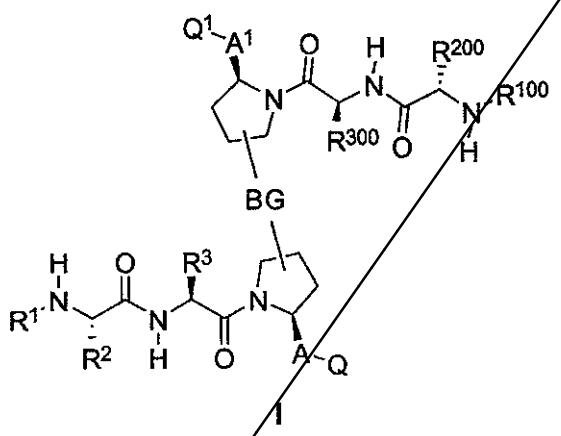
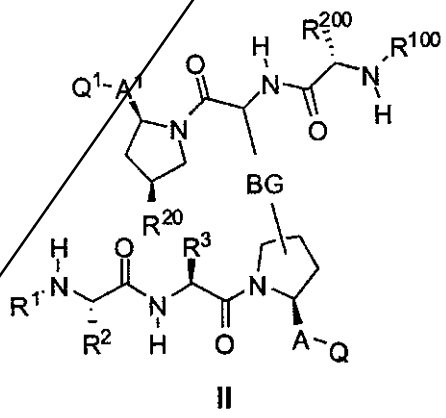
CLAIMS

We claim:

1. An isomer, enantiomer, diastereoisomer or tautomer of a compound represented by Formula I or II



I



II

wherein

m is 0, 1 or 2;

Y is NH, O or S;

BG is

1) –X-L-X^1–;

X and X^1 are independently selected from

1) O,

2) NR^{13},

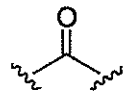
3) S,

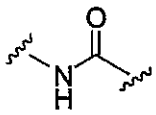
4) -C_1-C_6 alkyl-,

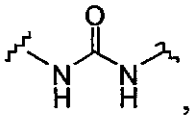
5) -C_1-C_6 alkyl-O,

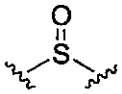
6) -C_1-C_6 alkyl-NR^{13}-,

7) -C_1-C_6 alkyl-S-,

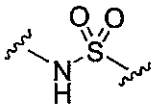
8)  ,

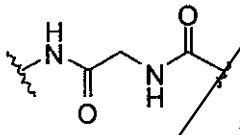
9)  ,

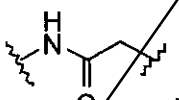
10)  ,

11)  ,

12)  ,

13)  ,

14)  , or

15)  ;

L is selected from:

1) –C_1-C_{20} alkyl–,

2) –C_2-C_6 alkenyl–,

3) –C_2–C_4 alkynyl–,

4) –C_3-C_7 cycloalkyl–,

5) –aryl–,

6) –biphenyl–,

7) – heteroaryl–,

8) – heterocyclyl–,

9) –C_1-C_6 alkyl–(C_2-C_6 alkenyl)– C_1-C_6 alkyl–,

10) –C_1-C_6 alkyl–(C_2–C_4 alkynyl)–C_1-C_6 alkyl–

11) –C_1-C_6 alkyl–(C_3-C_7 cycloalkyl)–C_1-C_6 alkyl–,

12) –C_1-C_6 alkyl– aryl–C_1-C_6 alkyl–,

13) –C_1-C_6 alkyl–biphenyl–C_1-C_6 alkyl–,

14) –C_1-C_6 alkyl–heteroaryl–C_1-C_6 alkyl–,

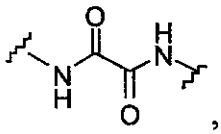
15) –C_1-C_6 alkyl-heterocycyl–C_1-C_6 alkyl–,

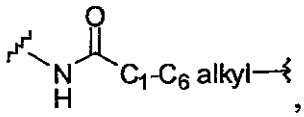
16) –C_1-C_6 alkyl-Y-C_1-C_6 alkyl–,

17) –aryl-Y-aryl–,

18) –heteroaryl-Y-heteroaryl–,

19) –heterocyclyl-Y-heterocyclyl–,

20)  , or

21)  ,

wherein the alkyl, alkenyl, alkynyl and cycloalkyl are optionally substituted with one or more R^6 substituents, and the aryl, biphenyl, heteroaryl, and heterocyclyl are optionally substituted with one or more R^{10} substituents;

Q and Q^1 are independently selected from

1) NR^4R^5,

2) OR^{11}, or

3) $S(O)_mR^{11}$; or

Q and Q^1 are independently selected from

1) aryl, or

2) heteroaryl, the aryl and the heteroaryl being optionally substituted with one or more R^{10} substituents;

A and A^1 are independently selected from

1) –CH_2–,

2) $-CH_2CH_2-$,

3) $-CH(C_1-C_6$ alkyl)–,

4) $-CH(C_3-C_7$ cycloalkyl)–,

5) $-C_3-C_7$ cycloalkyl–,

6) $-CH(C_1-C_6$ alkyl–C_3-C_7 cycloalkyl)–,

7) –C(O) –, or

8) $-C(O)OR^{13}$;

R^1 and R^{100} are independently selected from

1) H, or

2) C_1-C_6 alkyl optionally substituted with one or more R^6 substituents;

R^2 and R^{200} are independently selected from

1) H, or

2) C_1-C_6 alkyl optionally substituted with one or more R^6 substituents;

R^3 and R^{300} are independently C_1-C_6 alkyl optionally substituted with one or more R^6 substituents;

R^4 and R^5 are each independently selected from

1) H,

2) haloalkyl,

3) ←C_1-C_6 alkyl,

4) ←C_2-C_6 alkenyl,

5) ←C_2-C_4 alkynyl,

6) ←C_3-C_7 cycloalkyl,

7) ←C_3-C_7 cycloalkenyl,

8) ←aryl,

9) ←heteroaryl,

10) ←heterocyclyl,

11) ←heterobicyclyl,

12) ←C(O)-R^{11},

13) ←C(O)O-R^{11},

14) ←$C(=Y)NR^8R^9$, or

15) ←$S(O)_2$-R^{11},

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl is optionally substituted with one or more R^6 substituents; and wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl is optionally substituted with one or more R^{10} substituents;

R^6 is

1) halogen,
2) NO_2,
3) CN,
4) haloalkyl,
5) C_1–C_6 alkyl,
6) C_2-C_6 alkenyl,
7) C_2-C_4 alkynyl,
8) C_3–C_7 cycloalkyl,
9) C_3-C_7 cycloalkenyl,
10) aryl,
11) heteroaryl,
12) heterocyclyl,
13) heterobicyclyl,
14) OR^7,
15) $S(O)_mR^7$,
16) NR^8R^9 ,
17) $NR^8S(O)_2R^{11}$,
18) COR^7,
19) $C(O)OR^7$,
20) $CONR^8R^9$,
21) $S(O)_2NR^8R^9$
22) $OC(O)R^7$,
23) $OC(O)Y\text{-}R^{11}$,
24) $SC(O)R^7$, or
25) $NC(Y)NR^8R^9$,

wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl is optionally substituted with one or more R^{10} substituents;

R^7 is

1) H,

2) haloalkyl,
3) C_1–C_6 alkyl,
4) C_2-C_6 alkenyl,
5) C_2-C_4 alkynyl,
6) C_3–C_7 cycloalkyl,
7) C_3-C_7 cycloalkenyl,
8) aryl,
9) heteroaryl,
10) heterocyclyl,
11) heterobicyclyl,
12) $R^8R^9NC(=Y)$, or
13) C_1-C_6 alkyl-C_2-C_4 alkenyl, or
14) C_1-C_6 alkyl-C_2-C_4 alkynyl,

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl is optionally substituted with one or more R^6 substituents; and wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl is optionally substituted with one or more R^{10} substituents;

R^8 and R^9 are each independently
1) H,
2) haloalkyl,
3) C_1–C_6 alkyl,
4) C_2-C_6 alkenyl,
5) C_2-C_4 alkynyl,
6) C_3–C_7 cycloalkyl,
7) C_3-C_7 cycloalkenyl,
8) aryl,
9) heteroaryl,
10) heterocyclyl,
11) heterobicyclyl,
12) $C(O)R^{11}$,
13) $C(O)Y$-R^{11}, or
14) $S(O)_2$-R^{11},

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl is optionally substituted with one or more R^6 substituents; and wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl is optionally substituted with one or more R^{10} substituents;

or R^8 and R^9 together with the nitrogen atom to which they are bonded form a five, six or seven membered heterocyclic ring optionally substituted with one or more R^6 substituents;

R^{10} is

1) halogen,
2) NO_2,
3) CN,
4) $B(OR^{13})(OR^{14})$,
5) C_1-C_6 alkyl,
6) C_2-C_6 alkenyl,
7) C_2-C_4 alkynyl,
8) C_3-C_7 cycloalkyl,
9) C_3-C_7 cycloalkenyl,
10) haloalkyl,
11) OR^7,
12) NR^8R^9,
13) SR^7,
14) COR^7,
15) $C(O)OR^7$,
16) $S(O)_mR^7$,
17) $CONR^8R^9$,
18) $S(O)_2NR^8R^9$,
19) aryl,
20) heteroaryl,
21) heterocyclyl, or
22) heterobicyclyl,

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more R^6 substituents;

R^{11} is

1) haloalkyl,
2) C_1–C_6 alkyl,
3) C_2-C_6 alkenyl,
4) C_2-C_4 alkynyl,

5) C_3–C_7 cycloalkyl,
6) C_3-C_7 cycloalkenyl,
7) aryl,
8) heteroaryl,
9) heterocyclyl, or
10) heterobicyclyl,

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl is optionally substituted with one or more R^6 substituents; and wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl is optionally substituted with one or more R^{10} substituents;

R^{12} is
1) haloalkyl,
2) C_1–C_6 alkyl,
3) C_2-C_6 alkenyl,
4) C_2-C_4 alkynyl,
5) C_3–C_7 cycloalkyl,
6) C_3-C_7 cycloalkenyl,
7) aryl,
8) heteroaryl,
9) heterocyclyl,
10) heterobicyclyl,
11) C(O)-R^{11},
12) C(O)O-R^{11},
13) C(O)NR^8R^9,
14) $S(O)_m$-R^{11}, or
15) C(=Y)NR^8R^9,

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl is optionally substituted with one or more R^6 substituents; and wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl is optionally substituted with one or more R^{10} substituents;

R^{13} and R^{14} are each independently
1) H, or
2) C_1-C_6 alkyl; or

R^{13} and R^{14} are combined to form a heterocyclic ring or a heterobicyclyl ring;

R^{20} is

1) H,

2) NH_2, or

3)NHFmoc;

or a prodrug; or the compound of Formula I or II is labeled with a detectable label or an affinity tag.

2. The compound, according to claim 1, in which A and A^1 are both CH_2.

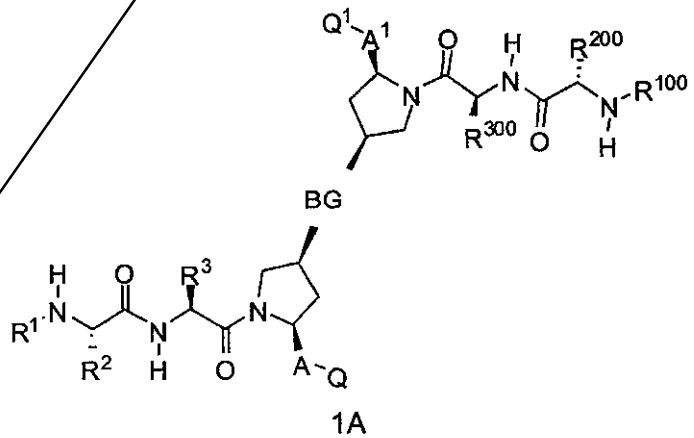
3. The compound, according to claim 1, in which A and A^1 are both C=O.

4. The compound, according to claim 1, in which A is CH_2 and A^1 is C=O.

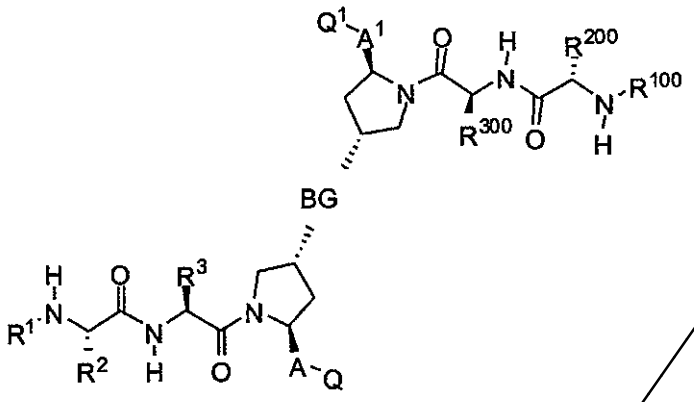
5. The compound, according to claim 1, in which A and A^1 are both $C(O)OCH_3$.

6. The compound, according to claim 1, in which A and A^1 are both C(O)OH.

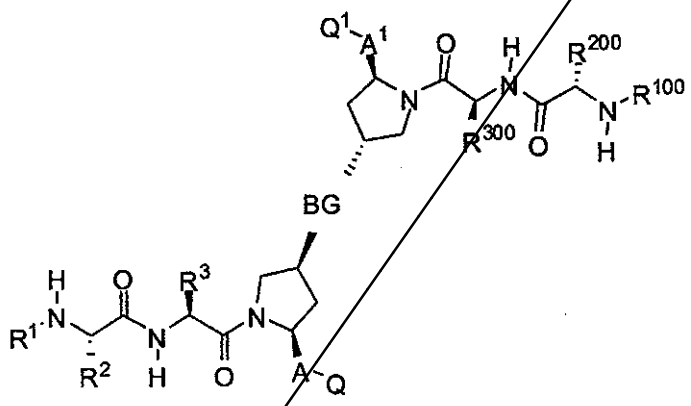
7. The compound, according to claim 1, comprises compounds of Formula 1A through 1C:



1A



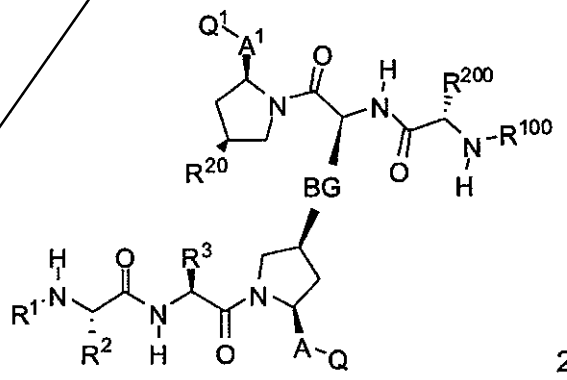
1B



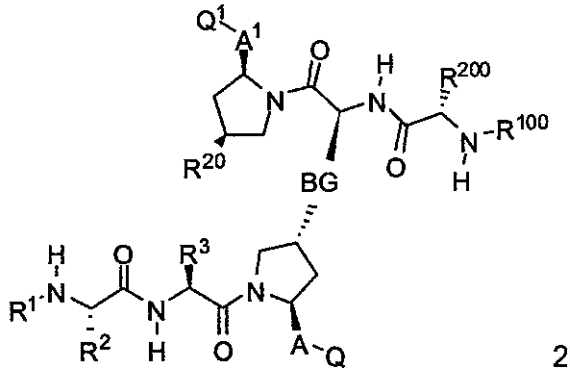
1C

wherein BG, A, A^1, Q, Q^1, R^1, R^{100}, R^2, R^{200}, R^3, and R^{300} are as defined in claim 1.

8. The compound, according to claim 1, comprise compounds of Formula 2A and 2B:



2A

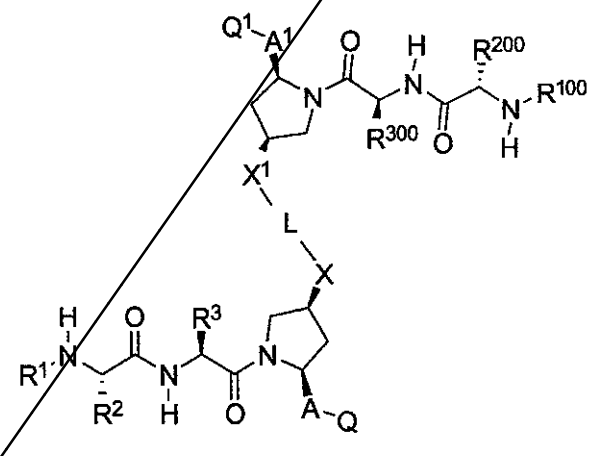


2B

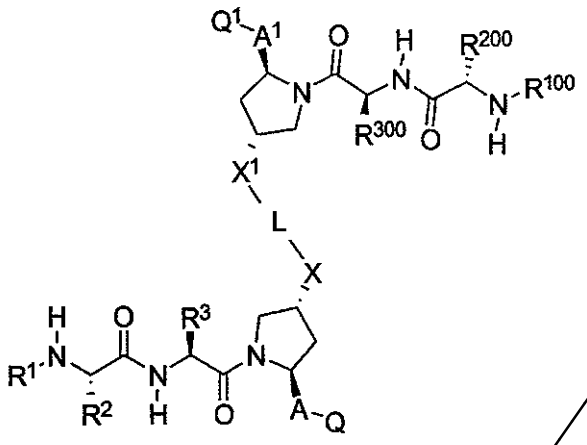
wherein BG, A, A^1, Q, Q^1, R^1, R^{100}, R^2, R^{200} R^3, and R^{20} are as defined in claim 1.

9. The compound, according to claim 1, in which BG is –X-L-X^1–.

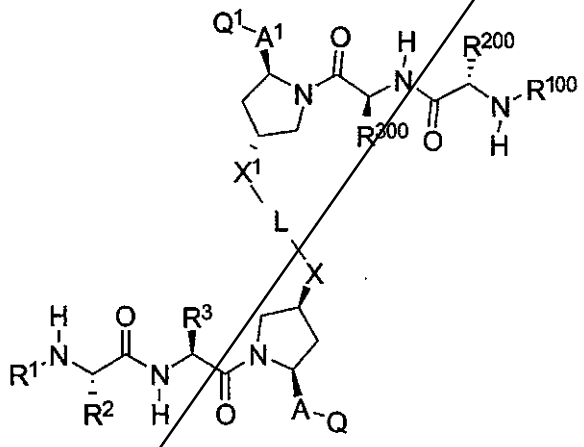
10. The compound, according to claim 1, comprises compounds of Formula 1a through 1c:



1a



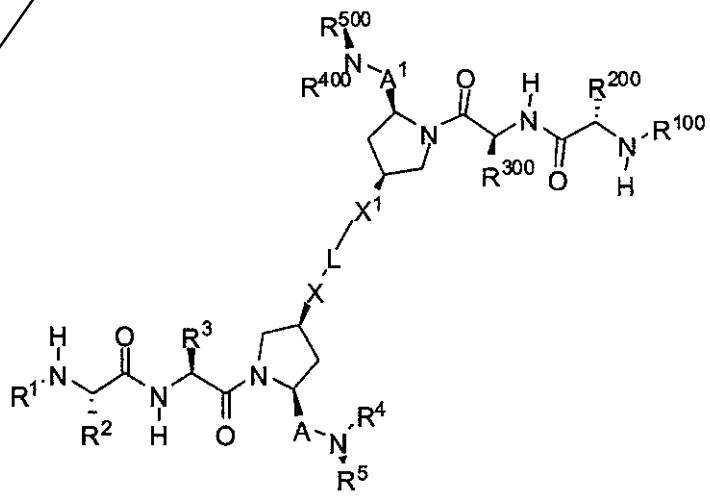
1b



1c.

wherein L, X, X^1, A, A^1, Q, Q^1, R^1, R^{100}, R^2, R^{200}, R^3, and R^{300} are as defined in claim 1.

11. The compound, according to claim 1, comprises compounds of Formula 1.1a through 1.1c:



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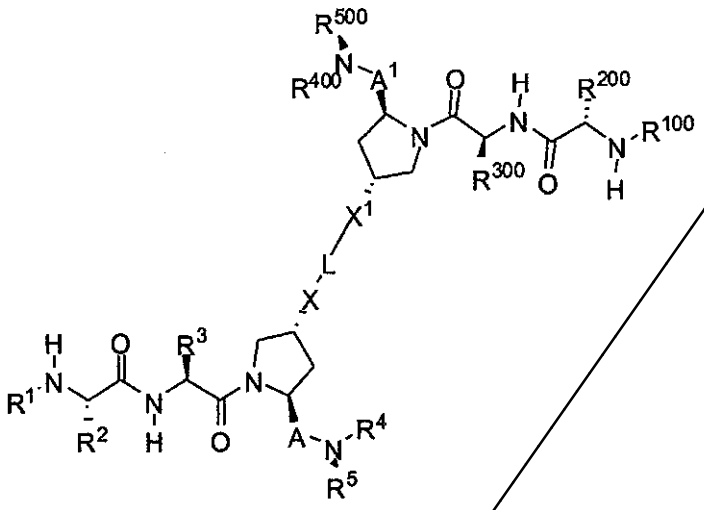
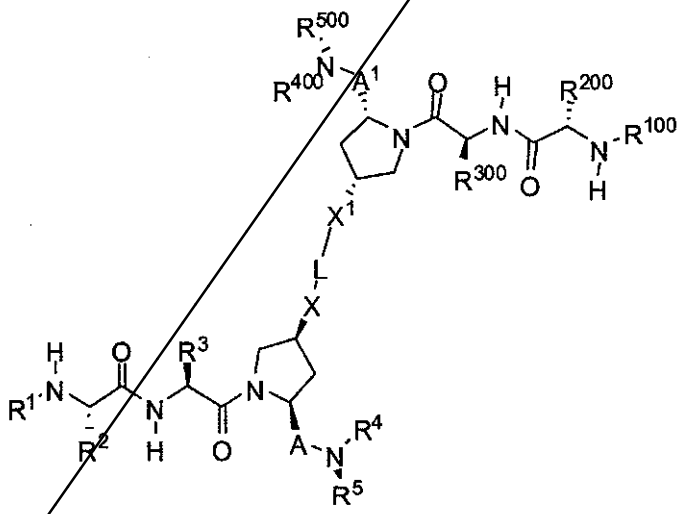
1.1a



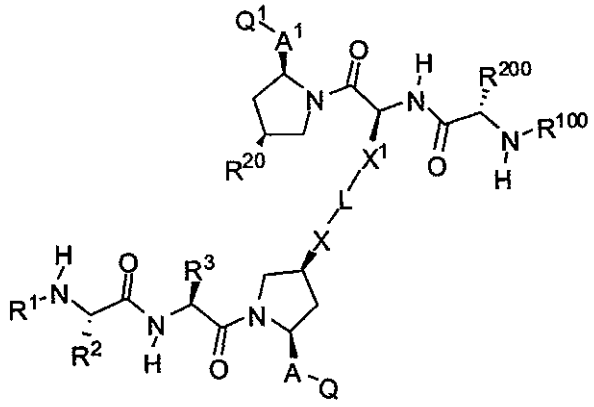
1.1b



1.1c

wherein L, X, X^1, A, A^1, Q, Q^1, R^1, R^{100}, R^2, R^{200}, R^3, R^{300}, R^4, R^{400}, R^5 and R^{500} are as defined in claim 1.

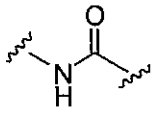
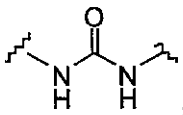
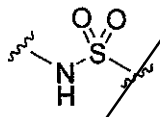
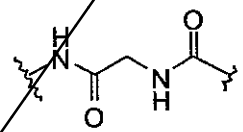
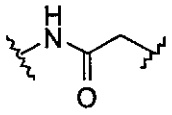
12. The compound, according to claim 1, comprises compounds of Formula 2a:



2a

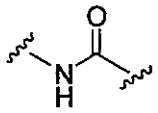
wherein L, X. X^1, A, A^1, B, Q, Q^1, R^1, R^{100}, R^2, R^{200}, R^3 and R^{20} are as defined in claim 1.

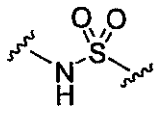
13. The compound, according to claim 1, in which X and X^1 are independently selected from

1) O,
2) NR^{13},
3) S,
4) -C_1-C_6 alkyl-O-,
5) -C_1-C_6 alkyl,
6)  ,
7)  ,
8)  ,
9)  , or
10)  .

14. The compound, according to claim 13, in which X and X^1 are independently selected from:

1) O,

2)  , or

3)  .

15. The compound, according to claim 1, in which L is selected from:

1) $-C_1$-C_{20} alkyl–,

2) $-C_3$-C_7 cycloalkyl–,

3) –aryl–,

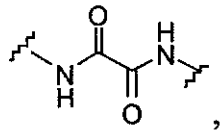
4) –biphenyl–,

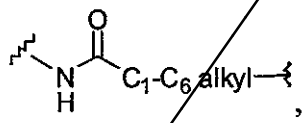
5) – heteroaryl–,

6) $-C_1$-C_6 alkyl–(C_2–C_4 alkynyl)–C_1-C_6 alkyl–

7) $-C_1$-C_6 alkyl– aryl–C_1-C_6 alkyl–,

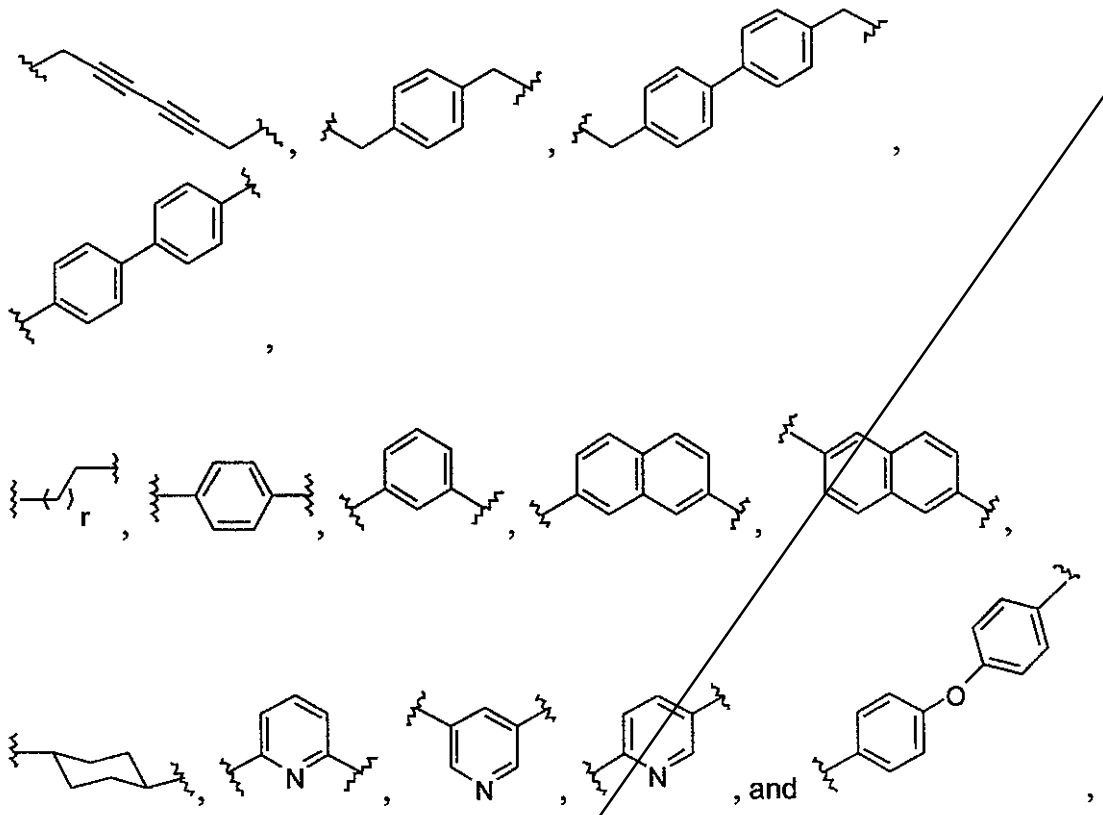
8) –aryl-Y-aryl–,

9)  , or

10)  ,

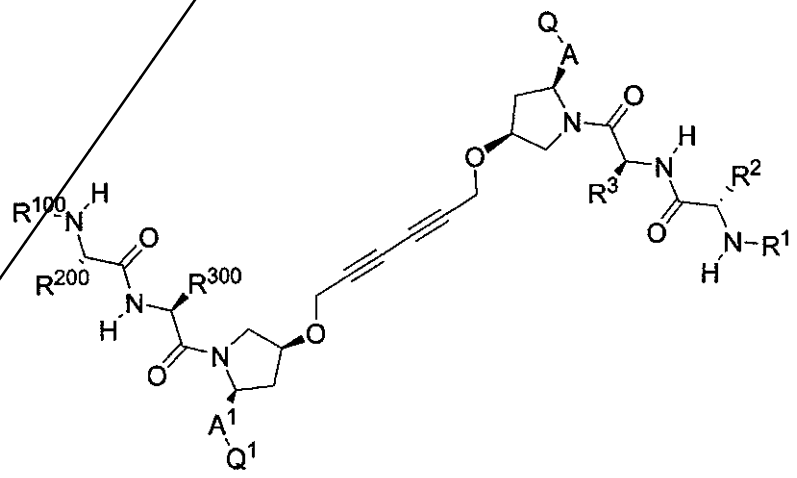
wherein the alkyl and cycloalkyl are optionally substituted with one or more R^6 substituents, and the aryl, biphenyl and heteroaryl are optionally substituted with one or more R^{10} substituents.

16. The compound, according to claim 15, in which L is selected from the group consisting of:

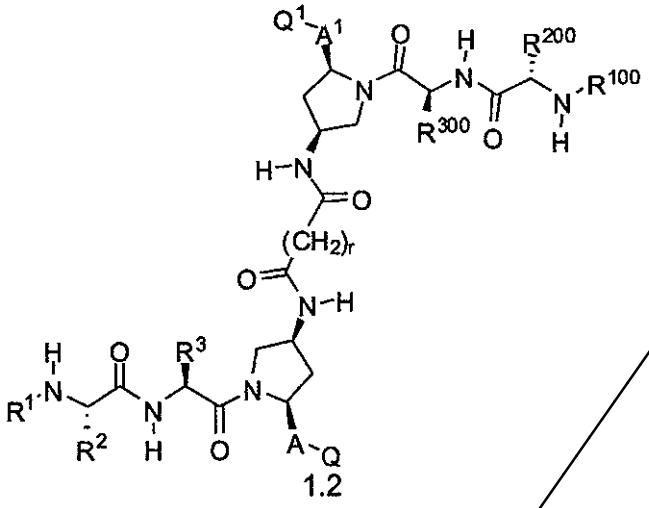


17. The compound, according to claim 16, in which r is an integer of 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10.

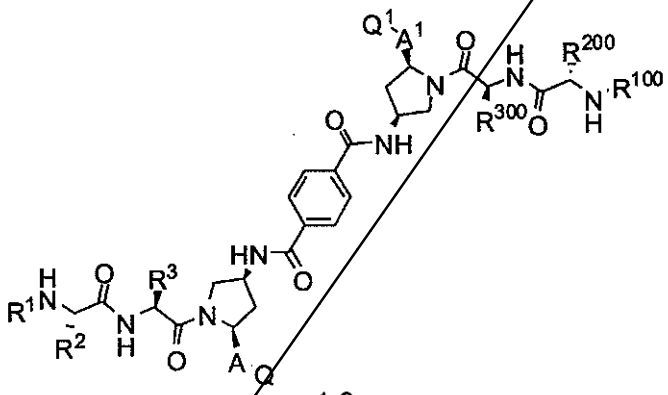
18. The compound, according to claim 1, comprises compounds of Formula 1.1 through 1.18:



