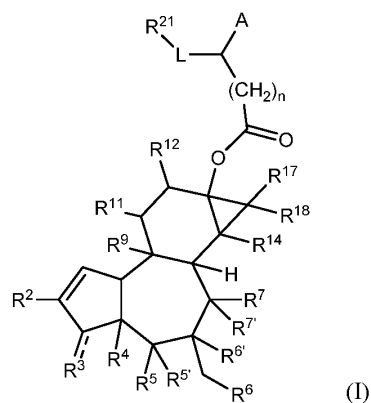


CLAIMS

What is claimed is:

1. A compound of formula (I):



or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;

wherein

A is -OH, -C(O)OR¹, or -NR¹³R^{13'};

R¹ is H or a M⁺ counterion;

R² is a C₁-C₄alkyl;

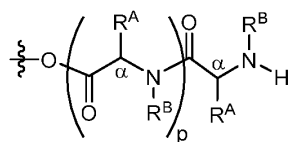
R³ is O double bonded to the ring carbon when (- -) is a bond, or -OR^a; wherein R^a is H or -C(O)R^{a1}, wherein R^{a1} is C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl;

R⁴ and R⁵ are each independently H or -OR^b, wherein R^b is H, C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl;

R^{5'} and R^{6'} are H, or R^{5'} and R^{6'} form a bond or are bonded to a common O atom to form an epoxide ring as permitted by valency;

R⁶ is OH, halo, or -OC(O)R^c, wherein R^c is -C₁-C₆alkyl, -C₁-C₆alkyl-(NR^{c1})₂ or -C₁-C₆alkylC(O)OR^k, R^{c1} is H, C₁-C₆alkyl, or two R^{c1} together with the N atom form a 5 to 7 membered heterocyclyl containing 1 to 3 heteroatoms selected from N, O, and S; or

R⁶ is



wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-

natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with the adjacent R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each occurrence of R^B is same or different; and

p is 0, 1, or 2;

R^{6'} and R^{7'} are H, or R^{6'} and R^{7'} form a bond or are bonded to a common O atom to form an epoxide ring, as permitted by valency;

R⁷ is H or OH;

R⁹ is OR^e, wherein R^e is H, C₁-C₆alkyl, or aryl;

R¹¹ is C₁-C₄alkyl;

R¹² is H, -OH, -OC(O)R^f, wherein R^f is C₁-C₁₂alkyl, C₂-C₁₂alkenyl, -C₀-C₁₂aliphatic-C₃-C₇cycloalkyl, -C₀-C₁₂aliphatic-heterocycloalkyl, -C₀-C₁₂aliphatic-aryl, or -C₀-C₁₂aliphatic-heteroaryl;

R¹³ and R^{13'} are each independently H or C₁-C₄alkyl;

R¹⁴ is H or OR^g; wherein R^g is H or C₁-C₆alkyl;

R¹⁷ and R¹⁸ are each independently C₁-C₄alkyl or C₁-C₄alkyl-OR^h, wherein R^h is H or C₁-C₆alkyl;

L is absent, C₁-C₁₂alkylene, or C₂-C₁₂alkenylene, wherein the C₁-C₁₂alkylene or C₂-C₁₂alkenylene is optionally substituted with C₁-C₄alkyl;

R²¹ is H, -S(O)₂R^j, -SR^j, -N(R^j)₂, -Si(R^j)₃, C₃-C₇cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂ cycloalkyl, 5 to 12 membered bridged bicycyl, adamantyl, or -C(O)OR^k, wherein the C₃-C₇cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂ cycloalkyl, bridged bicycyl, or adamantyl is optionally substituted with 1 to 3 of J¹, and wherein optionally 1 to 2 carbon atoms of the spiroC₅-C₁₂cycloalkyl or bridged bicycyl is replaced with a heteroatom selected from N, O and S, and optionally substituted with C₁-C₄alkyl, or when an N atom is present an N-protecting group;

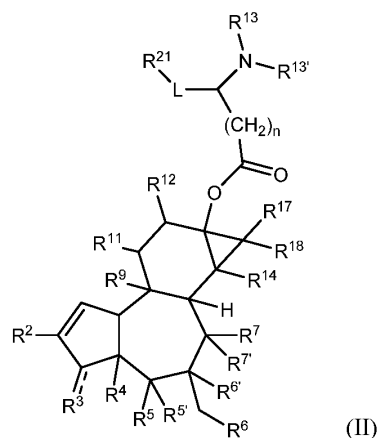
each R^j is independently C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkyl-C₃-C₇cycloalkyl, C₀-C₆alkylheterocyclyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl, wherein the C₃-C₇cycloalkyl, heterocyclyl, alkylaryl, or heteroaryl is optionally substituted with 1 to 3 of J¹;

R^k is H or M⁺ counterion;

J¹ is selected from OH, CN, halo, C₁-C₄alkyl, and haloC₁-C₄alkyl; and

n is 0 or 1.

2. The compound of claim 1, wherein A is -OH.
3. The compound of claim 1, wherein A is -C(O)OR¹, wherein R¹ is H or a M⁺ counterion.
4. The compound of claim 1 having the structure of formula (II):



or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;

wherein

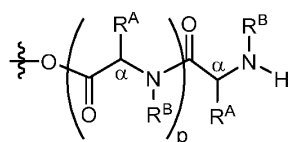
R² is a C₁-C₄alkyl;

R³ is O double bonded to the ring carbon when (- -) is a bond, or -OR^a, wherein R^a is H or -C(O)R^{a1}, wherein R^{a1} is C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl;

R⁴ and R⁵ are each independently H or -OR^b, wherein R^b is H, C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl;

R^{5'} and R^{6'} are H, or R^{5'} and R^{6'} form a bond or are bonded to a common O atom to form an epoxide ring as permitted by valency;

R⁶ is OH, halo, or -OC(O)R^c, wherein R^c is -C₁-C₆alkyl, -C₁-C₆alkyl-(NR^{cl})₂ or -C₁-C₆alkylC(O)OR^k, R^{cl} is H, C₁-C₆alkyl, or two R^{cl} together with the N atom form a 5 to 7 membered heterocyclyl containing 1 to 3 heteroatoms selected from N, O, and S; or

 $\mathbb{R}^6$ is

wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with the adjacent R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each occurrence of R^B is same or different; and

p is 0, 1, or 2;

$R^{6''}$ and $R^{7''}$ are H, or $R^{6''}$ and $R^{7''}$ form a bond or are bonded to a common O atom to form an epoxide ring, as permitted by valency;

R^7 is H or OH;

R^9 is OR^e , wherein R^e is H, C_1 - C_6 alkyl, or aryl;

R^{11} is C_1 - C_4 alkyl;

R^{12} is H, -OH, $-OC(O)R^f$, wherein R^f is C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, $-C_0$ - C_{12} aliphatic- C_3 - C_7 cycloalkyl, $-C_0$ - C_{12} aliphatic-heterocycloalkyl, $-C_0$ - C_{12} aliphatic-aryl, or $-C_0$ - C_{12} aliphatic-heteroaryl;

R^{13} and $R^{13'}$ are each independently H or C_1 - C_4 alkyl;

R^{14} is H or OR^g , wherein R^g is H or C_1 - C_6 alkyl;

R^{17} and R^{18} are each independently C_1 - C_4 alkyl or C_1 - C_4 alkyl- OR^h , wherein R^h is H or C_1 - C_6 alkyl;

L is absent, C_1 - C_{12} alkylene, or C_2 - C_{12} alkenylene, wherein the C_1 - C_{12} alkylene or C_2 - C_{12} alkenylene is optionally substituted with C_1 - C_4 alkyl;

R^{21} is H, $-S(O)_2R^j$, $-SR^j$, $-N(R^j)_2$, $-Si(R^j)_3$, C_3 - C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiro C_5 - C_{12} cycloalkyl, 5 to 12 membered bridged bicyclyl, adamantyl, or $-C(O)OR^k$, wherein the C_3 - C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiro C_5 - C_{12} cycloalkyl, bridged bicyclyl, or adamantyl is optionally substituted with 1 to 3 of J^1 , and wherein optionally 1 to 2 carbon atoms of the spiro C_5 - C_{12} cycloalkyl or bridged bicyclyl is replaced with a heteroatom selected from N, O and S, and optionally substituted with C_1 - C_4 alkyl, or when an N atom is present an N-protecting group;

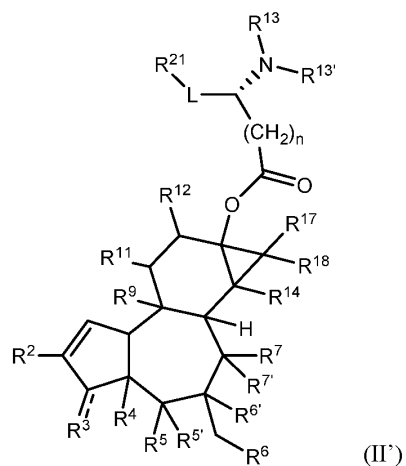
each R^j is independently C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkyl C_3 - C_7 cycloalkyl, C_0 - C_6 alkylheterocyclyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl, wherein the C_3 - C_7 cycloalkyl, heterocyclyl, alkylaryl, or heteroaryl is optionally substituted with 1 to 3 of J^1 ;

R^k is H or M^+ counterion;

J^1 is selected from OH, CN, halo, C_1 - C_4 alkyl, and halo C_1 - C_4 alkyl; and

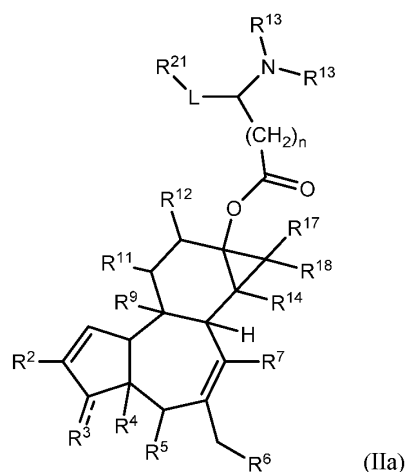
n is 0 or 1.

5. The compound of claim 4, having the structure of formula (II'):



or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof.

