hydrogen, optionally substituted alkyl, or a nitrogen protecting group, each instance of R^{LL} is independently hydrogen, halogen, or optionally substituted alkyl, and p is 0, 1, or 2;

R^{B3} is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, provided that when L_1 is a bond, then R^{B3} is not hydrogen;

each instance of R^A is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, carbonyl, silyl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen; optionally when attached to N the two R^A groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring; and optionally when R^{B1} and R^{B2} are each $-\text{X}^A\text{R}^A$ then two R^A groups may be joined to form an optionally substituted heterocyclyl ring; and

R^O is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $-\text{C}(=\text{O})\text{R}^A$, $-\text{C}(=\text{O})\text{OR}^A$, $-\text{C}(=\text{O})\text{N}(\text{R}^A)_2$, or an oxygen protecting group.

53. The compound of claim 52, wherein R^O is an optionally substituted alkyl.

54. The compound of claim 53, wherein R^O is $-\text{CH}_3$.

55. The compound of claim 53, wherein R^O is alkyl substituted with one or more amino, substituted amino, hydroxyl, substituted hydroxyl, thiol, substituted thiol, or sulfonyl substituents.

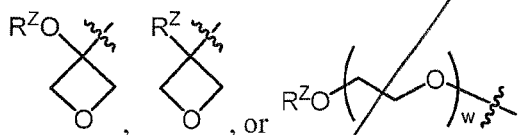
56. The compound of claim 53, wherein R⁰ is a group of formula:



wherein:

p is 1, 2, 3, 4, 5, or 6; and

Z is $-\text{CH}_2\text{X}^Z$, $-\text{CH}(\text{X}^Z)_2$, $-\text{C}(\text{X}^Z)_3$, $-\text{OR}^Z$, $-\text{SR}^Z$, $-\text{N}(\text{R}^Z)_2$, $-\text{S}(\text{O})_2\text{N}(\text{R}^Z)_2$,



wherein each instance of R^Z is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $-C(=O)R^Z$, $-C(=O)OR^Z$, $-C(=O)N(R^Z)_2$, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen, optionally when attached to N the two R^Z groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring;

each instance of X^Z is independently fluoro, chloro, bromo, or iodo; and

w is an integer between 1 and 10, inclusive.

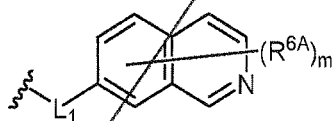
57. The compound of claim 52, wherein R^O is $-C(=O)R^A$, $-C(=O)OR^A$, or $-C(=O)N(R^A)_2$.

58. The compound of claim 52, wherein R^O is -C(=O)CH₃, -C(=O)OCH₃, -C(=O)N(CH₃)₂, or -C(=O)NHCH₃.

~~59. The compound of any one of claims 52 to 58, wherein R³ is optionally substituted alkyl.~~

60. The compound of claim 59, wherein R³ is -CH₃.

61. The compound of any one of claims 52 to 60, wherein R^4 is hydrogen.
62. The compound of any one of claims 52 to 61, wherein R^5 is hydrogen.
63. The compound of any one of claims 52 to 62, wherein each instance of ~~----~~ designated as (a), and (b) is a double bond.
64. The compound of any one of claims 52 to 63, wherein ~~----~~ designated as (c) represents a single bond.
65. The compound of any one of claims 52 to 64, wherein R^{B1} is L_1-R^{B3} and R^{B2} is hydrogen.
66. The compound of claim 65, wherein L_1 is a bond.
67. The compound of claim 65 or 66, wherein $-L_1-R^{B3}$ is:



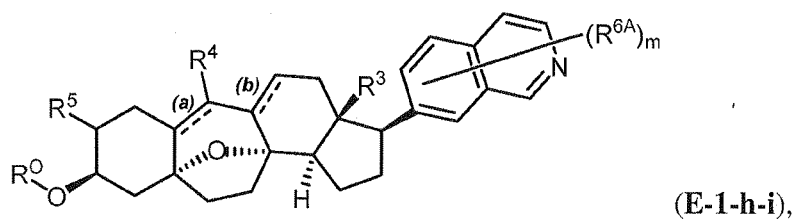
wherein:

each instance of R^{6A} is independently halogen, $-\text{NO}_2$, $-\text{CN}$, $-\text{OR}^{6C}$, SR^{6C} , $\text{N}(\text{R}^{6C})_2$, $-\text{C}(=\text{O})\text{R}^{6C}$, $-\text{C}(=\text{O})\text{OR}^{6C}$, $-\text{C}(=\text{O})\text{N}(\text{R}^{6C})_2$, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl;

wherein each instance of R^{6C} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to oxygen, a sulfur protecting group when attached to sulfur, or a nitrogen protecting group when attached to nitrogen, optionally when attached to N the two R^{6C} groups may be joined to form an optionally substituted heterocyclyl or optionally substituted heteroaryl ring; and

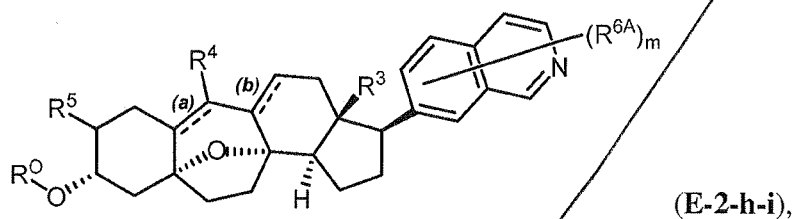
m is 0 or an integer between 1 and 4, inclusive.

68. The compound of claim 67, wherein the compound is:



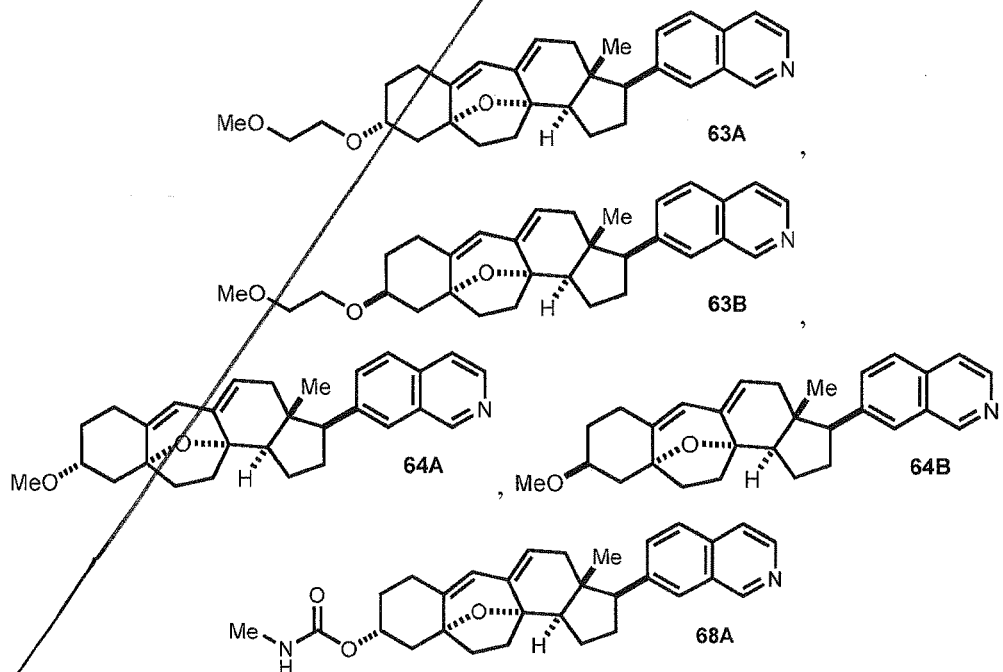
or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof.

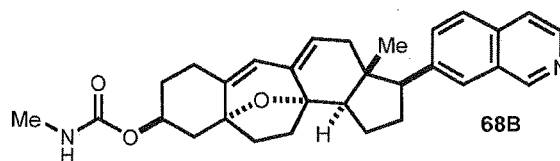
69. The compound of claim 67, wherein the compound is:



or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof.

70. The compound of claim 52, wherein the compound is selected from the group consisting of:





and pharmaceutically acceptable salts thereof.