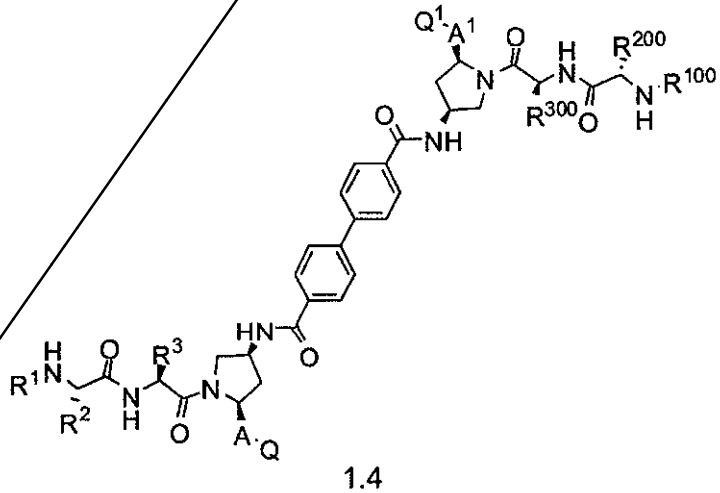
1.1



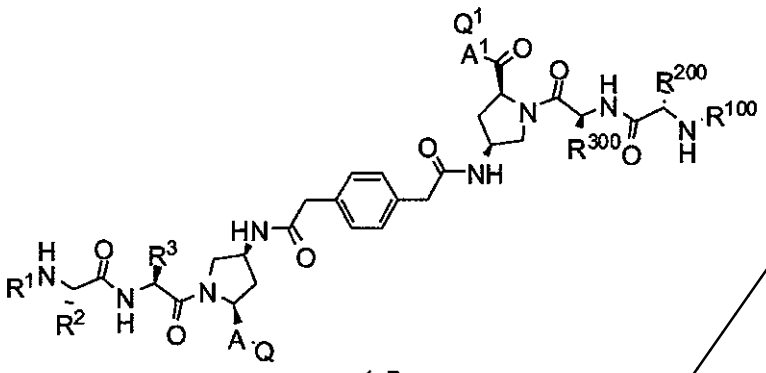
1.2



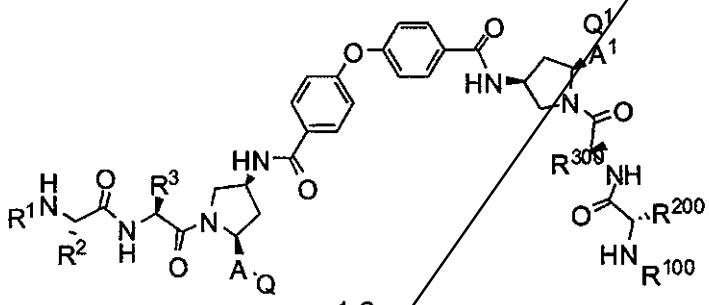
1.3



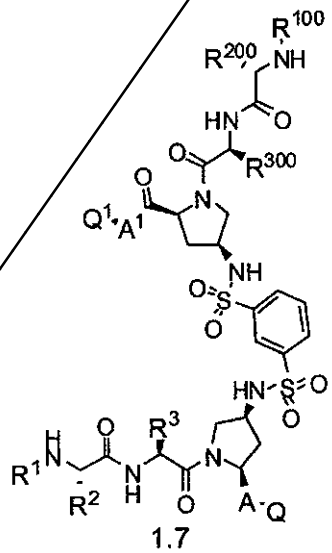
1.4



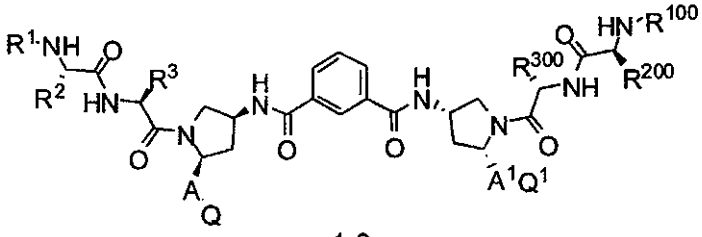
1.5



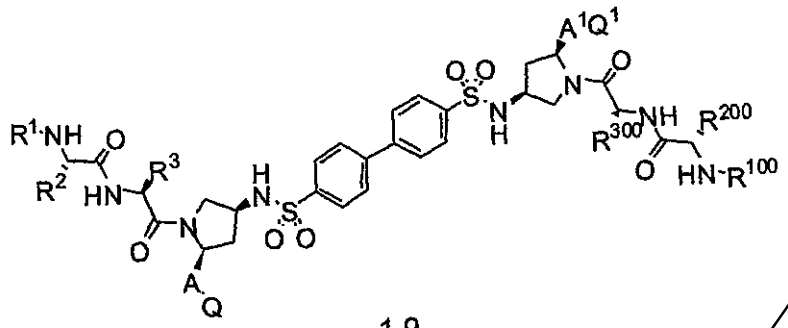
1.6



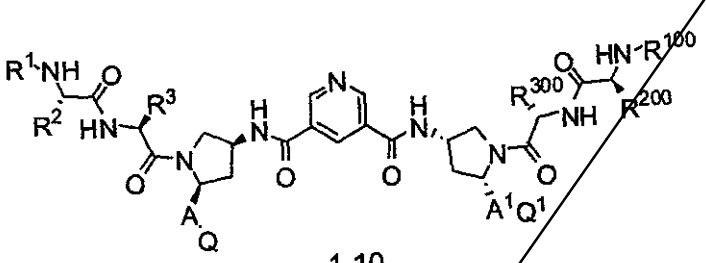
1.7



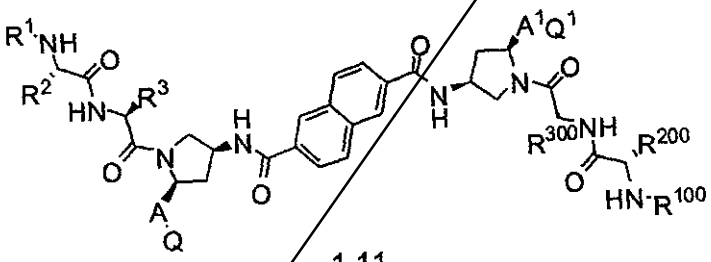
1.8



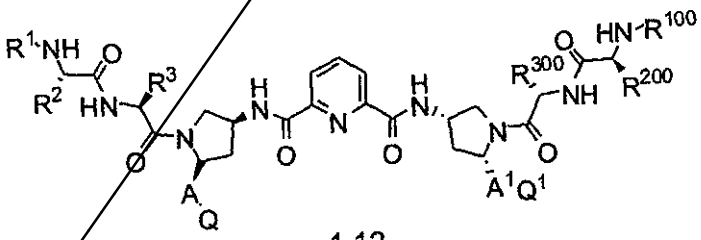
1.9



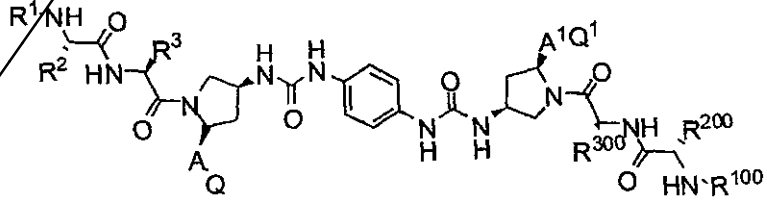
1.10



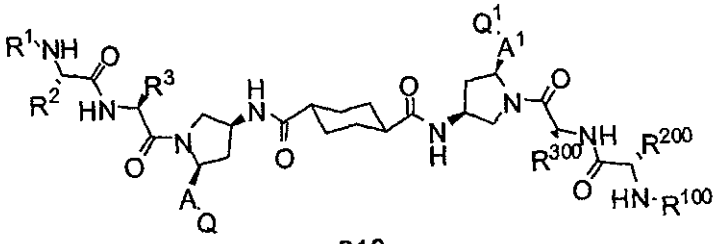
1.11



1.12

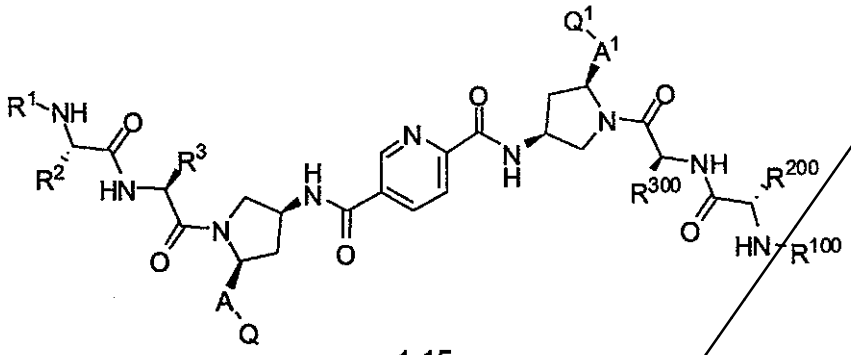


1.13

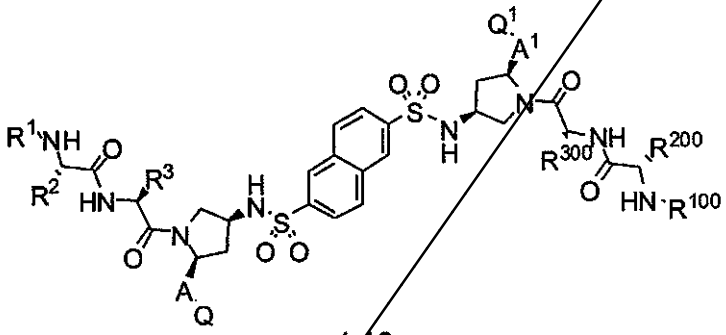


218

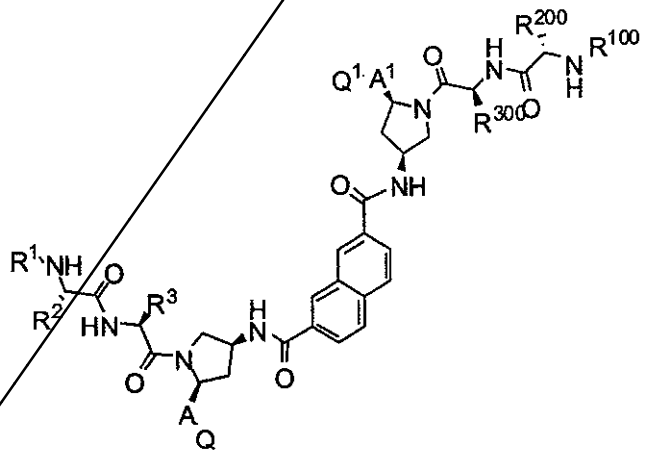
1.14



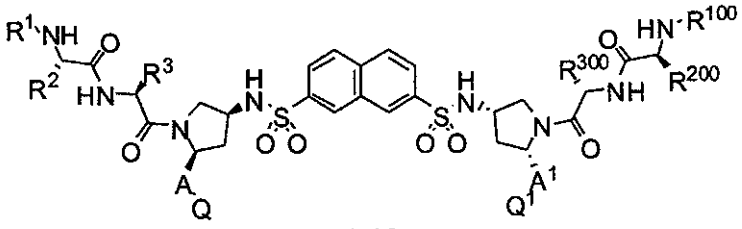
1.15



1.16



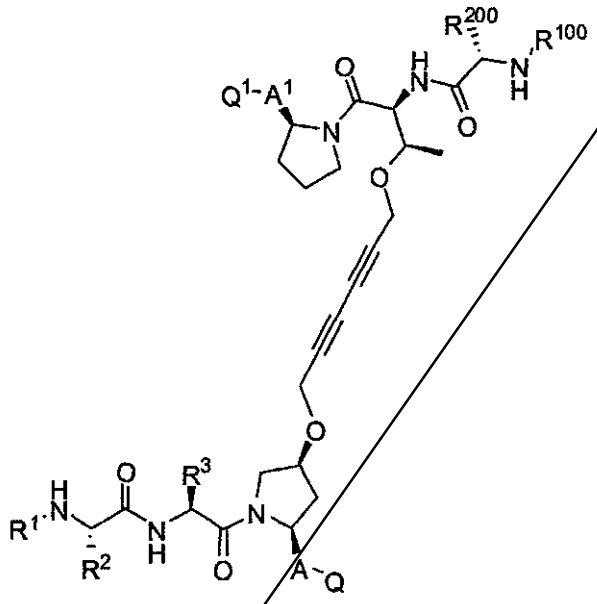
1.17



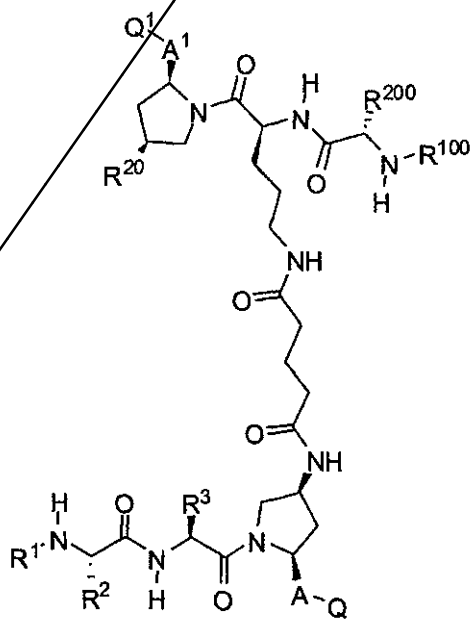
1.18

wherein r is an integer of 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10, and A, A^1, Q, Q^1, R^1, R^{100}, R^2, R^{200}, R^3 and R^{300} are as defined in claim 1.

19. The compound, according to claim 1, comprises compounds of Formula 2.1 and 2.2:



2.1



2.2

wherein A, A^1, Q, Q^1, R^1, R^{100}, R^2, R^{200}, R^3, R^{300} and R^{20} are as defined in claim 1.

20. The compound, according to claim 1, in which R^1 and R^{100} are both H.

21. The compound, according to claim 1, in which R^1 and R^{100} are both C_1-C_6 alkyl.

22. The compound, according to claim 21, in which R^1 and R^{100} are both CH_3.

23. The compound, according to claim 1, in which R^2 and R^{200} are both C_1-C_6 alkyl optionally subtituted with OH.

24. The compound, according to claim 23, in which R^2 and R^{200} are both CH_3.

25. The compound, according to claim 23, in which R^2 is CH_2OH and R^{300} is CH_3.

26. The compound, according to claim 23, in which R^2 and R^{200} are both CH_2OH.

27. The compound, according to claim 23, in which R^2 and R^{200} are both CH_2CH_3.

28. The compound, according to claim 1, in which R^3 and R^{300} are both C_1-C_6 alkyl.

29. The compound, according to claim 28, in which R^3 and R^{300} are both $C(CH_3)_3$.

30. The compound, according to claim 1, in which Q and Q^1 are both NR^4R^5.

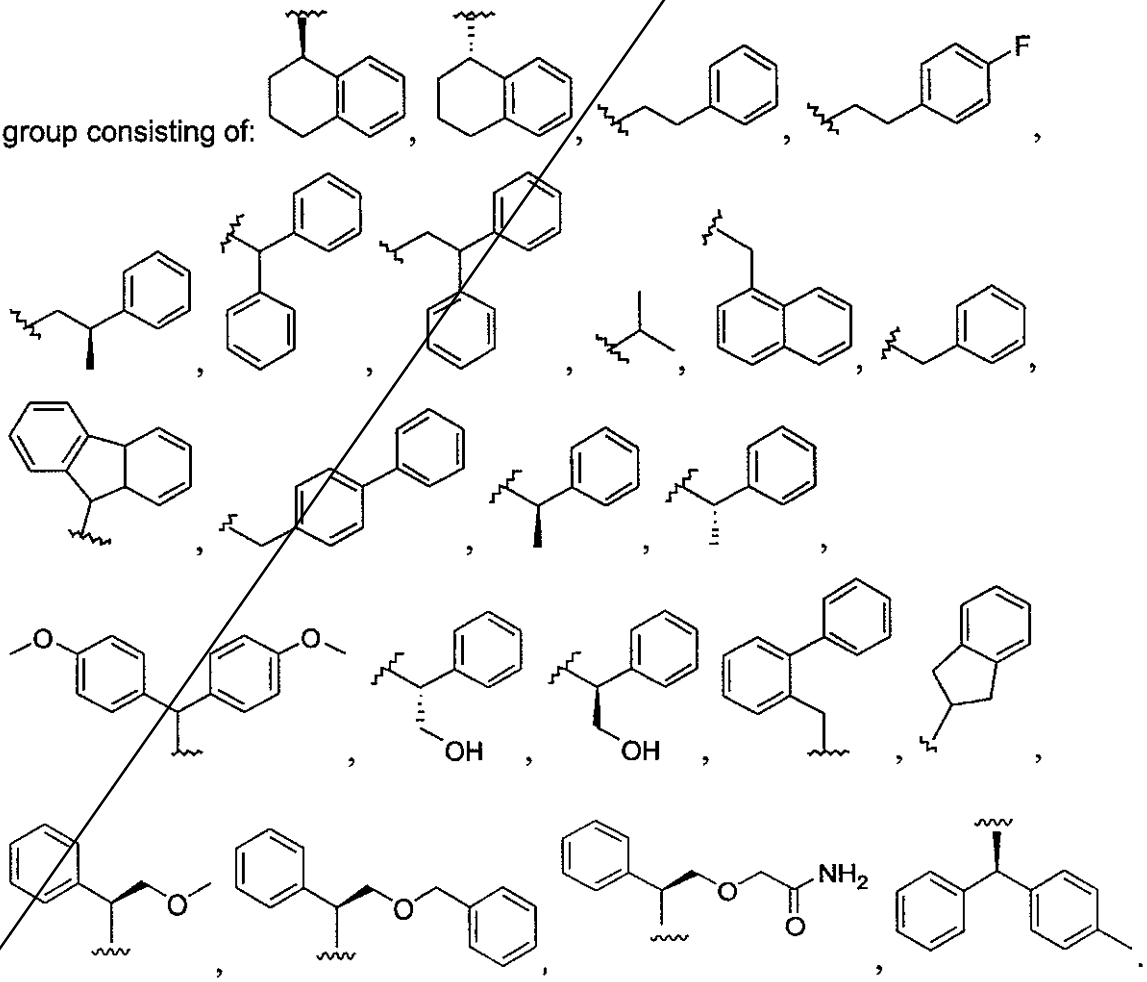
31. The compound, according to claim 1, in which A and A^1 are both C=O, Q and Q^1 are both NR^4R^5, R^4 is H and
R^5 is selected from

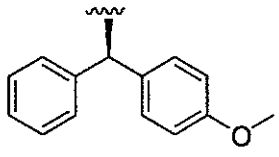
1) ←C_1–C_6 alkyl,
2) ←C_2-C_6 alkenyl,
3) ←C_2-C_4 alkynyl,
4) ←C_3–C_7 cycloalkyl,
5) ←C_3-C_7 cycloalkenyl,
6) ←aryl,
7) ←heteroaryl,
8) ←heterocyclyl, or
9) ←heterobicyclyl,

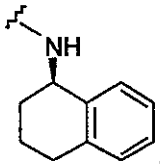
wherein the alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl is optionally substituted with one or more R^6 substituents; and wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl is optionally substituted with one or more R^{10} substituents;
wherein R^6 and R^{10} are as defined herein.

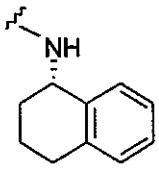
32. The compound, according to claim 31, in which R^4 is H and R^5 is selected from:
1) ←C_1–C_6 alkyl, or
2) ←aryl,
wherein the alkyl is optionally substituted with one or two R^6 substituents; and wherein the aryl is optionally substituted with one R^{10} substituent;
wherein R^6 and R^{10} are as defined herein.

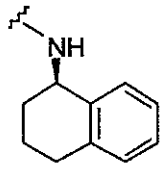
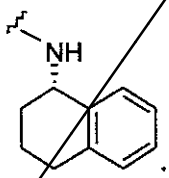
33. The compound, according to claim 32, in which R^4 is H and R^5 is selected from the group consisting of:

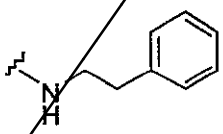


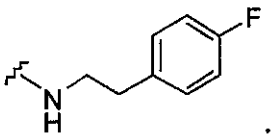
and  .

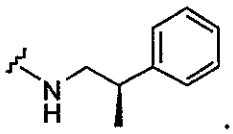
34. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

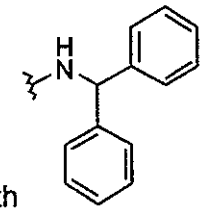
35. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

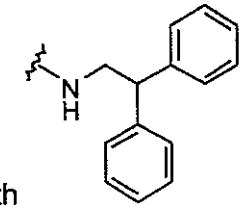
36. The compound, according to claim 1, in which A and A^1 are both C=O, and Q is  and Q^1 is  .

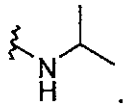
37. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

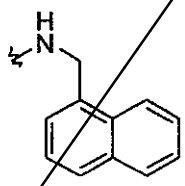
38. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

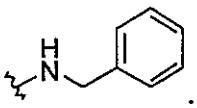
39. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

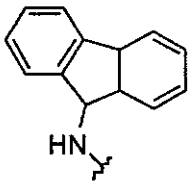
40. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

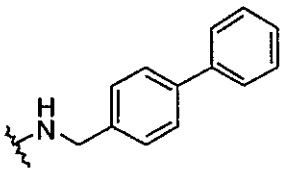
41. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

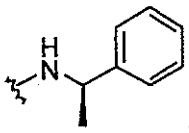
42. The compound ,according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

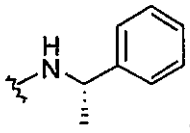
43. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

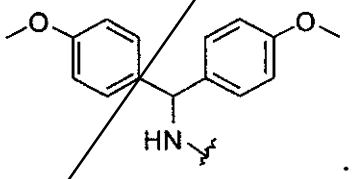
44. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

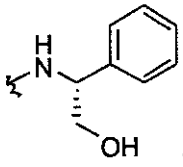
45. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

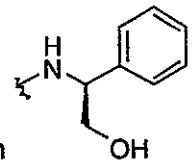
46. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

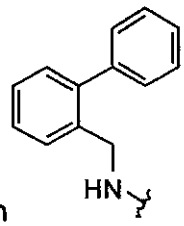
47. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

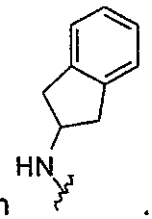
48. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

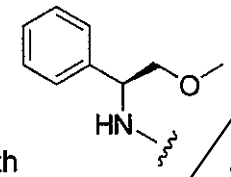
49. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

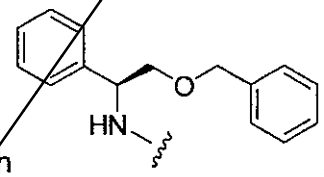
50. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

51. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

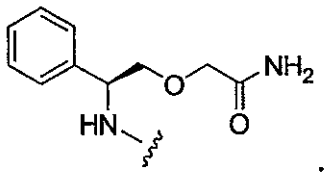
52. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

53. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

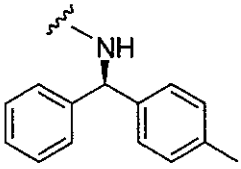
54. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

55. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

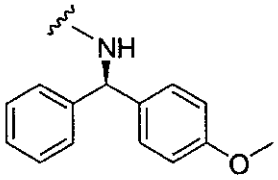
56. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both



57. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both



58. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both



59. The compound, according to claim 1, in which A and A^1 are both CH_2 andQ and Q^1 are both NR^4R^5, then R^4 and R^5 are each independently

1) haloalkyl,
2) ←C_1–C_6 alkyl,
3) ←C_2-C_6 alkenyl,
4) ←C_2-C_4 alkynyl,
5) ←C_3–C_7 cycloalkyl,
6) ←C_3-C_7 cycloalkenyl,
7) ←aryl,
8) ←heteroaryl,
9) ←heterocyclyl,
10) ←heterobicyclyl,
11) ←C(O)-R^{11},
12) ←C(O)O-R^{11},
13) ←C(=Y)NR^8R^9, or
14) ←$S(O)_2$-R^{11},

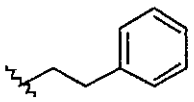
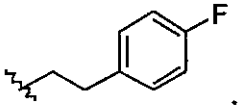
wherein the alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl is optionally substituted with one or more R^6 substituents; and wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl is optionally substituted with one or more R^{10} substituents;
wherein Y, R^6, R^8, R^9, R^{10} and R^{11} are as defined herein.

60. The compound, according to claim 59, in which R^4 and R^5 are independently selected from

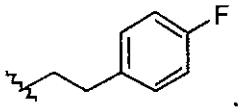
1) C_1-C_6 alkyl,
2) ←C(O)-R^{11},
3) ←C(O)O-R^{11}, or
4) ←$S(O)_2$-R^{11},

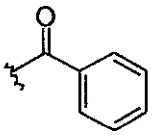
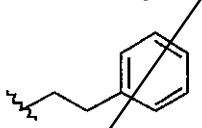
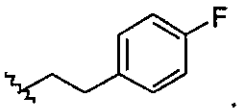
wherein the alkyl is substituted with an R^6 substituent;
wherein R^6 and R^{11} are as defined herein.

61. The compound, according to claim 60, in which R^4 is $S(O)_2CH_3$ and R^5 is

 or  .

62. The compound, according to claim 60, in which R^4 is $C(O)CH_3$ and R^5 is

 .

63. The compound, according to claim 60, in which R^4 is  and R^5 is  or  .

64. The compound, according to claim 1, in which R^{11} is

1) C_1–C_6 alkyl, or
2) aryl,

wherein the alkylis optionally substituted with one or more R^6 substituents; and wherein the aryl is optionally substituted with one or more R^{10} substituents;
wherein R^6 and R^{10} are as defined herein.

65. The compound, according to claim 64, in which R^{11} is
1) C_1–C_6 alkyl optionally substituted with one or two R^6 substituents, or
2) phenyl optionally substituted with one R^{10} substituent;
wherein the R^6 and the R^{10} substituents are as defined herein.

66. The compound, according to claim 1, in which R^6 is
1) halogen,
2) NO_2,
3) CN,
4) aryl,
5) heteroaryl,
6) heterocyclyl,
7) heterobicyclyl,
8) OR^7,
9) SR^7, or
10) NR^8R^9 ,
wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl is optionally substituted with one or more R^{10} substituents;
wherein R^7, R^8, R^9 and R^{10} are as defined herein.

67. The compound, according to claim 66, in which R^6 is
1) halogen,
2) aryl, or
3) NR^8R^9 ,
wherein the aryl is optionally substituted with one R^{10} substituent;
wherein R^8, R^9 and R^{10} are as defined herein.

68. The compound, according to claim 1, in which R^8 and R^9 are each independently
1) H,
2) haloalkyl,
3) C_1–C_6 alkyl,

4) C_2-C_6 alkenyl,

5) C_2-C_4 alkynyl,

6) C_3–C_7 cycloalkyl, or

7) C_3-C_7 cycloalkenyl,

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl is optionally substituted with one or more R^6 substituents;

wherein the R^6 substituents are as defined herein.

69. The compound, according to claim 1, in which R^{10} is

1) halogen,

2) NO_2,

3) CN,

4) haloalkyl,

5) OR^7,

6) NR^8R^9, or

7) SR^7;

wherein R^7, R^8, and R^9 are as defined herein.

70. A compound, according to claim 1, selected from the group consisting of:

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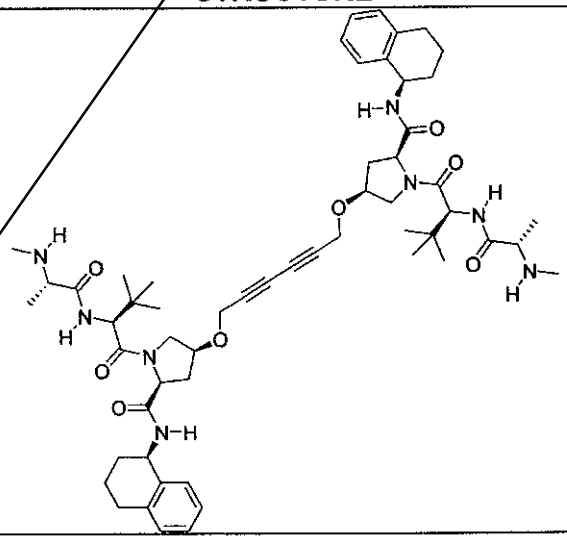
1	

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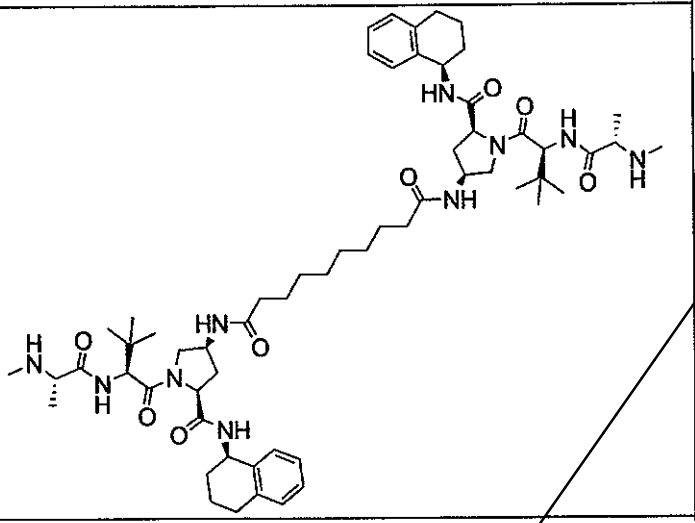
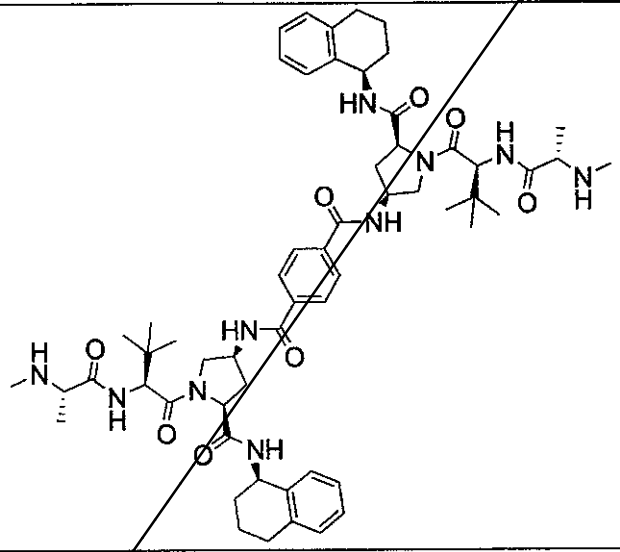
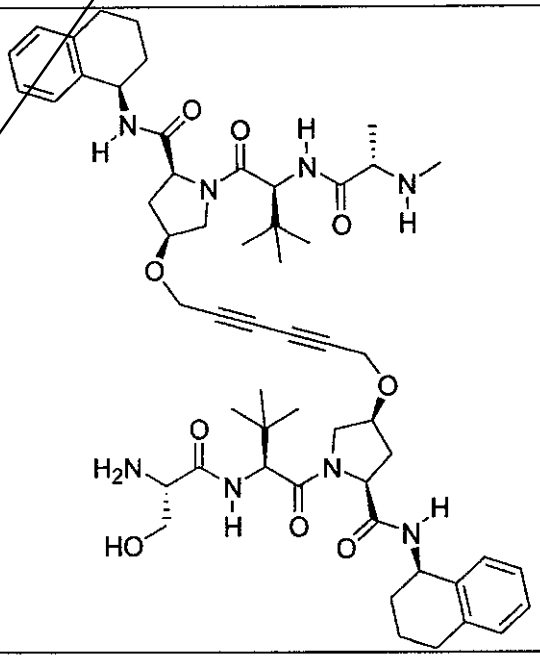
2	 ;
3	 ;
4	 ;

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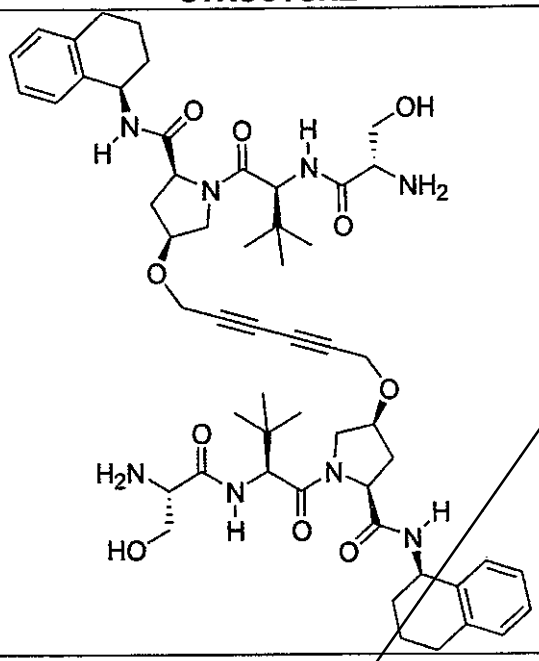
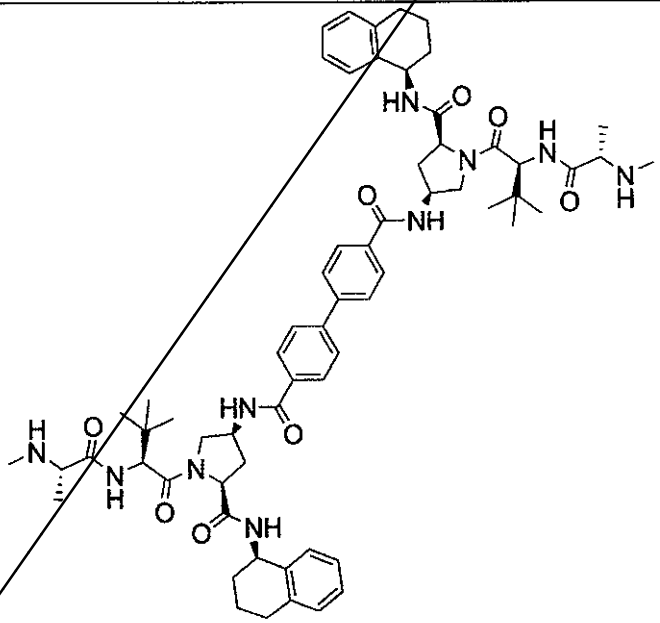
5	
10	

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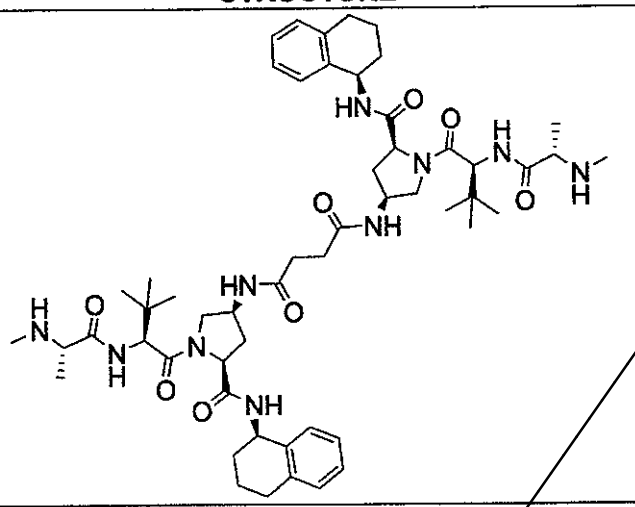
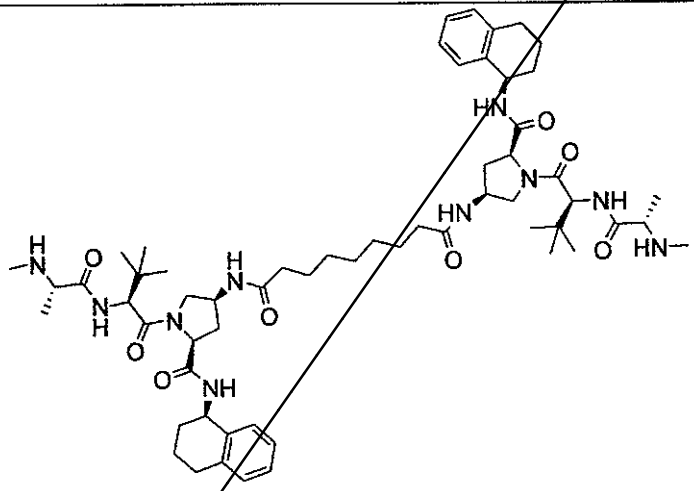
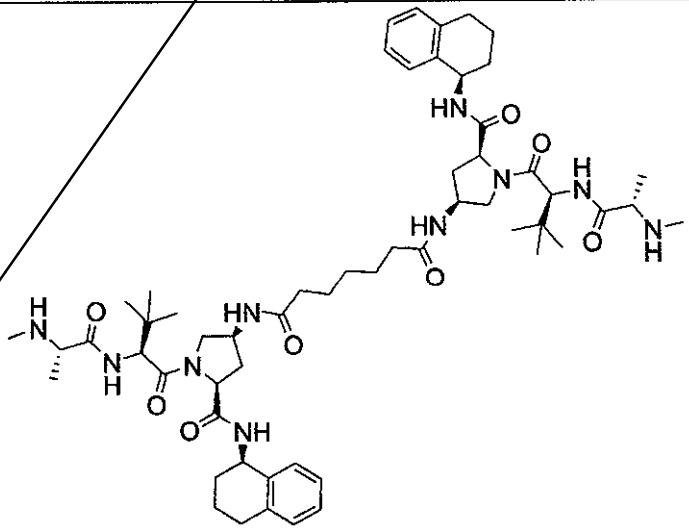
11	 ;
12	 ;
13	 ;

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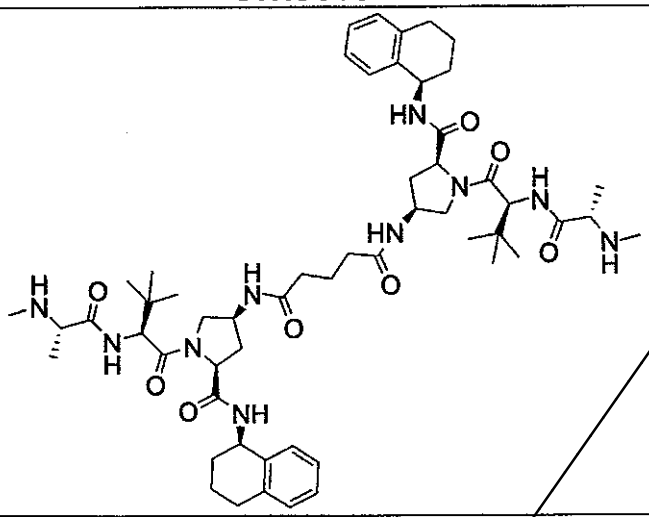
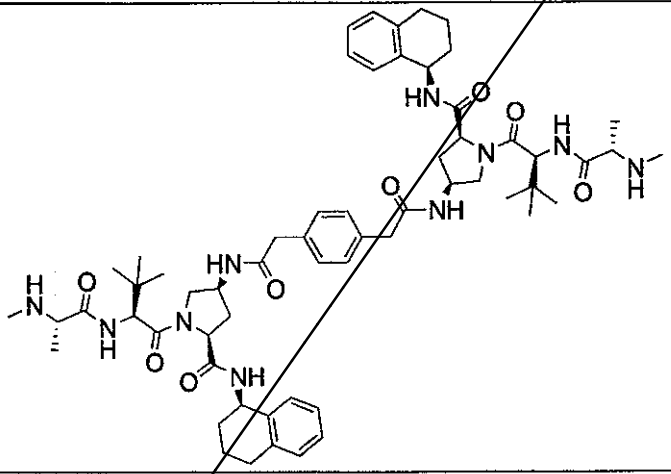
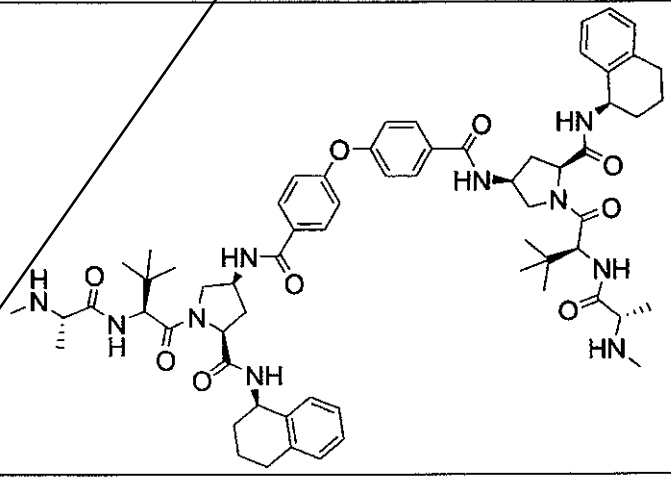
14	 ;
15	 ;
16	 ;