6. The compound of claim 4, having the structure of formula (IIa):



or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;

wherein

R^2 is a C_1 - C_4 alkyl;

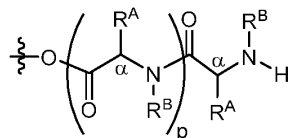
R^3 is O double bonded to the ring carbon when (---) is a bond, or $-OR^a$; wherein R^a is H or $-C(O)R^{a1}$, wherein R^{a1} is C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl;

R^4 and R^5 are each independently H or $-OR^b$, wherein R^b is H, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl;

R^6 is OH, halo, or $-OC(O)R^c$, wherein R^c is $-C_1$ - C_6 alkyl, $-C_1$ - C_6 alkyl-(NR^{c1})₂ or $-C_1$ - C_6 alkylC(O)OR^k, R^{c1} is H, C_1 - C_6 alkyl, or two R^{c1} together with the N atom form a 5 to 7 membered

heterocyclyl containing 1 to 3 heteroatoms selected from N, O, and S; or

R⁶ is



wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with the adjacent R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each occurrence of R^B is same or different; and

p is 0, 1, or 2;

R⁷ is H or OH;

R⁹ is OR^e, wherein R^e is H, C₁-C₆alkyl, or aryl;

R¹¹ is C₁-C₄alkyl;

R¹² is H, -OH, -OC(O)R^f, wherein R^f is C₁-C₁₂alkyl, C₂-C₁₂alkenyl, -C₀-C₁₂aliphatic-C₃-C₇cycloalkyl, -C₀-C₁₂aliphatic-heterocycloalkyl, -C₀-C₁₂aliphatic-aryl, or -C₀-C₁₂aliphatic-heteroaryl;

R¹³ and R^{13'} are each independently H or C₁-C₄alkyl;

R¹⁴ is H or OR^g; wherein R^g is H or C₁-C₆alkyl;

R¹⁷ and R¹⁸ are each independently C₁-C₄alkyl or C₁-C₄alkyl-OR^h, wherein R^h is H or C₁-C₆alkyl;

L is absent, C₁-C₁₂alkylene, or C₂-C₁₂alkenylene, wherein the C₁-C₁₂alkylene or C₂-C₁₂alkenylene is optionally substituted with C₁-C₄alkyl;

R²¹ is H, -S(O)₂R^j, -SR^j, -N(R^j)₂, -Si(R^j)₃, C₃-C₇cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂ cycloalkyl, 5 to 12 membered bridged bicyclyl, adamantyl, or -C(O)OR^k, wherein the C₃-C₇cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂ cycloalkyl, bridged bicyclyl, or adamantyl is optionally substituted with 1 to 3 of J¹, and wherein optionally 1 to 2 carbon atoms of the spiroC₅-C₁₂cycloalkyl or bridged bicyclyl is replaced with a heteroatom selected from N, O and S, and optionally substituted with C₁-C₄alkyl, or when an N atom is present an N-protecting group;

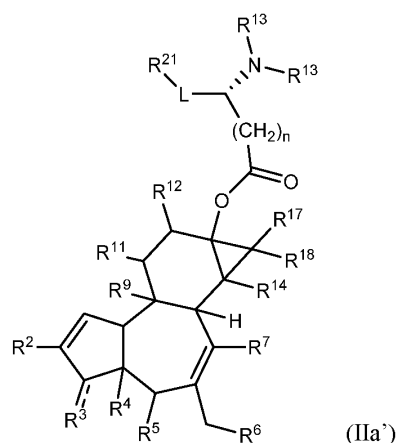
each R^j is independently C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkyl-C₃-C₇cycloalkyl, C₀-C₆alkylheterocyclyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl, wherein the C₃-C₇cycloalkyl, heterocyclyl, alkylaryl, or heteroaryl is optionally substituted with 1 to 3 of J¹;

R^k is H or M⁺ counterion;

J¹ is selected from OH, CN, halo, C₁-C₄alkyl, and haloC₁-C₄alkyl; and

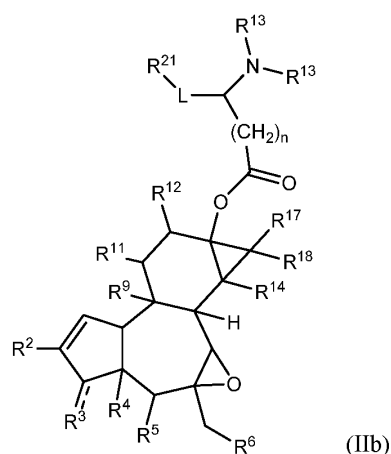
n is 0 or 1.

7. The compound of claim 6, having the structure of formula (IIa'):



or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof.

8. The compound of claim 4, having the structure of formula (IIb):



or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;

wherein

R^2 is a C_1 - C_4 alkyl;

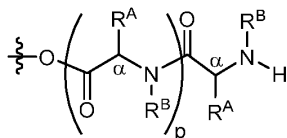
R^3 is O double bonded to the ring carbon when $(- - -)$ is a bond, or $-OR^a$; wherein R^a is H or $-C(O)R^{a1}$, wherein R^{a1} is C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl;

R^4 and R^5 are each independently H or $-OR^b$, wherein R^b is H, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl;

R^6 is OH, halo, or $-OC(O)R^c$, wherein R^c is $-C_1$ - C_6 alkyl, $-C_1$ - C_6 alkyl- $(NR^{c1})_2$ or $-C_1$ - C_6 alkyl $C(O)OR^k$, R^{c1} is H, C_1 - C_6 alkyl, or two R^{c1} together with the N atom form a 5 to 7 membered

heterocyclyl containing 1 to 3 heteroatoms selected from N, O, and S; or

R⁶ is



wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with the adjacent R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each occurrence of R^B is same or different; and

p is 0, 1, or 2;

R⁹ is OR^e, wherein R^e is H, C₁-C₆alkyl, or aryl;

R¹¹ is C₁-C₄alkyl;

R¹² is H, -OH, -OC(O)R^f, wherein R^f is C₁-C₁₂alkyl, C₂-C₁₂alkenyl, -C₀-C₁₂aliphatic-C₃-C₇cycloalkyl, -C₀-C₁₂aliphatic-heterocycloalkyl, -C₀-C₁₂aliphatic-aryl, or -C₀-C₁₂aliphatic-heteroaryl;

R¹³ and R^{13'} are each independently H or C₁-C₄alkyl;

R¹⁴ is H or OR^g, wherein R^g is H or C₁-C₆alkyl;

R¹⁷ and R¹⁸ are each independently C₁-C₄alkyl or C₁-C₄alkyl-OR^h, wherein R^h is H or C₁-C₆alkyl;

L is absent, C₁-C₁₂alkylene, or C₂-C₁₂alkenylene, wherein the C₁-C₁₂alkylene or C₂-C₁₂alkenylene is optionally substituted with C₁-C₄alkyl;

R²¹ is H, -S(O)₂R^j, -SR^j, -N(R^j)₂, -Si(R^j)₃, C₃-C₇cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂cycloalkyl, 5 to 12 membered bridged bicyclyl, adamantyl, or -C(O)OR^k, wherein the C₃-C₇cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂cycloalkyl, bridged bicyclyl, or adamantyl is optionally substituted with 1 to 3 of J¹, and wherein optionally 1 to 2 carbon atoms of the spiroC₅-C₁₂cycloalkyl or bridged bicyclyl is replaced with a heteroatom selected from N, O and S, and optionally substituted with C₁-C₄alkyl, or when an N atom is present an N-protecting group;

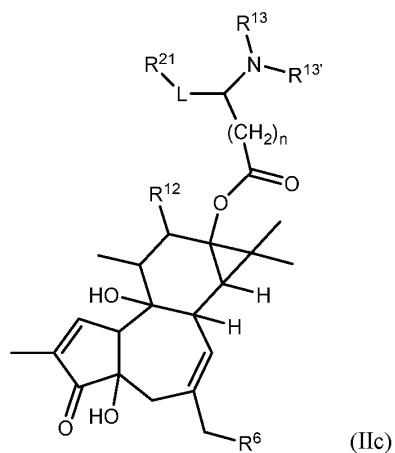
each R^j is independently C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkyl-C₃-C₇cycloalkyl, C₀-C₆alkylheterocyclyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl, wherein the C₃-C₇cycloalkyl, heterocyclyl, alkylaryl, or heteroaryl is optionally substituted with 1 to 3 of J¹;

R^k is H or M⁺ counterion;

J¹ is selected from OH, CN, halo, C₁-C₄alkyl, and haloC₁-C₄alkyl; and

n is 0 or 1.

9. The compound of claim 6, having the structure of formula (IIc):

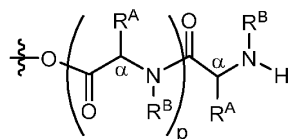


or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;

wherein

R^6 is OH, halo, or $-OC(O)R^c$, wherein R^c is $-C_1-C_6$ alkyl, $-C_1-C_6$ alkyl- $(NR^{c1})_2$ or $-C_1-C_6$ alkylC(O)OR^k, R^{c1} is H, C_1-C_6 alkyl, or two R^{c1} together with the N atom form a 5 to 7 membered heterocyclyl containing 1 to 3 heteroatoms selected from N, O, and S; or

R^6 is



wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with the adjacent R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each occurrence of R^B is same or different; and

p is 0, 1, or 2;

R^{12} is H, -OH, $-OC(O)R^f$, wherein R^f is C_1-C_{12} alkyl, C_2-C_{12} alkenyl, $-C_0-C_{12}$ aliphatic- C_3-C_7 cycloalkyl, $-C_0-C_{12}$ aliphatic-heterocycloalkyl, $-C_0-C_{12}$ aliphatic-aryl, or $-C_0-C_{12}$ aliphatic-heteroaryl;

R^{13} and $R^{13'}$ are each independently H or C_1-C_4 alkyl;

L is absent, C_1-C_{12} alkylene, or C_2-C_{12} alkenylene, wherein the C_1-C_{12} alkylene or C_2-C_{12} alkenylene is optionally substituted with C_1-C_4 alkyl;

R^{21} is H, $-S(O)_2R^j$, $-SR^j$, $-N(R^j)_2$, $-Si(R^j)_3$, C_3-C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiro C_5-C_{12} cycloalkyl, 5 to 12 membered bridged bicycyl, adamantyl, or $-C(O)OR^k$, wherein the C_3-C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiro C_5-C_{12} cycloalkyl, bridged bicycyl, or adamantyl is

optionally substituted with 1 to 3 of J^1 , and wherein optionally 1 to 2 carbon atoms of the spiroC₅-C₁₂cycloalkyl or bridged bicycyl is replaced with a heteroatom selected from N, O and S, and optionally substituted with C₁-C₄alkyl, or when an N atom is present an N-protecting group;

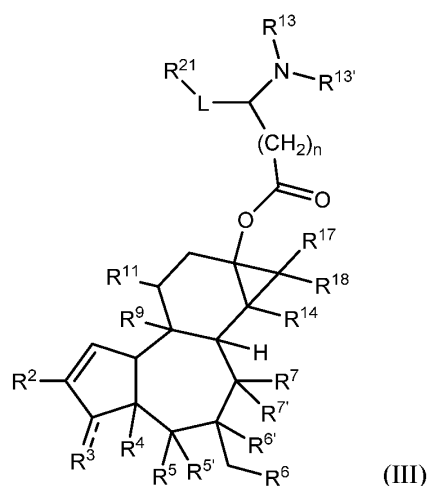
each R^j is independently C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylC₃-C₇cycloalkyl, C₀-C₆alkylheterocyclyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl, wherein the C₃-C₇cycloalkyl, heterocyclyl, alkylaryl, or heteroaryl is optionally substituted with 1 to 3 of J^1 ;

R^k is H or M^+ counterion;

J^1 is selected from OH, CN, halo, C₁-C₄alkyl, and haloC₁-C₄alkyl; and

n is 0 or 1.

