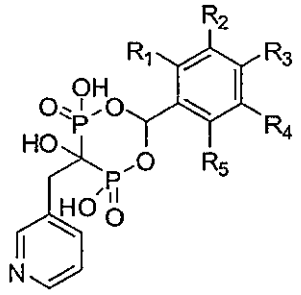
We claim:

1. A compound of Formula I,



(I)

or a pharmaceutically acceptable salt or hydrate thereof,

wherein R_1, R_2, R_3, R_4 and R_5 are each independently

a) hydrogen;

b) halogen, -CN, $-CF_3$, or $-NO_2$;

c) C_1-C_8 alkyl or C_1-C_8 haloalkyl;

d) C_2-C_8 alkenyl or C_2-C_8 haloalkenyl;

e) C_2-C_8 alkynyl or C_2-C_8 haloalkynyl;

f) optionally substituted aryl or optionally substituted heteroaryl;

g) $-C(O)R_6$;

h) $-C(O)OR_6$, or $-CO_2R_6$;

i) $-OR_6$, $-O-L-OC(O)R_6$, or $-O-L-OC(O)OR_6$;

j) $-OC(O)R_6$, or $-OC(O)-L-OC(O)R_6$;

k) $-OC(O)OR_6$, $-OC(O)O-L-C(O)R_7$, $-OC(O)O-L-C(O)OR_7$, or $-L-OC(O)R_6$;

l) $-C(O)NR_6R_7$, or $-CNR_6R_7$;

m) $-OC(O)NR_6R_7$, $-OC(O)N(R_6)$-L-$OC(O)R_7$, $-OC(O)O$-L-(R_6)-L-$C(O)R_7$, $-OC(O)$-$C(R_6)(R_7)$-L-$OC(O)R_8$, $-OC(O)N(-L-OC(O)R_7)(-L-OC(O)R_8)$;

n) $-SR_6$, or $-NR_6R_7$;

o) $-NR_6C(O)R_7$;

p) $-NR_6C(O)OR_7$;

q) $-NR_6C(O)NR_7$;

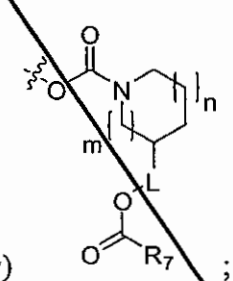
r) $-OSO_2R_6$;

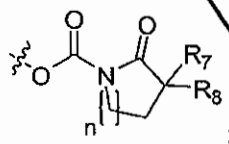
s) $-SO_2OR_6$;

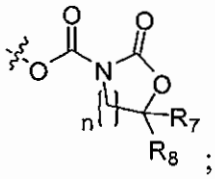
t) $-SO_2R_6$;

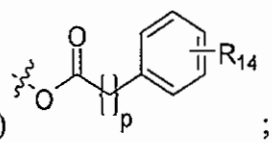
u) $-NR_6SO_2R_7$;

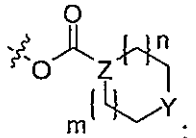
v) $-SO_2NR_6R_7$;

w) ;

x) ;

y) ;

z) ;

aa)  ; or

bb) R_1 and R_2, R_2 and R_3, R_3 and R_4, or R_4 and R_5 taken together form an optionally substituted 4- to 8-membered carbocyclic or heterocyclic ring, wherein the ring is saturated, unsaturated or aromatic;

wherein m and n are each independently an integer from 0 to 2;

Y is $-CH_2-$, -O-, $-NR_7-$, or -S-;

p is an integer from 1 to 3;

R_{14} is hydrogen, halogen, C_1-C_8 alkyl, or C_1-C_8 alkoxyl;