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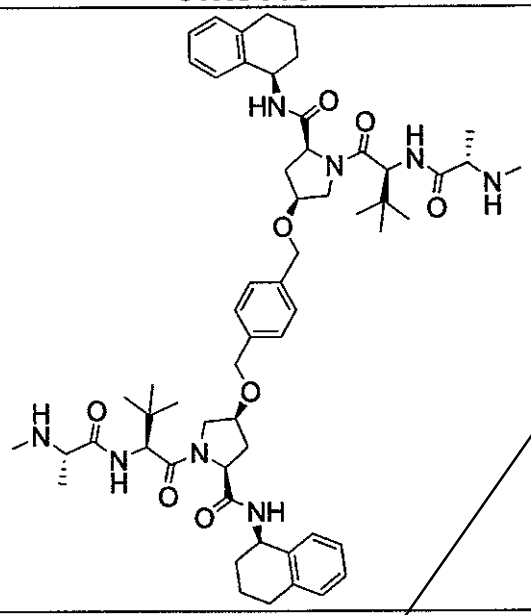
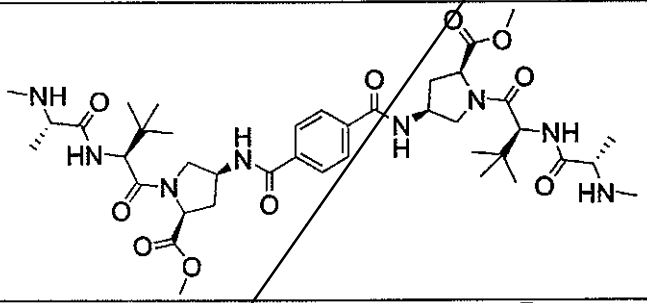
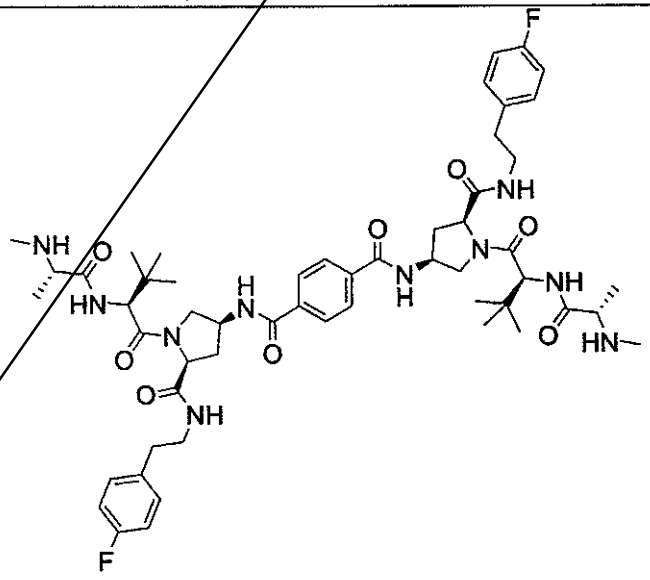
17	 ;
18	 ;
19	 ;

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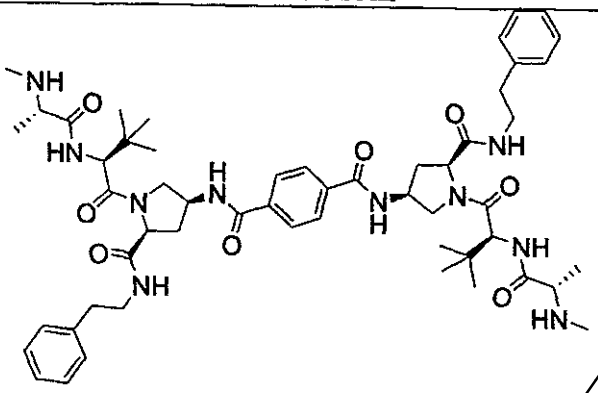
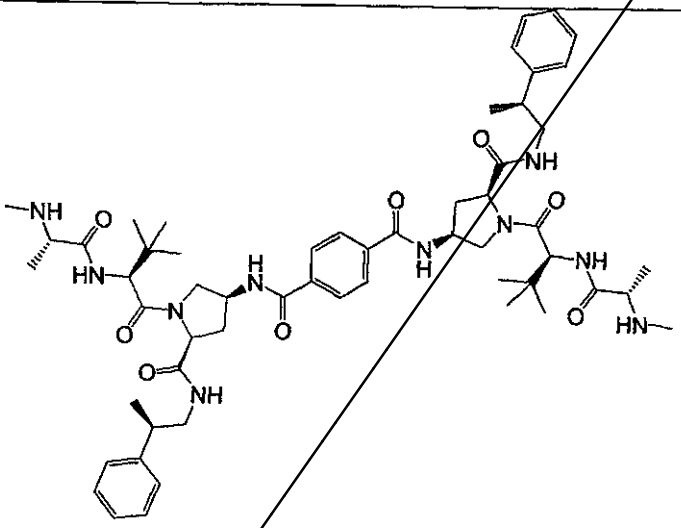
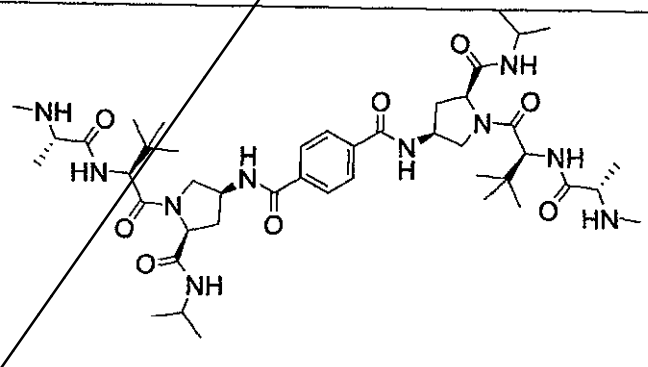
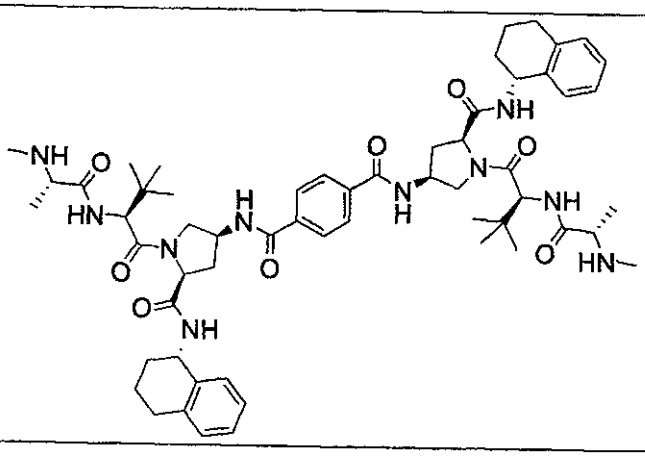
20	 ;
21	 ;
22	 ;
23	 ;

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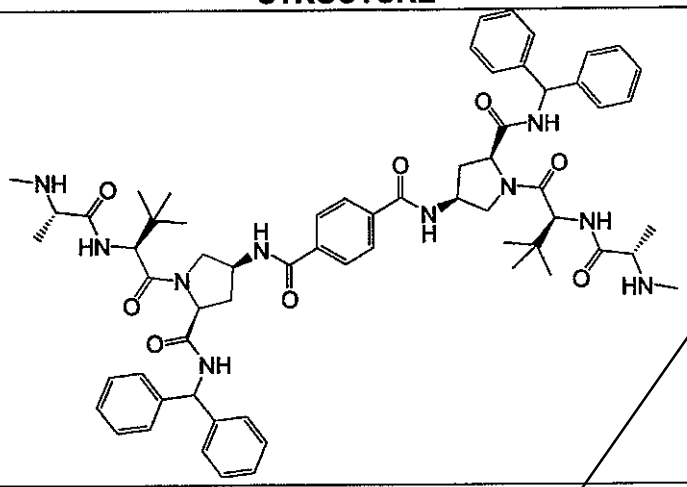
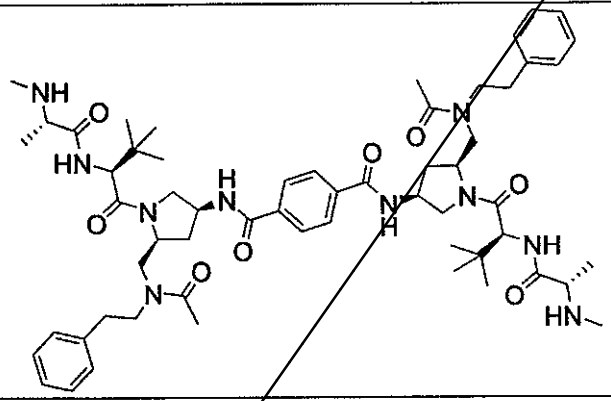
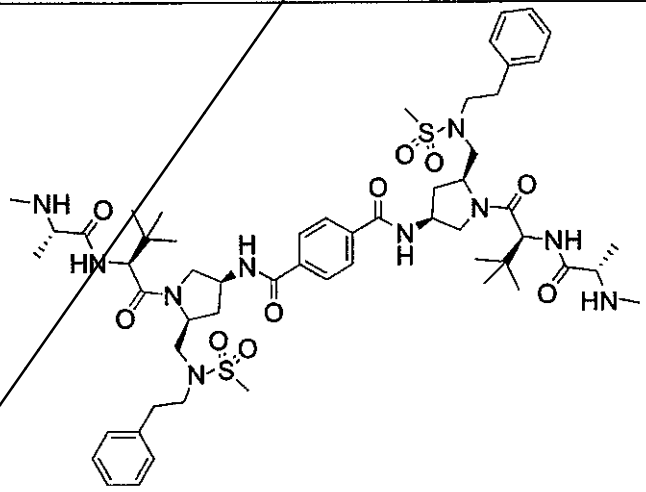
24	 ;
25	 ;
26	 ;

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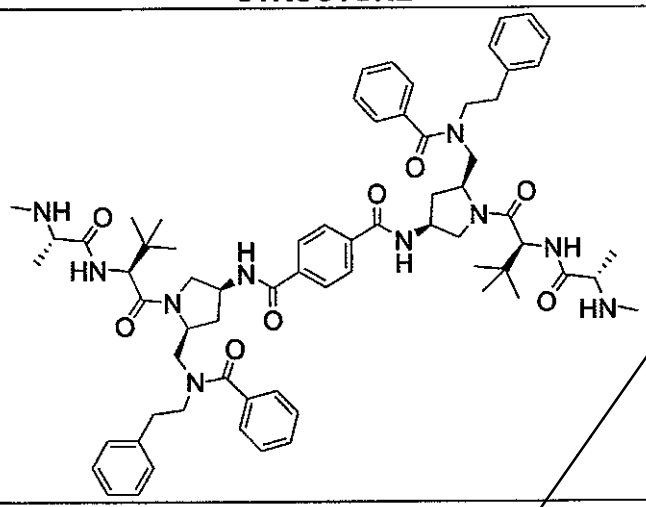
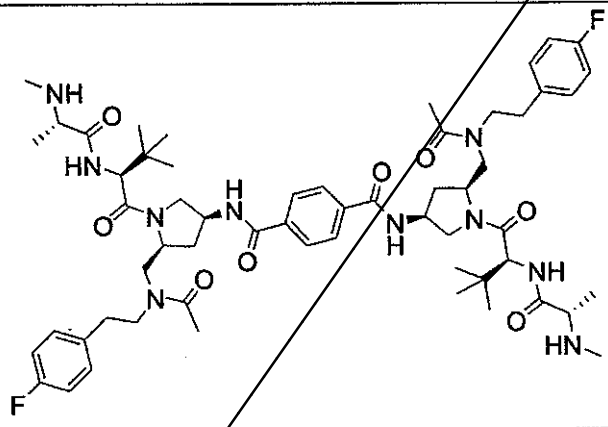
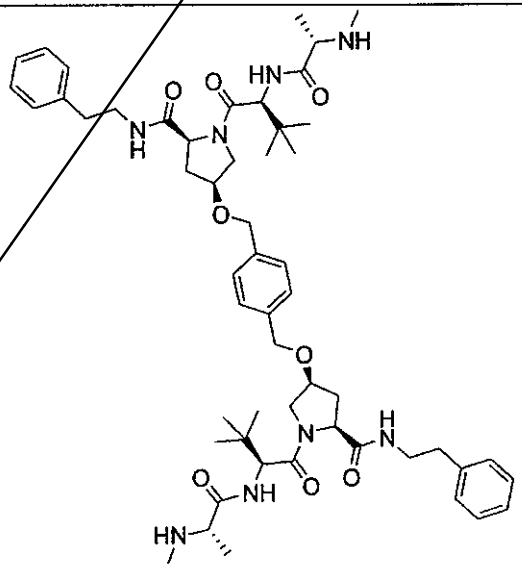
27	 ;
28	 ;
29	 ;

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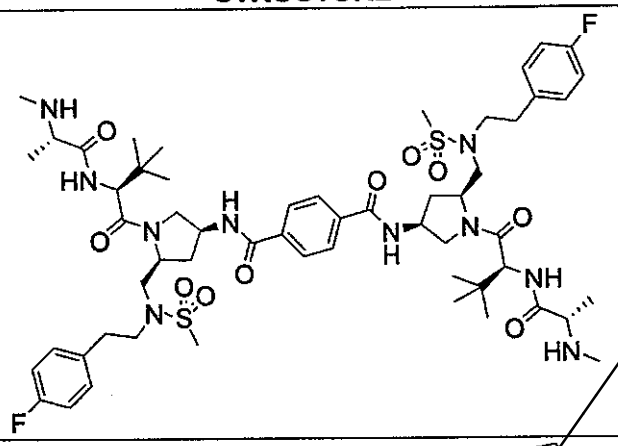
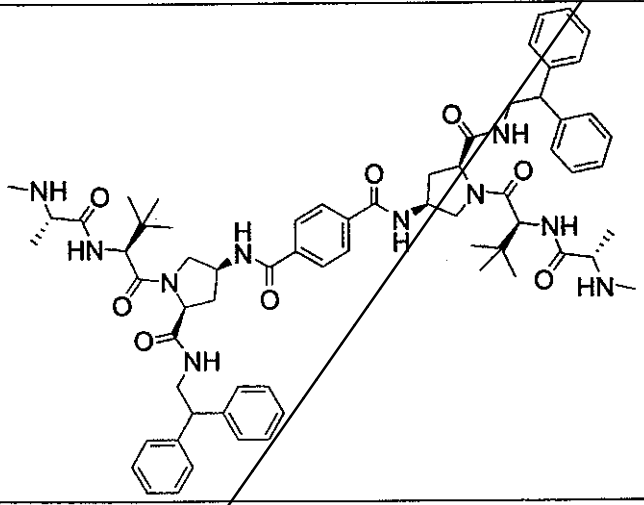
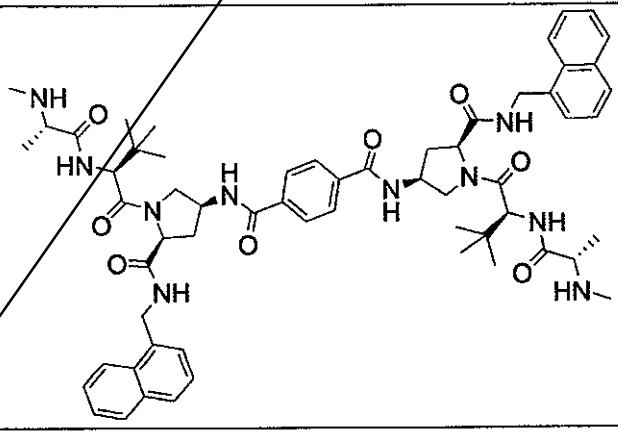
30	 ;
31	 ;
32	 ;

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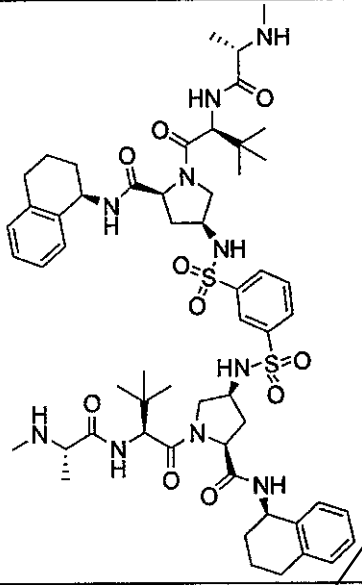
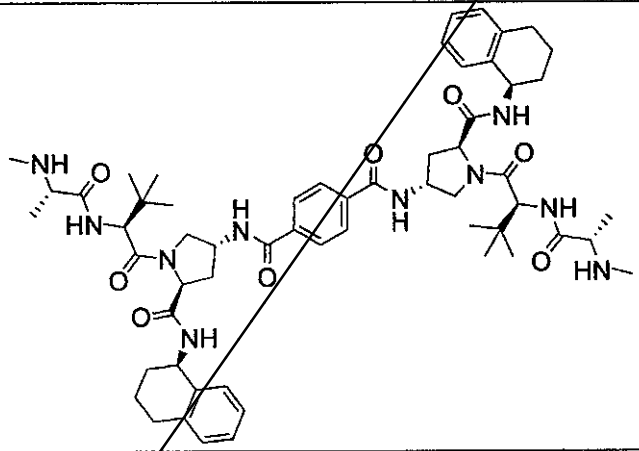
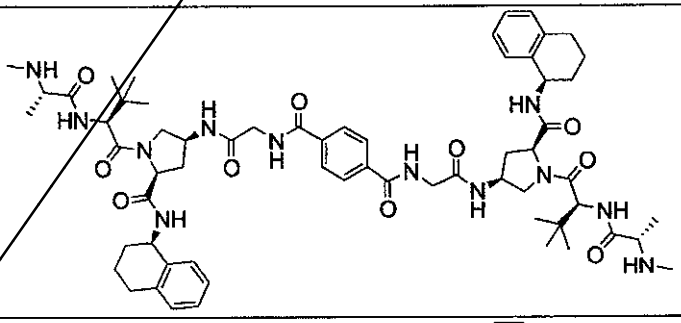
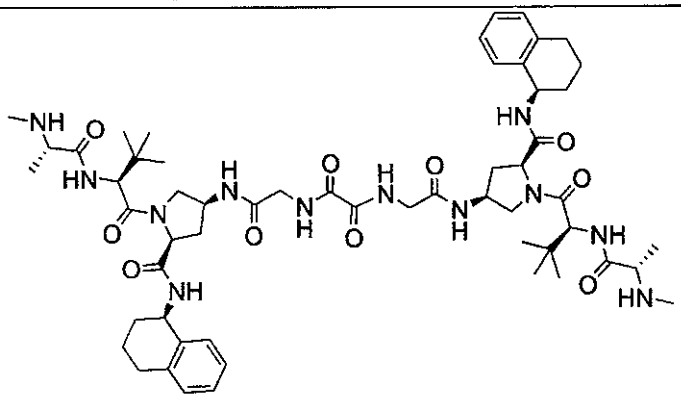
33	 ;
34	 ;
35	 ;
36	 ;

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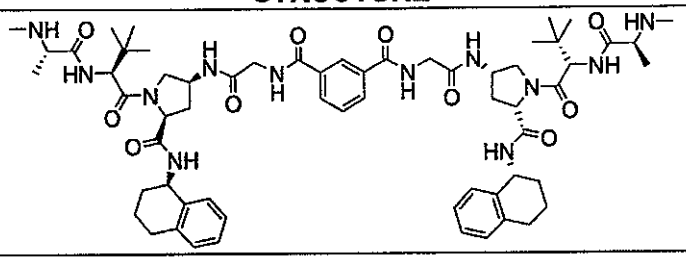
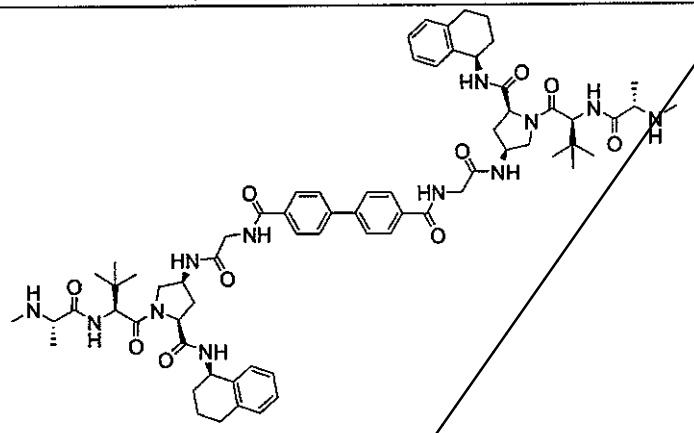
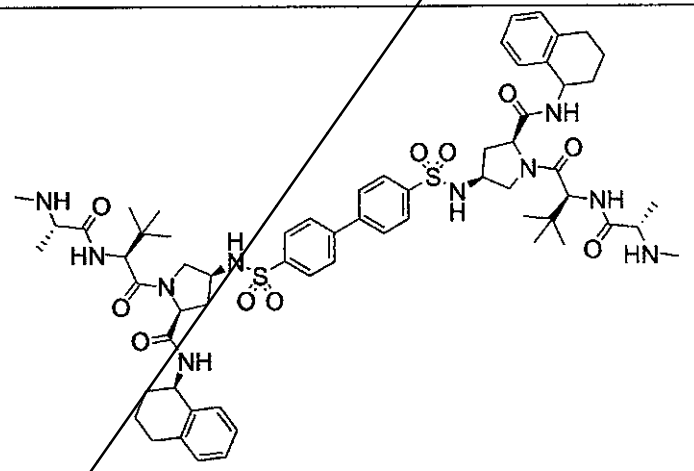
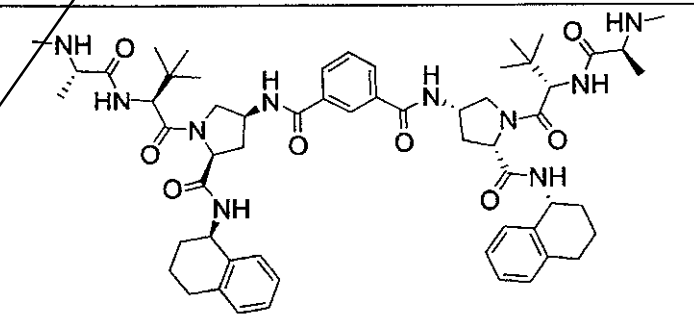
37	 ;
38	 ;
39	 ;
40	 ;

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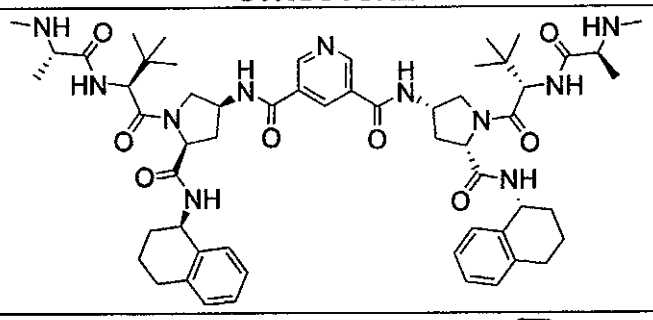
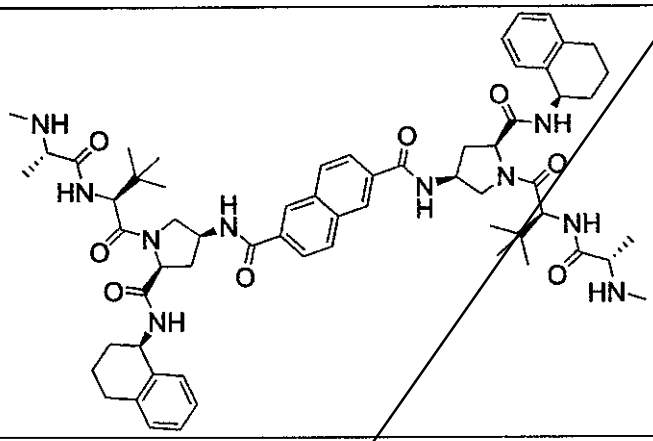
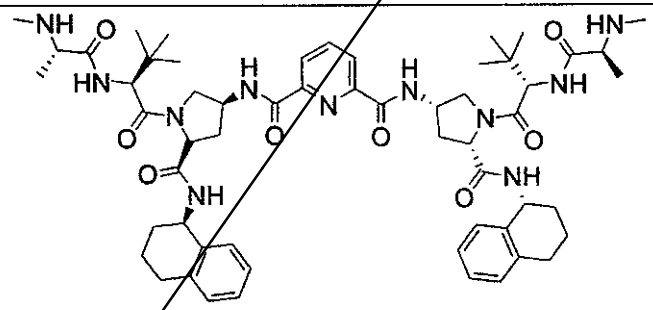
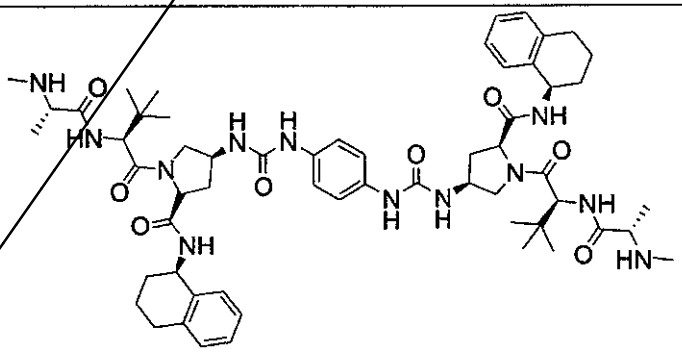
41	 ;
42	 ;
43	 ;
44	 ;

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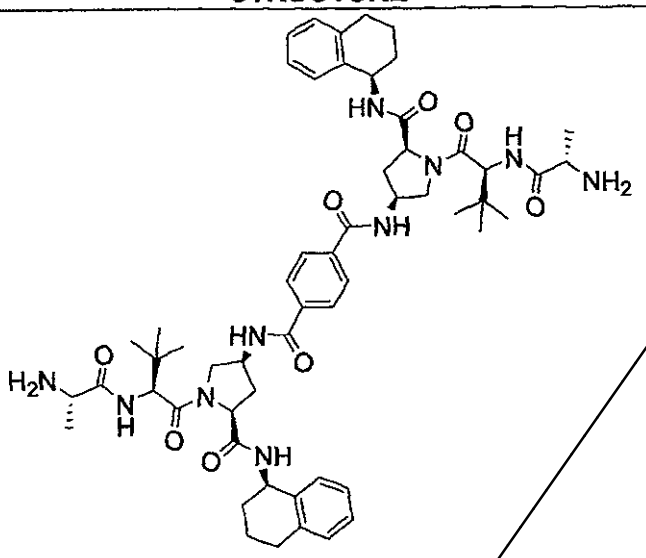
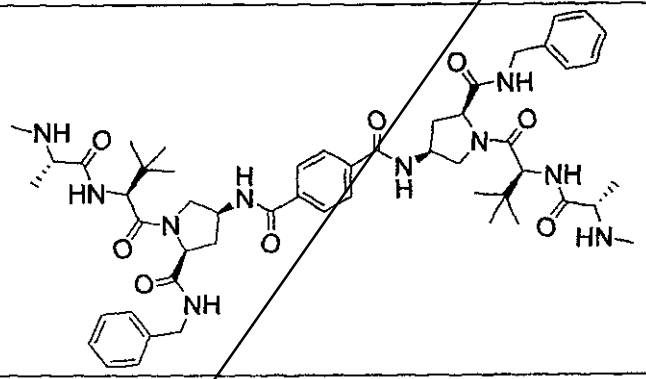
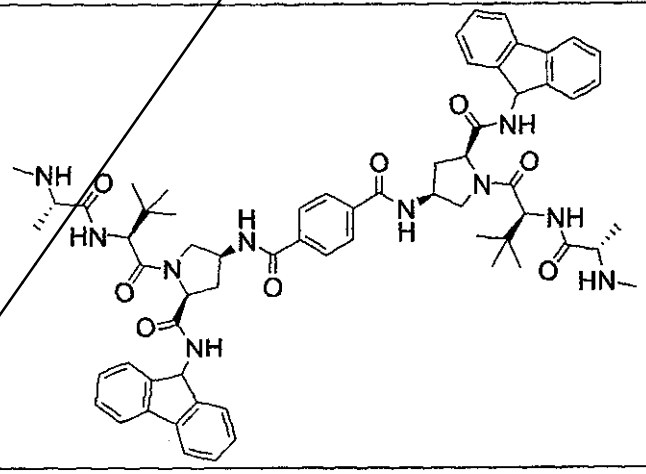
45	 ;
46	 ;
47	 ;

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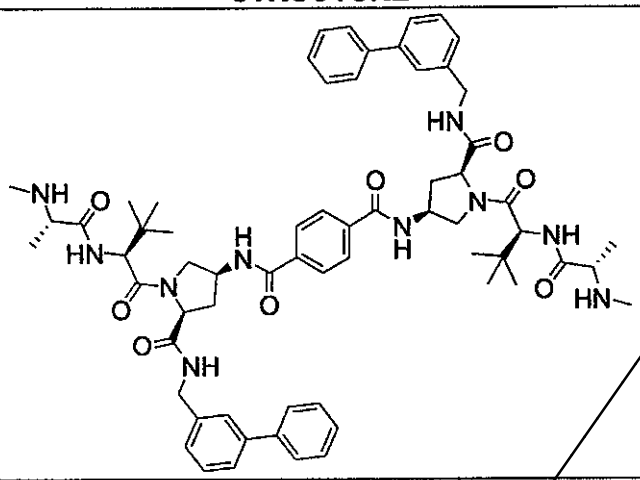
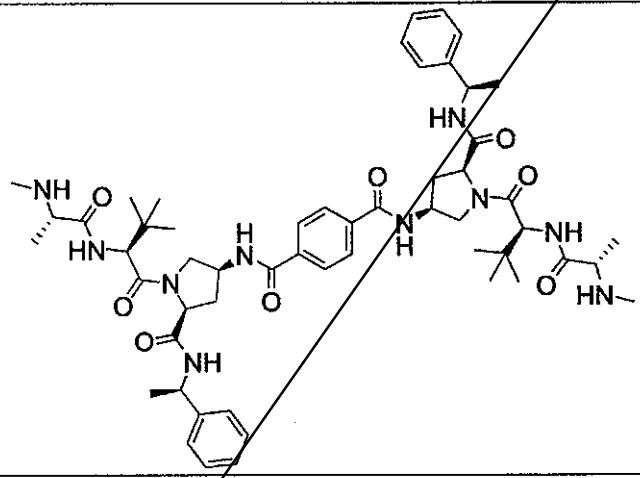
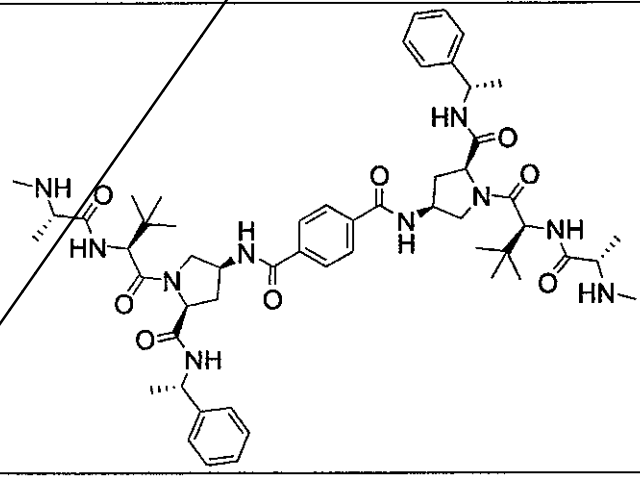
48	 ;
49	 ;
50	 ;

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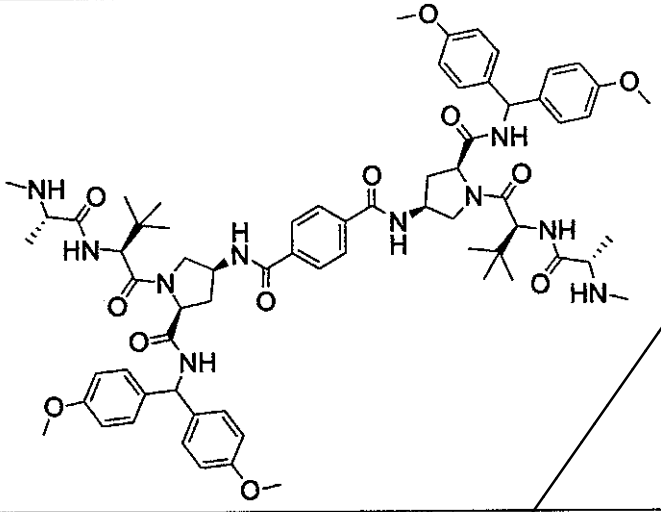
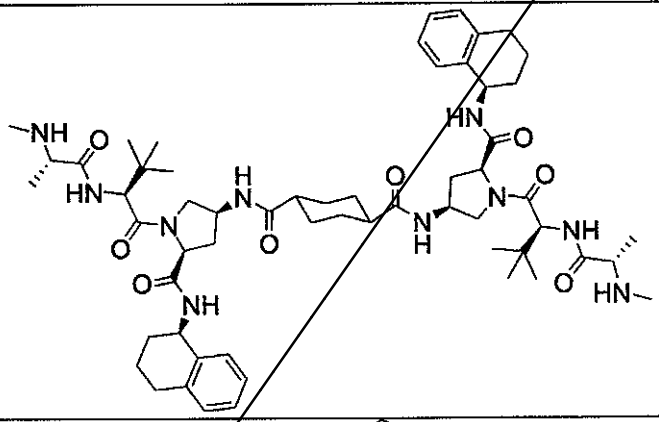
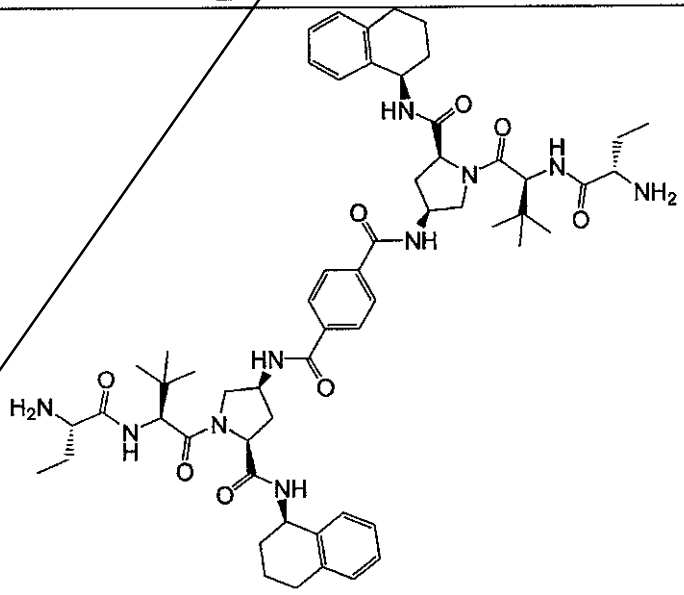
51	 ;
52	 ;
53	 ;

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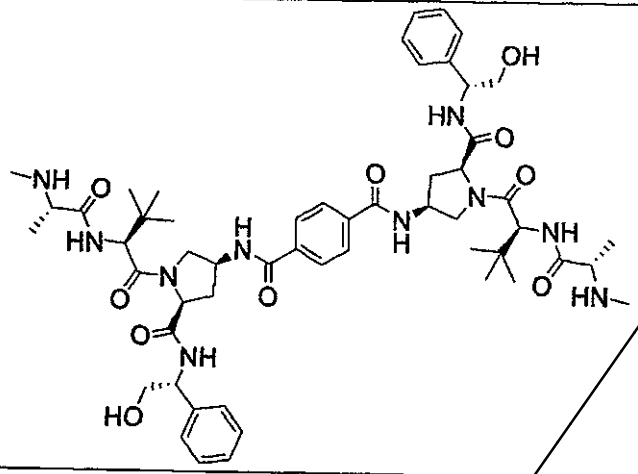
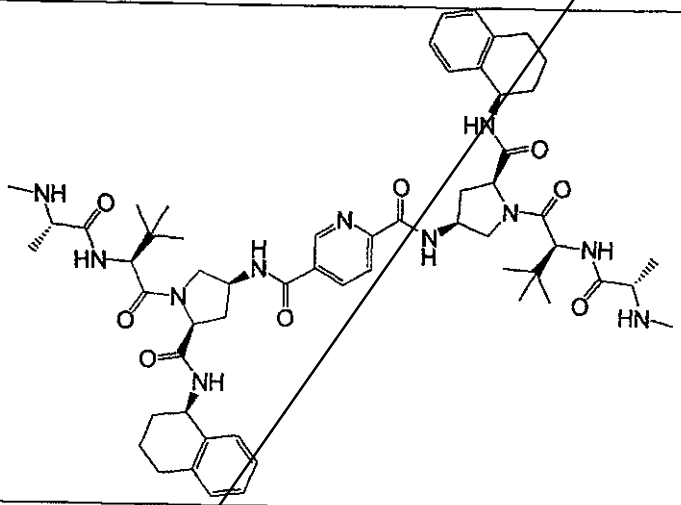
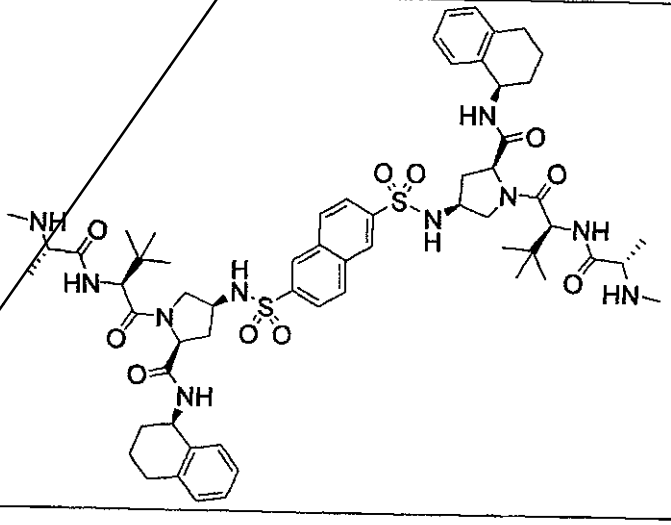
54	 ;
55	 ;
56	 ;