10. The compound of claim 4 having the structure of formula (III):



or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;

wherein

R^2 is a C₁-C₄alkyl;

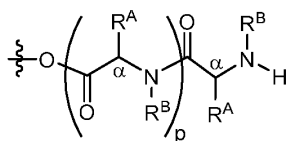
R^3 is O double bonded to the ring carbon when (---) is a bond, or -OR^a; wherein R^a is H or -C(O)R^{a1}, wherein R^{a1} is C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl;

R^4 and R^5 are each independently H or -OR^b, wherein R^b is H, C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl;

$R^{5'}$ and $R^{6'}$ are H, or $R^{5'}$ and $R^{6'}$ form a bond or are bonded to a common O atom to form an epoxide ring as permitted by valency;

R^6 is OH, halo, or -OC(O)R^c, wherein R^c is -C₁-C₆alkyl, -C₁-C₆alkyl-(NR^{c1})₂ or -C₁-C₆alkylC(O)OR^k, R^{c1} is H, C₁-C₆alkyl, or two R^{c1} together with the N atom form a 5 to 7 membered heterocyclyl containing 1 to 3 heteroatoms selected from N, O, and S; or

R^6 is



wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with the adjacent R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each occurrence of R^B is same or different; and

p is 0, 1, or 2;

R^{6*} and R^{7*} are H, or R^{6*} and R^{7*} form a bond or are bonded to a common O atom to form an epoxide ring, as permitted by valency;

R^7 is H or OH;

R^9 is OR^e , wherein R^e is H, C₁-C₆alkyl, or aryl;

R^{11} is C₁-C₄alkyl;

R^{13} and $R^{13'}$ are each independently H or C₁-C₄alkyl;

R^{14} is H or OR^g , wherein R^g is H or C₁-C₆alkyl;

R^{17} and R^{18} are each independently C₁-C₄alkyl or C₁-C₄alkyl- OR^h , wherein R^h is H or C₁-C₆alkyl;

L is absent, C₁-C₁₂alkylene, or C₂-C₁₂alkenylene, wherein the C₁-C₁₂alkylene or C₂-C₁₂alkenylene is optionally substituted with C₁-C₄alkyl;

R^{21} is H, $-S(O)_2R^j$, $-SR^j$, $-N(R^j)_2$, $-Si(R^j)_3$, C₃-C₇cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂ cycloalkyl, 5 to 12 membered bridged bicyclyl, adamantyl, or $-C(O)OR^k$, wherein the C₃-C₇cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂ cycloalkyl, bridged bicyclyl, or adamantyl is optionally substituted with 1 to 3 of J^1 , and wherein optionally 1 to 2 carbon atoms of the spiroC₅-C₁₂cycloalkyl or bridged bicyclyl is replaced with a heteroatom selected from N, O and S, and optionally substituted with C₁-C₄alkyl, or when an N atom is present an N-protecting group;

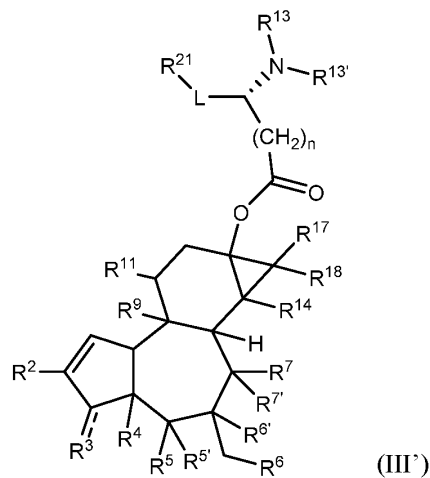
each R^j is independently C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylC₃-C₇cycloalkyl, C₀-C₆alkylheterocyclyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl, wherein the C₃-C₇cycloalkyl, heterocyclyl, alkylaryl, or heteroaryl is optionally substituted with 1 to 3 of J^1 ;

R^k is H or M^+ counterion;

J^1 is selected from OH, CN, halo, C₁-C₄alkyl, and haloC₁-C₄alkyl; and

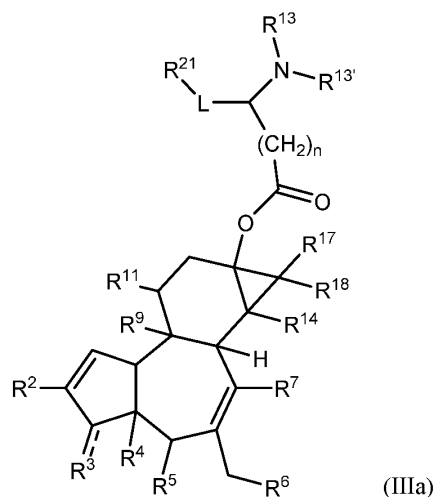
n is 0 or 1.

11. The compound of claim 10 having the structure of formula (III'):



or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof.

12. The compound of claim 10 having the structure of formula (IIIa):



or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;

wherein

R^2 is a C_1 - C_4 alkyl;

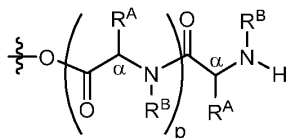
R^3 is O double bonded to the ring carbon when (- -) is a bond, or $-OR^a$, wherein R^a is H or $-C(O)R^{a1}$, wherein R^{a1} is C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl;

R^4 and R^5 are each independently H or $-OR^b$, wherein R^b is H, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl;

R^6 is OH, halo, or $-OC(O)R^c$, wherein R^c is $-C_1$ - C_6 alkyl, $-C_1$ - C_6 alkyl- $(NR^{c1})_2$ or $-C_1$ - C_6 alkylC(O)OR^k, R^{c1} is H, C_1 - C_6 alkyl, or two R^{c1} together with the N atom form a 5 to 7 membered

heterocyclyl containing 1 to 3 heteroatoms selected from N, O, and S; or

R⁶ is



wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with the adjacent R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each occurrence of R^B is same or different; and

p is 0, 1, or 2;

R⁷ is H or OH;

R⁹ is OR^e, wherein R^e is H, C₁-C₆alkyl, or aryl;

R¹¹ is C₁-C₄alkyl;

R¹³ and R^{13'} are each independently H or C₁-C₄alkyl;

R¹⁴ is H or OR^g, wherein R^g is H or C₁-C₆alkyl;

R¹⁷ and R¹⁸ are each independently C₁-C₄alkyl or C₁-C₄alkyl-OR^h, wherein R^h is H or C₁-C₆alkyl;

L is absent, C₁-C₁₂alkylene, or C₂-C₁₂alkenylene, wherein the C₁-C₁₂alkylene or C₂-C₁₂alkenylene is optionally substituted with C₁-C₄alkyl;

R²¹ is H, -S(O)₂R^j, -SR^j, -N(R^j)₂, -Si(R^j)₃, C₃-C₇cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂ cycloalkyl, 5 to 12 membered bridged bicyclyl, adamantyl, or -C(O)OR^k, wherein the C₃-C₇cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂ cycloalkyl, bridged bicyclyl, or adamantyl is optionally substituted with 1 to 3 of J¹, and wherein optionally 1 to 2 carbon atoms of the spiroC₅-C₁₂cycloalkyl or bridged bicyclyl is replaced with a heteroatom selected from N, O and S, and optionally substituted with C₁-C₄alkyl, or when an N atom is present an N-protecting group;

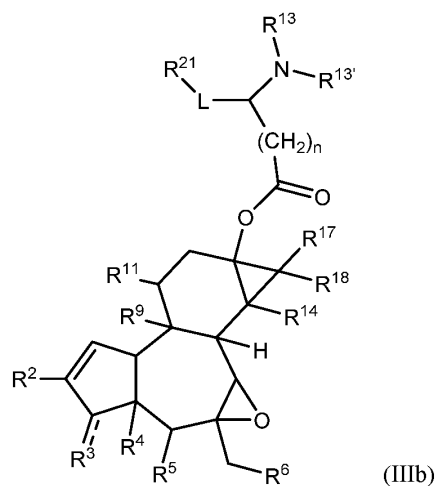
each R^j is independently C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylC₃-C₇cycloalkyl, C₀-C₆alkylheterocyclyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl, wherein the C₃-C₇cycloalkyl, heterocyclyl, alkylaryl, or heteroaryl is optionally substituted with 1 to 3 of J¹;

R^k is H or M⁺ counterion;

J¹ is selected from OH, CN, halo, C₁-C₄alkyl, and haloC₁-C₄alkyl; and

n is 0 or 1.