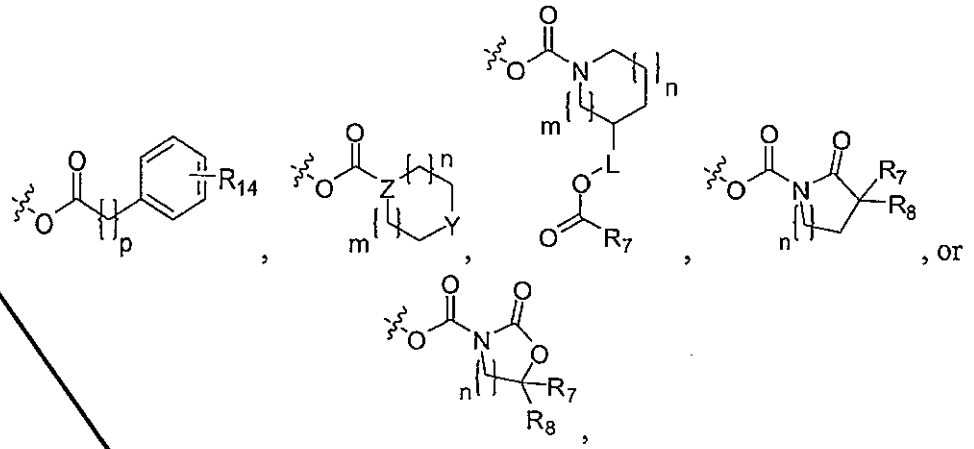
Z is  or ;

each R_6 is independently hydrogen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_2-C_8 alkenyl, C_2-C_8 haloalkenyl, C_2-C_8 alkynyl, C_2-C_8 haloalkynyl, an optionally substituted 4-8 membered saturated carbocyclic or heterocyclic ring, optionally substituted aryl, optionally substituted heteroaryl, -L-optionally substituted aryl or -L-optionally substituted heteroaryl;

R_7 and R_8 are each independently hydrogen or C_1-C_8 alkyl; and L is C_1-C_8 alkyl; or

R_6 and R_7 taken together form an optionally substituted 4- to 8-membered carbocyclic or heterocyclic ring, wherein the ring is saturated, unsaturated or aromatic.

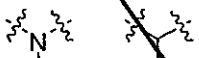
2. The compound of claim 1, wherein R_1, R_2, R_3, R_4, and R_5 are each independently hydrogen, halogen, $-CF_3$, C_1-C_8 alkyl, optionally substituted phenyl, $-OR_6$, -O-L-OC(O)R_6, -O-L-OC(O)OR_6, $-OC(O)R_6$, -OC(O)-L-OC(O)R_6, $-C(O)OR_6$, $-OC(O)OR_6$, -OC(O)O-L-C(O)R_7, $-OC(O)NR_6R_7$, $-OC(O)N(R_6)$-L-OC(O)R_7, -OC(O)N(-L-OC(O)R_7)(-L-OC(O)R_8),



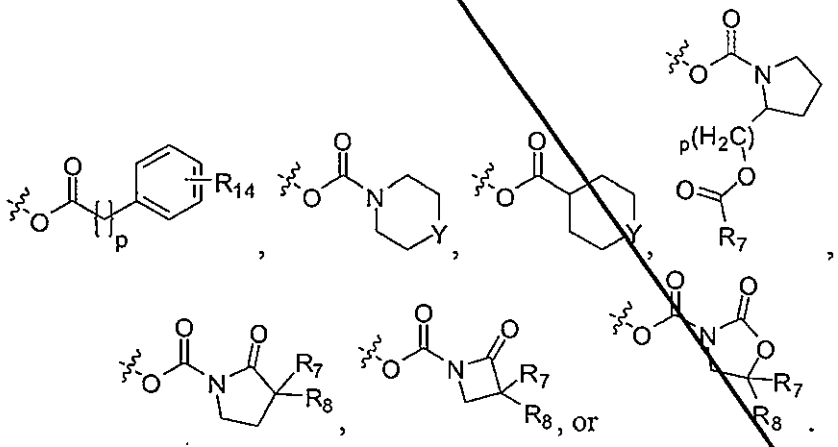
wherein Y is $-CH_2-$, -O-, $-NR_7-$, or -S-;

p is an integer from 1 to 3;

R_{14} is hydrogen, halogen, C_1-C_8 alkyl, or C_1-C_8 alkoxyl; and

Z is  or .

3. The compound of claim 1, wherein R_1, R_2, R_3, R_4, and R_5 are each independently $-OR_6$, $-O-(CH_2)_p-OC(O)R_6$, $-O-(CH_2)_p-OC(O)OR_6$, $-OC(O)R_6$, $-OC(O)-C(R_6)(R_7)-(CH_2)_p-OC(O)R_8$, $-C(O)OR_6$, $-OC(O)OR_6$, $-OC(O)O-CH(R_6)(CH_2)_pC(O)R_7$, $-OC(O)NR_6R_7$, $-OC(O)N(R_6)(CH_2)_p-OC(O)R_7$, $-OC(O)N(-(CH_2)_p-OC(O)R_7)(-(CH_2)_p-OC(O)R_8)$,



4. The compound of claim 1, wherein R_6 is C_1-C_8 alkyl, C_2-C_8 alkenyl, C_3-C_6 cycloalkyl, benzyl;

R_7 and R_8 are each independently hydrogen, methyl, or ethyl;

Y is -O-;

L is C_1-C_3 alkyl;

m is 0; and

n is 0 or 1.