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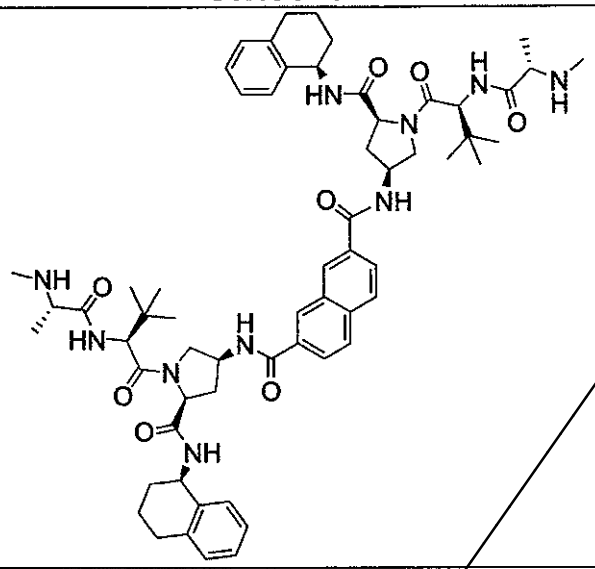
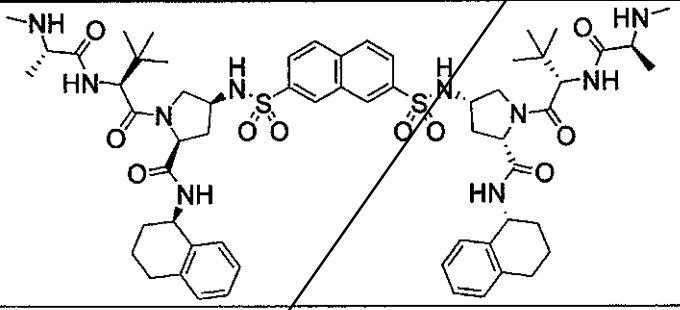
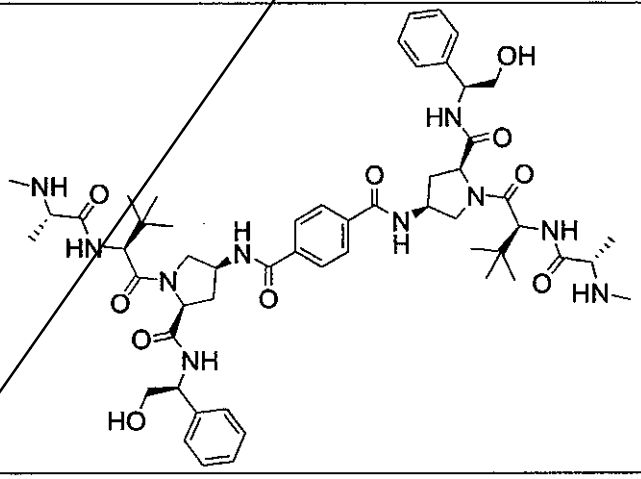
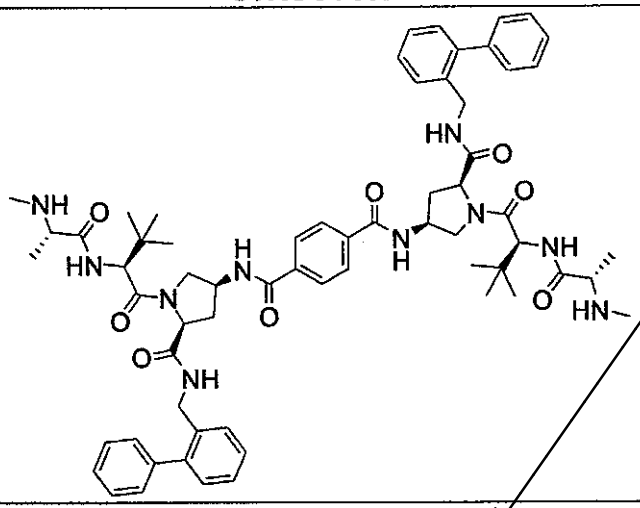
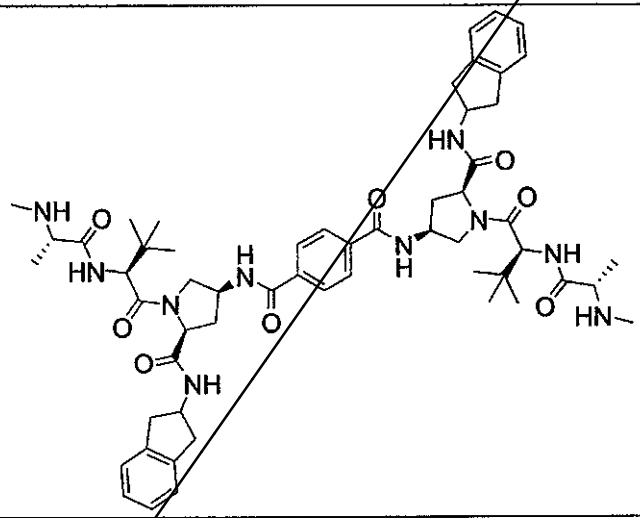
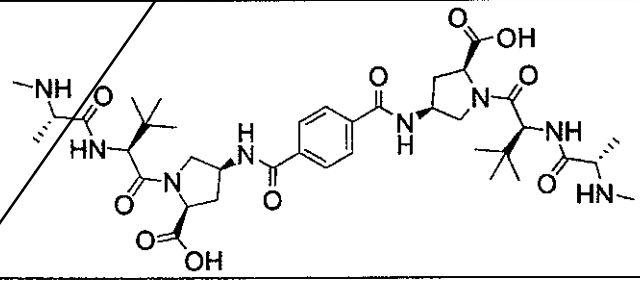
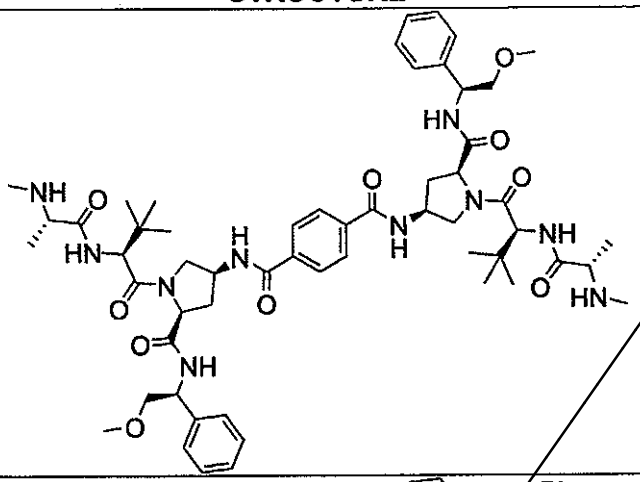
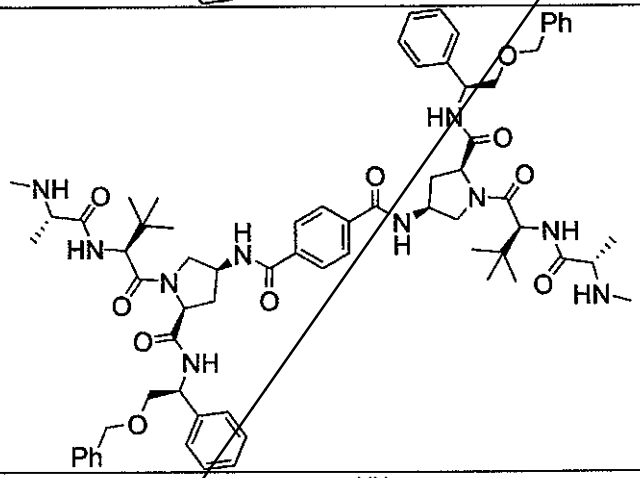
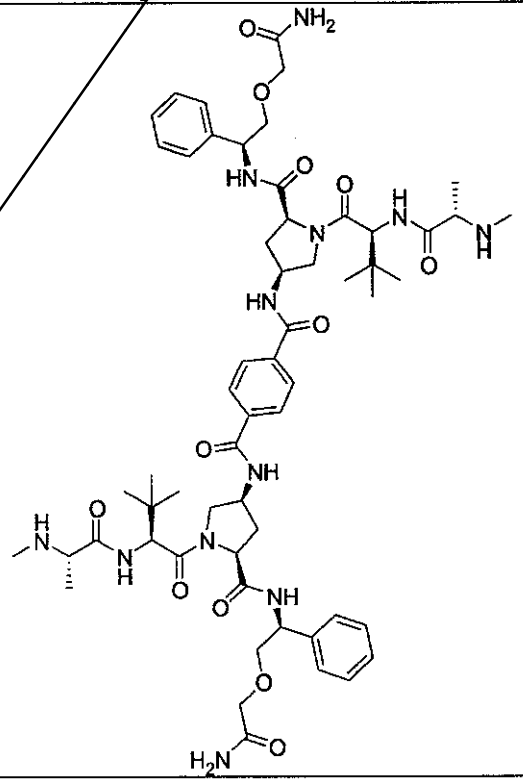
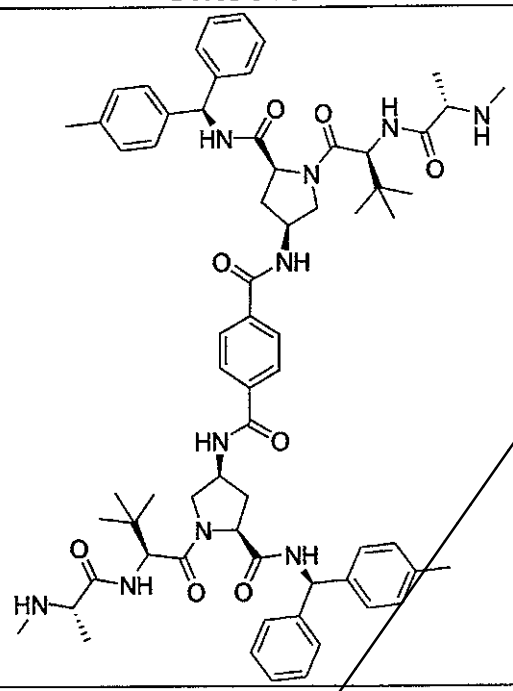
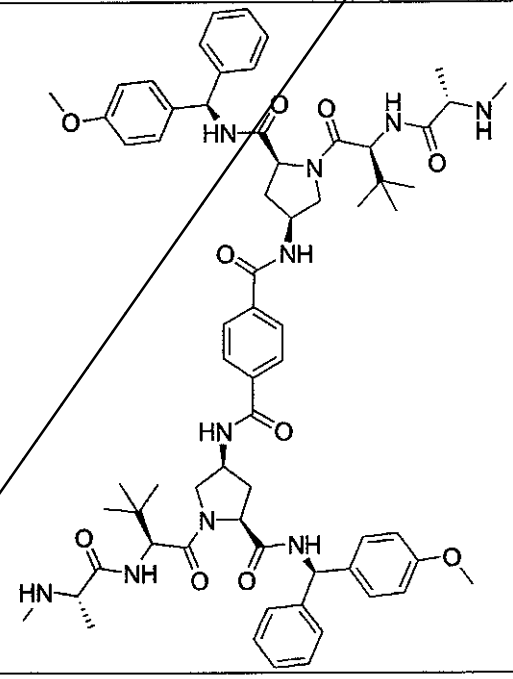
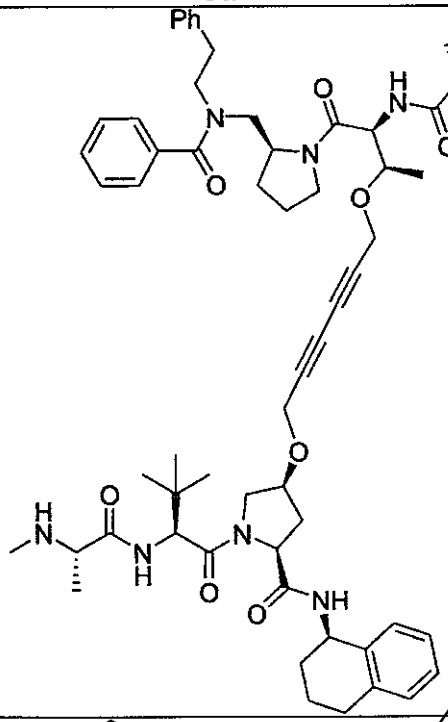
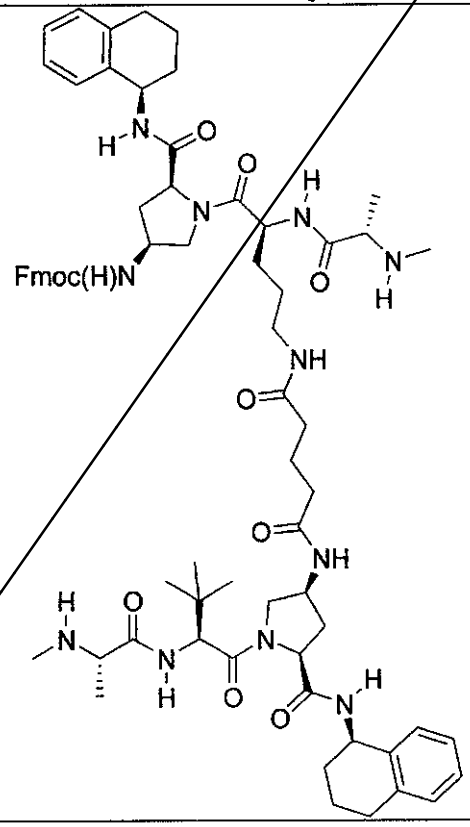
57	 ;
58	 ;
59	 ;

Cpd	STRUCTURE	
60		;
61		;
62		;
63		; and

Cpd	STRUCTURE
	
64	
65	

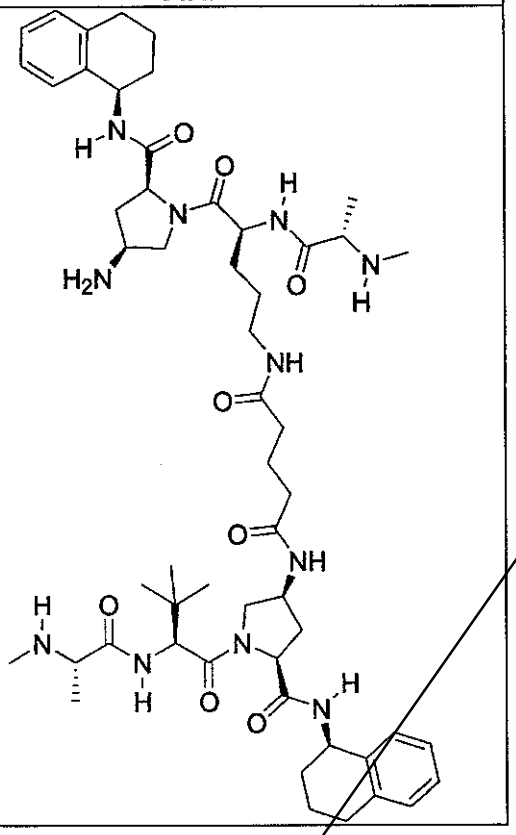
Cpd	STRUCTURE
66	
67	

71. A compound, according to claim 1, selected from the group consisting of:

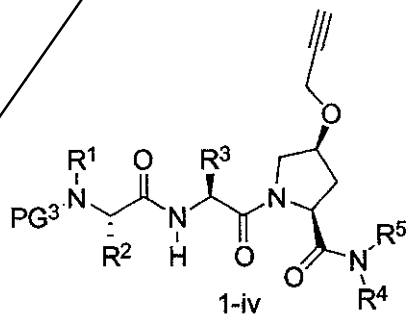
Cpd	Structure
6	
7	

;

; and

Cpd	Structure
8	

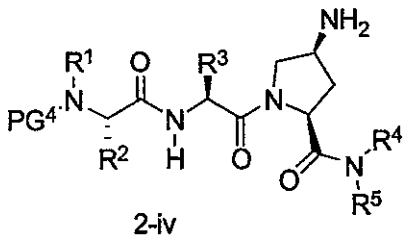
72. An intermediate compound represented by Formula 1-iv:



1-iv

wherein PG^3, R^1, R^2, R^3, A, and Q are as defined in claim 1.

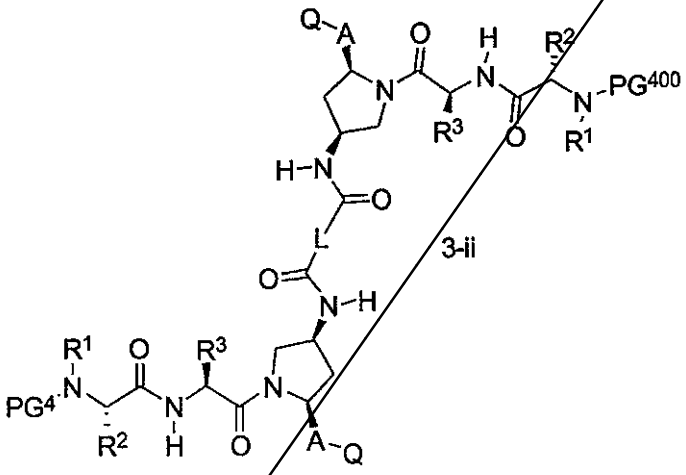
73. An intermediate compound represented by Formula 2-iv:



2-iv

wherein PG^4, R^1, R^2, R^3, A, and Q are as defined in claim 1.

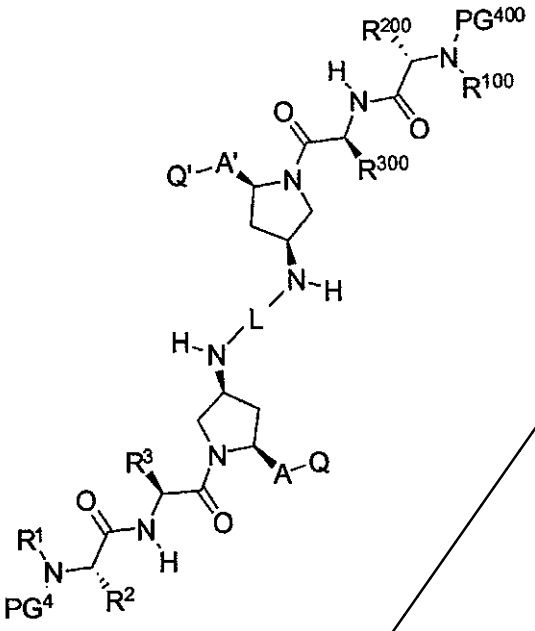
74. An intermediate compound represented by Formula 3-ii:



3-ii

wherein PG^4, PG^{400}, R^1, R^2, R^3, A and Q are as defined in claim 1, and L is $-(CH_2)_r$ -, -$(CH_2)_r$-Y-$(CH_2)_r$-, -alkyl-aryl-alkyl-, -alkyl-heteroaryl-alkyl-, cycloalkyl, aryl or heteroaryl.

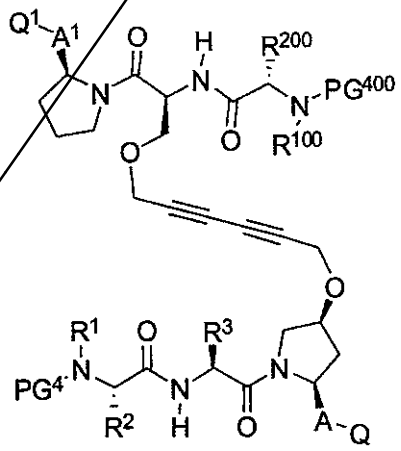
75. An intermediate compound represented by Formula 4-i:



4-i

wherein PG^4, PG^{400}, L, R^1, R^{100}, R^2, R^{200}, R^3, R^{300}, A, A^1, X, X^1, Q and Q^1 are as defined in claim 1.

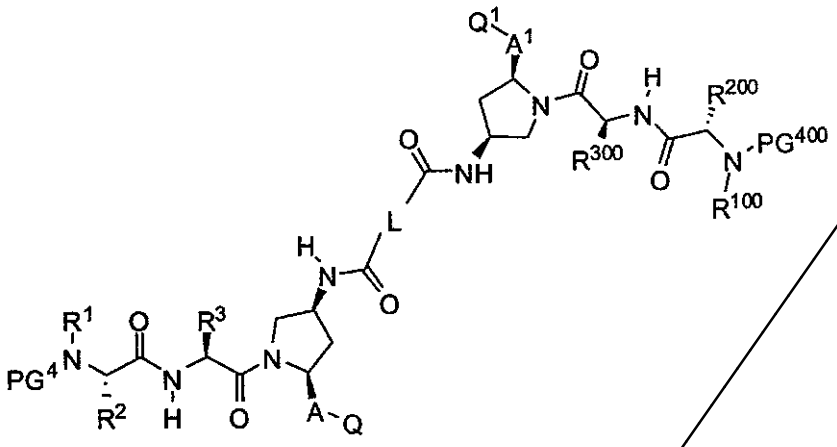
76. An intermediate compound represented by Formula 6-ii:



6-ii

wherein PG^4, PG^{400}, R^1, R^{100}, R^2, R^{200}, R^3, R^{300}, A, A^1, Q and Q^1 are as defined in claim 1.

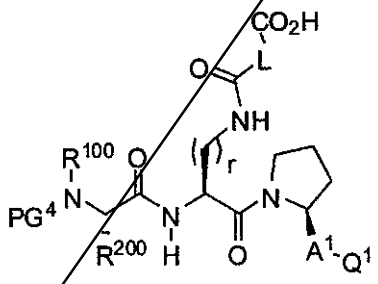
77. An intermediate compound represented by Formula 7-v:



7-v

wherein PG^4, PG^{400}, L, R^1, R^{100}, R^2, R^{200}, R^3, R^{300}, A, A^1, Q and Q^1 are as defined in claim 1.

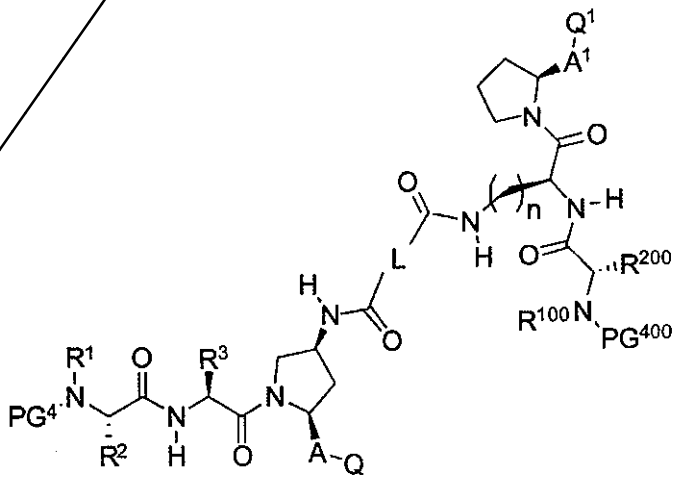
78. An intermediate compound represented by Formula 8-ii:



8-ii

wherein PG^4, r, L, R^{100}, R^{200}, A^1, and Q^1 are as defined in claim 1.

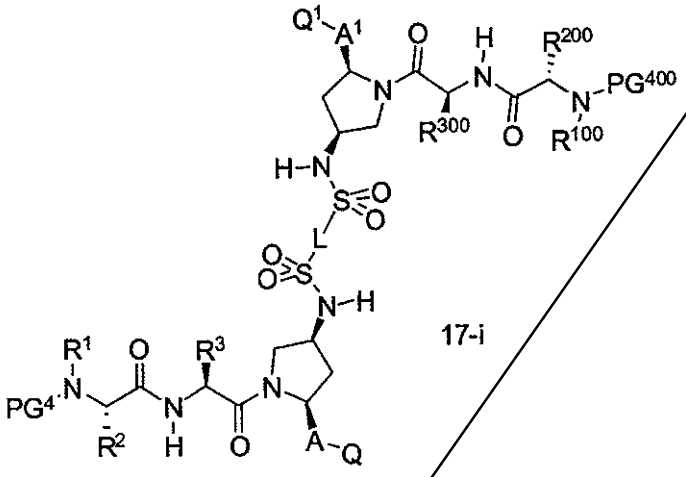
79. An intermediate compound represented by Formula 8-iii:



8-iii

wherein PG^4, PG^{400}, r, L, R^1, R^{100}, R^2, R^{200}, R^3, R^{300}, A, A^1, Q and Q^1 are as defined in claim 1.

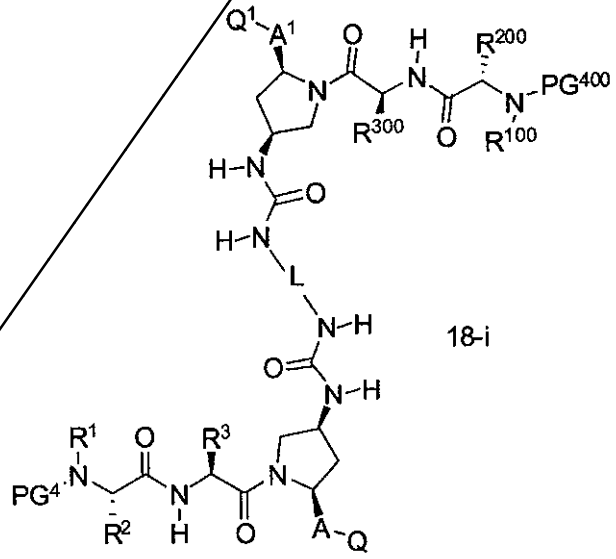
80. An intermediate compound represented by Formula 17-i:



17-i

wherein PG^4, PG^{400}, L, R^1, R^{100}, R^2, R^{200}, R^3, R^{300}, A, A^1, Q and Q^1 are as defined in claim 1.

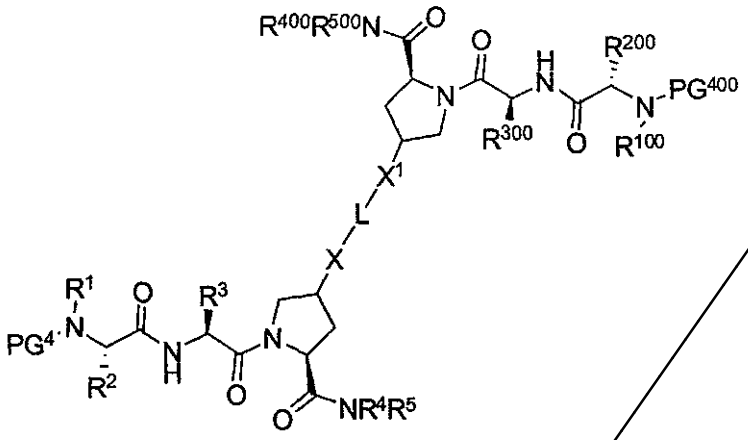
81. An intermediate compound represented by Formula 18-i:



18-i

wherein PG^4, PG^{400}, L, R^1, R^{100}, R^2, R^{200}, R^3, R^{300}, A, A^1, Q and Q^1 are as defined in claim 1.

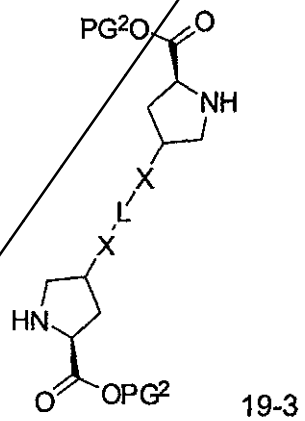
82. An intermediate compound represented by Formula 19-8:



19-8

wherein PG^4, PG^{400}, L, X, X^1, R^1, R^{100}, R^2, R^{200}, R^3, R^{300}, R^4, R^{400}, R^5 and R^{500} are as defined in claim 1.

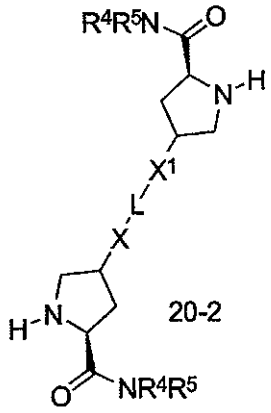
83. An intermediate compound represented by Formula 19-3:



19-3

wherein PG^2, L, and X are as defined in claim 1.

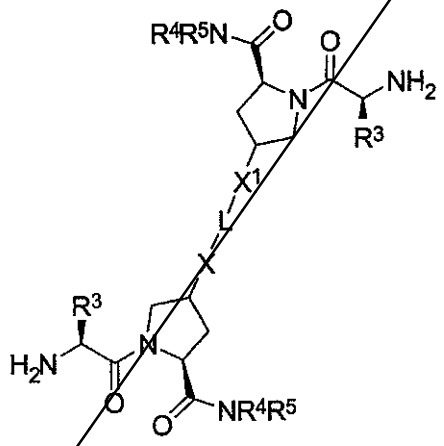
84. An intermediate compound represented by Formula 20-2:



20-2

wherein L, X, X^1, R^4 and R^5 are as defined in claim 1.

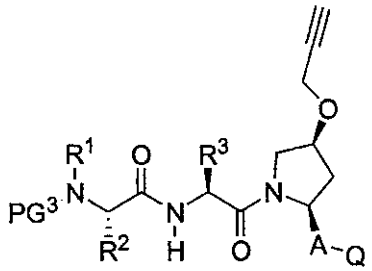
85. An intermediate compound represented by Formula 20-4:



wherein L, X, X^1, R^3, R^4, and R^5 are as defined in claim 1.

86. A process for producing compounds represented by Formula I, described hereinabove, the process comprising:

a) coupling two intermediates represented by Formula 1(iv):



1 (iv)

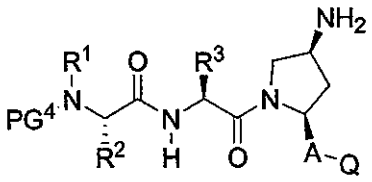
wherein PG^3, R^1, R^2, R^3, A, and Q are as defined herein,

in a solvent; and

b) removing the protecting groups so as to form compounds of Formula I.

87. A process for producing compounds represented by Formula I, described hereinabove, the process comprising:

a) coupling an intermediate represented by Formula 2(iv):



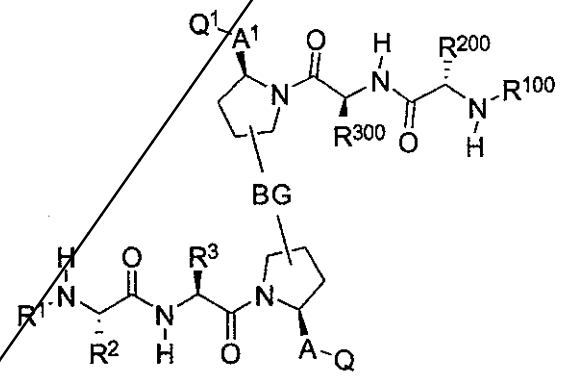
2(iv)

wherein PG^4 is a protecting group, and R^1, R^2, R^3, A, and Q are as defined herein.

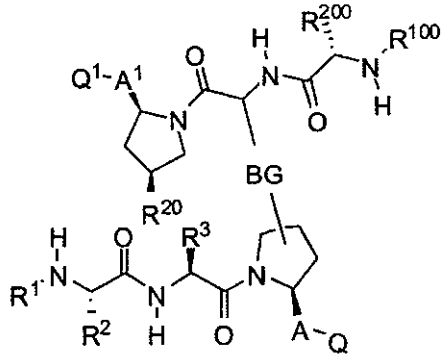
and an activated diacid (0.5 equiv) in a solvent; and

b) removing the protecting groups so as to form compounds of Formula I.