13. The compound of claim 10 having structure of formula (IIIb):



or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;

wherein

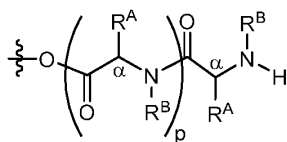
R^2 is a C_1 - C_4 alkyl;

R^3 is O double bonded to the ring carbon when (---) is a bond, or $-OR^a$, wherein R^a is H or $-C(O)R^{a1}$, wherein R^{a1} is C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl;

R^4 and R^5 are each independently H or $-OR^b$, wherein R^b is H, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl;

R^6 is OH, halo, or $-OC(O)R^c$, wherein R^c is $-C_1$ - C_6 alkyl, $-C_1$ - C_6 alkyl- $(NR^{c1})_2$ or $-C_1$ - C_6 alkyl $C(O)OR^k$, R^{c1} is H, C_1 - C_6 alkyl, or two R^{c1} together with the N atom form a 5 to 7 membered heterocycle containing 1 to 3 heteroatoms selected from N, O, and S; or

R^6 is



wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with the adjacent R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each occurrence of R^B is same or different; and

p is 0, 1, or 2;

R^9 is OR^e , wherein R^e is H, C_1 - C_6 alkyl, or aryl;

R^{11} is C_1 - C_4 alkyl;

R^{13} and $R^{13'}$ are each independently H or C_1 - C_4 alkyl;

R^{14} is H or OR^g , wherein R^g is H or C_1 - C_6 alkyl;

R^{17} and R^{18} are each independently C_1 - C_4 alkyl or C_1 - C_4 alkyl- OR^h , wherein R^h is H or C_1 - C_6 alkyl;

L is absent, C_1 - C_{12} alkylene, or C_2 - C_{12} alkenylene, wherein the C_1 - C_{12} alkylene or C_2 - C_{12} alkenylene is optionally substituted with C_1 - C_4 alkyl;

R^{21} is H, $-S(O)_2R^j$, $-SR^j$, $-N(R^j)_2$, $-Si(R^j)_3$, C_3 - C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiro C_5 - C_{12} cycloalkyl, 5 to 12 membered bridged bicycyl, adamantyl, or $-C(O)OR^k$, wherein the C_3 - C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiro C_5 - C_{12} cycloalkyl, bridged bicycyl, or adamantyl is optionally substituted with 1 to 3 of J^1 , and wherein optionally 1 to 2 carbon atoms of the spiro C_5 - C_{12} cycloalkyl or bridged bicycyl is replaced with a heteroatom selected from N, O and S, and optionally substituted with C_1 - C_4 alkyl, or when an N atom is present an N-protecting group;

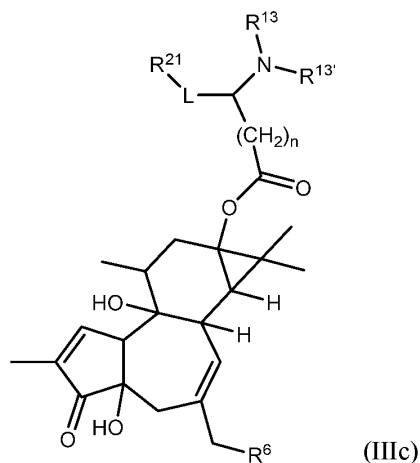
each R^j is independently C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkyl C_3 - C_7 cycloalkyl, C_0 - C_6 alkylheterocyclyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl, wherein the C_3 - C_7 cycloalkyl, heterocyclyl, alkylaryl, or heteroaryl is optionally substituted with 1 to 3 of J^1 ;

R^k is H or M^+ counterion;

J^1 is selected from OH, CN, halo, C_1 - C_4 alkyl, and halo C_1 - C_4 alkyl; and

n is 0 or 1.

14. The compound of claim 10 having the structure of formula (IIIc):



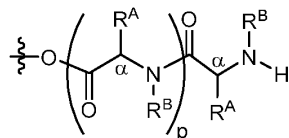
or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;

wherein

R^6 is OH, halo, or $-OC(O)R^c$, wherein R^c is $-C_1$ - C_6 alkyl, $-C_1$ - C_6 alkyl- $(NR^{c1})_2$ or $-C_1$ - C_6 alkyl $C(O)OR^k$, R^{c1} is H, C_1 - C_6 alkyl, or two R^{c1} together with the N atom form a 5 to 7 membered

heterocyclyl containing 1 to 3 heteroatoms selected from N, O, and S; or

R⁶ is



wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with the adjacent R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each occurrence of R^B is same or different; and

p is 0, 1, or 2;

R¹³ and R^{13'} are each independently H or C₁-C₄alkyl;

L is absent, C₁-C₁₂alkylene, or C₂-C₁₂alkenylene, wherein the C₁-C₁₂alkylene or C₂-C₁₂alkenylene is optionally substituted with C₁-C₄alkyl;

R²¹ is H, -S(O)₂R^j, -SR^j, -N(R^j)₂, -Si(R^j)₃, C₃-C₇cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂ cycloalkyl, 5 to 12 membered bridged bicycyl, adamantyl, or -C(O)OR^k, wherein the C₃-C₇cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂ cycloalkyl, bridged bicycyl, or adamantyl is optionally substituted with 1 to 3 of J¹, and wherein optionally 1 to 2 carbon atoms of the spiroC₅-C₁₂cycloalkyl or bridged bicycyl is replaced with a heteroatom selected from N, O and S, and optionally substituted with C₁-C₄alkyl, or when an N atom is present an N-protecting group;

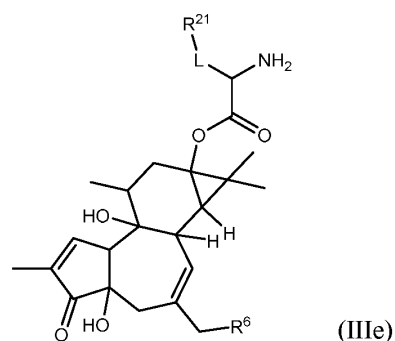
each R^j is independently C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylC₃-C₇cycloalkyl, C₀-C₆alkylheterocyclyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl, wherein the C₃-C₇cycloalkyl, heterocyclyl, alkylaryl, or heteroaryl is optionally substituted with 1 to 3 of J¹;

R^k is H or M⁺ counterion;

J¹ is selected from OH, CN, halo, C₁-C₄alkyl, and haloC₁-C₄alkyl; and

n is 0 or 1.

15. The compound of claim 14 having the structure of formula (IIIe):

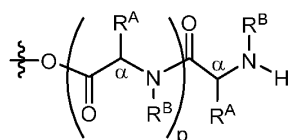


or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;

wherein

R^6 is OH, halo, or $-OC(O)R^c$, wherein R^c is $-C_1-C_6$ alkyl, $-C_1-C_6$ alkyl- $(NR^{c1})_2$ or $-C_1-C_6$ alkylC(O)OR^k, R^{c1} is H, C_1-C_6 alkyl, or two R^{c1} together with the N atom form a 5 to 7 membered heterocyclyl containing 1 to 3 heteroatoms selected from N, O, and S; or

R^6 is



wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with the adjacent R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each occurrence of R^B is same or different; and

p is 0, 1, or 2;

L is absent, C_1-C_{12} alkylene, or C_2-C_{12} alkenylene, wherein the C_1-C_{12} alkylene or C_2-C_{12} alkenylene is optionally substituted with C_1-C_4 alkyl;

R^{21} is H, $-S(O)_2R^j$, $-SR^j$, $-N(R^j)_2$, $-Si(R^j)_3$, C_3-C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiro C_5-C_{12} cycloalkyl, 5 to 12 membered bridged bicycyl, adamantyl, or $-C(O)OR^k$, wherein the C_3-C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiro C_5-C_{12} cycloalkyl, bridged bicycyl, or adamantyl is optionally substituted with 1 to 3 of J^1 , and wherein optionally 1 to 2 carbon atoms of the spiro C_5-C_{12} cycloalkyl or bridged bicycyl is replaced with a heteroatom selected from N, O and S, and optionally substituted with C_1-C_4 alkyl, or when an N atom is present an N-protecting group;

each R^j is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_0-C_6 alkyl C_3-C_7 cycloalkyl, C_0-C_6 alkylheterocyclyl, C_0-C_6 alkylaryl, or C_0-C_6 alkylheteroaryl, wherein the C_3-C_7 cycloalkyl,

heterocyclyl, alkylaryl, or heteroaryl is optionally substituted with 1 to 3 of J¹;

R^k is H or M⁺ counterion; and

J¹ is selected from OH, CN, halo, C₁-C₄alkyl, and haloC₁-C₄alkyl.

16. The compound of any one of claims 1 to 15, wherein R²¹ is C₃-C₇cycloalkyl, wherein the C₃-C₇cycloalkyl is optionally substituted with 1 to 3 of J¹.

17. The compound of claim 16, wherein the C₃-C₇cycloalkyl is selected from the group consisting of cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl, wherein the C₃-C₇cycloalkyl is optionally substituted with 1 to 3 of J¹.

18. The compound of any one of claims 1 to 15, wherein R²¹ is heterocyclyl, wherein the heterocyclyl is optionally substituted with 1 to 3 of J¹.

19. The compound of claim 18, wherein the heterocyclyl is selected from the group consisting of oxiranyl, oxetanyl, azetidynyl, oxazolyl, thiazolidinyl, thiazolyl, morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidinyl, piperazinyl, 2,3-dihydrofuranyl, dihydropyranyl, tetrahydrofuranyl, tetrahydropyranyl, dihydropyridinyl, tetrahydropyridinyl, tetrahydropyrimidinyl, tetrahydrothiophenyl, tetrahydrothiopyranyl, and azapanyl, wherein the heterocyclyl is optionally substituted with 1 to 3 of J¹.

20. The compound of any one of claims 1 to 15, wherein R²¹ is aryl, wherein the aryl is optionally substituted with 1 to 3 of J¹.

21. The compound of claim 20, wherein R²¹ is a phenyl or naphthyl, wherein the phenyl or naphthyl is optionally substituted with 1 to 3 of J¹.

22. The compound of any one of claims 1 to 15, wherein R²¹ is heteroaryl, wherein the heteroaryl is optionally substituted with 1 to 3 of J¹.

23. The compound of claim 22, wherein the heteroaryl is selected from the group consisting of pyrrolyl, pyrazolyl, imidazolyl, pyrazinyl, oxazolyl, isoxazolyl, thiazolyl, furyl, thienyl, pyridyl, pyrimidyl, benzoxazolyl, benzothiazolyl, purinyl, benzimidazolyl, indolyl, isoquinolyl, quinoxalinyl, and quinolyl, wherein the heteroaryl is optionally substituted with 1 to 3 of J¹.

24. The compound of any one of claims 1 to 15 wherein R²¹ is adamantyl, wherein the adamantyl is optionally substituted with OH, halo, or C₁-C₄alkyl.