5. The compound of claim 3, wherein R_6 is C_1-C_8 alkyl, C_2-C_8 alkenyl, C_3-C_6 cycloalkyl, benzyl;

R_7 and R_8 are each independently hydrogen, methyl, or ethyl; and

Y is -O-.

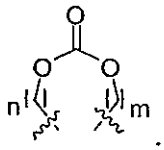
6. The compound of claim 1, wherein R_1 and R_2, R_2 and R_3, R_3 and R_4, or R_4 and R_5 taken together form an optionally substituted 5- to 7-membered carbocyclic or heterocyclic ring, wherein the ring is saturated, unsaturated or aromatic.

7. The compound of claim 6, wherein the 5- to 7-membered carbocyclic or heterocyclic ring is unsubstituted.

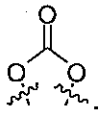
8. The compound of claim 6, wherein the 5- to 7-membered carbocyclic or heterocyclic ring is saturated or aromatic.

9. The compound of claim 6, wherein the 5- to 7-membered heterocyclic ring includes 1 or 2 heteroatoms.

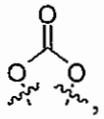
10. The compound of claim 6, wherein R_1 and R_2, R_2 and R_3, R_3 and R_4, or R_4 and R_5 taken together form



11. The compound of claim 10, wherein R_1 and R_2, R_2 and R_3, R_3 and R_4, or R_4 and R_5 taken together are

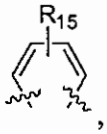


12. The compound of claim 10, wherein R_1 and R_2, R_2 and R_3, R_3 and R_4, or R_4 and R_5 taken together are



and the remaining R-groups of R_1, R_2, R_3, R_4, and R_5 are each hydrogen.

13. The compound of claim 6, wherein R_1 and R_2, R_2 and R_3, R_3 and R_4, or R_4 and R_5 taken together are



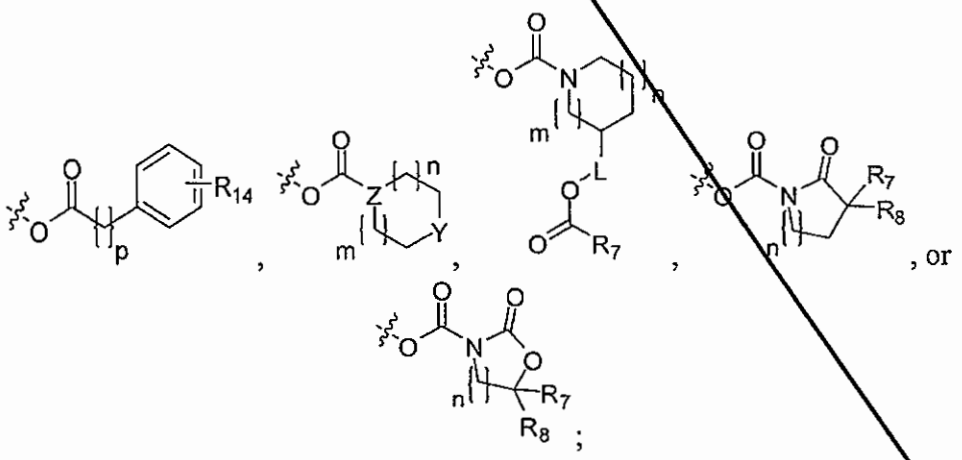
wherein R_{15} is hydrogen, halogen, or $-OR_6$.