71. A pharmaceutical composition comprising a compound according to any one of the preceding claims, or a pharmaceutically acceptable salt, quaternary amine, or N-oxide thereof, and a pharmaceutically acceptable excipient.

72. A method of treating a condition associated with angiogenesis comprising administering to a subject in need thereof a compound according to any one of the preceding claims, or a pharmaceutically acceptable salt, quaternary amine, or N-oxide thereof, or a pharmaceutical composition thereof.

73. The method of claim 72, wherein the condition is a diabetic condition, an inflammatory condition, macular degeneration, obesity, atherosclerosis, or a proliferative disorder.

74. A method of treating a condition associated with CDK8 and/or CDK19 kinase activity, comprising administering to a subject in need thereof a compound according to any one of the preceding claims, or a pharmaceutically acceptable salt, quaternary amine, or N-oxide thereof, or a pharmaceutical composition thereof.

75. The method of claim 74, wherein the condition is a proliferative disorder.

76. The method of claim 75, wherein the proliferative disorder is cancer.

77. The method of claim 76, wherein the cancer is a hematopoietic cancer.

78. The method of claim 77, wherein the hematopoietic cancer is lymphoma or leukemia.

79. The method of claim 77, wherein the hematopoietic cancer is multiple myeloma.

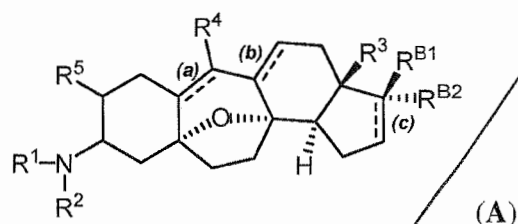
80. The method of claim 78, wherein the leukemia is acute myelocytic leukemia (AML).
81. The method of claim 75, wherein the proliferative disorder is a myeloproliferative neoplasm.
82. The method of claim 81, wherein the myeloproliferative neoplasm is primary myelofibrosis (PMF).
83. The method of claim 76, wherein the cancer is a solid tumor.
84. A method of inhibiting CDK8 and/or CDK19 kinase activity in a cell comprising contacting a compound according to any one of the preceding claims, or a pharmaceutically acceptable salt, quaternary amine, or N-oxide thereof, or a pharmaceutical composition thereof, with the cell.
85. A method of modulating the β -catenin pathway in a cell comprising contacting a compound according to any one of the preceding claims, or a pharmaceutically acceptable salt, quaternary amine, or N-oxide thereof, or a pharmaceutical composition thereof, with the cell.
86. A method of modulating STAT1 activity in a cell comprising contacting a compound according to any one of the preceding claims, or a pharmaceutically acceptable salt, quaternary amine, or N-oxide thereof, or a pharmaceutical composition thereof, with the cell.
87. A method of modulating the TGF β /BMP pathway in a cell comprising contacting a compound according to any one of the preceding claims, or a pharmaceutically acceptable salt, quaternary amine, or N-oxide thereof, or a pharmaceutical composition thereof, with the cell.
88. A method of modulating HIF-1-alpha activity in a cell comprising contacting a compound according to any one of the preceding claims, or a pharmaceutically acceptable salt, quaternary amine, or N-oxide thereof, or a pharmaceutical composition thereof, with the cell.

89. A method of increasing BIM expression to induce apoptosis in a cell comprising contacting a compound according to any one of the preceding claims, or a pharmaceutically acceptable salt, quaternary amine, or N-oxide thereof, or a pharmaceutical composition thereof, with the cell.
90. The method of any one of claims 84 to 89, wherein the method is an *in vitro* method.
91. The method of any one of claims 84 to 89, wherein the method is an *in vivo* method.
92. A method of validating CDK8 and /or CDK19 kinase activity in a cell by contacting a CDK8 or CDK19 Trp105 point mutant and a cortistatin or cortistatin analog.
93. The method of claim 92, wherein the cortistatin analog is a compound according to any one of the preceding claims, or a pharmaceutically acceptable salt, quaternary amine, or N-oxide thereof.
94. The method of claim 92, wherein the CDK8 Trp105 point mutant has an amino acid sequence which has a degree of homology to the amino acid sequence of SEQ ID NO: 1 of at least about 80%.
95. The method of claim 92, wherein the CDK19 Trp105 point mutant has an amino acid sequence which has a degree of homology to the amino acid sequence of SEQ ID NO: 2 of at least about 80%.
96. A CDK8 Trp105 point mutant.
97. The CDK8 Trp105 point mutant of claim 56 having an amino acid sequence which has a degree of homology to the amino acid sequence of SEQ ID NO: 1 of at least about 80%.
98. A protein that has a degree of homology to the amino acid sequence of SEQ ID NO: 1 of at least about 80%.
99. A CDK19 Trp105 point mutant.