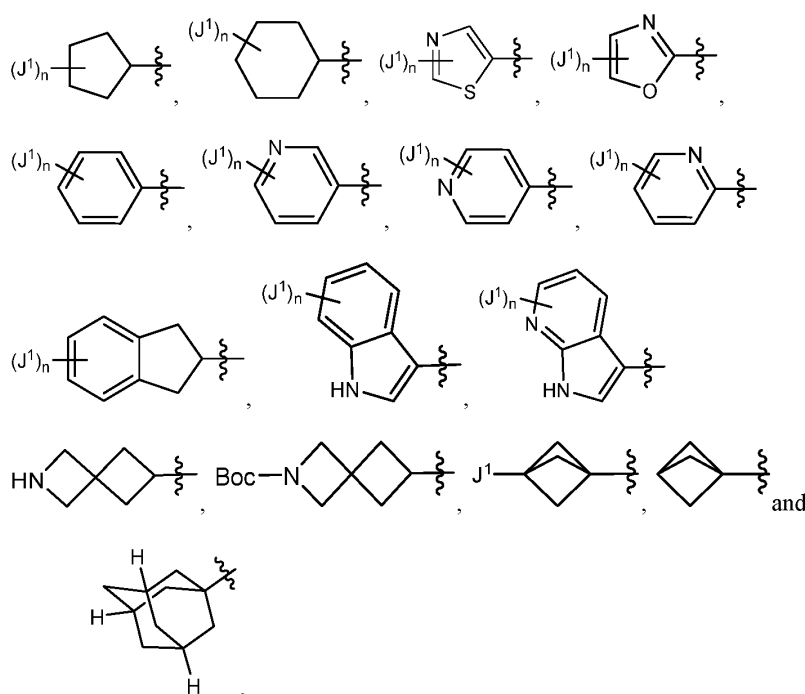
25. The compound of any one of claims 1 to 15, wherein

R²¹ is spiroC₅-C₁₂ cycloalkyl, wherein the spiroC₅-C₁₂ cycloalkyl has 0-2 carbon atoms replaced with 0-2 heteroatoms selected from N, O and S, and is optionally substituted with 1 to 3 of J¹, or when an N atom is present an N-protecting group.

26. The compound of any one of claims 1 to 15, wherein

R²¹ is 5 to 12 membered bridged bicycyl, wherein the bridged bicycyl has 0-2 carbon atoms replaced with 0-2 heteroatoms selected from N, O or S, and is optionally substituted with 1 to 3 of J¹, or when an N atom is present an N-protecting group.

27. The compound of any one of claims 1 to 15, wherein R²¹ is selected from:



wherein J¹ is OH, CN, halo, C₁-C₄alkyl, and haloC₁-C₄alkyl, and n is 0-3.

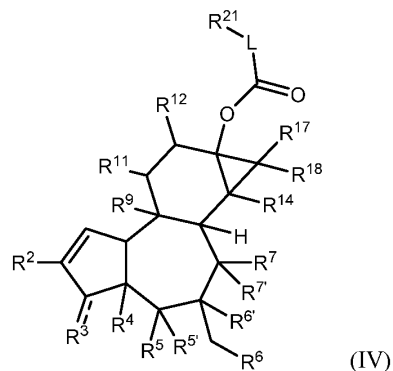
28. The compound of any one of claims 1 to 27, wherein L is C₁-C₆alkylene, C₃-C₆alkylene, or C₃-C₁₂alkylene.

29. The compound of any one of claims 1 to 27, wherein L is C₁-C₆alkenylene, C₃-C₆alkenylene, or C₃-C₁₂alkenylene.

30. The compound of any one of claims 1-29, wherein n is 0.

30. The compound of claim 1 selected from the group consisting of the compounds of **Table 1**, or an amino acid prodrug thereof.

31. A compound of formula (IV):



or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;

wherein

R^2 is a C_1 - C_4 alkyl;

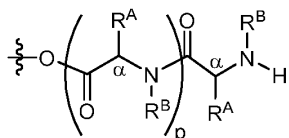
R^3 is O double bonded to the ring carbon when (---) is a bond, or $-OR^a$; wherein R^a is H or $-C(O)R^{a1}$, wherein R^{a1} is C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl;

R^4 and R^5 are each independently H or $-OR^b$, wherein R^b is H, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl;

R^{5*} and R^{6*} are H, or R^{5*} and R^{6*} form a bond or are bonded to a common O atom to form an epoxide ring as permitted by valency;

R^6 is OH, halo, or $-OC(O)R^c$, wherein R^c is $-C_1$ - C_6 alkyl, $-C_1$ - C_6 alkyl- $(NR^{c1})_2$ or $-C_1$ - C_6 alkylC(O)OR^k, R^{c1} is H, C_1 - C_6 alkyl, or two R^{c1} together with the N atom form a 5 to 7 membered heterocyclyl containing 1 to 3 heteroatoms selected from N, O, and S; or

R^6 is



wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein

each occurrence of R^B is same or different; and

p is 0, 1, or 2;

$R^{6'}$ and $R^{7'}$ are H, or $R^{6'}$ and $R^{7'}$ form a bond or are bonded to a common O atom to form an epoxide ring, as permitted by valency;

R^7 is H or OH;

R^9 is OR^e , wherein R^e is H, C_1 - C_6 alkyl, or aryl;

R^{11} is C_1 - C_4 alkyl;

R^{12} is H, -OH, $-OC(O)R^f$, wherein R^f is C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, $-C_0$ - C_{12} aliphatic- C_3 - C_7 cycloalkyl, $-C_0$ - C_{12} aliphatic-heterocycloalkyl, $-C_0$ - C_{12} aliphatic-aryl, or $-C_0$ - C_{12} aliphatic-heteroaryl;

R^{14} is H or OR^g , wherein R^g is H or C_1 - C_6 alkyl;

R^{17} and R^{18} are each independently C_1 - C_4 alkyl or C_1 - C_4 alkyl- OR^h , wherein R^h is H or C_1 - C_6 alkyl;

L is C_0 - C_6 alkylarylene, C_0 - C_6 alkylheteroarylene, C_0 - C_6 alkyl- C_3 - C_7 cycloalkylene, C_1 - C_{12} alkylene or C_2 - C_{12} alkenylene, wherein the C_1 - C_{12} alkylene or C_2 - C_{12} alkenylene is optionally substituted with OH or C_1 - C_4 alkyl; and

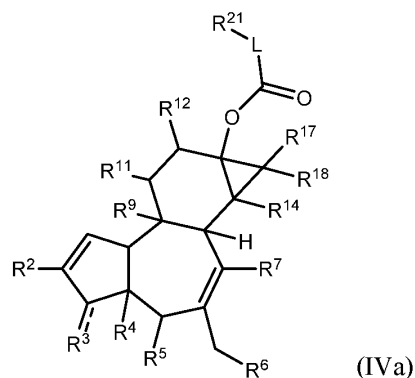
R^{21} is H, -OH, -SH, $-S(O)_2R^j$, $-SR^j$, $-N(R^j)_2$, $-Si(R^j)_3$, C_3 - C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiro- C_5 - C_{12} cycloalkyl, 5 to 12 membered bridged bicyclyl, adamantyl, or $-C(O)OR^k$, wherein the C_3 - C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiro- C_5 - C_{12} cycloalkyl, bridged bicyclyl, or adamantyl is optionally substituted with 1 to 3 of J^1 ; and wherein optionally 1 to 2 carbon atoms of the spiro- C_5 - C_{12} cycloalkyl or bridged bicyclyl is replaced with a heteroatom selected from N, O and S, and optionally substituted with C_1 - C_4 alkyl or, when an N atom is present an N-protecting group;

each R^j is independently C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkyl- C_3 - C_7 cycloalkyl, C_0 - C_6 alkylheterocyclyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl, wherein the C_3 - C_7 cycloalkyl, heterocyclyl, alkylaryl, or heteroaryl is optionally substituted with 1 to 3 of J^1 ;

J^1 is selected from OH, CN, halo, C_1 - C_4 alkyl, and halo- C_1 - C_4 alkyl; and

R^k is H or M^+ counterion.

32. The compound of claim 31, having the structure of formula (IVa):



or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;

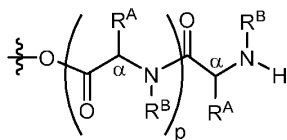
wherein

R² is a C₁-C₄alkyl;

R³ is O double bonded to the ring carbon when (---) is a bond, or -OR^a, wherein R^a is H or -C(O)R^{a1}, wherein R^{a1} is C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl;

R⁴ and R⁵ are each independently H or -OR^b, wherein R^b is H, C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl;

R⁶ is OH, halo, or -OC(O)R^c, wherein R^c is -C₁-C₆alkyl, -C₁-C₆alkyl-(NR^{c1})₂ or -C₁-C₆alkylC(O)OR^k, R^{c1} is H, C₁-C₆alkyl, or two R^{c1} together with the N atom form a 5 to 7 membered heterocycl containing 1 to 3 heteroatoms selected from N, O, and S; or

 $\mathbb{R}^6$ is

wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each occurrence of R^B is same or different; and

p is 0, 1, or 2;

R⁷ is H or OH;

R⁹ is OR^e, wherein R^e is H, C₁-C₆alkyl, or aryl;

R¹¹ is C₁-C₄alkyl;

R¹² is H, -OH, -OC(O)R^f, wherein R^f is C₁-C₁₂alkyl, C₂-C₁₂alkenyl, -C₀-C₁₂aliphatic-C₃-

C₇cycloalkyl, -C₀-C₁₂aliphatic-heterocycloalkyl, -C₀-C₁₂aliphatic-aryl, or -C₀-C₁₂aliphatic-heteroaryl;

R¹⁴ is H or OR^g; wherein R^g is H or C₁-C₆alkyl;

R¹⁷ and R¹⁸ are each independently C₁-C₄alkyl or C₁-C₄alkyl-OR^h, wherein R^h is H or C₁-C₆alkyl;

L is C₀-C₆alkylarylene, C₀-C₆alkylheteroarylene, C₀-C₆alkylC₃-C₇cycloalkylene, C₁-C₁₂alkylene or C₂-C₁₂alkenylene, wherein the C₁-C₁₂alkylene or C₂-C₁₂alkenylene is optionally substituted with OH or C₁-C₄alkyl; and

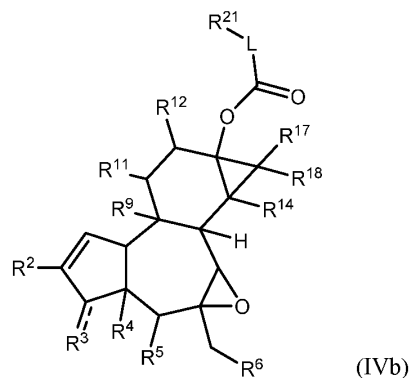
R²¹ is H, -OH, -SH, -S(O)₂R^j, -SR^j, -N(R^j)₂, -Si(R^j)₃, C₃-C₇cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂cycloalkyl, 5 to 12 membered bridged bicycyl, adamantyl, or -C(O)OR^k, wherein the C₃-C₇cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂cycloalkyl, bridged bicycyl, or adamantyl is optionally substituted with 1 to 3 of J¹; and wherein optionally 1 to 2 carbon atoms of the spiroC₅-C₁₂cycloalkyl or bridged bicycyl is replaced with a heteroatom selected from N, O and S, and optionally substituted with C₁-C₄alkyl or, when an N atom is present an N-protecting group;

each R^j is independently C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylC₃-C₇cycloalkyl, C₀-C₆alkylheterocyclyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl, wherein the C₃-C₇cycloalkyl, heterocyclyl, alkylaryl, or heteroaryl is optionally substituted with 1 to 3 of J¹;

J¹ is selected from OH, CN, halo, C₁-C₄alkyl, and haloC₁-C₄alkyl; and

R^k is H or M⁺ counterion.