88. Use of a compound represented by Formula I or II:



I



II

or a salt thereof, for the manufacture of a medicament for treating or preventing a disease state characterized by insufficient apoptosis,

wherein:

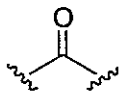
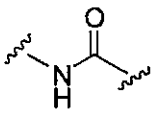
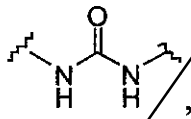
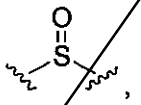
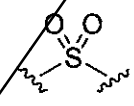
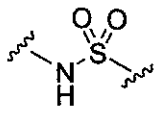
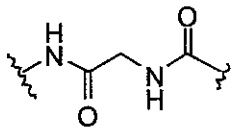
m is 0, 1 or 2;

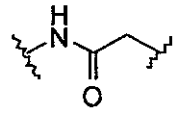
Y is NH, O or S;

BG is

1) –X-L-X^1–;

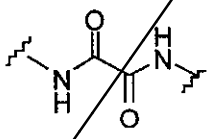
X and X^1 are independently selected from

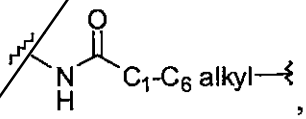
1) O,
2) NR^{13},
3) S,
4) -C_1-C_6 alkyl-,
5) -C_1-C_6 alkyl-O,
6) -C_1-C_6 alkyl-NR^{13}-,
7) -C_1-C_6 alkyl-S-,
8)  ,
9)  ,
10)  ,
11)  ,
12)  ,
13)  ,
14)  , or

15)  ;

L is selected from:

1) $-C_1$-C_{20} alkyl–,
2) $-C_2$-C_6 alkenyl–,
3) $-C_2$–C_4 alkynyl–,
4) $-C_3$-C_7 cycloalkyl–,
5) –aryl–,
6) –biphenyl–,
7) – heteroaryl–,
8) – heterocyclyl–,
9) $-C_1$-C_6 alkyl–(C_2-C_6 alkenyl)– C_1-C_6 alkyl–,
10) $-C_1$-C_6 alkyl–(C_2–C_4 alkynyl)–C_1-C_6 alkyl–
11) $-C_1$-C_6 alkyl–(C_3-C_7 cycloalkyl)–C_1-C_6 alkyl–,
12) $-C_1$-C_6 alkyl– aryl–C_1-C_6 alkyl–,
13) $-C_1$-C_6 alkyl–biphenyl–C_1-C_6 alkyl–,
14) $-C_1$-C_6 alkyl–heteroaryl–C_1-C_6 alkyl–,
15) $-C_1$-C_6 alkyl-heterocycyl–C_1-C_6 alkyl–,
16) $-C_1$-C_6 alkyl-Y-C_1-C_6 alkyl–,
17) –aryl-Y-aryl–,
18) –heteroaryl-Y-heteroaryl–,
19) –heterocyclyl-Y-heterocyclyl–,

20)  , or

21)  ,

wherein the alkyl, alkenyl, alkynyl and cycloalkyl are optionally substituted with one or more R^6 substituents, and the aryl, biphenyl, heteroaryl, and heterocyclyl are optionally substituted with one or more R^{10} substituents;

Q and Q^1 are independently selected from

1) NR^4R^5,

2) OR^{11}, or

3) $S(O)_mR^{11}$; or

Q and Q^1 are independently selected from

1) aryl, or

2) heteroaryl, the aryl and the heteroaryl being optionally substituted with one or more R^{10} substituents;

A and A^1 are independently selected from

1) $-CH_2-$,

2) $-CH_2CH_2-$,

3) $-CH(C_1-C_6$ alkyl$)-$,

4) $-CH(C_3-C_7$ cycloalkyl$)-$,

5) $-C_3-C_7$ cycloalkyl$-$,

6) $-CH(C_1-C_6$ alkyl$-C_3-C_7$ cycloalkyl$)-$,

7) $-C(O)-$, or

8) $-C(O)OR^{13}$;

R^1 and R^{100} are independently selected from

1) H, or

2) C_1-C_6 alkyl optionally substituted with one or more R^6 substituents;

R^2 and R^{200} are independently selected from

1) H, or

2) C_1-C_6 alkyl optionally substituted with one or more R^6 substituents;

R^3 and R^{300} are independently C_1-C_6 alkyl optionally substituted with one or more R^6 substituents;

R^4 and R^5 are each independently selected from

1) H,

2) haloalkyl,

3) $\leftarrow C_1-C_6$ alkyl,

4) $\leftarrow C_2-C_6$ alkenyl,

5) ←C_2-C_4 alkynyl,
6) ←C_3–C_7 cycloalkyl,
7) ←C_3-C_7 cycloalkenyl,
8) ←aryl,
9) ←heteroaryl,
10) ←heterocyclyl,
11) ←heterobicyclyl,
12) ←C(O)-R^{11},
13) ←C(O)O-R^{11},
14) ←C(=Y)NR^8R^9, or
15) ←$S(O)_2$-R^{11},

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl is optionally substituted with one or more R^6 substituents; and wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl is optionally substituted with one or more R^{10} substituents;

R^6 is

1) halogen,
2) NO_2,
3) CN,
4) haloalkyl,
5) C_1–C_6 alkyl,
6) C_2-C_6 alkenyl,
7) C_2-C_4 alkynyl,
8) C_3–C_7 cycloalkyl,
9) C_3-C_7 cycloalkenyl,
10) aryl,
11) heteroaryl,
12) heterocyclyl,
13) heterobicyclyl,
14) OR^7,
15) $S(O)_mR^7$,
16) NR^8R^9 ,
17) $NR^8S(O)_2R^{11}$,
18) COR^7,
19) $C(O)OR^7$,

20) $CONR^8R^9$,
21) $S(O)_2NR^8R^9$
22) $OC(O)R^7$,
23) $OC(O)Y\text{-}R^{11}$,
24) $SC(O)R^7$, or
25) $NC(Y)NR^8R^9$,

wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl is optionally substituted with one or more R^{10} substituents;

R^7 is

1) H,
2) haloalkyl,
3) C_1–C_6 alkyl,
4) C_2-C_6 alkenyl,
5) C_2-C_4 alkynyl,
6) C_3–C_7 cycloalkyl,
7) C_3-C_7 cycloalkenyl,
8) aryl,
9) heteroaryl,
10) heterocyclyl,
11) heterobicyclyl,
12) $R^8R^9NC(=Y)$, or
13) C_1-C_6 alkyl-C_2-C_4 alkenyl, or
14) C_1-C_6 alkyl-C_2-C_4 alkynyl,

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl is optionally substituted with one or more R^6 substituents; and wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl is optionally substituted with one or more R^{10} substituents;

R^8 and R^9 are each independently

1) H,
2) haloalkyl,
3) C_1–C_6 alkyl,
4) C_2-C_6 alkenyl,
5) C_2-C_4 alkynyl,
6) C_3–C_7 cycloalkyl,

7) C_3-C_7 cycloalkenyl,
8) aryl,
9) heteroaryl,
10) heterocyclyl,
11) heterobicyclyl,
12) $C(O)R^{11}$,
13) $C(O)Y$-R^{11}, or
14) $S(O)_2$-R^{11},

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl is optionally substituted with one or more R^6 substituents; and wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl is optionally substituted with one or more R^{10} substituents;

or R^8 and R^9 together with the nitrogen atom to which they are bonded form a five, six or seven membered heterocyclic ring optionally substituted with one or more R^6 substituents;

R^{10} is

1) halogen,
2) NO_2,
3) CN,
4) $B(OR^{13})(OR^{14})$,
5) C_1-C_6 alkyl,
6) C_2-C_6 alkenyl,
7) C_2-C_4 alkynyl,
8) C_3-C_7 cycloalkyl,
9) C_3-C_7 cycloalkenyl,
10) haloalkyl,
11) OR^7,
12) NR^8R^9,
13) SR^7,
14) COR^7,
15) $C(O)O\,R^7$,
16) $S(O)_mR^7$,
17) $CONR^8R^9$,
18) $S(O)_2NR^8R^9$,
19) aryl,

20) heteroaryl,
21) heterocyclyl, or
22) heterobicyclyl,

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more R^6 substituents;

R^{11} is

1) haloalkyl,
2) C_1–C_6 alkyl,
3) C_2-C_6 alkenyl,
4) C_2-C_4 alkynyl,
5) C_3–C_7 cycloalkyl,
6) C_3-C_7 cycloalkenyl,
7) aryl,
8) heteroaryl,
9) heterocyclyl, or
10) heterobicyclyl,

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl is optionally substituted with one or more R^6 substituents; and wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl is optionally substituted with one or more R^{10} substituents;

R^{12} is

1) haloalkyl,
2) C_1–C_6 alkyl,
3) C_2-C_6 alkenyl,
4) C_2-C_4 alkynyl,
5) C_3–C_7 cycloalkyl,
6) C_3-C_7 cycloalkenyl,
7) aryl,
8) heteroaryl,
9) heterocyclyl,
10) heterobicyclyl,
11) C(O)-R^{11},
12) C(O)O-R^{11},
13) C(O)NR^8R^9,

14) $S(O)_m$-R^{11}, or

15) $C(=Y)NR^8R^9$,

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl is optionally substituted with one or more R^6 substituents; and wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl is optionally substituted with one or more R^{10} substituents;

R^{13} and R^{14} are each independently

1) H, or

2) C_1-C_6 alkyl; or

R^{13} and R^{14} are combined to form a heterocyclic ring or a heterobicyclyl ring; and

R^{20} is

1) H,

2) NH_2, or

3)NHFmoc.

89. Use of the compound of any one of claims 1 to 71 for the manufacture of a medicament for treating or preventing a disease state characterized by insufficient apoptosis.

90. Use, according to claims 88 or 89, in which the disease state is cancer.

91. Use of the compound of any one of claims 1 to 71 for the manufacture of a medicament for treating or preventing a proliferative disorder.

92. Use of the compound of any one of claims 1 to 71 in combination with an agent for the manufacture of a medicament for treating or preventing a proliferative disorder, wherein the agent is selected from:

a) an estrogen receptor modulator,

b) an androgen receptor modulator,

c) retinoid receptor modulator,

d) a cytotoxic agent,

e) an antiproliferative agent,

f) a prenyl-protein transferase inhibitor,

g) an HMG-CoA reductase inhibitor,

h) an HIV protease inhibitor,

i) a reverse transcriptase inhibitor,

k) an angiogenesis inhibitor,

l) a PPAR-.γ agonist,

m) a PPAR-.δ. agonist,

n) an inhibitor of inherent multidrug resistance,

o) an anti-emetic agent,

p) an agent useful in the treatment of anemia,

q) agents useful in the treatment of neutropenia,

r) an immunologic-enhancing drug.

s) a proteasome inhibitor;

t) an HDAC inhibitor;'

u) an inhibitor of the chemotrypsin-like activity in the proteasome; or

v) E3 ligase inhibitors;

w) a modulator of the immune system such as, but not limited to, interferon-alpha, Bacillus Calmette-Guerin (BCG), and ionizing radition (UVB) that can induce the release of cytokines, such as the interleukins, TNF, or induce release of death receptor ligands such as TRAIL;

x) a modulator of death receptors TRAIL and TRAIL agonists such as the humanized antibodies HGS-ETR1 and HGS-ETR2;

or in combination or sequentially with radiation therapy.

93. Use of the compound of any one of claims 1 to 71 in combination with a death receptor agonist for the manufacture of a medicament the treatment or prevention of a proliferative disorder in a subject.

94. Use, according to claim 93, in which the death receptor agonist is TRAIL.

95. Use, according to claim 93, in which the death receptor agonist is a TRAIL antibody.

96. Use, according to claim 93, in which the death receptor agonist is in an amount that produces a synergistic effect.

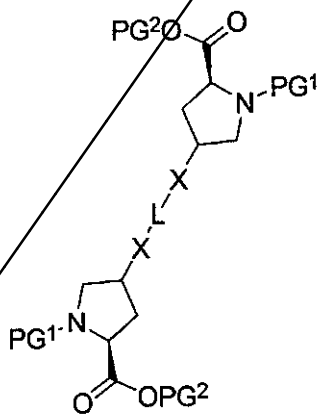
97. Use, according to claims 92 or 93, in which the proliferative disorder is cancer.

98. A pharmaceutical composition comprising the compound of any one of claims 1 to 71, mixed with a pharmaceutically acceptable carrier, diluent or excipient, for treating or preventing a disease state characterized by insufficient apoptosis.

99. A pharmaceutical composition comprising the compound of any one of claims 1 to 71 in combination with any compound that increases the circulating level of one or more death receptor agonists for preventing or treating a proliferative disorder.

100. A method of preparing a pharmaceutical composition, the method comprising: mixing the compound of any one of claims 1 to 71, with a pharmaceutically acceptable carrier, diluent or excipient.

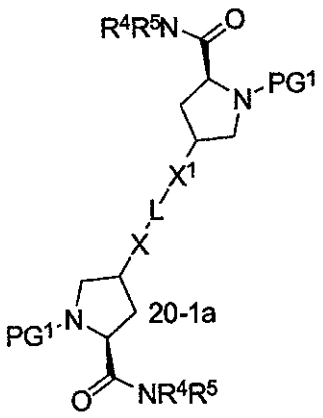
101. An intermediate compound represented by Formula 19-2:



19-2

wherein PG^1, PG^2, L, X are as defined herein

102. An intermediate compound represented by Formula 20-1a:



wherein PG^1, L, X, X^1, R^4 and R^5 are as defined herein.

103. A method for the preparation of a pharmaceutically acceptable salt of compound of Formula I and II, by the treatment of a compound of Formula I or II with 1 to 2 equiv of a pharmaceutically acceptable acid, as defined herein.

104. A method of detecting loss of function or suppression of IAPs in vivo, the method comprising: a) administering to a subject, a therapeutically effective amount of a pharmaceutical composition, according to claim 88; b) isolating a tissue sample from the subject; and c) detecting a loss of function or suppression of IAPs from the sample.

105 The method, according to claim 104, wherein the IAP is XIAP.

106. The method, according to claim 104, wherein the IAP is c-IAP1.

107. The method, according to claim 104, wherein the IAP is c-IAP2.

108. The method, according to claim 104, wherein the tissue is a tumor sample.

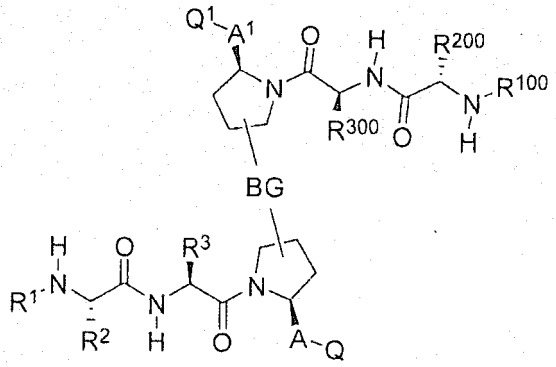
109. The method according to claim 104, wherein the tissue is normal tissue.

110. The method, according to claim 104, wherein the tissue is isolated from the hematopeotic system.

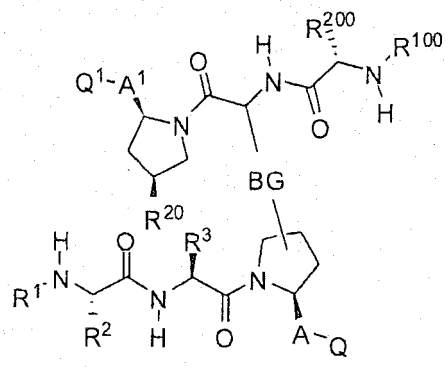
111. The method, according to claim 104, wherein mononuclear cells are isolated from blood, and IAP suppression or loss is measured in the mononeclear cells.

CLAIMS

1. A compound represented by Formula I or II



I



II

or an enantiomer, diastereoisomer or tautomer thereof,

or a salt thereof;

wherein

m is 0, 1 or 2;

Y is NH, O or S;

BG is

–X-L-X^1–;

X and X^1 are independently

1) O,

2) NR^{13},

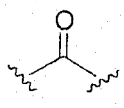
3) S,

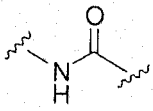
4) -C_1-C_6 alkyl-,

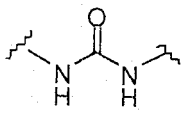
5) -C_1-C_6 alkyl-O,

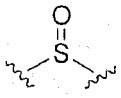
6) -C_1-C_6 alkyl-NR^{13}-,

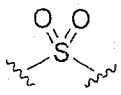
7) -C_1-C_6 alkyl-S-,

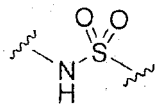
8)  ,

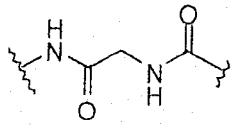
9)  ,

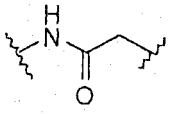
10)  ,

11)  ,

12)  ,

13)  ,

14)  , or

15)  ;

L is:

1) –C_1-C_{20} alkyl–,

2) –C_2-C_6 alkenyl–,

3) –C_2–C_4 alkynyl–,

4) –C_3-C_7 cycloalkyl–,

5) –aryl–,

6) –biphenyl–,

7) – heteroaryl–,

8) – heterocyclyl–,

9) –C_1-C_6 alkyl–(C_2-C_6 alkenyl)–C_1-C_6 alkyl–,

10) $-C_1$-C_6 alkyl–(C_2–C_4 alkynyl)–C_1-C_6 alkyl–

11) $-C_1$-C_6 alkyl–(C_3-C_7 cycloalkyl)–C_1-C_6 alkyl–,

12) $-C_1$-C_6 alkyl– aryl–C_1-C_6 alkyl–,

13) $-C_1$-C_6 alkyl–biphenyl–C_1-C_6 alkyl–,

14) $-C_1$-C_6 alkyl–heteroaryl–C_1-C_6 alkyl–,

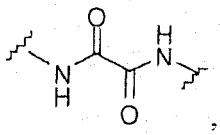
15) $-C_1$-C_6 alkyl-heterocycyl–C_1-C_6 alkyl–,

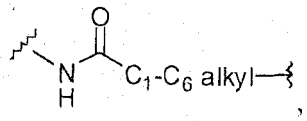
16) $-C_1$-C_6 alkyl-Y-C_1-C_6 alkyl–,

17) –aryl-Y-aryl–,

18) –heteroaryl-Y-heteroaryl–,

19) –heterocyclyl-Y-heterocyclyl–,

20)  , or

21)  ,

wherein the alkyl, alkenyl, alkynyl and cycloalkyl are optionally substituted with one or more R^6 substituents, and the aryl, biphenyl, heteroaryl, and heterocyclyl are optionally substituted with one or more R^{10} substituents;

Q and Q^1 are independently

1) $-NR^4R^5$,

2) $-OR^{11}$, or

3) $-S(O)_mR^{11}$; or

Q and Q^1 are independently

1) aryl, or

2) heteroaryl, the aryl and the heteroaryl being optionally substituted with one or more R^{10} substituents;

A and A^1 are independently

1) $-CH_2-$,

2) $-CH_2CH_2-$,

3) $-CH(C_1-C_6$ alkyl)–,

4) –CH(C_3–C_7 cycloalkyl)–,

5) –C_3–C_7 cycloalkyl–,

6) –CH(C_1–C_6 alkyl–C_3–C_7 cycloalkyl)–, or

7) –C(O)–;

R^1 and R^{100} are independently

1) H, or

2) C_1–C_6 alkyl optionally substituted with one or more R^6 substituents;

R^2 and R^{200} are independently

1) H, or

2) C_1–C_6 alkyl optionally substituted with one or more R^6 substituents;

R^3 and R^{300} are independently C_1–C_6 alkyl optionally substituted with one or more R^6 substituents;

R^4 and R^5 are each independently

1) H,

2) haloalkyl,

3) C_1–C_6 alkyl,

4) C_2-C_6 alkenyl,

5) C_2-C_4 alkynyl,

6) C_3–C_7 cycloalkyl,

7) C_3-C_7 cycloalkenyl,

8) aryl,

9) heteroaryl,

10) heterocyclyl,

11) heterobicyclyl,

12) -C(O)-R^{11},

13) -C(O)O-R^{11},

14) -C(=Y)NR^8R^9, or

15) -$S(O)_2$-R^{11},

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, and cycloalkenyl are optionally substituted with one or more R^6 substituents; and wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl are optionally substituted with one or more R^{10} substituents;

R^6 is

1) halogen,
2) $-NO_2$,
3) -CN,
4) haloalkyl,
5) C_1–C_6 alkyl,
6) C_2-C_6 alkenyl,
7) C_2-C_4 alkynyl,
8) C_3–C_7 cycloalkyl,
9) C_3-C_7 cycloalkenyl,
10) aryl,
11) heteroaryl,
12) heterocyclyl,
13) heterobicyclyl,
14)-OR^7,
15) -$S(O)_mR^7$,
16) -NR^8R^9 ,
17) -$NR^8S(O)_2R^{11}$,
18) -COR^7,
19) -$C(O)OR^7$,
20) -$CONR^8R^9$,
21) -$S(O)_2NR^8R^9$
22) -$OC(O)R^7$,
23) -$OC(O)Y$-R^{11},
24) -$SC(O)R^7$, or
25) -$NC(Y)NR^8R^9$,

wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl are optionally substituted with one or more R^{10} substituents;

R^7 is

1) H,

2) haloalkyl,

3) C_1–C_6 alkyl,

4) C_2-C_6 alkenyl,

5) C_2-C_4 alkynyl,

6) C_3–C_7 cycloalkyl,

7) C_3-C_7 cycloalkenyl,

8) aryl,

9) heteroaryl,

10) heterocyclyl,

11) heterobicyclyl,

12) -C(=Y)NR^8R^9,

13) C_1-C_6 alkyl-C_2-C_4 alkenyl, or

14) C_1-C_6 alkyl-C_2-C_4 alkynyl,

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, and cycloalkenyl are optionally substituted with one or more R^6 substituents; and wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl are optionally substituted with one or more R^{10} substituents;

R^8 and R^9 are each independently

1) H,

2) haloalkyl,

3) C_1–C_6 alkyl,

4) C_2-C_6 alkenyl,

5) C_2-C_4 alkynyl,

6) C_3–C_7 cycloalkyl,

7) C_3-C_7 cycloalkenyl,

8) aryl,

9) heteroaryl,

10) heterocyclyl,

11) heterobicyclyl,

12) -C(O)R^{11},

13) -C(O)Y-R^{11}, or

14) -$S(O)_2$-R^{11},

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, and cycloalkenyl are optionally substituted with one or more R^6 substituents; and wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl are optionally substituted with one or more R^{10} substituents;

or R^8 and R^9 together with the nitrogen atom to which they are bonded form a five, six or seven membered heterocyclic ring optionally substituted with one or more R^6 substituents;

R^{10} is

1) halogen,
2) $-NO_2$,
3) -CN,
4) $-B(OR^{13})(OR^{14})$,
5) C_1-C_6 alkyl,
6) C_2-C_6 alkenyl,
7) C_2-C_4 alkynyl,
8) C_3-C_7 cycloalkyl,
9) C_3-C_7 cycloalkenyl,
10) haloalkyl,
11) $-OR^7$,
12) $-NR^8R^9$,
13) $-SR^7$,
14) $-COR^7$,
15) $-C(O)O\,R^7$,
16) $-S(O)_mR^7$,
17) $-CONR^8R^9$,
18) $-S(O)_2NR^8R^9$,
19) aryl,
20) heteroaryl,
21) heterocyclyl, or
22) heterobicyclyl,

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, and cycloalkenyl are optionally substituted with one or more R^6 substituents;

R^{11} is

1) haloalkyl,
2) C_1–C_6 alkyl,
3) C_2-C_6 alkenyl,
4) C_2-C_4 alkynyl,
5) C_3–C_7 cycloalkyl,
6) C_3-C_7 cycloalkenyl,
7) aryl,
8) heteroaryl,
9) heterocyclyl, or
10) heterobicyclyl,

wherein the alkyl, alkenyl, alkynyl, cycloalkyl, and cycloalkenyl are optionally substituted with one or more R^6 substituents; and wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl are optionally substituted with one or more R^{10} substituents;

R^{13} and R^{14} are each independently
1) H, or
2) C_1-C_6 alkyl; or

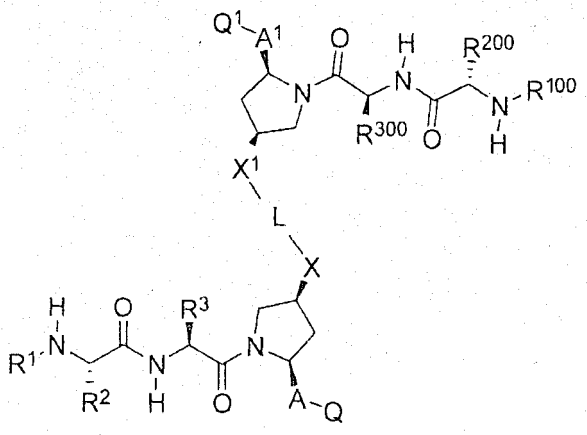
R^{13} and R^{14} are combined to form a heterocyclic ring or a heterobicyclyl ring;

R^{20} is
1) H,
2) -NH_2, or
3) -NHFmoc.

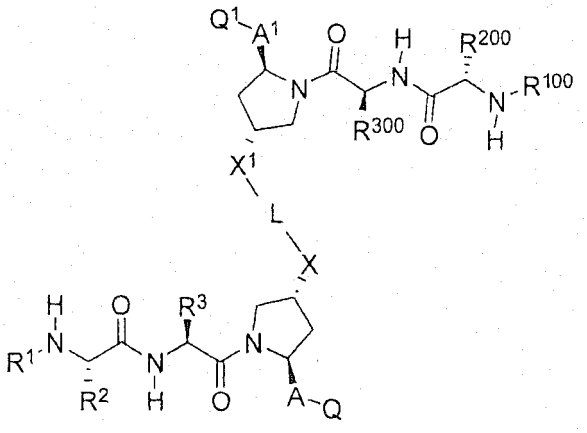
2. The compound, according to claim 1, in which A and A^1 are both CH_2.

3. The compound, according to claim 1, in which A and A^1 are both C=O.

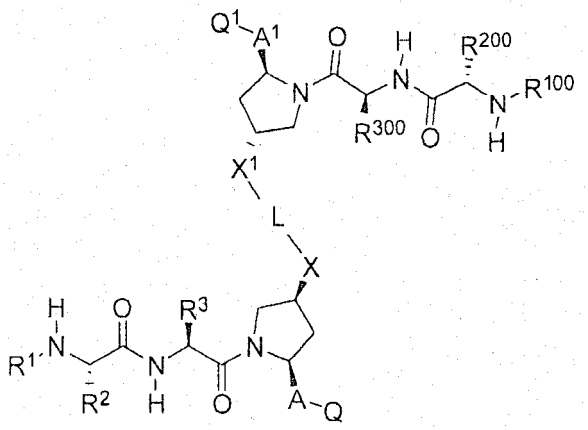
4. The compound, according to claim 1, of Formula 1a through 1c:



1a



1b



1c

wherein L, X, X^1, A, A^1, Q, Q^1, R^1, R^{100}, R^2, R^{200}, R^3, and R^{300} are as defined in claim 1.

5. The compound, according to any one of claims 1 to 4, in which X and X^1 are independently

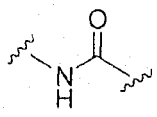
1) O,

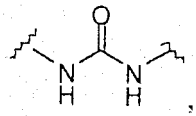
2) NR^{13},

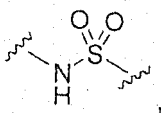
3) S,

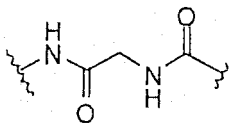
4) -C_1-C_6 alkyl-O-,

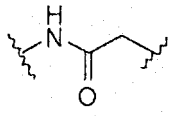
5) -C_1-C_6 alkyl,

6)  ,

7)  ,

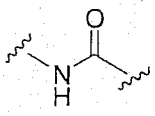
8)  ,

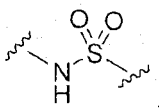
9)  , or

10)  .

6. The compound, according to claim 5, in which X and X^1 are independently:

1) O,

2)  , or

3)  .

7. The compound, according to any one of claims 1 to 6, in which L is selected from:

1) –C_1-C_{20} alkyl–,

2) –C_3-C_7 cycloalkyl–,

3) –aryl–,

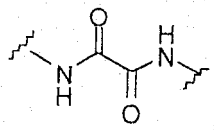
4) –biphenyl–,

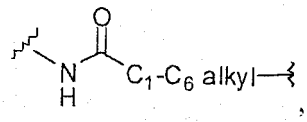
5) – heteroaryl–,

6) –C_1-C_6 alkyl–(C_2–C_4 alkynyl)–C_1-C_6 alkyl–

7) –C_1-C_6 alkyl– aryl–C_1-C_6 alkyl–,

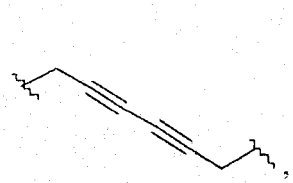
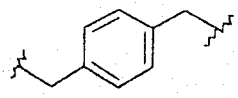
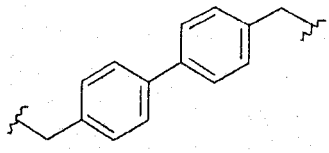
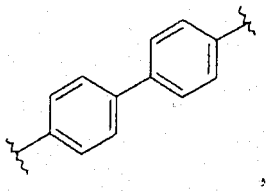
8) –aryl-Y-aryl–,

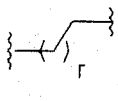
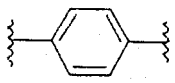
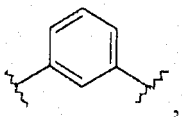
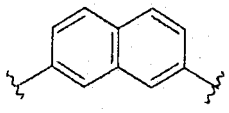
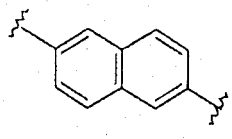
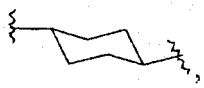
9)  , or

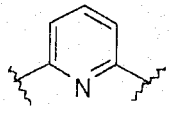
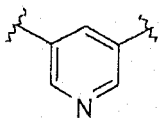
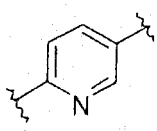
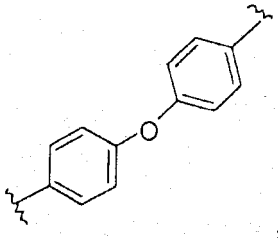
10)  ,

wherein the alkyl and cycloalkyl are optionally substituted with one or more R^6 substituents, and the aryl, biphenyl and heteroaryl are optionally substituted with one or more R^{10} substituents.

8. The compound, according to claim 7, in which L is selected from the group consisting of:

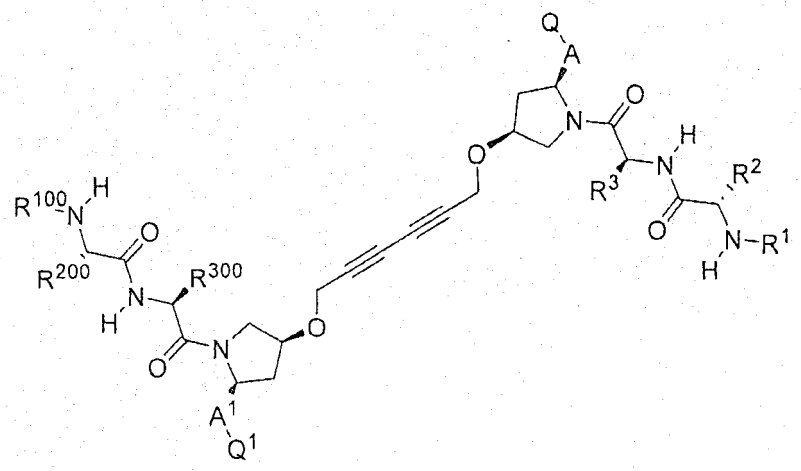
 ,  ,  ,  ,

 ,  ,  ,  ,  ,  ,

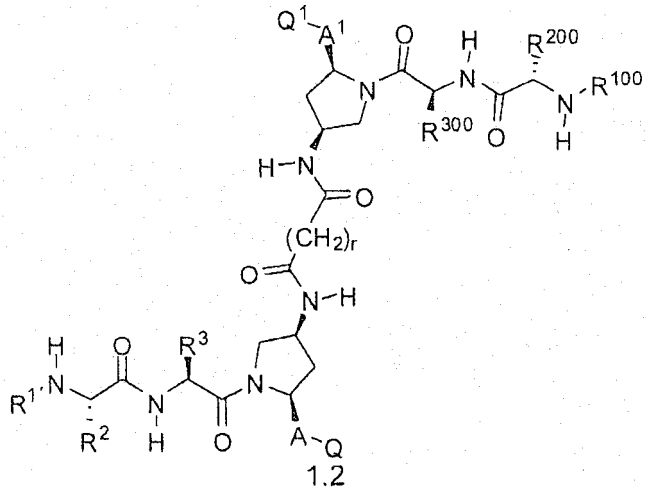
 ,  ,  , and  ,

wherein r is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

9. The compound, according to claim 1, of Formula 1.1 through 1.18:



1.1



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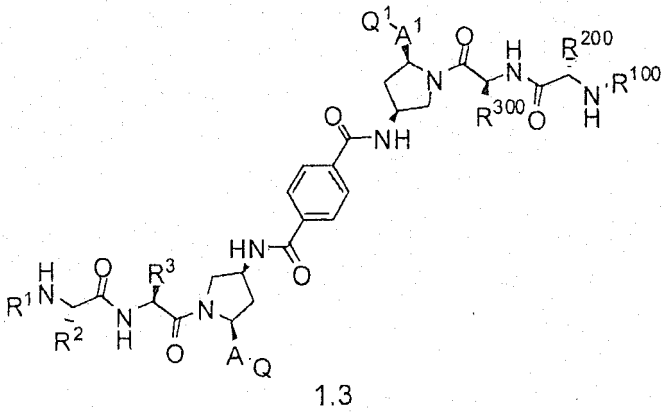

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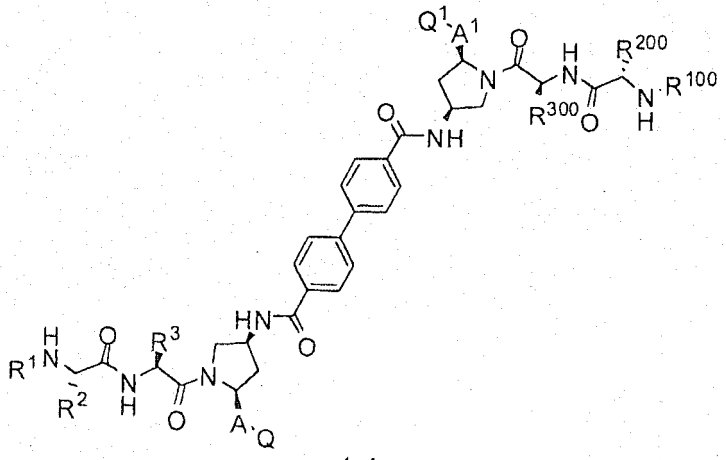
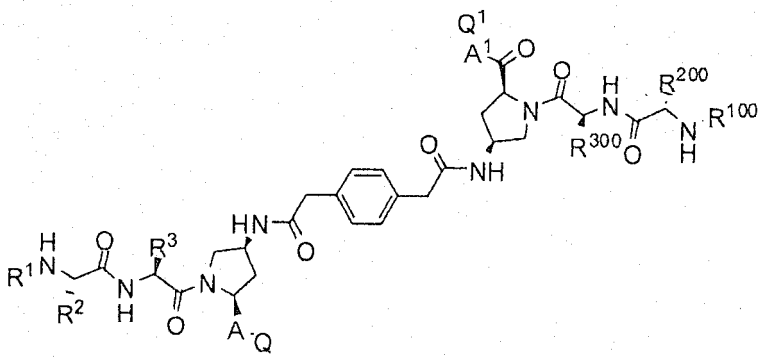
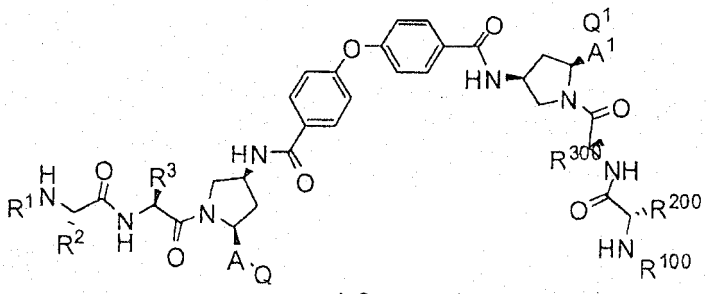


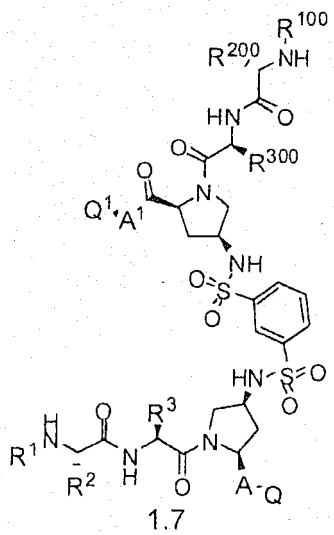
1.4



1.5



1.6



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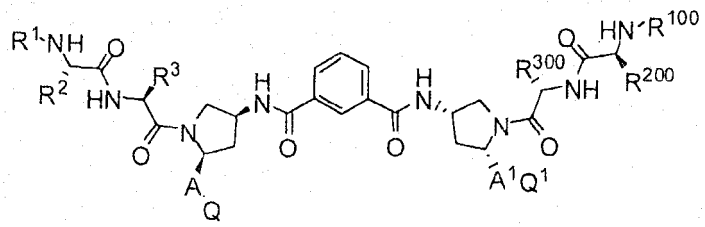
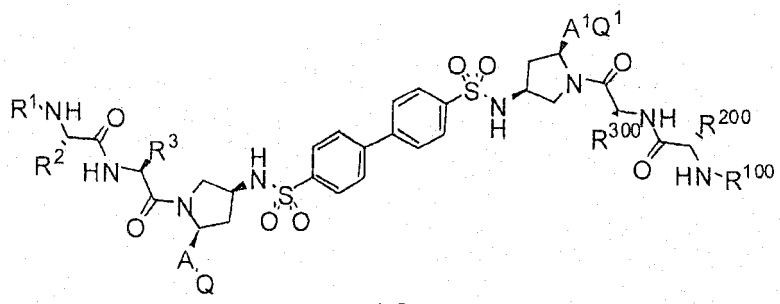
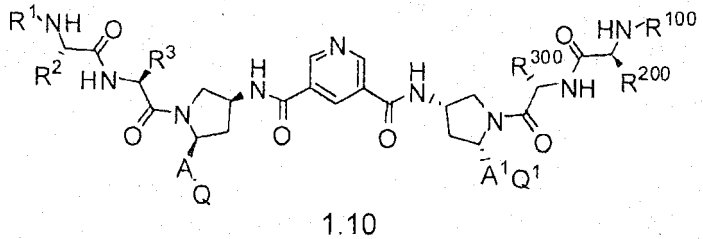


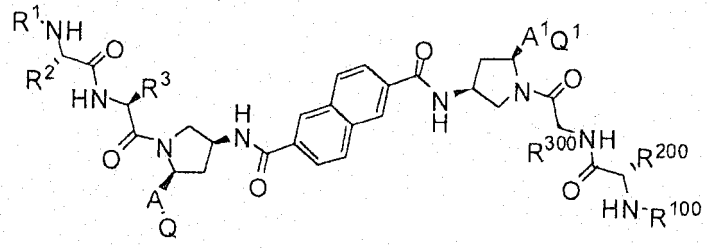
1.8



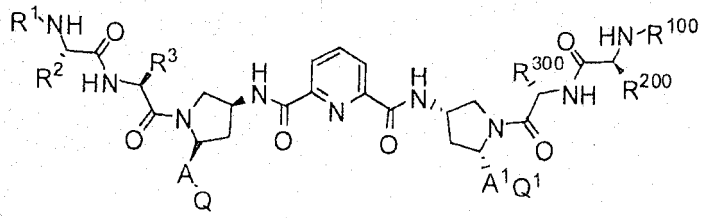
1.9



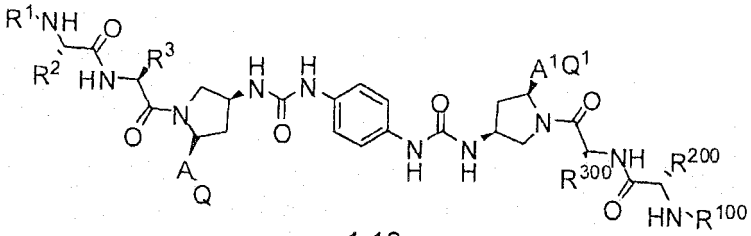
1.10



1.11



1.12



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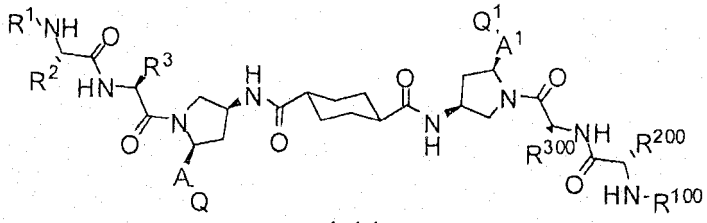

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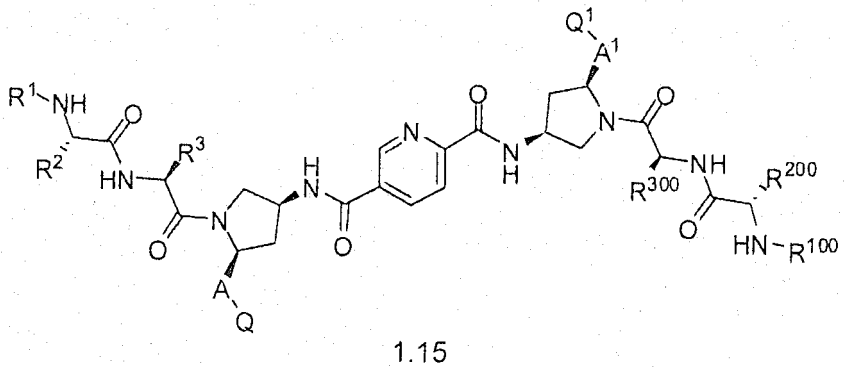
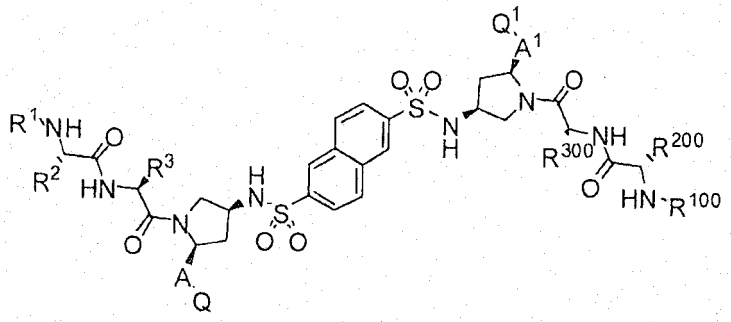
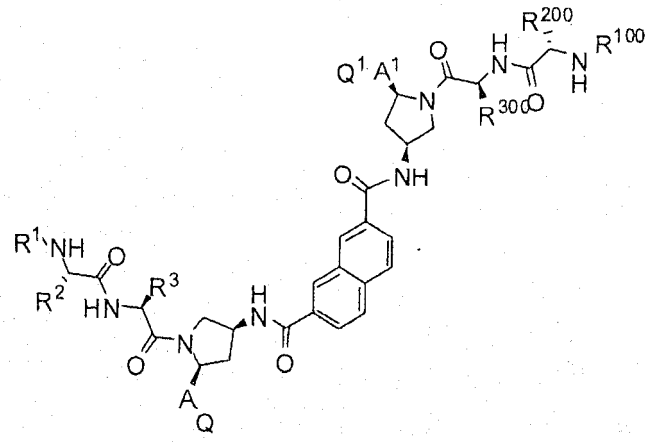


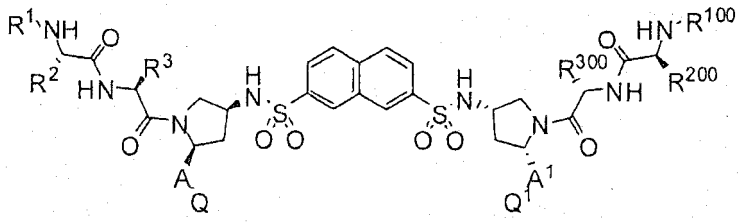
1.15



1.16



1.17



1.18

wherein r is an integer of 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10, and A, A^1, Q, Q^1, R^1, R^{100}, R^2, R^{200}, R^3 and R^{300} are as defined in claim 1.