14. The compound of claim 13, wherein R_1 and R_2, R_2 and R_3, R_3 and R_4, or R_4 and R_5 taken together are



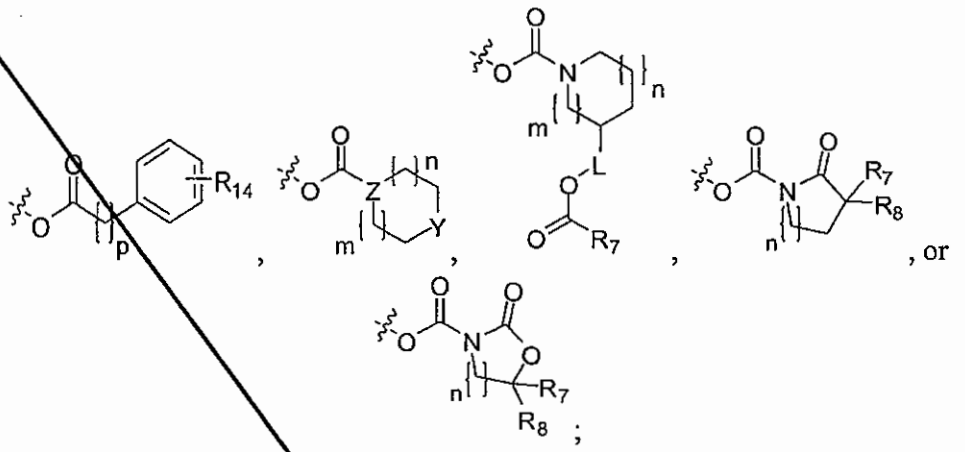
and the remaining R-groups of R_1, R_2, R_3, R_4, and R_5 are each independently -H or $-OC(O)OR_6$.

15. The compound of claim 1, wherein one of R_1, R_2, R_3, R_4, and R_5 is $-OR_6$, $-O-L-OC(O)R_6$, $-O-L-OC(O)OR_6$, $-OC(O)R_6$, $-OC(O)-L-OC(O)R_6$, $-OC(O)OR_6$, $-OC(O)O-L-C(O)R_7$, $-OC(O)NR_6R_7$, $-OC(O)N(R_6)-L-OC(O)R_7$, $-OC(O)N(-L-OC(O)R_7)(-L-OC(O)R_8)$,



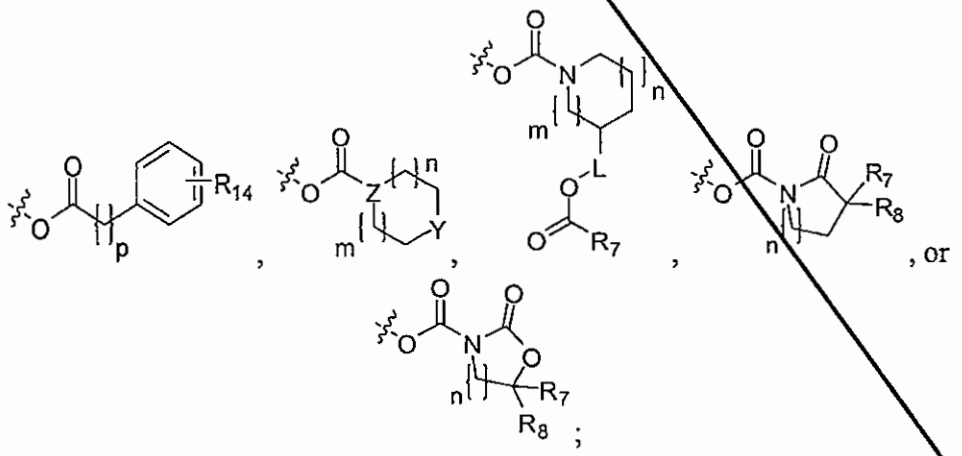
any two of the remaining R_1, R_2, R_3, R_4, and R_5 are halogen; and each of the remaining R-groups of R_1, R_2, R_3, R_4, and R_5 are hydrogen.

16. The compound of claim 1, wherein one of R_1, R_2, R_3, R_4, and R_5 is $-OR_6$, $-O-L-OC(O)R_6$, $-O-L-OC(O)OR_6$, $-OC(O)R_6$, $-OC(O)-L-OC(O)R_6$, $-OC(O)OR_6$, $-OC(O)O-L-C(O)R_7$, $-OC(O)NR_6R_7$, $-OC(O)N(R_6)-L-OC(O)R_7$, $-OC(O)N(-L-OC(O)R_7)(-L-OC(O)R_8)$,



one of the remaining R-groups of R_1, R_2, R_3, R_4, and R_5 is halogen, $-CF_3$, C_1-C_8 alkyl, phenyl, $-OR_6$, or $-C(O)OR_6$; and each remaining R-group of R_1, R_2, R_3, R_4, and R_5 is hydrogen.