33. The compound of claim 31, having the structure of formula (IVb)



or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;

wherein

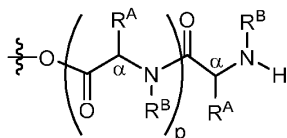
R² is a C₁-C₄alkyl;

R³ is O double bonded to the ring carbon when (- -) is a bond, or -OR^a, wherein R^a is H or -C(O)R^{a1}, wherein R^{a1} is C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl;

R⁴ and R⁵ are each independently H or -OR^b, wherein R^b is H, C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl;

R^6 is OH, halo, or $-OC(O)R^c$, wherein R^c is $-C_1-C_6$ alkyl, $-C_1-C_6$ alkyl- $(NR^{c1})_2$ or $-C_1-C_6$ alkylC(O)OR^k, R^{c1} is H, C_1-C_6 alkyl, or two R^{c1} together with the N atom form a 5 to 7 membered heterocyclyl containing 1 to 3 heteroatoms selected from N, O, and S; or

R^6 is



wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each occurrence of R^B is same or different; and

p is 0, 1, or 2;

R^7 is H or OH;

R^9 is OR^e, wherein R^e is H, C_1-C_6 alkyl, or aryl;

R^{11} is C_1-C_4 alkyl;

R^{12} is H, -OH, $-OC(O)R^f$, wherein R^f is C_1-C_{12} alkyl, C_2-C_{12} alkenyl, $-C_0-C_{12}$ aliphatic- C_3-C_7 cycloalkyl, $-C_0-C_{12}$ aliphatic-heterocycloalkyl, $-C_0-C_{12}$ aliphatic-aryl, or $-C_0-C_{12}$ aliphatic-heteroaryl;

R^{14} is H or OR^g, wherein R^g is H or C_1-C_6 alkyl;

R^{17} and R^{18} are each independently C_1-C_4 alkyl or C_1-C_4 alkyl-OR^h, wherein R^h is H or C_1-C_6 alkyl;

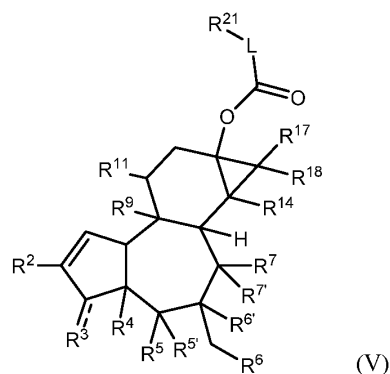
L is C_0-C_6 alkylarylene, C_0-C_6 alkylheteroarylene, C_0-C_6 alkyl C_3-C_7 cycloalkylene, C_1-C_{12} alkylene or C_2-C_{12} alkenylene, wherein the C_1-C_{12} alkylene or C_2-C_{12} alkenylene is optionally substituted with OH or C_1-C_4 alkyl; and

R^{21} is H, -OH, -SH, $-S(O)_2R^j$, $-SR^j$, $-N(R^j)_2$, $-Si(R^j)_3$, C_3-C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiro C_5-C_{12} cycloalkyl, 5 to 12 membered bridged bicyclyl, adamantyl, or $-C(O)OR^k$, wherein the C_3-C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiro C_5-C_{12} cycloalkyl, bridged bicyclyl, or adamantyl is optionally substituted with 1 to 3 of J^1 ; and wherein optionally 1 to 2 carbon atoms of the spiro C_5-C_{12} cycloalkyl or bridged bicyclyl is replaced with a heteroatom selected from N, O and S, and optionally substituted with C_1-C_4 alkyl or, when an N atom is present an N-protecting group;

each R^j is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_0-C_6 alkyl C_3-C_7 cycloalkyl, C_0-C_6 alkylheterocyclyl, C_0-C_6 alkylarylene, or C_0-C_6 alkylheteroaryl, wherein the C_3-C_7 cycloalkyl, heterocyclyl, alkylarylene, or heteroaryl is optionally substituted with 1 to 3 of J^1 ;

J¹ is selected from OH, CN, halo, C₁-C₄alkyl, and haloC₁-C₄alkyl; and
R^k is H or M⁺ counterion.

34. The compound of claim 31, having the structure of formula (V):



or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;

wherein

R² is a C₁-C₄alkyl;

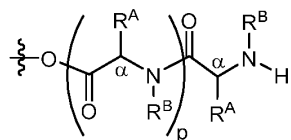
R³ is O double bonded to the ring carbon when (- -) is a bond, or -OR^a; wherein R^a is H or -C(O)R^{a1}, wherein R^{a1} is C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl;

R⁴ and R⁵ are each independently H or -OR^b, wherein R^b is H, C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl;

R^{5'} and R^{6'} are H, or R^{5'} and R^{6'} form a bond or are bonded to a common O atom to form an epoxide ring as permitted by valency;

R⁶ is OH, halo, or -OC(O)R^c, wherein R^c is -C₁-C₆alkyl, -C₁-C₆alkyl-(NR^{c1})₂ or -C₁-C₆alkylC(O)OR^k, R^{c1} is H, C₁-C₆alkyl, or two R^{c1} together with the N atom form a 5 to 7 membered heterocyclyl containing 1 to 3 heteroatoms selected from N, O, and S; or

R⁶ is



wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each

occurrence of R^B is same or different; and

p is 0, 1, or 2;

$R^{6'}$ and $R^{7'}$ are H, or $R^{6'}$ and $R^{7'}$ form a bond or are bonded to a common O atom to form an epoxide ring, as permitted by valency;

R^7 is H or OH;

R^9 is OR^e , wherein R^e is H, C_1 - C_6 alkyl, or aryl;

R^{11} is C_1 - C_4 alkyl;

R^{14} is H or OR^g , wherein R^g is H or C_1 - C_6 alkyl;

R^{17} and R^{18} are each independently C_1 - C_4 alkyl or C_1 - C_4 alkyl- OR^h , wherein R^h is H or C_1 - C_6 alkyl;

L is C_0 - C_6 alkylarylene, C_0 - C_6 alkylheteroarylene, C_0 - C_6 alkyl C_3 - C_7 cycloalkylene, C_1 - C_{12} alkylene or C_2 - C_{12} alkenylene, wherein the C_1 - C_{12} alkylene or C_2 - C_{12} alkenylene is optionally substituted with OH or C_1 - C_4 alkyl; and

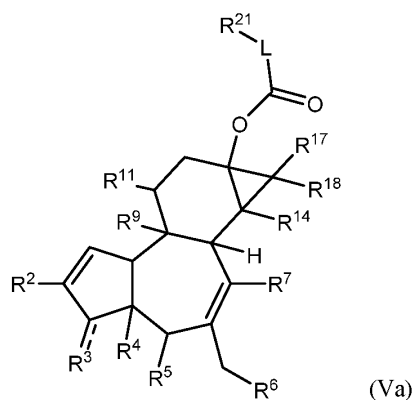
R^{21} is H, -OH, -SH, $-S(O)_2R^j$, $-SR^j$, $-N(R^j)_2$, $-Si(R^j)_3$, C_3 - C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiro C_5 - C_{12} cycloalkyl, 5 to 12 membered bridged bicycyl, adamantyl, or $-C(O)OR^k$, wherein the C_3 - C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiro C_5 - C_{12} cycloalkyl, bridged bicycyl, or adamantyl is optionally substituted with 1 to 3 of J^1 ; and wherein optionally 1 to 2 carbon atoms of the spiro C_5 - C_{12} cycloalkyl or bridged bicycyl is replaced with a heteroatom selected from N, O and S, and optionally substituted with C_1 - C_4 alkyl or, when an N atom is present an N-protecting group;

each R^j is independently C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkyl C_3 - C_7 cycloalkyl, C_0 - C_6 alkylheterocyclyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl, wherein the C_3 - C_7 cycloalkyl, heterocyclyl, alkylaryl, or heteroaryl is optionally substituted with 1 to 3 of J^1 ;

J^1 is selected from OH, CN, halo, C_1 - C_4 alkyl, and halo C_1 - C_4 alkyl; and

R^k is H or M^+ counterion.