10. The compound, according to any one of claims 1 to 9, in which R^1 and R^{100} are both C_1-C_6 alkyl.

11. The compound, according to claim 10, in which R^1 and R^{100} are both CH_3.

12. The compound, according to any one of claims 1 to 11, in which R^2 and R^{200} are both CH_3.

13. The compound, according to any one of claims 1 to 12, in which R^3 and R^{300} are both C_1-C_6 alkyl.

14. The compound, according to claim 13, in which R^3 and R^{300} are both $C(CH_3)_3$.

15. The compound, according to any one of claims 1 to 14, in which Q and Q^1 are both $-NR^4R^5$.

16. The compound, according to claim 1, in which A and A^1 are both C=O, Q and Q^1 are both $-NR^4R^5$, R^4 is H and
R^5 is

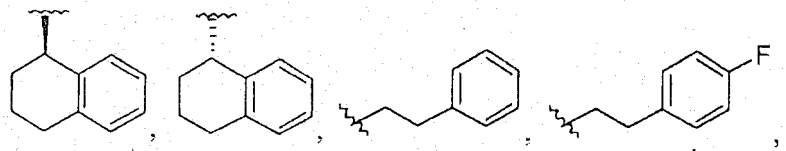
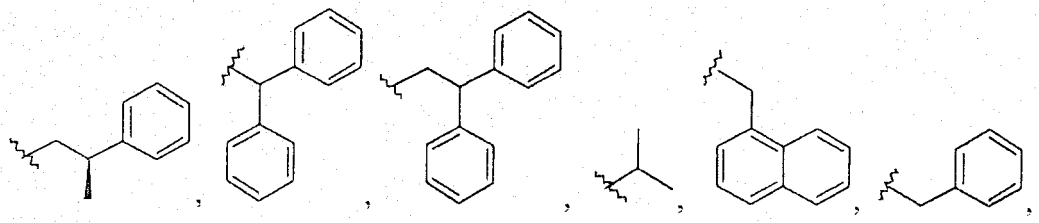
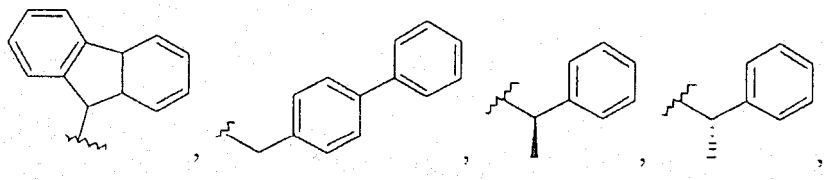
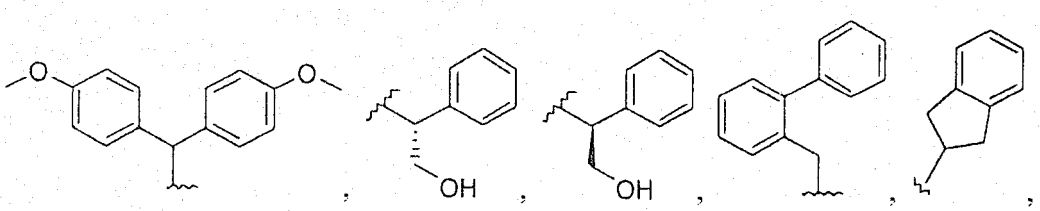
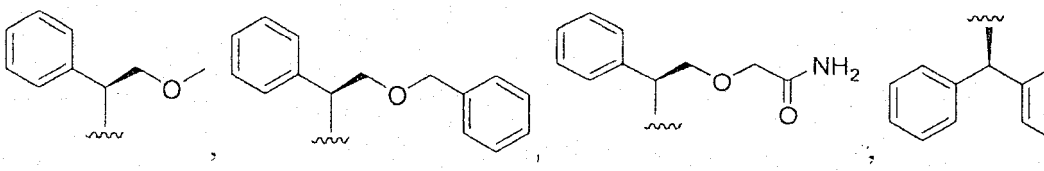
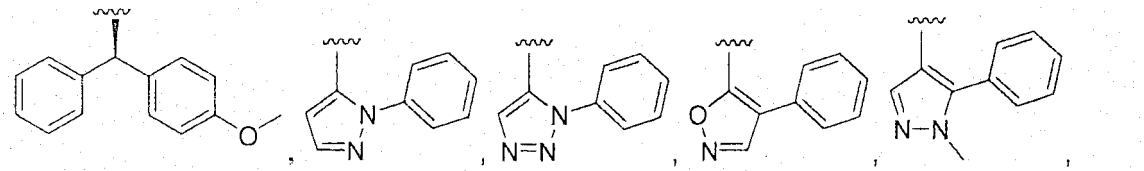
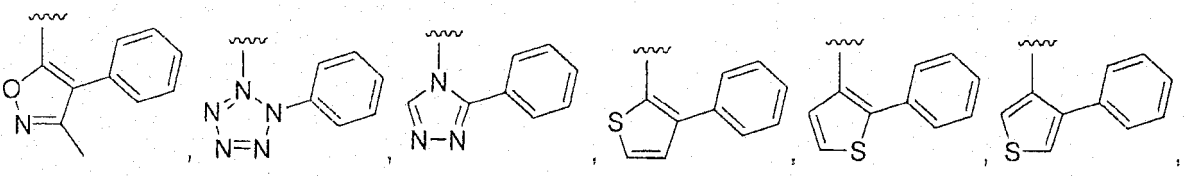
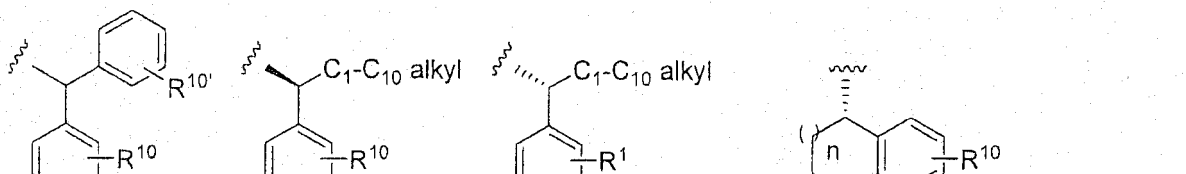
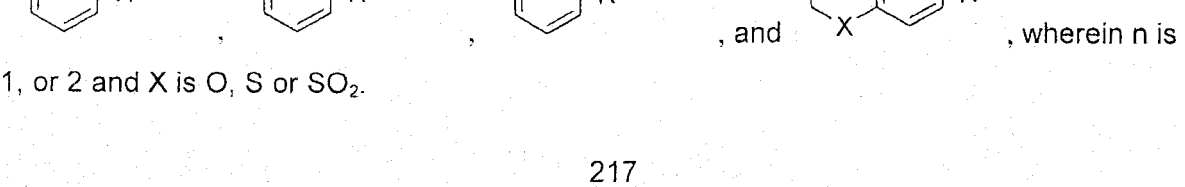
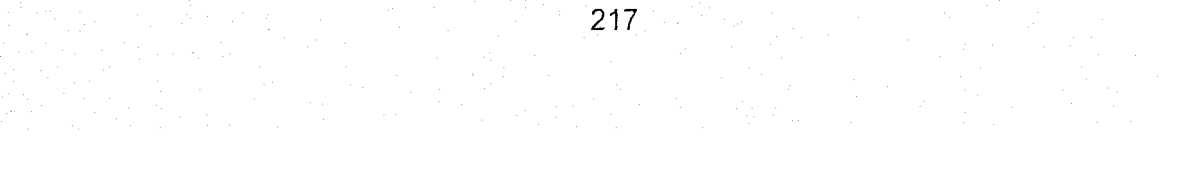
1) C_1–C_6 alkyl,
2) C_2-C_6 alkenyl,
3) C_2-C_4 alkynyl,
4) C_3–C_7 cycloalkyl,
5) C_3-C_7 cycloalkenyl,
6) aryl,
7) heteroaryl,
8) heterocyclyl, or
9) heterobicyclyl,

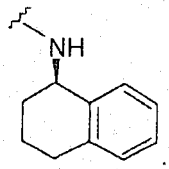
wherein the alkyl, alkenyl, alkynyl, cycloalkyl, and cycloalkenyl are optionally substituted with one or more R^6 substituents; and wherein the aryl, heteroaryl, heterocyclyl, and heterobicyclyl are optionally substituted with one or more R^{10} substituents.

17. The compound, according to claim 16, in which R^4 is H and R^5 is:

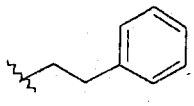
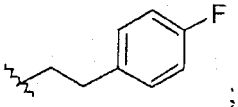
1) C_1–C_6 alkyl, or
2) aryl,

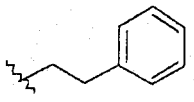
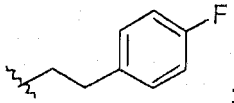
wherein the alkyl is optionally substituted with one or two R^6 substituents; and wherein the aryl is optionally substituted with one R^{10} substituent.

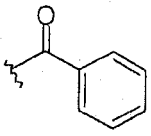
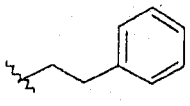
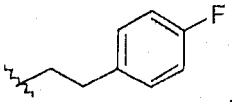
18. The compound, according to claim 17, in which R^4 is H and R^5 is selected from the group consisting of:  ,  ,  ,  ,  ,  ,  ,  ,  ,  , , ,  , and , wherein n is 0, 1, or 2 and X is O, S or SO_2.

19. The compound, according to claim 1, in which A and A^1 are both C=O, and Q and Q^1 are both  .

20. The compound, according to claim 1, in which A and A^1 are both CH_2, Q and Q^1 are both NR^4R^5, and

R^4 is $S(O)_2CH_3$ and R^5 is  or  ;

or R^4 is $C(O)CH_3$ and R^5 is  or  ;

or R^4 is  and R^5 is  or  .

21. A compound, according to claim 1, selected from the group consisting of:

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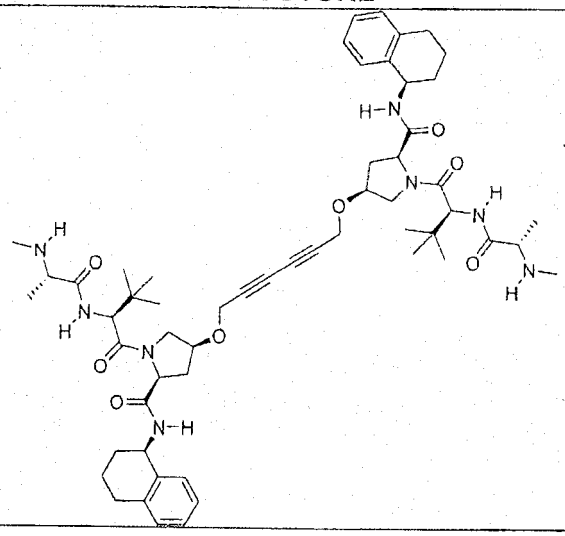
1	

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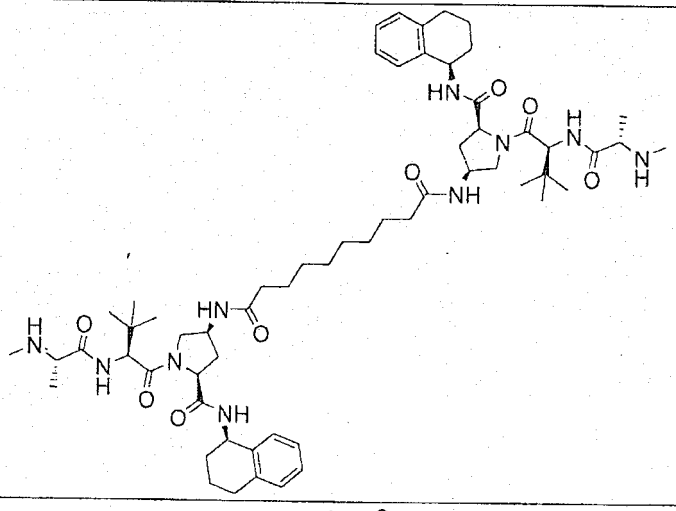
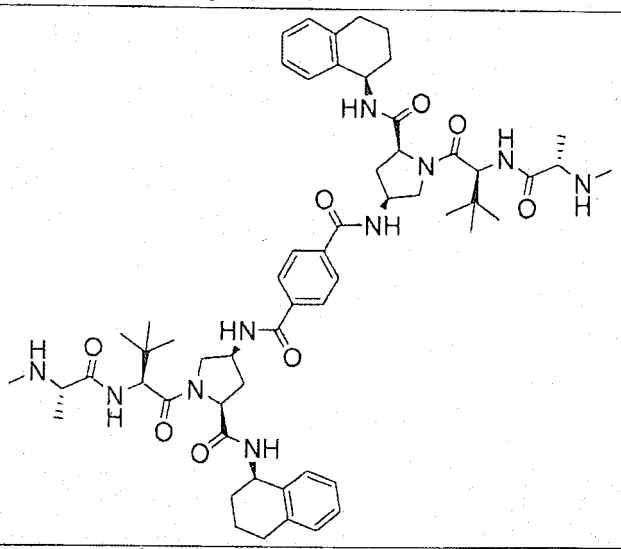
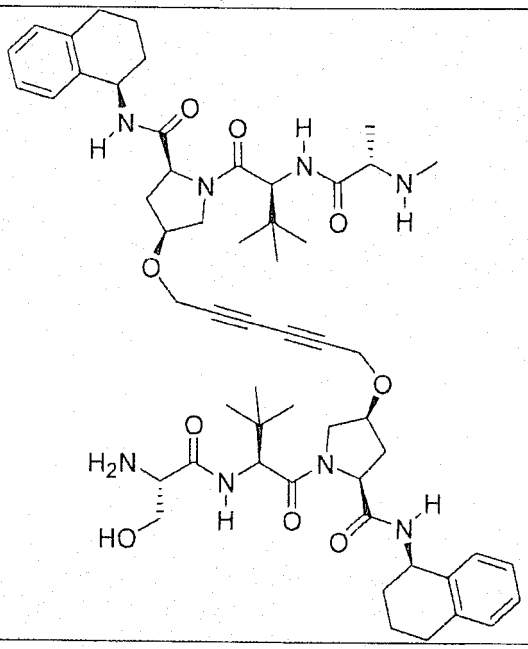
2	
3	
4	

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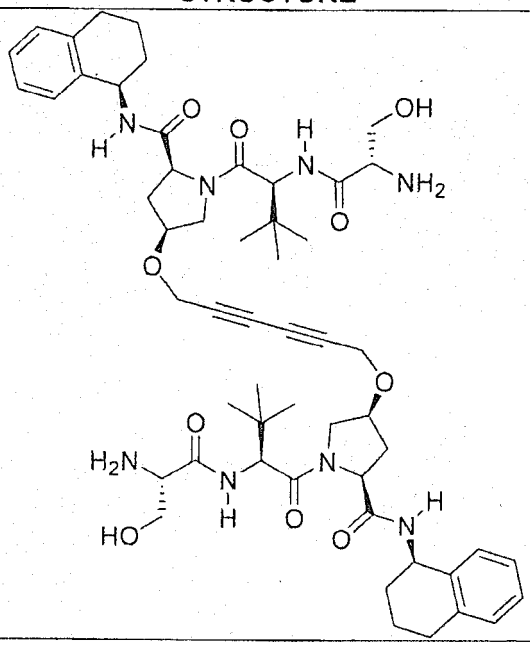
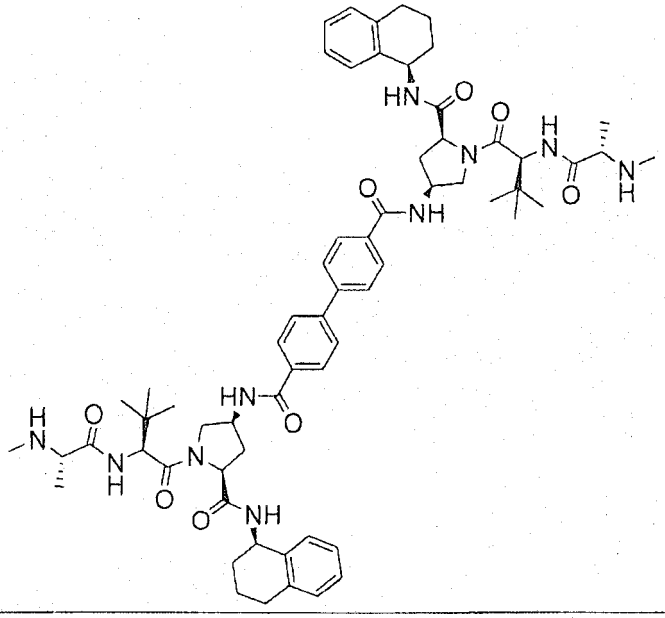
5	
10	

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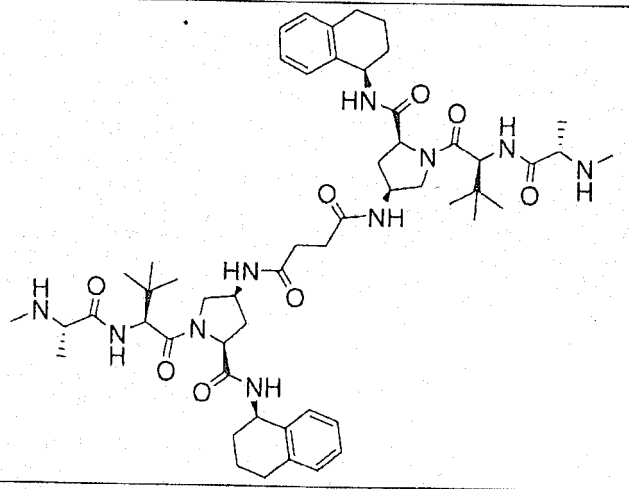
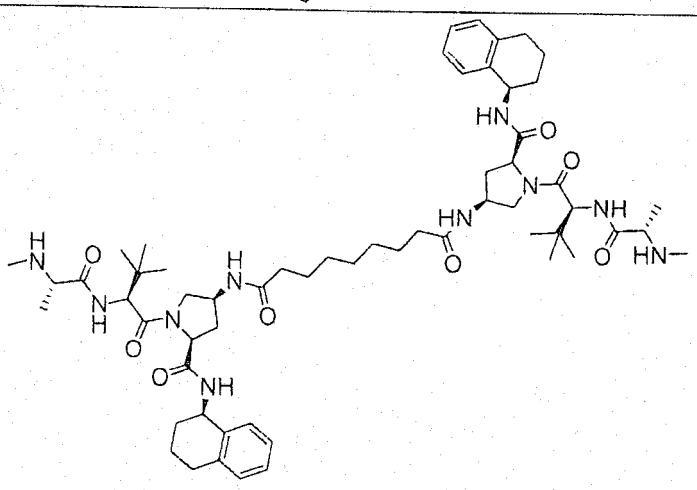
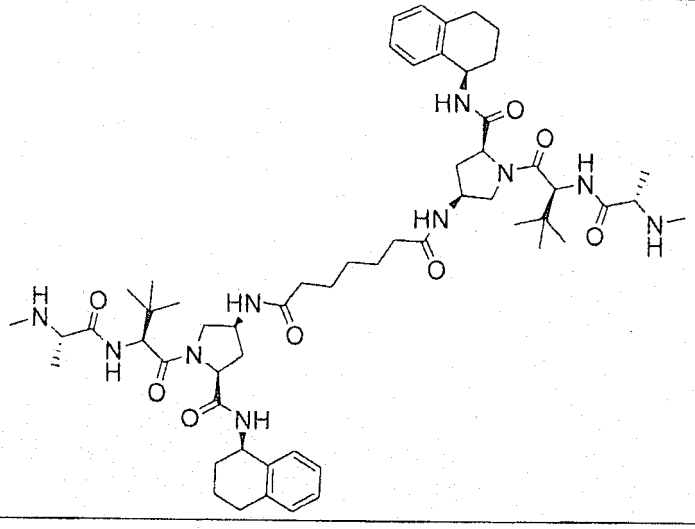
11	
12	
13	

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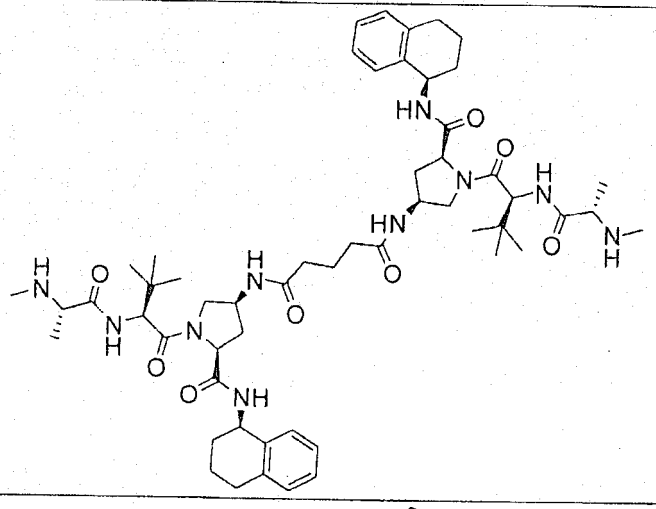
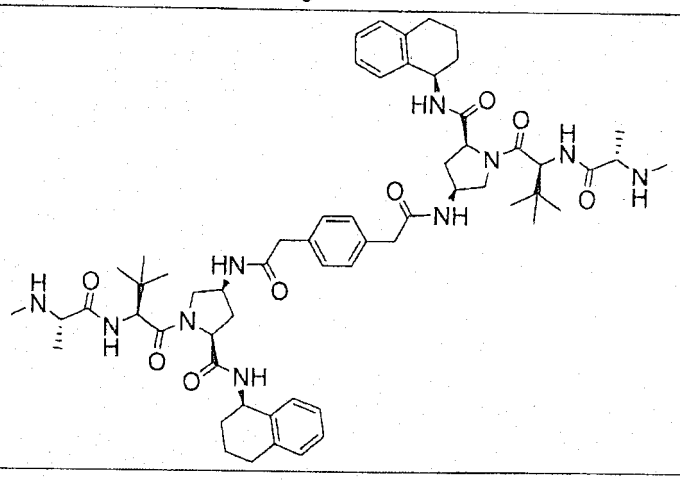
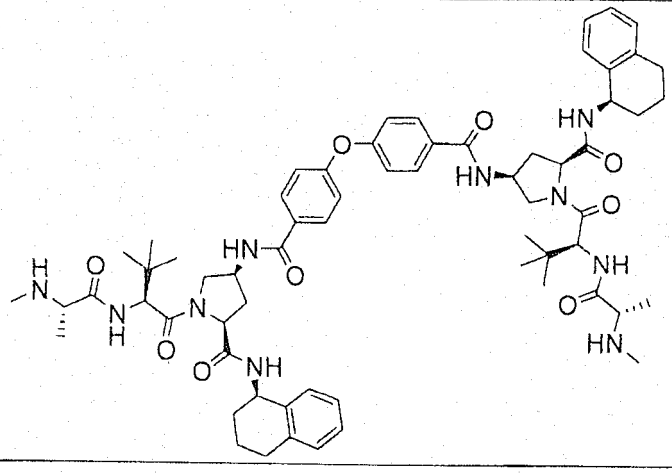
14	
15	
16	

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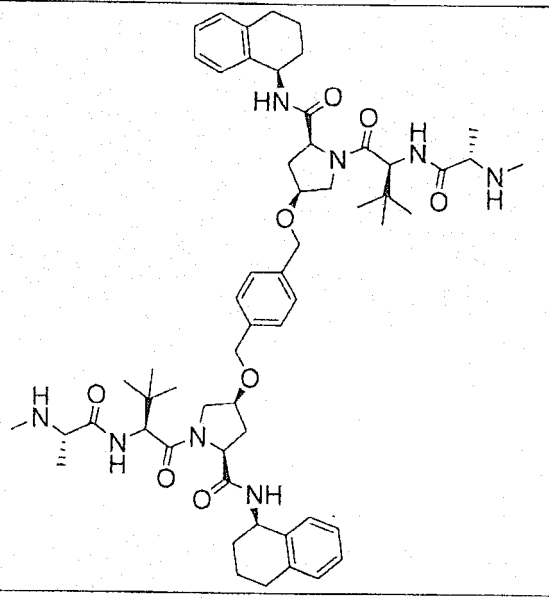
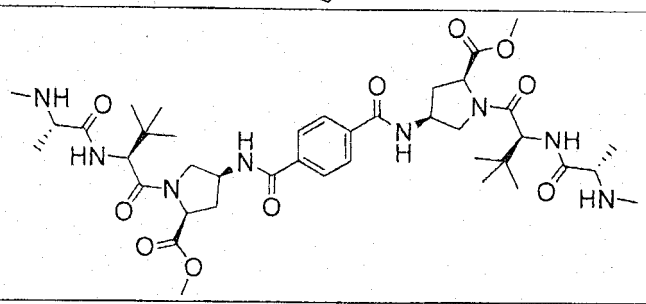
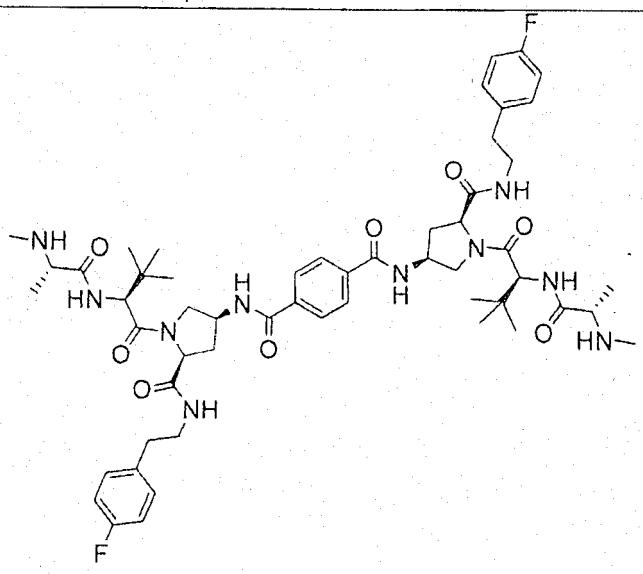
17	
18	
19	

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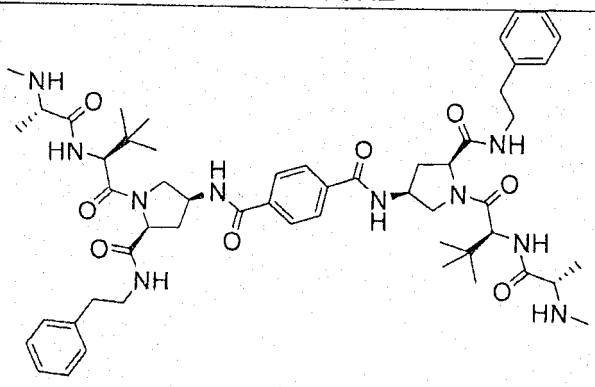
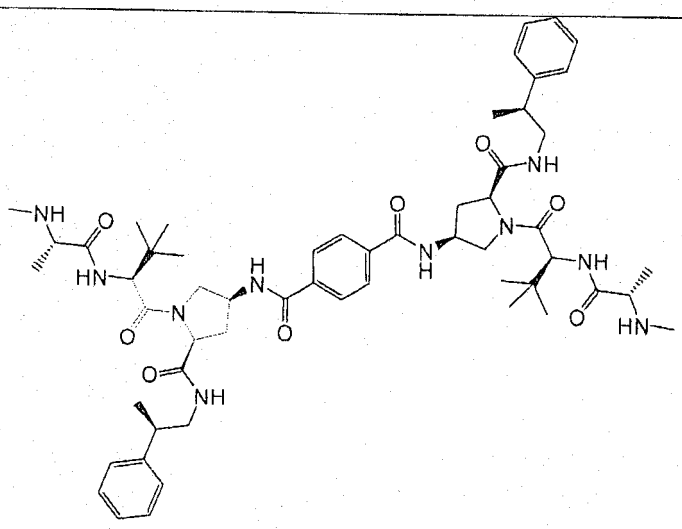
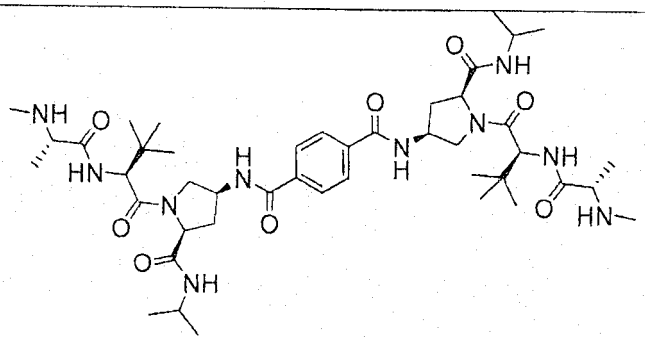
20	 ;
21	 ;
22	 ;

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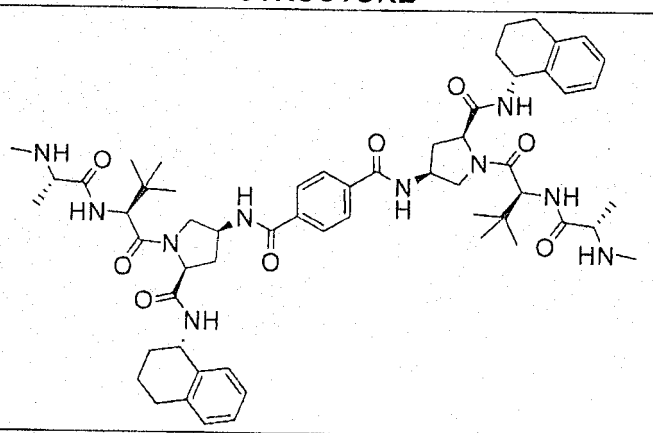
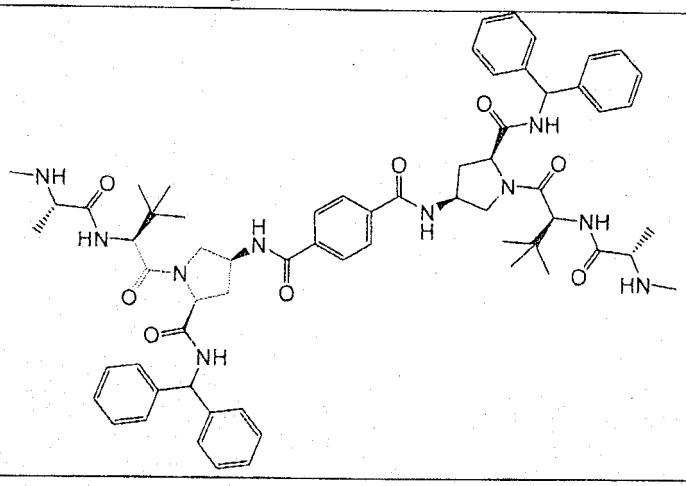
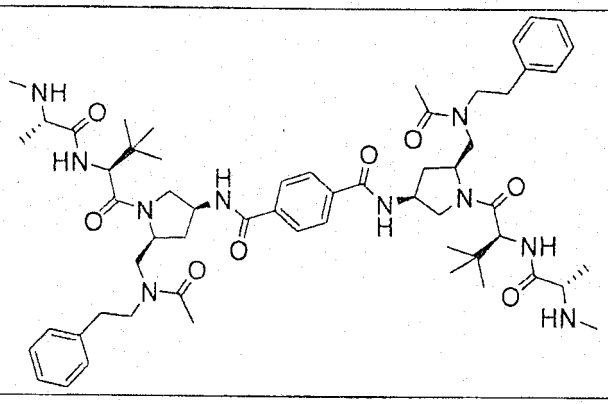
23	
24	
25	