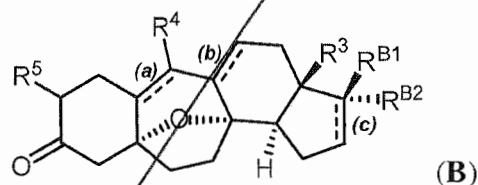
100. The CDK19 Trp105 point mutant of claim 99 having an amino acid sequence which has a degree of homology to the amino acid sequence of SEQ ID NO: 2 of at least about 80%.

101. A protein that has a degree of homology to the amino acid sequence of SEQ ID NO: 2 of at least about 80%.

102. A method of preparing a compound of Formula (A):



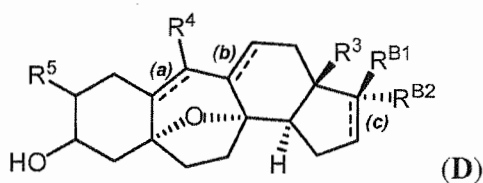
or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof;
the method comprising contacting a compound of Formula (B):



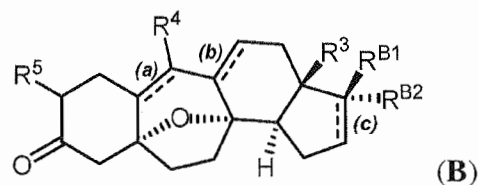
or a pharmaceutically acceptable salt, provided R^{B1} and R^{B2} are not joined to form an oxo group;

with an amine of formula HNR^1R^2 , or salt thereof, under reductive amination conditions.

103. A method of preparing a compound of Formula (D):

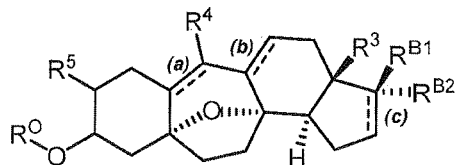


or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof;
the method comprising contacting a compound of Formula (B):

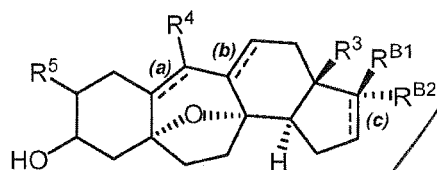


or a pharmaceutically acceptable salt thereof, with a reducing agent.

104. A method of preparing a compound of Formula (E):

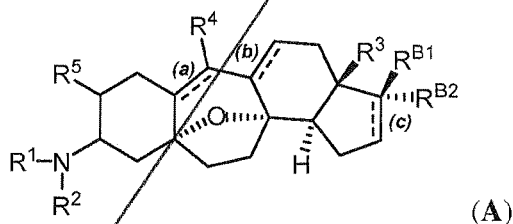


a pharmaceutically acceptable salt thereof; the method comprising contacting a compound of Formula (D):

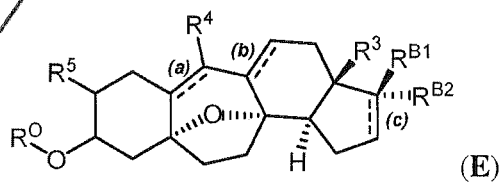


or a pharmaceutically acceptable salt thereof, with a compound of formula R^O-LG , wherein LG is a leaving group, to provide a compound of Formula (E).

105. A method of preparing a compound of Formula (A):



or a pharmaceutically acceptable salt, quaternary amine salt, or N-oxide thereof; the method comprising providing a compound of Formula (E):



wherein R^O is $-C(=O)R^A$, or a pharmaceutically acceptable salt thereof; and treating the compound of Formula (E) with a compound of formula NHR^1R^2 , to provide a compound of Formula (A).