35. The compound of claim 31, having the structure of formula (Va):



or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;

wherein

or an enantiomer or pharmaceutically acceptable salt thereof;

wherein

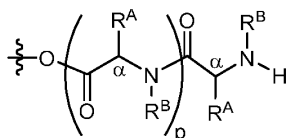
R^2 is a C_1 - C_4 alkyl;

R^3 is O double bonded to the ring carbon when (- -) is a bond, or $-OR^a$; wherein R^a is H or $-C(O)R^{a1}$, wherein R^{a1} is C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl;

R^4 and R^5 are each independently H or $-OR^b$, wherein R^b is H, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl;

R^6 is OH, halo, or $-OC(O)R^c$, wherein R^c is $-C_1$ - C_6 alkyl, $-C_1$ - C_6 alkyl- $(NR^{c1})_2$ or $-C_1$ - C_6 alkylC(O)OR^k, R^{c1} is H, C_1 - C_6 alkyl, or two R^{c1} together with the N atom form a 5 to 7 membered heterocyclyl containing 1 to 3 heteroatoms selected from N, O, and S; or

R^6 is



wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each occurrence of R^B is same or different; and

p is 0, 1, or 2;

R^7 is H or OH;

R^9 is OR^e , wherein R^e is H, C_1 - C_6 alkyl, or aryl;

R^{11} is C_1 - C_4 alkyl;

R^{14} is H or OR^g ; wherein R^g is H or C_1 - C_6 alkyl;

R^{17} and R^{18} are each independently C_1 - C_4 alkyl or C_1 - C_4 alkyl- OR^h , wherein R^h is H or C_1 - C_6 alkyl;

L is C_0 - C_6 alkylarylene, C_0 - C_6 alkylheteroarylene, C_0 - C_6 alkylC₃-C₇cycloalkylene, C_1 - C_{12} alkylene or C_2 - C_{12} alkenylene, wherein the C_1 - C_{12} alkylene or C_2 - C_{12} alkenylene is optionally substituted with OH or C_1 - C_4 alkyl; and

R^{21} is H, -OH, -SH, $-S(O)_2R^j$, $-SR^j$, $-N(R^j)_2$, $-Si(R^j)_3$, C_3 - C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂ cycloalkyl, 5 to 12 membered bridged bicycyl, adamantyl, or $-C(O)OR^k$, wherein the C_3 - C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂ cycloalkyl, bridged bicycyl,

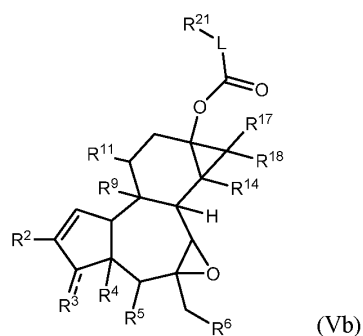
or adamantyl is optionally substituted with 1 to 3 of J^1 ; and wherein optionally 1 to 2 carbon atoms of the spiro C_5 - C_{12} cycloalkyl or bridged bicycyl is replaced with a heteroatom selected from N, O and S, and optionally substituted with C_1 - C_4 alkyl or, when an N atom is present an N-protecting group;

each R^1 is independently C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkyl C_3 - C_7 cycloalkyl, C_0 - C_6 alkylheterocyclyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl, wherein the C_3 - C_7 cycloalkyl, heterocyclyl, alkylaryl, or heteroaryl is optionally substituted with 1 to 3 of J^1 ;

J^1 is selected from OH, CN, halo, C_1 - C_4 alkyl, and halo C_1 - C_4 alkyl; and

R^k is H or M^+ counterion.

36. The compound of claim 31, having the structure of formula (Vb):



or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;

wherein

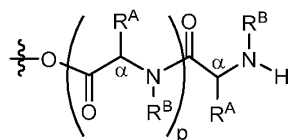
R^2 is a C_1 - C_4 alkyl;

R^3 is O double bonded to the ring carbon when (---) is a bond, or $-OR^a$; wherein R^a is H or $-C(O)R^{a1}$, wherein R^{a1} is C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl;

R^4 and R^5 are each independently H or $-OR^b$, wherein R^b is H, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl;

R^6 is OH, halo, or $-OC(O)R^c$, wherein R^c is $-C_1$ - C_6 alkyl, $-C_1$ - C_6 alkyl- $(NR^{c1})_2$ or $-C_1$ - C_6 alkyl $C(O)OR^k$, R^{c1} is H, C_1 - C_6 alkyl, or two R^{c1} together with the N atom form a 5 to 7 membered heterocyclyl containing 1 to 3 heteroatoms selected from N, O, and S; or

R^6 is



wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each occurrence of R^B is same or different; and

p is 0, 1, or 2;

R^9 is OR^e , wherein R^e is H, C_1 - C_6 alkyl, or aryl;

R^{11} is C_1 - C_4 alkyl;

R^{14} is H or OR^g , wherein R^g is H or C_1 - C_6 alkyl;

R^{17} and R^{18} are each independently C_1 - C_4 alkyl or C_1 - C_4 alkyl- OR^h , wherein R^h is H or C_1 - C_6 alkyl;

L is C_0 - C_6 alkylaryl, C_0 - C_6 alkylheteroaryl, C_0 - C_6 alkyl C_3 - C_7 cycloalkyl, C_1 - C_{12} alkylene or C_2 - C_{12} alkenylene, wherein the C_1 - C_{12} alkylene or C_2 - C_{12} alkenylene is optionally substituted with OH or C_1 - C_4 alkyl; and

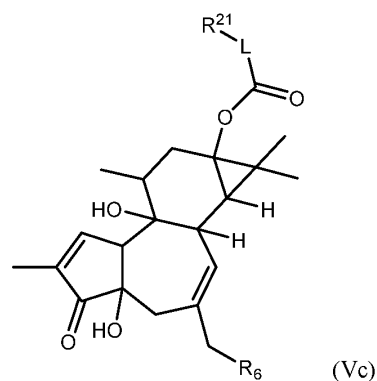
R^{21} is H, -OH, -SH, $-S(O)_2R^j$, $-SR^j$, $-N(R^j)_2$, $-Si(R^j)_3$, C_3 - C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiro C_5 - C_{12} cycloalkyl, 5 to 12 membered bridged bicyclyl, adamantyl, or $-C(O)OR^k$, wherein the C_3 - C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiro C_5 - C_{12} cycloalkyl, bridged bicyclyl, or adamantyl is optionally substituted with 1 to 3 of J^1 ; and wherein optionally 1 to 2 carbon atoms of the spiro C_5 - C_{12} cycloalkyl or bridged bicyclyl is replaced with a heteroatom selected from N, O and S, and optionally substituted with C_1 - C_4 alkyl or, when an N atom is present an N-protecting group;

each R^j is independently C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_0 - C_6 alkyl C_3 - C_7 cycloalkyl, C_0 - C_6 alkylheterocyclyl, C_0 - C_6 alkylaryl, or C_0 - C_6 alkylheteroaryl, wherein the C_3 - C_7 cycloalkyl, heterocyclyl, alkylaryl, or heteroaryl is optionally substituted with 1 to 3 of J^1 ;

J^1 is selected from OH, CN, halo, C_1 - C_4 alkyl, and halo C_1 - C_4 alkyl; and

R^k is H or M^+ counterion.

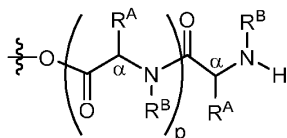
37. The compound of claim 31, having the structure formula (Vc):



or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;
wherein

R^6 is OH, halo, or $-OC(O)R^c$, wherein R^c is $-C_1-C_6$ alkyl, $-C_1-C_6$ alkyl- $(NR^{c1})_2$ or $-C_1-C_6$ alkylC(O)OR^k, R^{c1} is H, C_1-C_6 alkyl, or two R^{c1} together with the N atom form a 5 to 7 membered heterocyclyl containing 1 to 3 heteroatoms selected from N, O, and S; or

R^6 is



wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each occurrence of R^B is same or different; and

p is 0, 1, or 2;

L is C_0-C_6 alkylarylene, C_0-C_6 alkylheteroarylene, C_0-C_6 alkylC₃-C₇cycloalkylene, C_1-C_{12} alkylene or C_2-C_{12} alkenylene, wherein the C_1-C_{12} alkylene or C_2-C_{12} alkenylene is optionally substituted with OH or C_1-C_4 alkyl; and

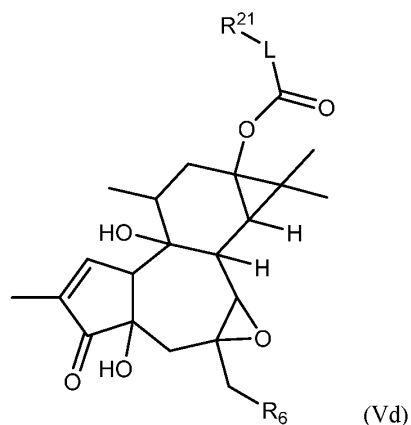
R^{21} is H, -OH, -SH, $-S(O)_2R^j$, $-SR^j$, $-N(R^j)_2$, $-Si(R^j)_3$, C_3-C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂cycloalkyl, 5 to 12 membered bridged bicycyl, adamantyl, or $-C(O)OR^k$, wherein the C_3-C_7 cycloalkyl, heterocyclyl, aryl, heteroaryl, spiroC₅-C₁₂cycloalkyl, bridged bicycyl, or adamantyl is optionally substituted with 1 to 3 of J^1 ; and wherein optionally 1 to 2 carbon atoms of the spiroC₅-C₁₂cycloalkyl or bridged bicycyl is replaced with a heteroatom selected from N, O and S, and optionally substituted with C_1-C_4 alkyl or, when an N atom is present an N-protecting group;

each R^j is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_0-C_6 alkylC₃-C₇cycloalkyl, C_0-C_6 alkylheterocyclyl, C_0-C_6 alkylaryl, or C_0-C_6 alkylheteroaryl, wherein the C_3-C_7 cycloalkyl, heterocyclyl, alkylaryl, or heteroaryl is optionally substituted with 1 to 3 of J^1 ;

J^1 is selected from OH, CN, halo, C_1-C_4 alkyl, and haloC₁-C₄alkyl; and

R^k is H or M^+ counterion.