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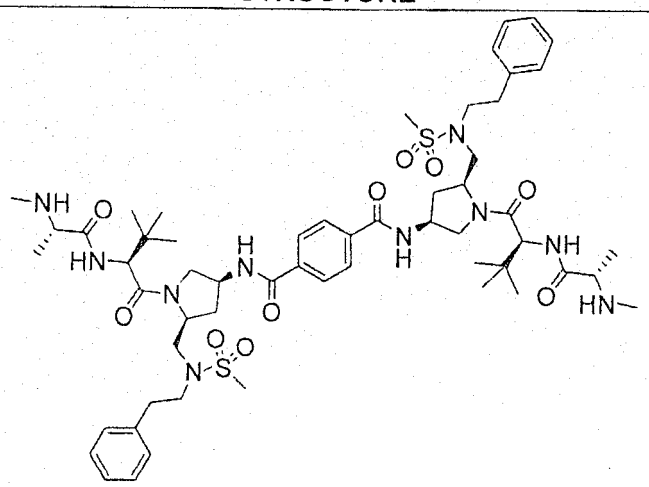
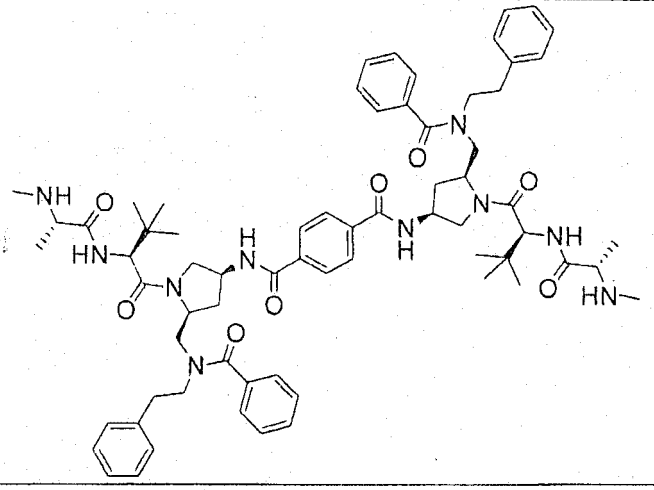
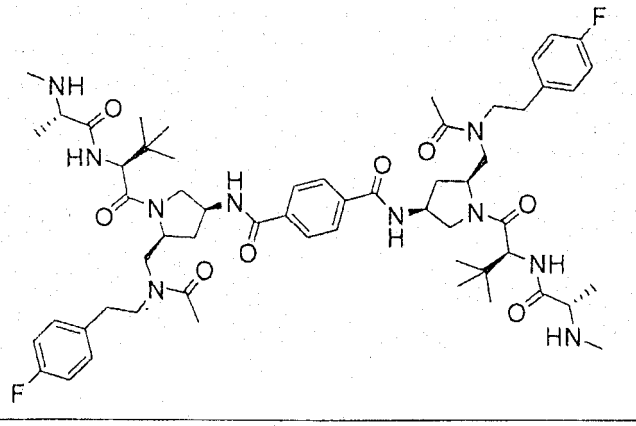
26	
27	
28	

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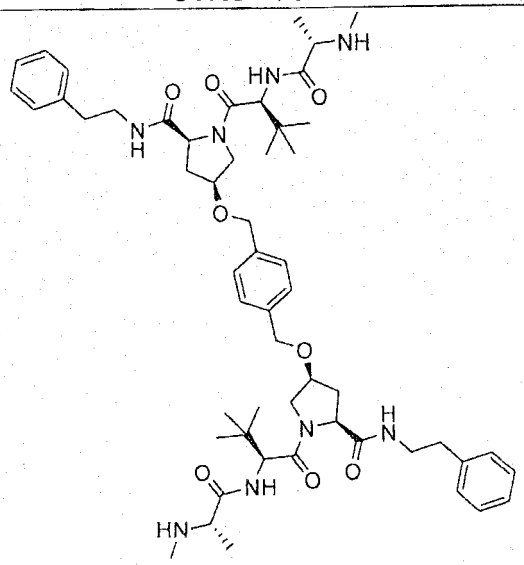
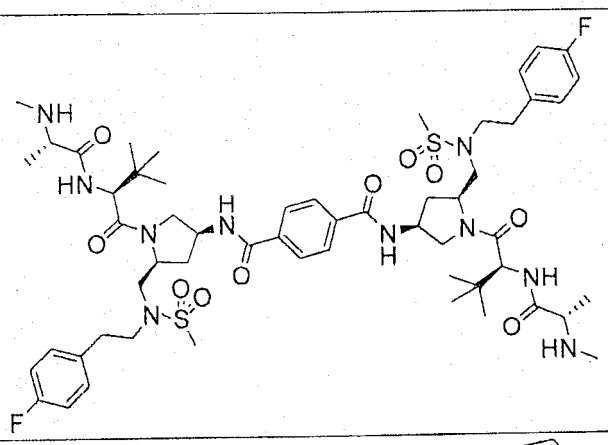
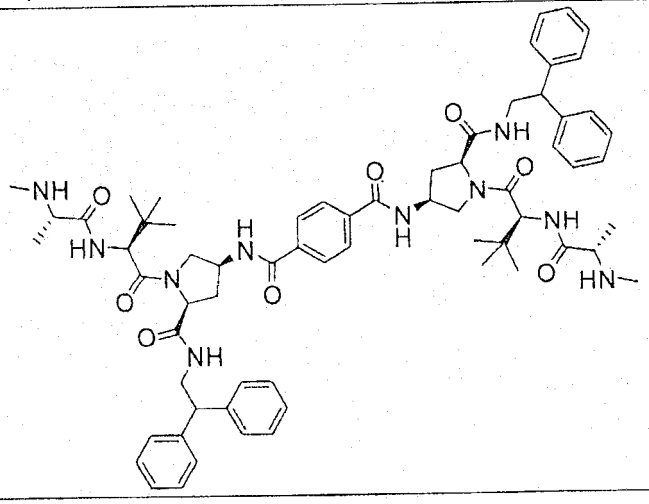
29	
30	
31	

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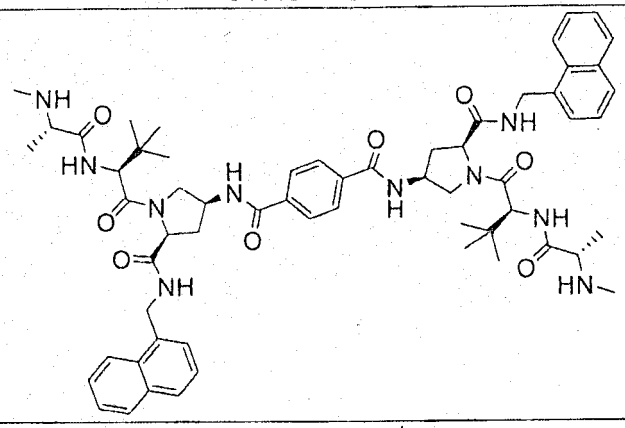
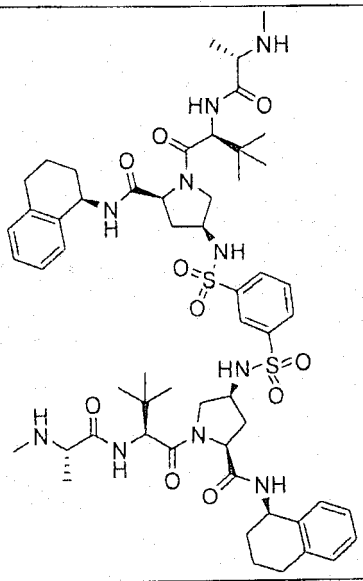
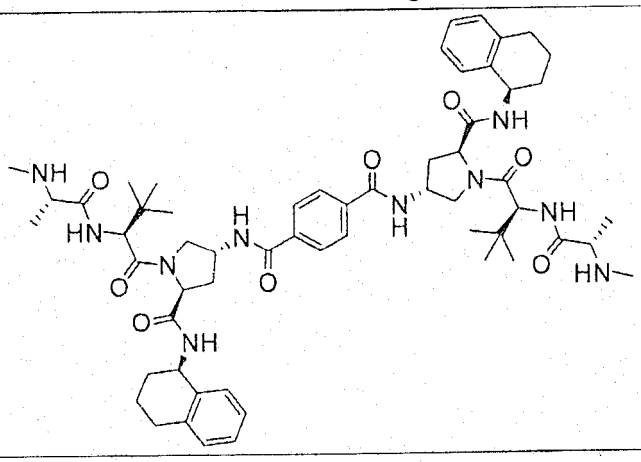
32	
33	
34	

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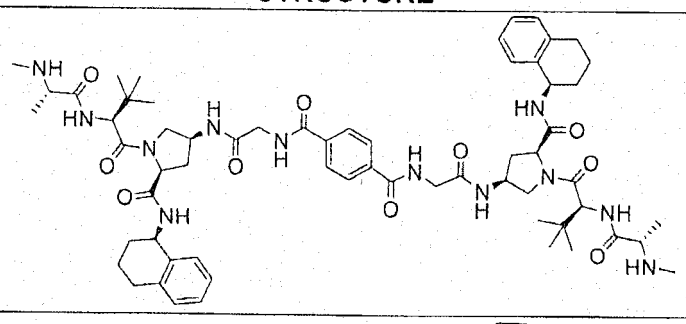
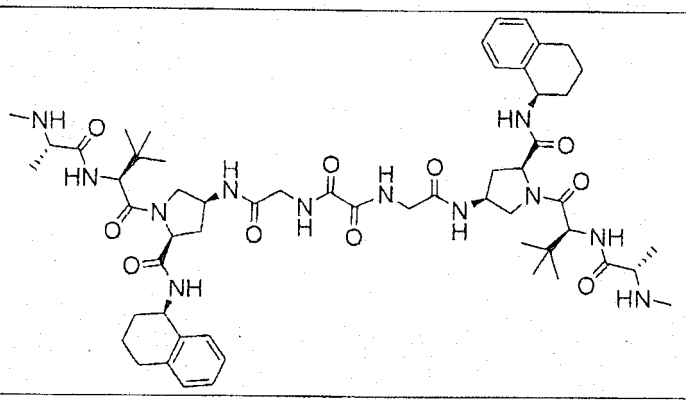
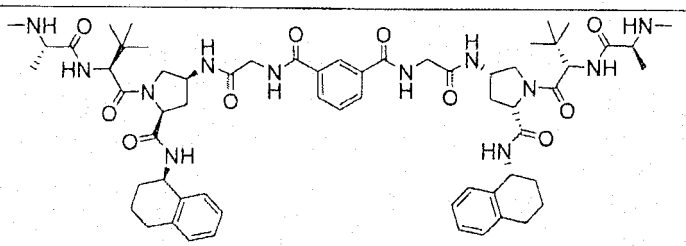
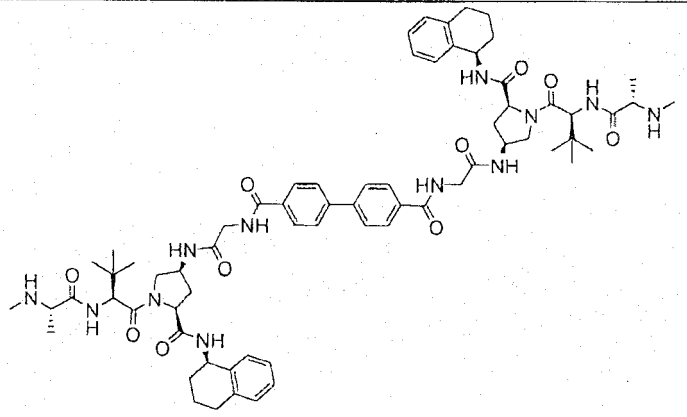
35	
36	
37	
38	

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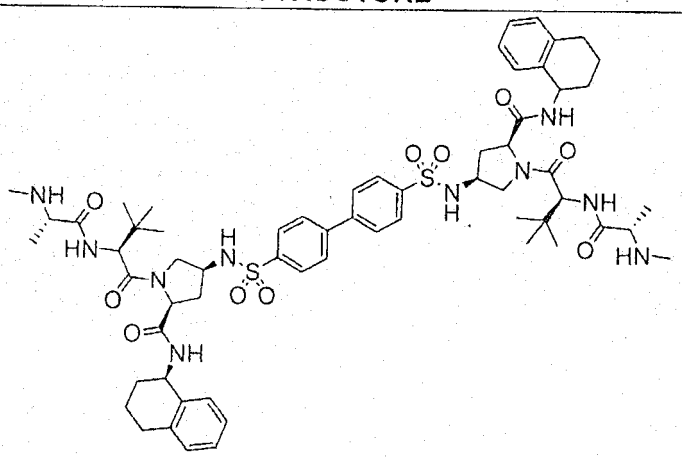
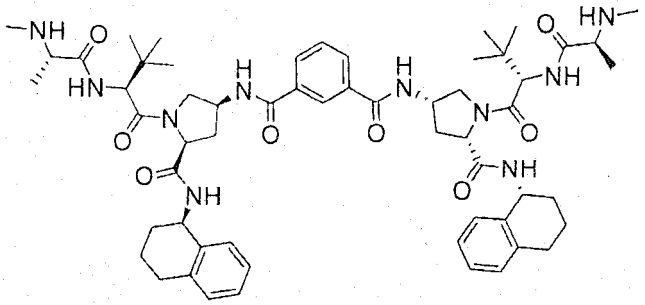
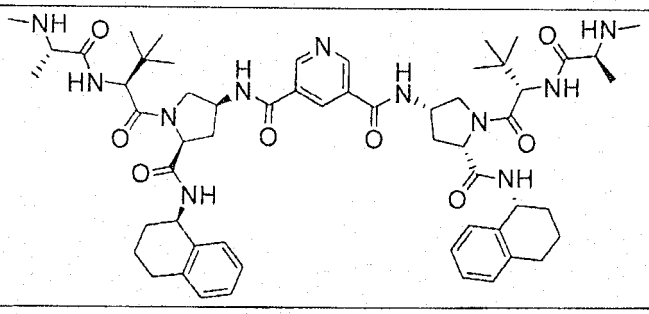
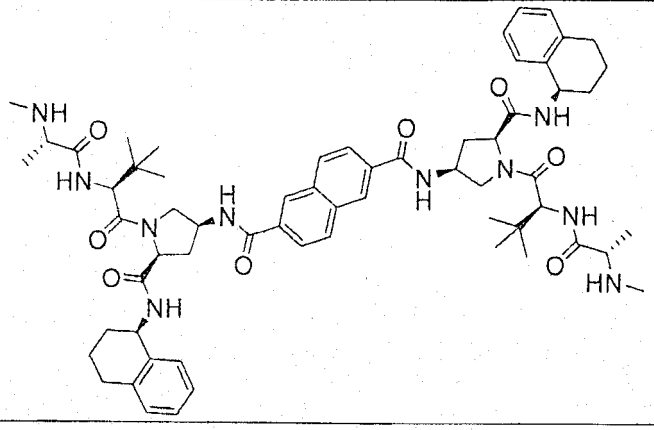
39	
40	
41	
42	

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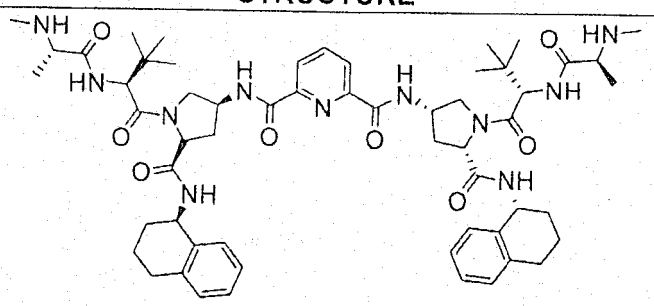
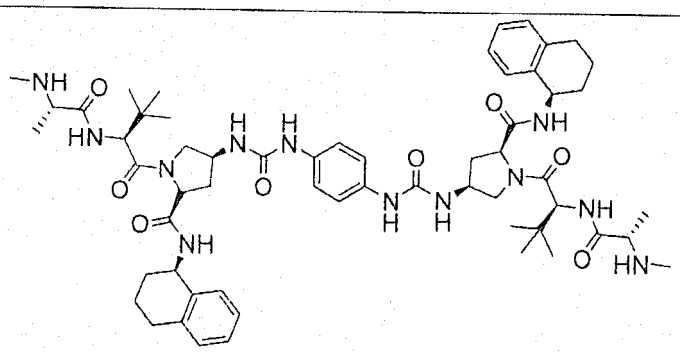
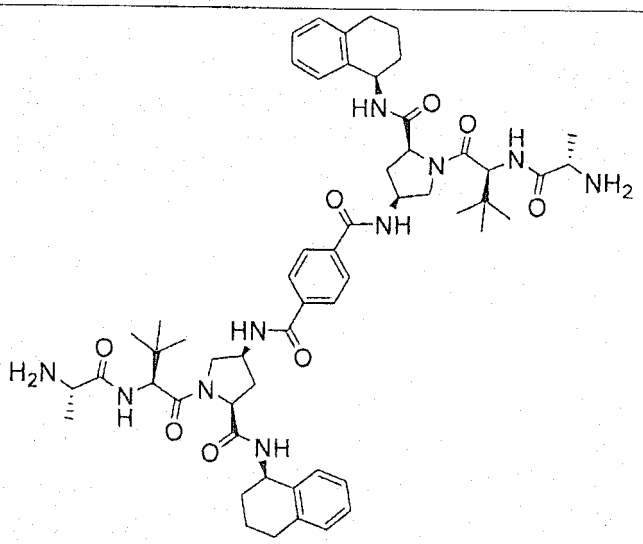
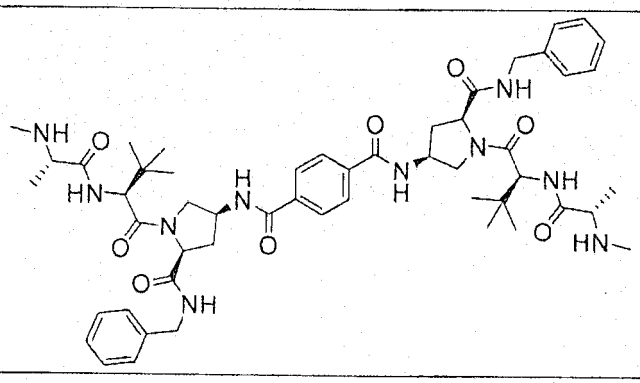
43	
44	
45	
46	

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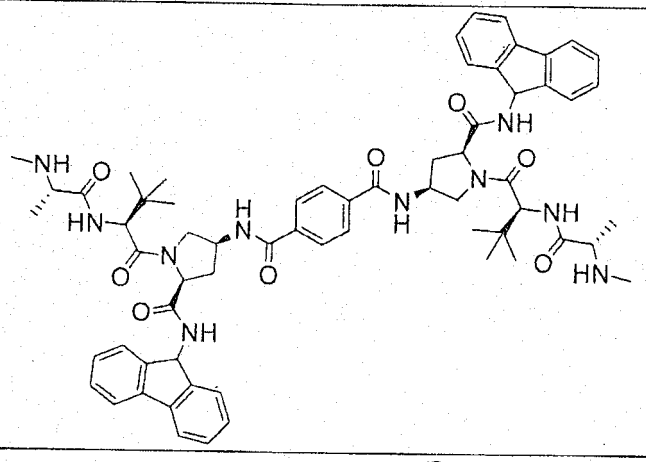
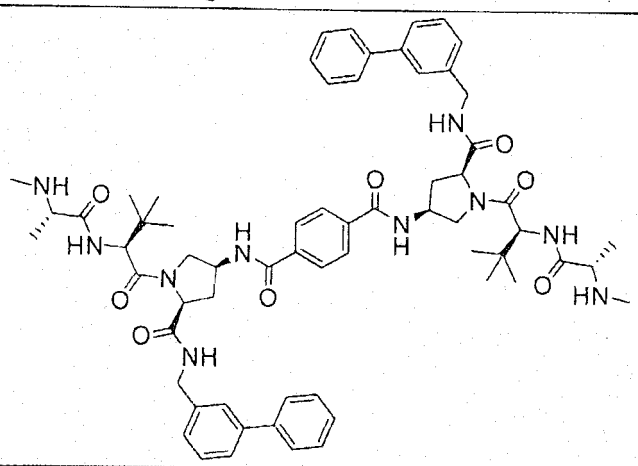
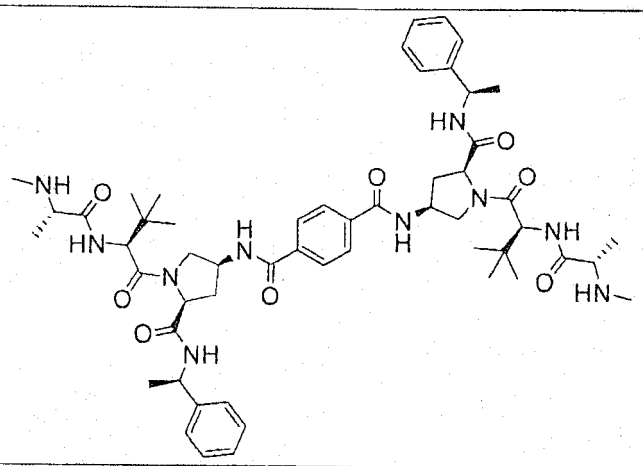
47	
48	
49	

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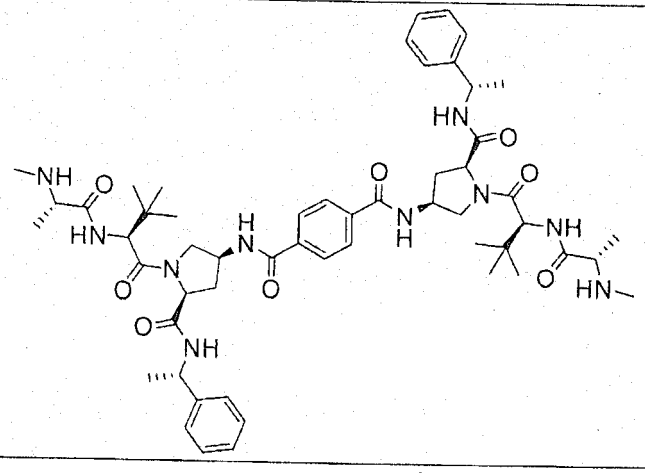
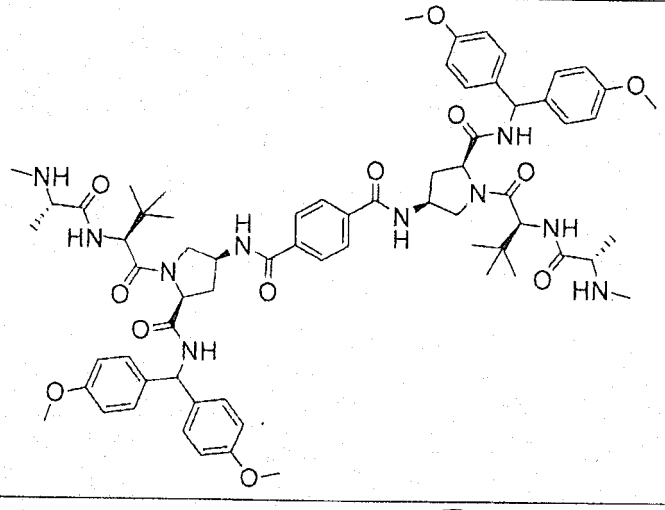
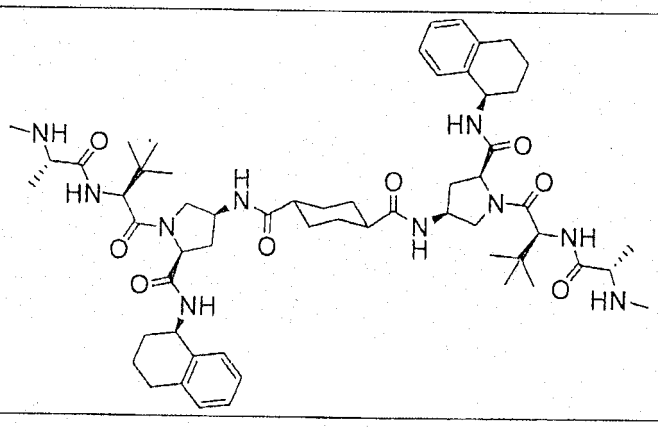
50	
51	
52	

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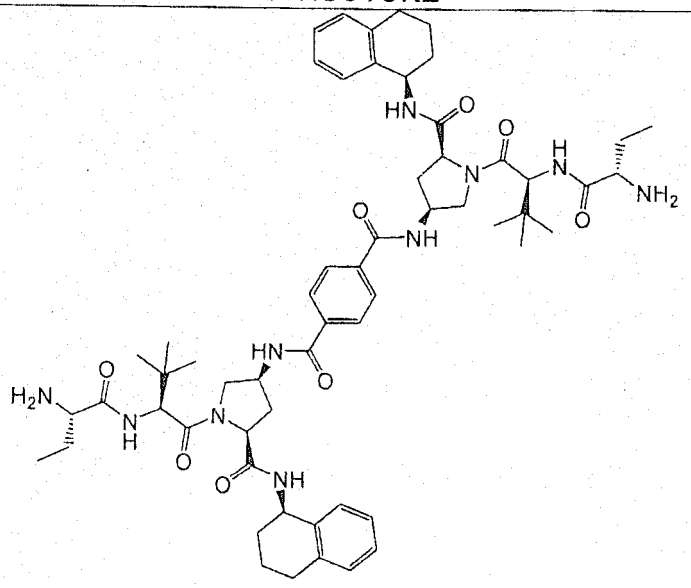
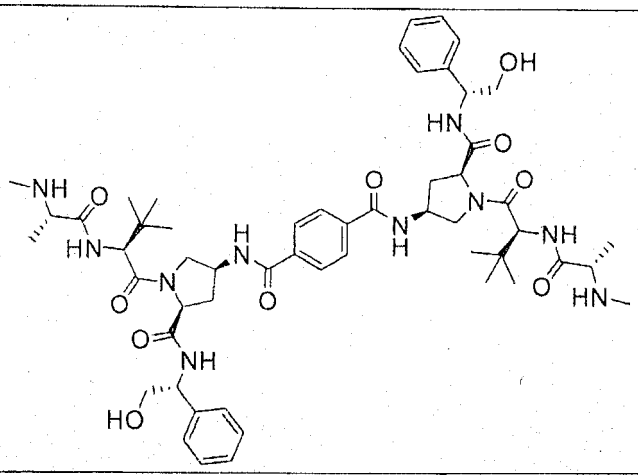
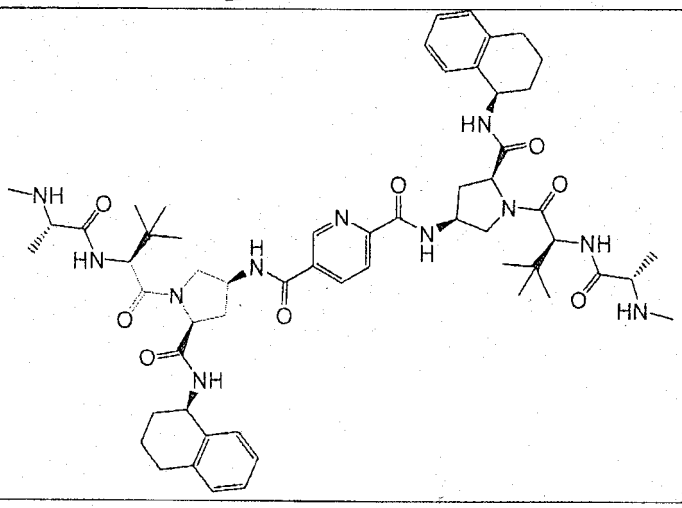
53	
54	
55	

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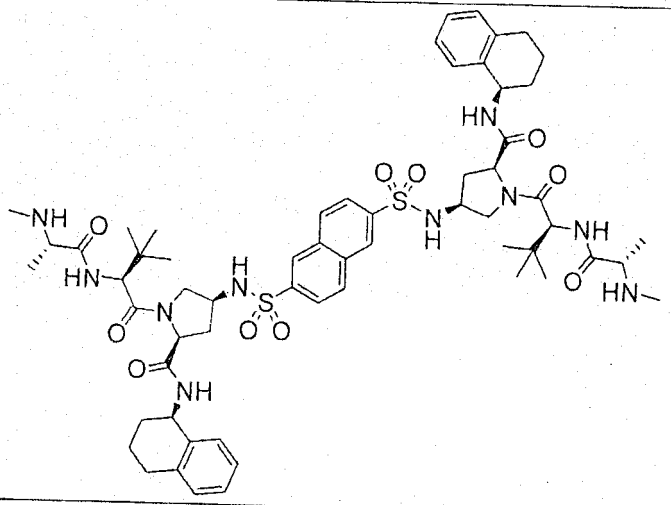
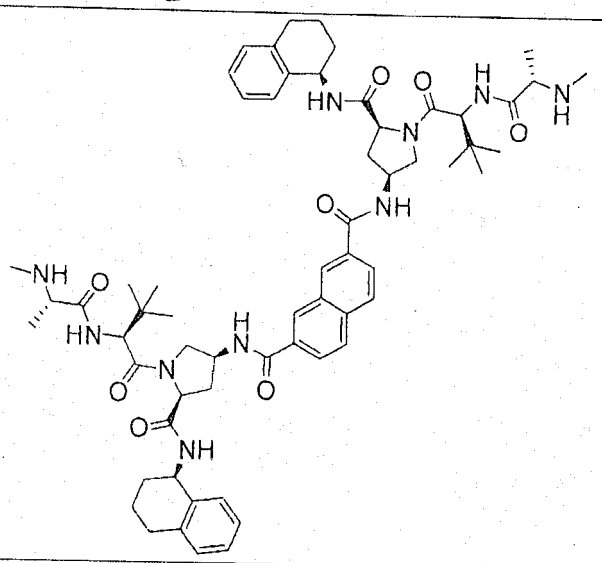
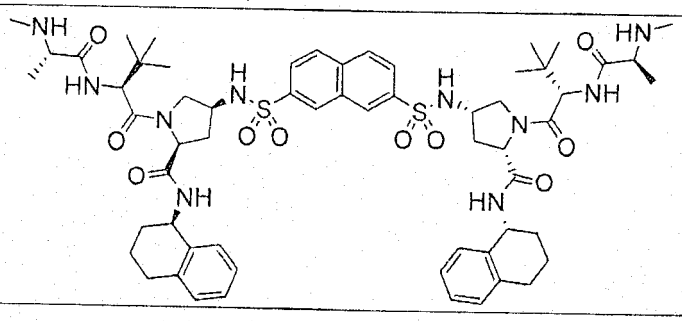
56	
57	
58	

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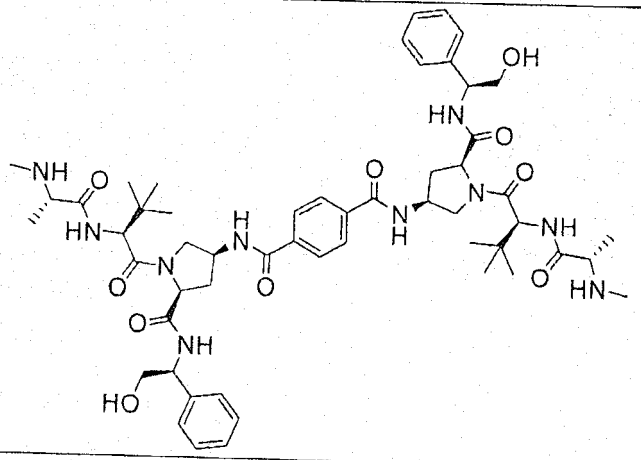
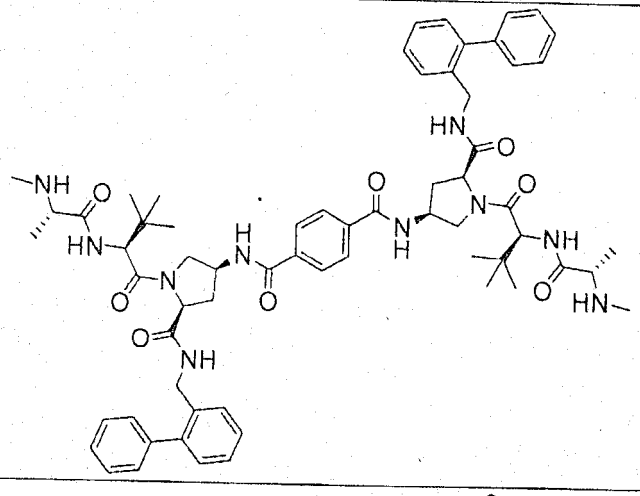
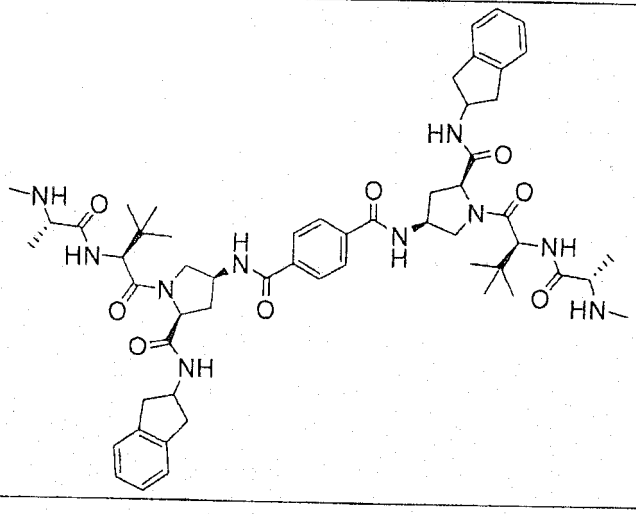
59	
60	
61	

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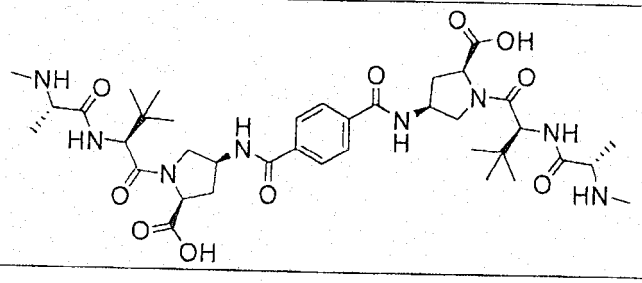
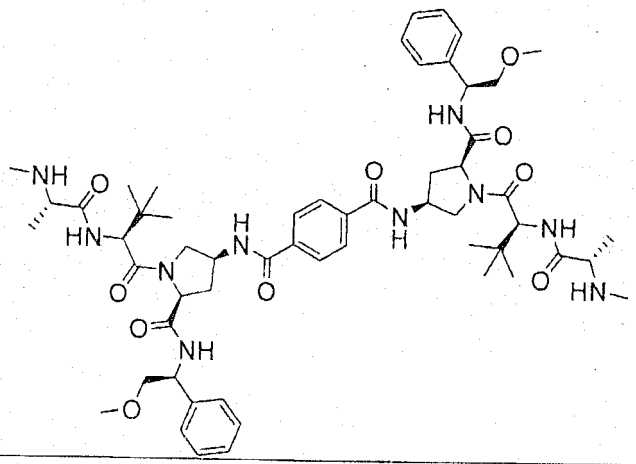
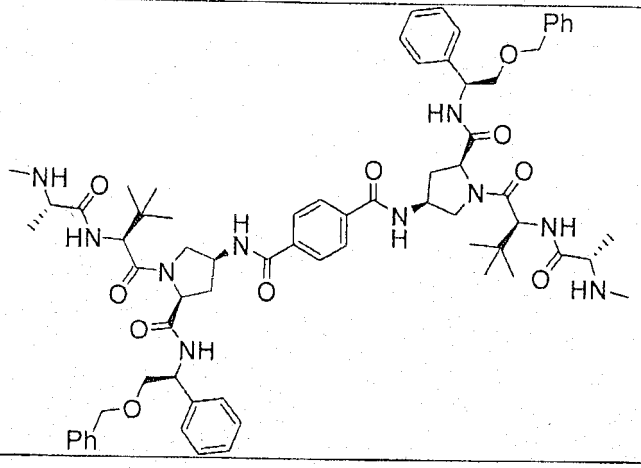
62	
63	
64	

;