38. The compound of claim 31, having the structure of formula (Vd):

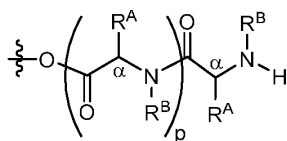


or a pharmaceutically acceptable salt, tautomer, or stereoisomer thereof;

wherein

R^6 is OH, halo, or $-OC(O)R^c$, wherein R^c is $-C_1-C_6$ alkyl, $-C_1-C_6$ alkyl- $(NR^{c1})_2$ or $-C_1-C_6$ alkylC(O)OR^k, R^{c1} is H, C_1-C_6 alkyl, or two R^{c1} together with the N atom form a 5 to 7 membered heterocycl containing 1 to 3 heteroatoms selected from N, O, and S; or

R^6 is



wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each occurrence of R^B is same or different; and

p is 0, 1, or 2;

L is C_0-C_6 alkylarylene, C_0-C_6 alkylheteroarylene, C_0-C_6 alkylC₃-C₇cycloalkylene, C_1-C_{12} alkylene or C_2-C_{12} alkenylene, wherein the C_1-C_{12} alkylene or C_2-C_{12} alkenylene is optionally substituted with OH or C_1-C_4 alkyl; and

R^{21} is H, -OH, -SH, $-S(O)_2R^j$, $-SR^j$, $-N(R^j)_2$, $-Si(R^j)_3$, C_3-C_7 cycloalkyl, heterocycl, aryl, heteroaryl, spiroC₅-C₁₂cycloalkyl, 5 to 12 membered bridged bicycl, adamantyl, or $-C(O)OR^k$, wherein the C_3-C_7 cycloalkyl, heterocycl, aryl, heteroaryl, spiroC₅-C₁₂cycloalkyl, bridged bicycl, or adamantyl is optionally substituted with 1 to 3 of J^1 ; and wherein optionally 1 to 2 carbon atoms of the spiroC₅-C₁₂cycloalkyl or bridged bicycl is replaced with a heteroatom selected from N, O and S,

and optionally substituted with C₁-C₄alkyl or, when an N atom is present an N-protecting group;

each R^l is independently C₁-C₆alkyl, C₂-C₆alkenyl, C₀-C₆alkylC₃-C₇cycloalkyl, C₀-C₆alkylheterocyclyl, C₀-C₆alkylaryl, or C₀-C₆alkylheteroaryl, wherein the C₃-C₇cycloalkyl, heterocyclyl, alkylaryl, or heteroaryl is optionally substituted with 1 to 3 of J¹;

J¹ is selected from OH, CN, halo, C₁-C₄alkyl, and haloC₁-C₄alkyl; and

R^k is H or M⁺ counterion.

39. The compound of any one of claims 31 to 38, wherein

R²¹ is C₃-C₇cycloalkyl, wherein the C₃-C₇cycloalkyl is optionally substituted with 1 to 3 of J¹.

40. The compound of claim 39, wherein the C₃-C₇cycloalkyl is selected from the group consisting of cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl, wherein the C₃-C₇cycloalkyl is optionally substituted with 1 to 3 of J¹.

41. The compound of any one of claims 31 to 38, wherein

R²¹ is heterocyclyl, wherein the heterocyclyl is optionally substituted with 1 to 3 of J¹.

42. The compound of claim 41, wherein the heterocyclyl is selected from the group consisting of oxiranyl, oxetanyl, azetidynyl, oxazolyl, thiazolidinyl, thiazolyl, morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidynyl, piperazinyl, 2,3-dihydrofuranyl, dihydropyranyl, tetrahydrofuranyl, tetrahydropyranyl, dihydropyridinyl, tetrahydropyridinyl, tetrahydropyrimidinyl, tetrahydrothiophenyl, tetrahydrothiopyranyl, and azapanyl, wherein the heterocyclyl is optionally substituted with 1 to 3 of J¹.

43. The compound of any one of claims 31 to 38, wherein

R²¹ is aryl, wherein the aryl is optionally substituted with 1 to 3 of J¹.

44. The compound of claim 43, wherein

R²¹ is a phenyl or naphthyl, wherein the phenyl or naphthyl is optionally substituted with 1 to 3 of J¹.

45. The compound of any one of claims 31 to 38, wherein

R²¹ is heteroaryl, wherein the heteroaryl is optionally substituted with 1 to 3 of J¹.

46. The compound of claim 45, wherein the heteroaryl is selected from the group consisting of pyrrolyl, pyrazolyl, imidazolyl, pyrazinyl, oxazolyl, isoxazolyl, thiazolyl, furyl, thienyl, pyridyl, pyrimidyl, benzoxazolyl, benzothiazolyl, purinyl, benzimidazolyl, indolyl, isoquinolyl, quinoxaliny, and quinolyl, wherein the heteroaryl is optionally substituted with 1 to 3 of J¹.

47. The compound of any one of claims 31 to 38, wherein

R^{21} is adamantyl, wherein the adamantyl is optionally substituted with 1 to 3 of J^1 .

48. The compound of any one of claims 31 to 38, wherein

R^{21} is spiro C_5 - C_{12} cycloalkyl, wherein the spiro C_5 - C_{12} cycloalkyl has 0-2 carbon atoms replaced with 0-2 heteroatoms selected from N, O and S, and is optionally substituted with 1 to 3 of J^1 , or when an N atom is present an N-protecting group.

49. The compound of any one of claims 31 to 38, wherein

R^{21} is 5 to 12 membered bridged bicycyl, wherein the bridged bicycyl has 0-2 carbon atoms replaced with 0-2 heteroatoms selected from N, O or S, and is optionally substituted with 1 to 3 of J^1 , or when an N atom is present an N-protecting group.

50. The compound of any one of claims 31 to 49, wherein L is C_1 - C_6 alkylene, C_3 -

C_6 alkylene, or C_3 - C_{12} alkylene.

51. The compound of any one of claims 31 to 49, wherein L is C_1 - C_6 alkenylene, C_3 -

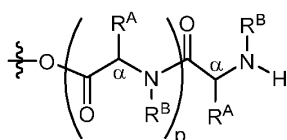
C_6 alkenylene, or C_3 - C_{12} alkenylene.

52. The compound of claim 31 selected from the group consisting of the compounds of

Table 2 or an amino acid prodrug thereof.

53. The compound of any one of claims 1 to 52, wherein:

R^6 is



wherein,

each occurrence of R^A is independently selected from a side chain of a natural or non-natural amino acid, wherein each occurrence of R^A is same or different;

each occurrence of R^B is independently H, or R^B together with R^A and the N atom to which it is attached form a heterocyclic ring of a natural or non-natural amino acid, wherein each occurrence of R^B is same or different; and

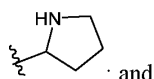
p is 0, 1, or 2.

54. The compound of claim 53, wherein

each R^A is independently hydrogen (glycine), methyl (alanine), propan-2-yl (valine), propan-1-yl (norvaline), 2-methylpropan-1-yl (leucine), 1-methylpropan-1-yl (isoleucine), butan-1-yl

(norleucine), phenyl (2-phenylglycine), benzyl (phenylalanine), p-hydroxybenzyl (tyrosine), indol-3-ylmethyl (tryptophan), imidazol-4-ylmethyl (histidine), hydroxymethyl (serine), 2-hydroxyethyl (homoserine), 1-hydroxyethyl (threonine), mercaptomethyl (cysteine), methylthiomethyl (S-methylcysteine), 2-mercaptoethyl (homocysteine), 2-methylthioethyl (methionine), carbamoylmethyl (asparagine), 2-carbamoylethyl (glutamine), carboxymethyl (aspartic acid), 2-carboxyethyl (glutamic acid), 4-aminobutan-1-yl (lysine), 4-amino-3-hydroxybutan-1-yl (hydroxylysine), 3-aminopropan-1-yl (ornithine), 3-guanidinopropan-1-yl (arginine), or 3-ureido-propan-1-yl (citrulline);

each R^B is H, or R^B together with the adjacent R_A and the N atom form a prolyl side chain:



p is 0, 1 or 2.

55. The compound of claim 54, wherein:

each R^A is independently methyl (alanine), propan-2-yl (valine), 2-methylpropan-1-yl (leucine), imidazol-4-ylmethyl (histidine), hydroxymethyl (serine), 1-hydroxyethyl (threonine), carbamoylmethyl (asparagine), 2-carbamoylethyl (glutamine), 4-aminobutan-1-yl (lysine), carboxymethyl (aspartic acid), 3-guanidinopropan-1-yl (arginine), benzyl (phenylalanine), or 4-aminobutan-1-yl (lysine);

R^B is H; and

p 0, 1, or 2.

56. The compound of claim 54, wherein

each R^A is independently propan-2-yl (valine), 2-methylpropan-1-yl (leucine), carboxymethyl (aspartic acid), benzyl (phenylalanine), or 4-aminobutan-1-yl (lysine);

each R^B is H; and

p is 0, 1, or 2.

57. The compound of claim 54, wherein p is 0.

58. The compound of claim 54, wherein p is 1.

59. The compound of claim 54, wherein p is 1;

first of R^A is propan-2-yl (valine) and second of R^A is propan-2-yl (valine); and each of R^B is H (dipeptide Val-Val); or

first of R^A is 2-methylpropan-1-yl (leucine), and second of R^A is 2-methylpropan-1-yl (leucine); and each of R^B is H (dipeptide Leu-Leu); or

first of R^A is methyl (alanine) and second of R^A is methyl (alanine); and each of R^B is H (dipeptide Ala-Ala); or

first of R^A is 4-aminobutan-1-yl (lysine); second of R^A is 4-aminobutan-1-yl (lysine); and each of R^B is H (dipeptide Lys-Lys); or

first of R^A is hydrogen; second of R^A is 4-aminobutan-1-yl, and each of R^B is H (dipeptide Gly-Lys).

60. The compound of any one of claims 53 to 59, wherein each of the α -carbon of the amino acid other than glycine is in the L or D configuration.

61. A pharmaceutical composition comprising a compound of any one of claims 1 to 60, and a pharmaceutically acceptable carrier.

62. A method of activating protein kinase C, comprising contacting a mammalian cell with an effective amount of a compound of any one of claims 1 to 60.

63. The method of claim 62, wherein the cell is a cancer cell.

64. A method of treating cancer, comprising administering to a subject in need thereof an effective amount of a compound of any one of claims 1 to 60.

65. The method of claim 64, wherein the cancer is selected from the group consisting of adrenocortical cancer, anal cancer, biliary cancer, bladder cancer, bone cancer, brain cancer, breast cancer, cervical cancer, colon cancer, endometrial cancer, esophageal cancer, head and neck cancer, intestinal cancer, liver cancer, lung cancer, oral cancer, ovarian cancer, pancreatic cancer, renal cancer, prostate cancer, salivary gland cancer, skin cancer, stomach cancer, testicular cancer, throat cancer, thyroid cancer, uterine cancer, vaginal cancer, sarcoma, and soft tissue carcinomas.

66. The method of claim 64, wherein the cancer is a hematological cancer.

67. The method of claim 66, wherein the hematological cancer is a leukemia or lymphoma.

68. The method of claim 67, wherein the hematological cancer is selected from the group consisting of acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), lymphoma (e.g., Hodgkin's lymphoma, Non-Hodgkin's lymphoma, Burkitt's lymphoma), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), Hairy Cell chronic myelogenous leukemia (CML), and multiple myeloma.