; and

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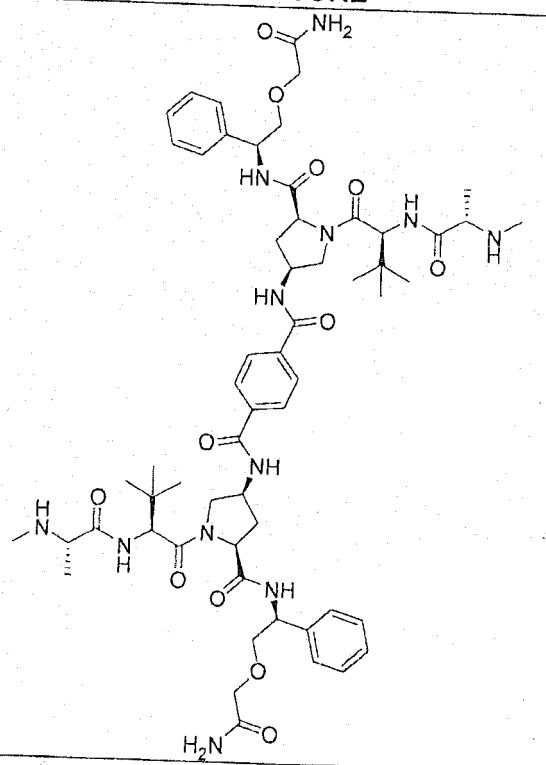
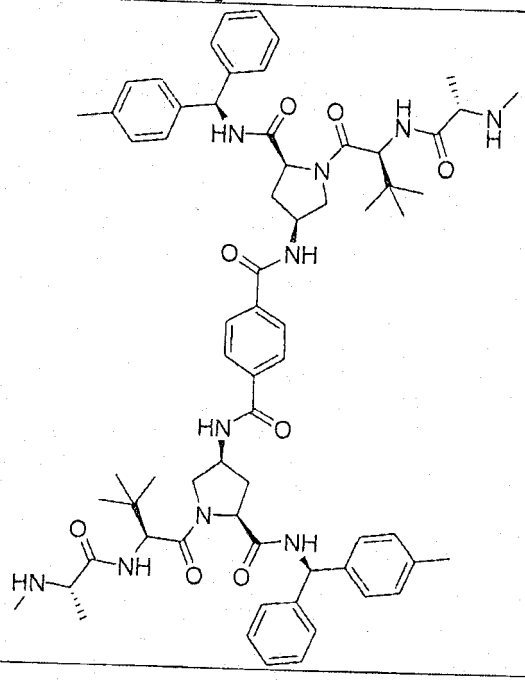
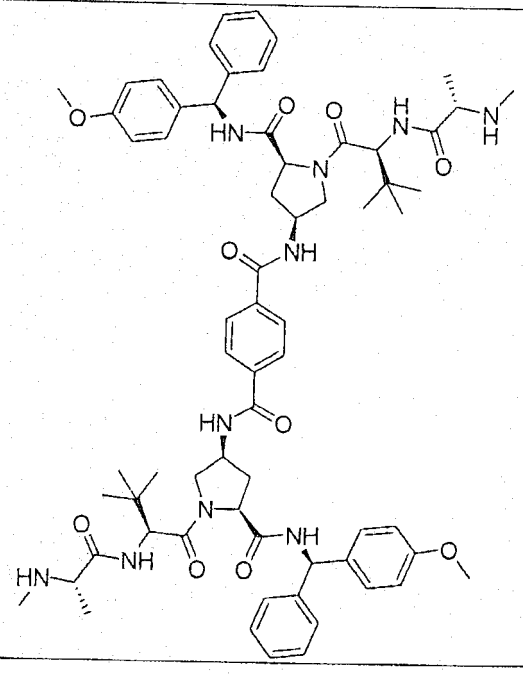
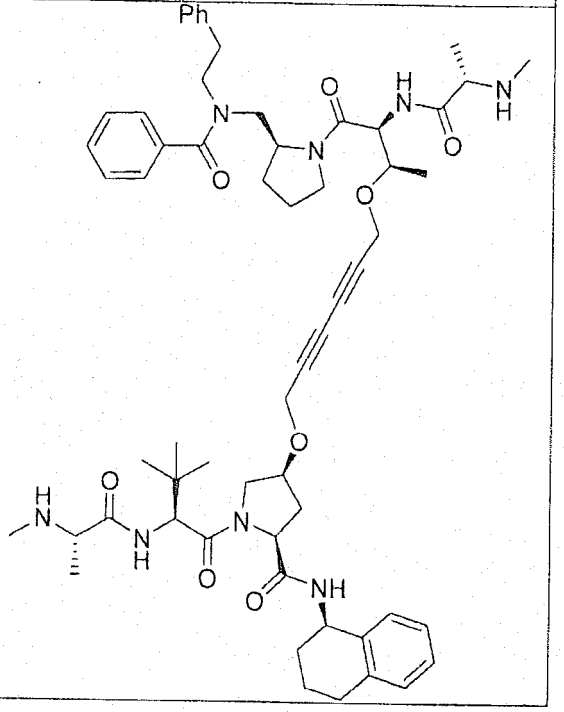
Cpd	STRUCTURE
65	
66	

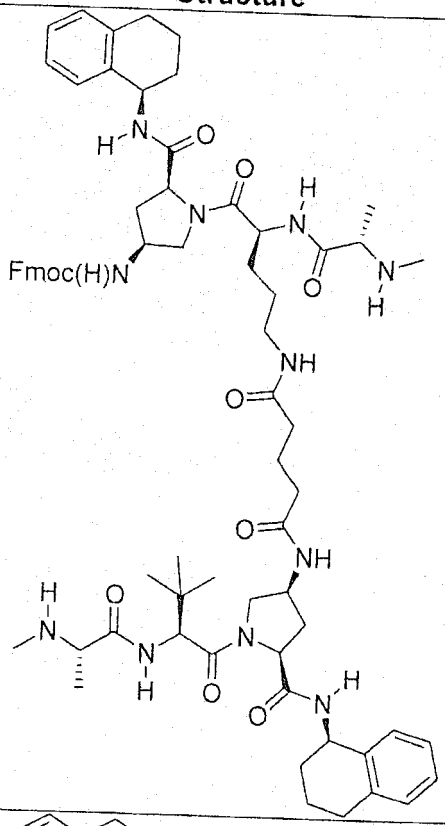
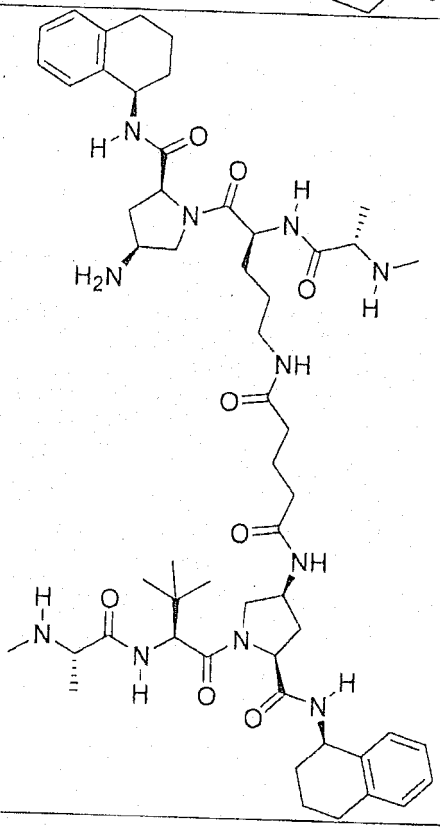
Cpd	STRUCTURE
67	

and salts thereof.

22. A compound, according to claim 1, selected from the group consisting of:

Cpd	Structure
6	

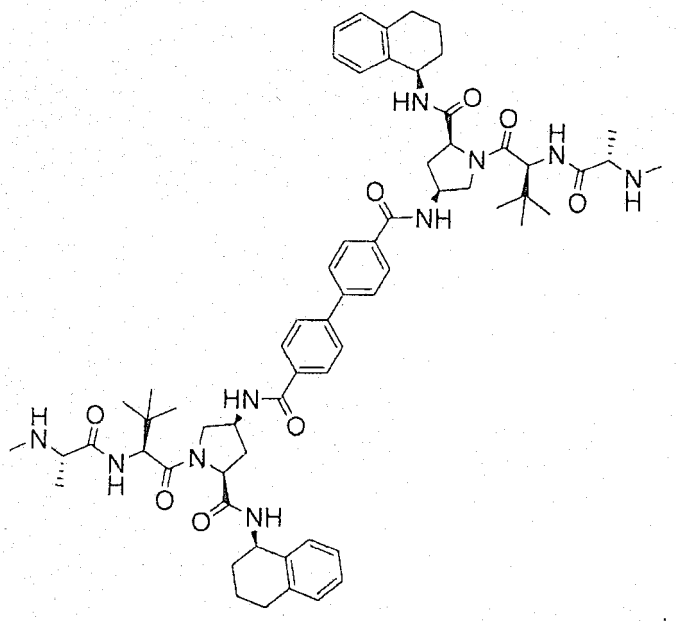
;

Cpd	Structure
7	
8	

; and

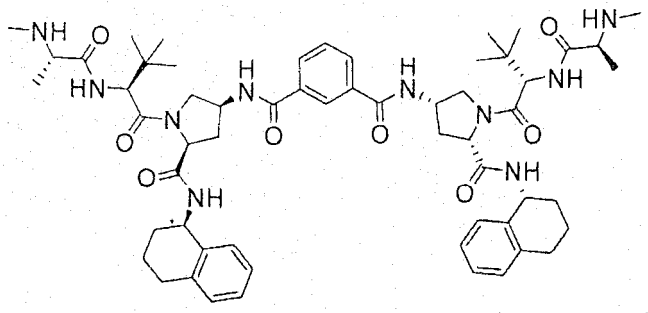
and salts thereof.

23. The compound, according to claim 1, wherein the compound is



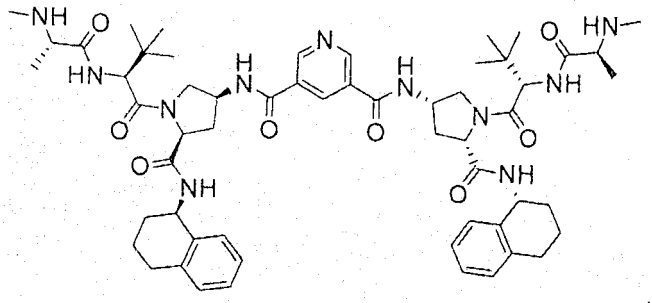
, or a salt thereof.

24. The compound, according to claim 1, wherein the compound is



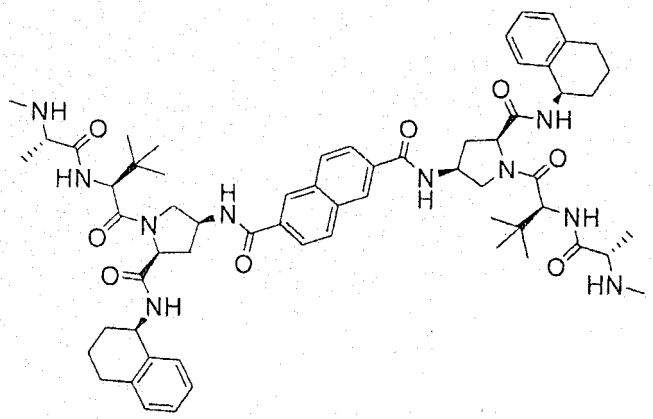
, or a salt thereof.

25. The compound, according to claim 1, wherein the compound is



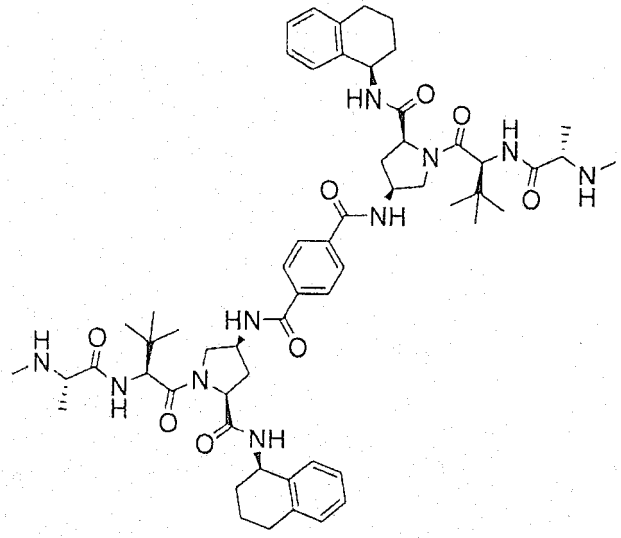
, or a salt thereof.

26. The compound, according to claim 1, wherein the compound is



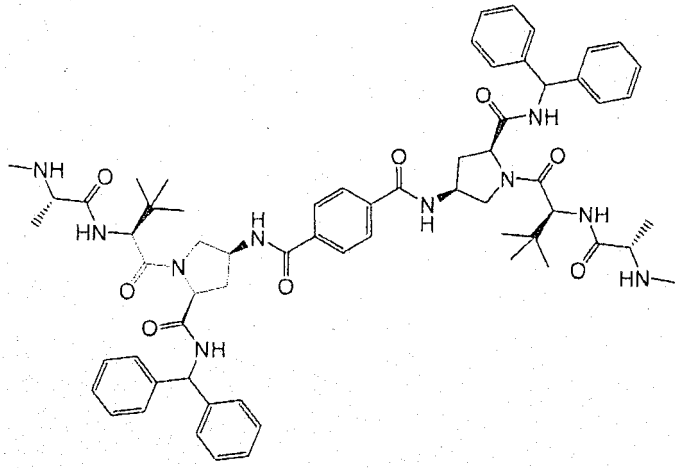
, or a salt thereof.

27. The compound, according to claim 1, wherein the compound is:



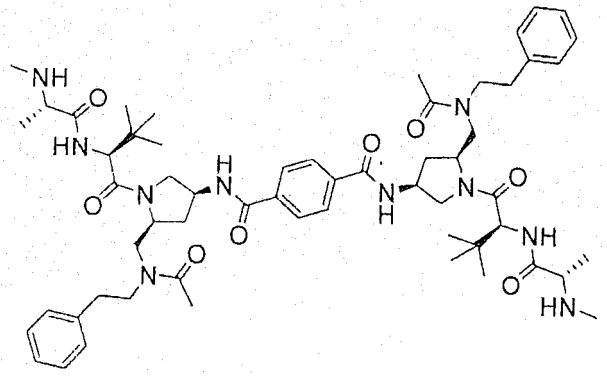
or a salt thereof.

28. The compound, according to claim 1, wherein the compound is:



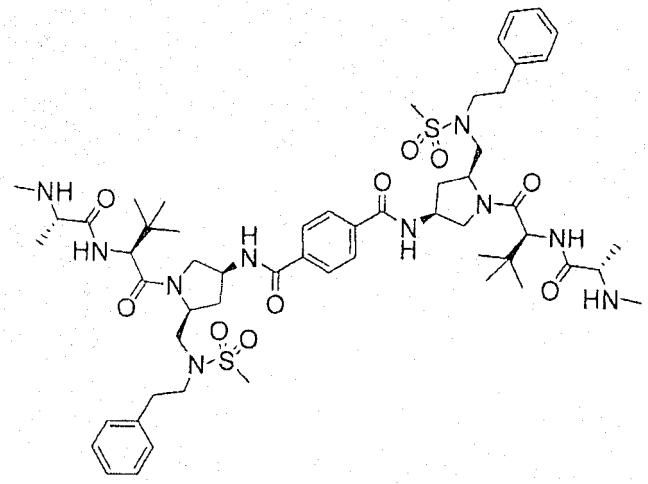
or a salt thereof.

29. The compound, according to claim 1, wherein the compound is:



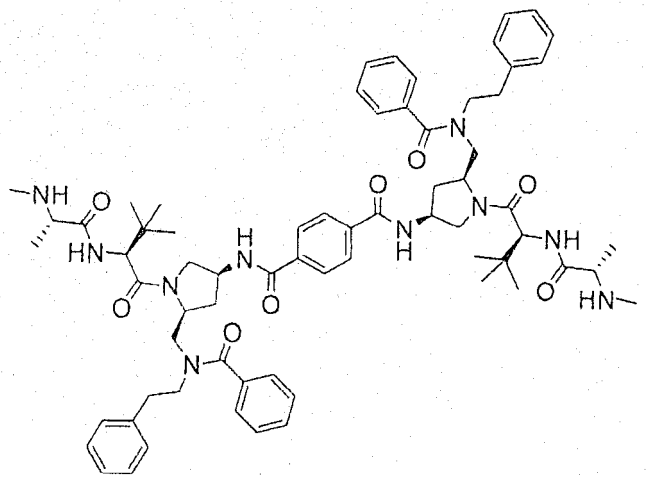
or a salt thereof.

30. The compound, according to claim 1, wherein the compound is:



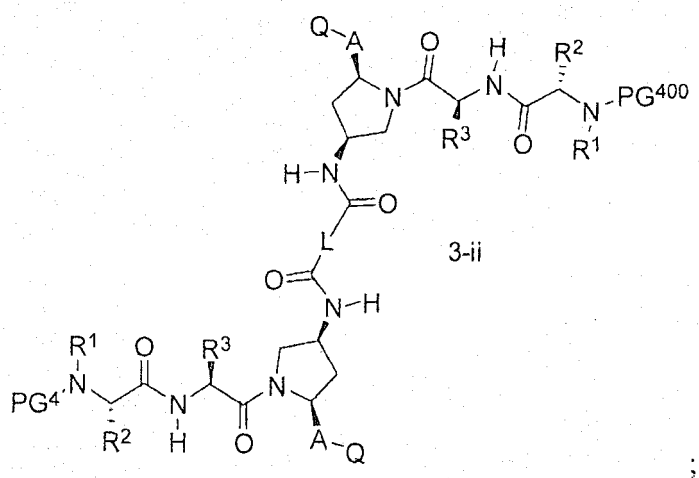
or a salt thereof.

31. The compound, according to claim 1, wherein the compound is:



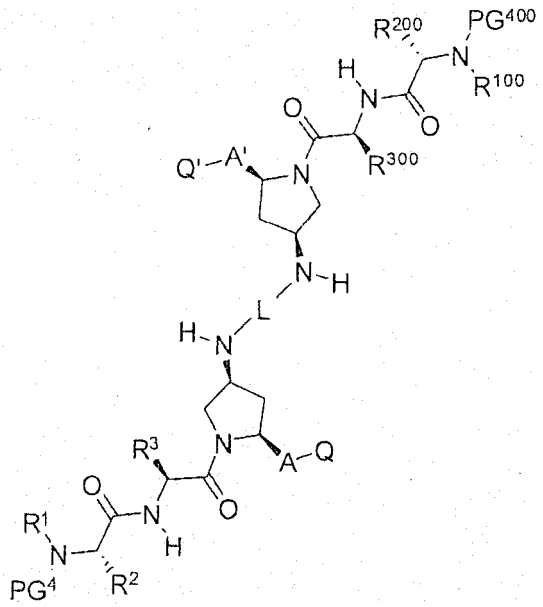
or a salt thereof.

32. An intermediate compound represented by Formula 3-ii, 4-i, 6-ii, 7-v, 8-ii, 8-iii, 17-i, 18-i, 19-8, 19-3, 20-2, 20-4, 19-2, or 20-1a:



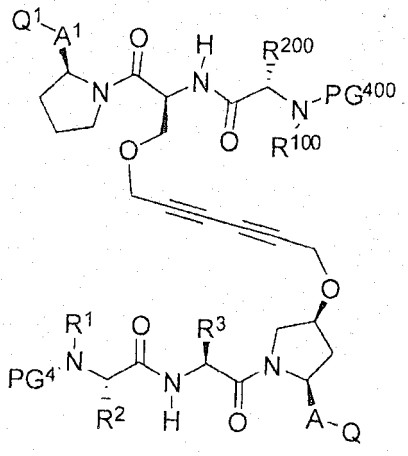
3-ii

;

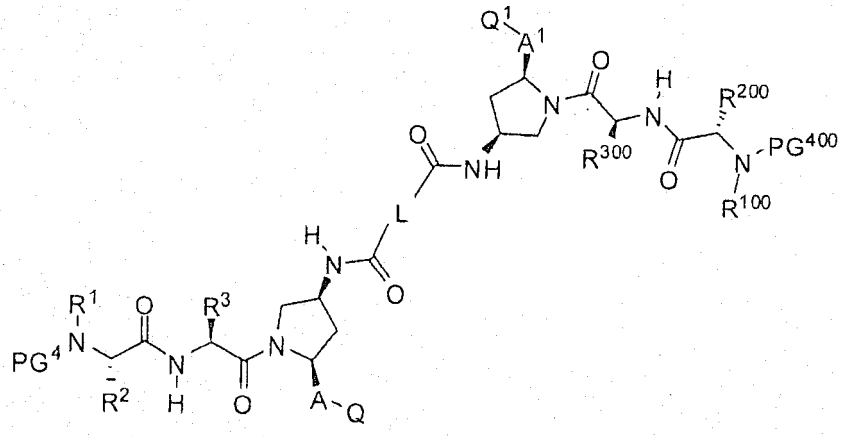


4-i

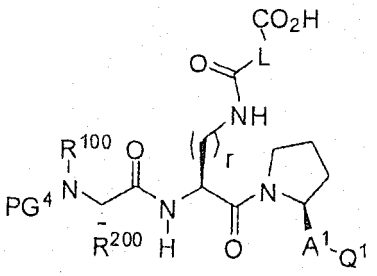
;



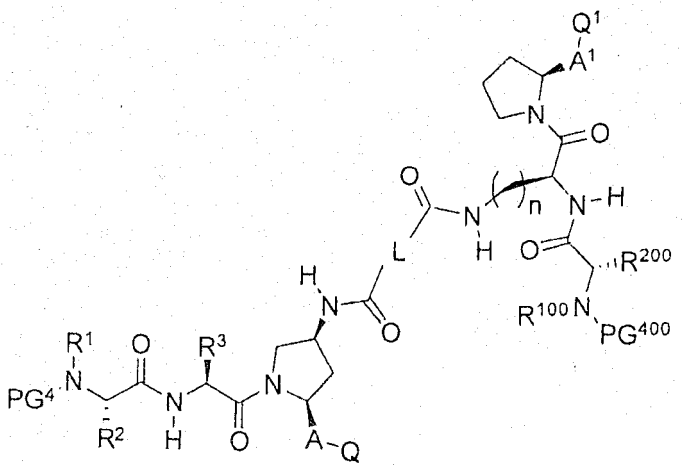
6-ii ;



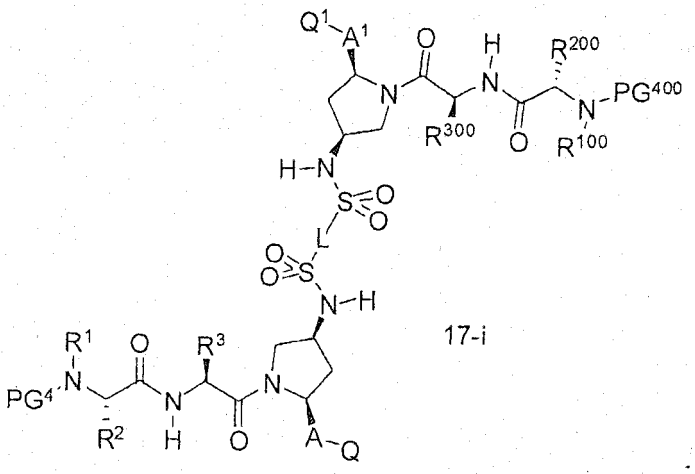
7-v ;



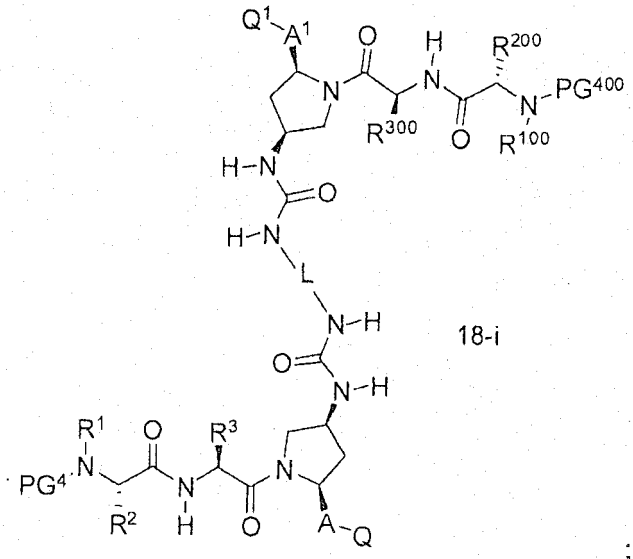
8-ii ;



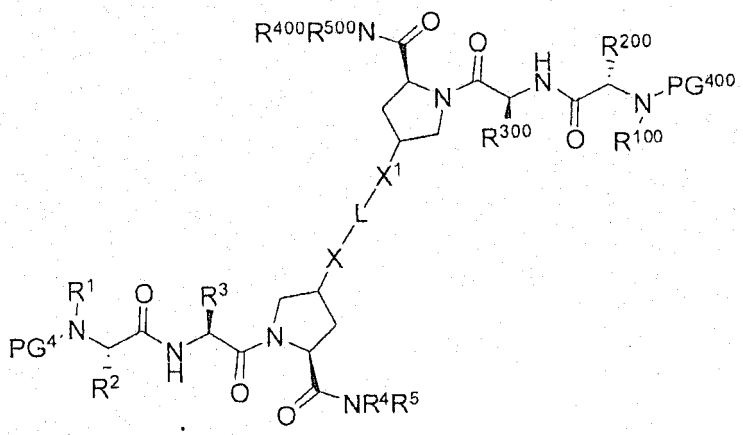
8-iii ;



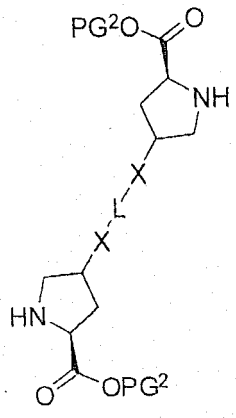
17-i ;



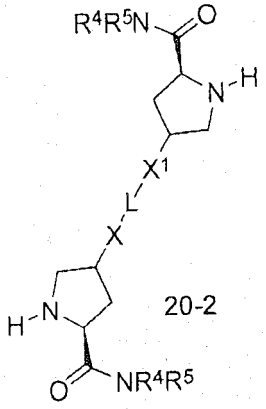
18-i ;



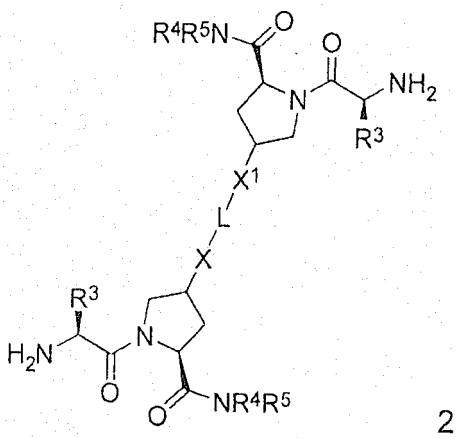
19-8 ;



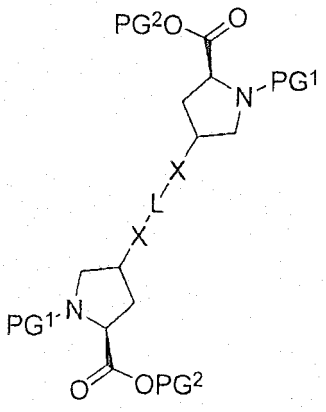
19-3;



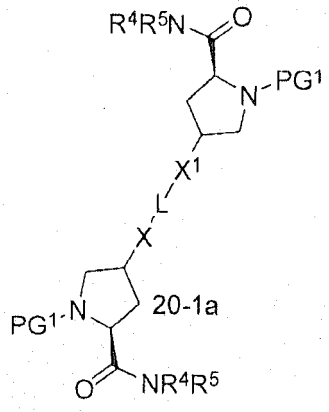
20-2 ;



20-4;



19-2; or

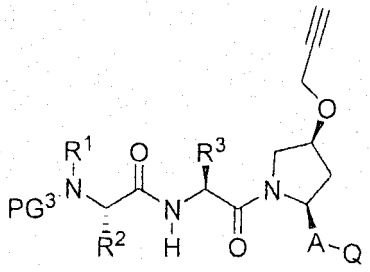


20-1a

wherein PG^1, PG^2, PG^3, PG^4, and PG^{400} are protecting groups, r is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, and L, X, X^1, A, A^1, Q, Q^1, R^1, R^{100}, R^2, R^{200}, R^3, R^{300}, R^4, R^{400}, R^5 and R^{500} are as defined in claim 1.

33. A process for producing compounds represented by Formula I of claim 1, the process comprising:

a) coupling two intermediates represented by Formula 1(iv):



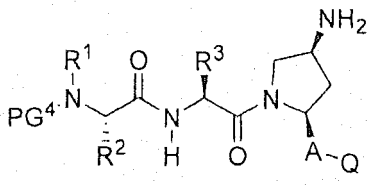
1 (iv)

wherein PG^3 is a protecting group, and R^1, R^2, R^3, A, and Q are as defined in claim 1, in a solvent; and

b) removing the protecting groups so as to form compounds of Formula I;

or

a) coupling an intermediate represented by Formula 2(iv):



2(iv)

wherein PG^4 is a protecting group, and R^1, R^2, R^3, A, and Q are as defined in claim 1 and an activated diacid (0.5 equiv) in a solvent; and

b) removing the protecting groups so as to form compounds of Formula I.

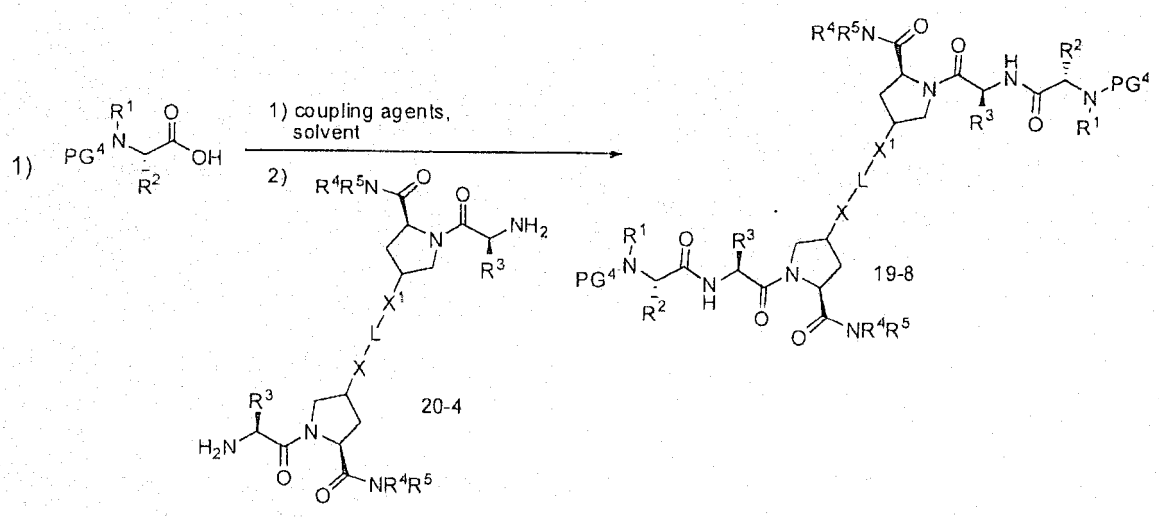
34. Use of a compound of any one of claims 1 to 31 for the manufacture of a medicament for treating or preventing a proliferative disorder or a disease state characterized by insufficient apoptosis.

35. Use, according to claim 34, in which the proliferative disorder or disease state is cancer.

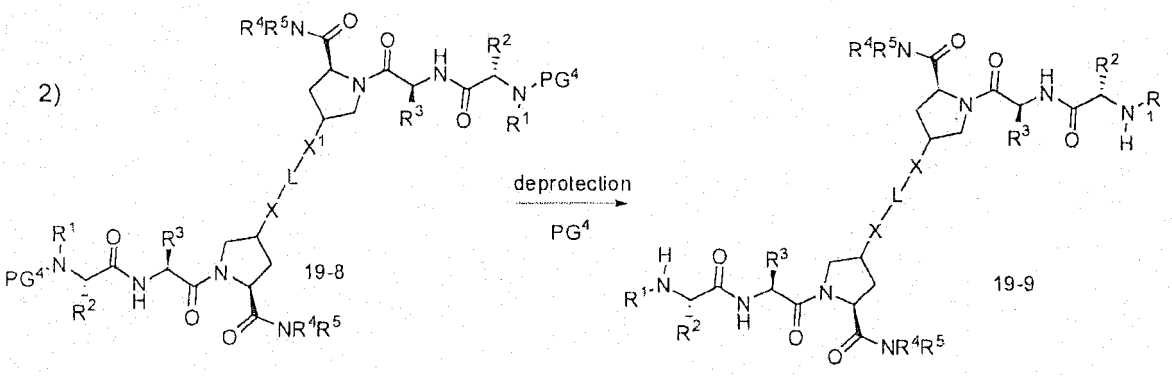
36. A pharmaceutical composition comprising a compound of any one of claims 1 to 31, and a pharmaceutically acceptable carrier, diluent or excipient, for treating or preventing a proliferative disorder or disease state characterized by insufficient apoptosis.

37. A pharmaceutical composition comprising a compound of any one of claims 1 to 31 in combination with any compound that increases the circulating level of one or more death receptor agonists for preventing or treating a proliferative disorder or disease state characterized by insufficient apoptosis.

38. A process for preparing a compound according to claim 1 of Formula 19-9, the process comprising the following steps:

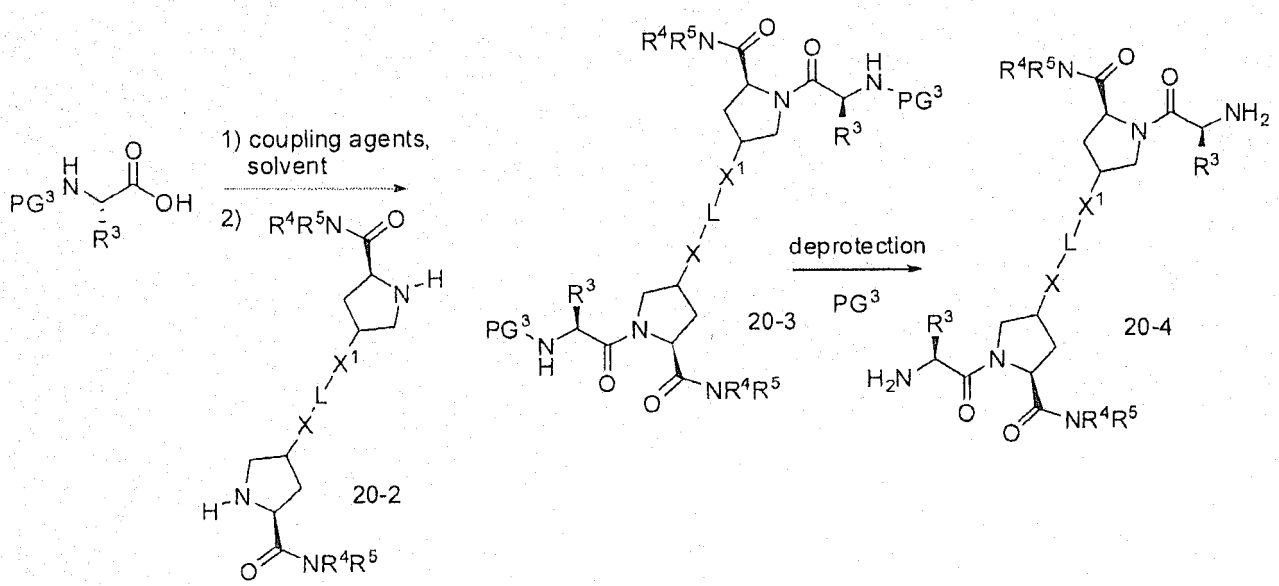


and



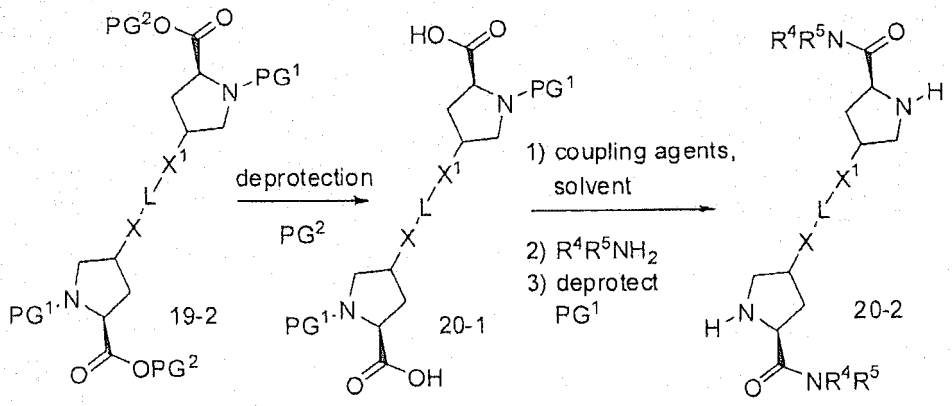
wherein PG^4 is a protecting group; and R^1, R^2, R^3, R^4, R^5, X, X^1, and L, are as defined in claim 1.

39. The process of claim 38, wherein 20-4 is prepared by a process comprising:



wherein PG^3 is a protecting group.

40. The process of claim 39, wherein 20-2 is prepared by a process comprising:



wherein PG^1 and PG^2 are protecting groups.