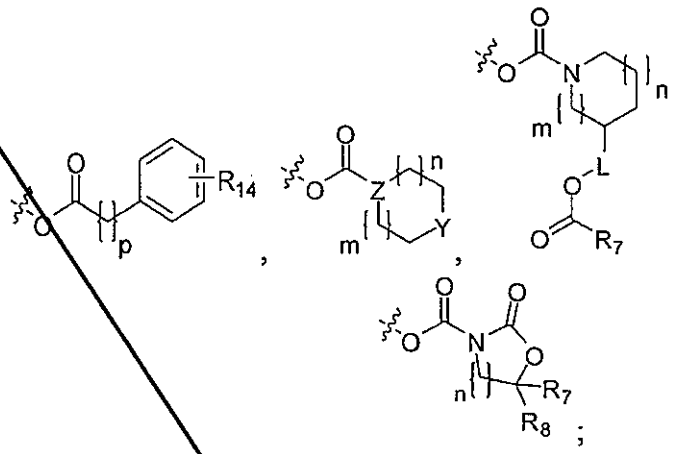
17. The compound of claim 1, wherein one of R_1, R_2, R_3, R_4, and R_5 is $-OR_6$, $-O-L-OC(O)R_6$, $-O-L-OC(O)OR_6$, $-OC(O)R_6$, $-OC(O)-L-OC(O)R_6$, $-OC(O)OR_6$, $-OC(O)O-L-C(O)R_7$, $-OC(O)NR_6R_7$, $-OC(O)N(R_6)-L-OC(O)R_7$, $-OC(O)N(-L-OC(O)R_7)(-L-OC(O)R_8)$,



and the remaining R-groups of R_1, R_2, R_3, R_4, and R_5 are each hydrogen.

18. The compound of claim 1, wherein R_1 and R_5 are each independently halogen; and

R_3 is $-OR_6$, $-O-L-OC(O)R_6$, $-O-L-OC(O)OR_6$, $-OC(O)R_6$, $-OC(O)-L-OC(O)R_6$, $-OC(O)OR_6$, $-OC(O)O-L-C(O)R_7$, $-OC(O)NR_6R_7$, $-OC(O)N(R_6)-L-OC(O)R_7$, $-OC(O)N(-L-OC(O)R_7)(-L-OC(O)R_8)$,



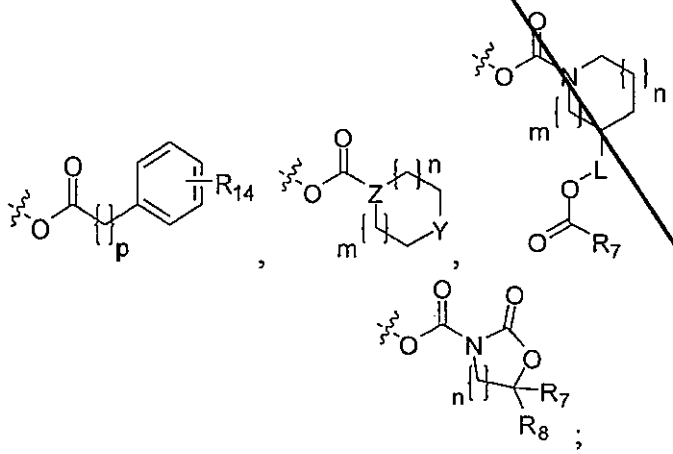
, or

;

and the remaining R-groups of R_1, R_2, R_3, R_4, and R_5 are each hydrogen.

19. The compound of claim 18, wherein R_1 and R_5 are each independently -F or -Cl.

20. The compound of claim 1, wherein R_1 is $-OR_6$, $-O-L-OC(O)R_6$, $-O-L-OC(O)OR_6$,$-OC(O)R_6$, $-OC(O)-L-OC(O)R_6$, $-OC(O)OR_6$, $-OC(O)O-L-C(O)R_7$, $-OC(O)NR_6R_7$, $-OC(O)N(R_6)-L-OC(O)R_7$, $-OC(O)N(-L-OC(O)R_7)(-L-OC(O)R_8)$,

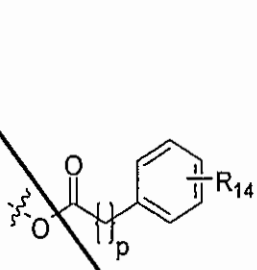
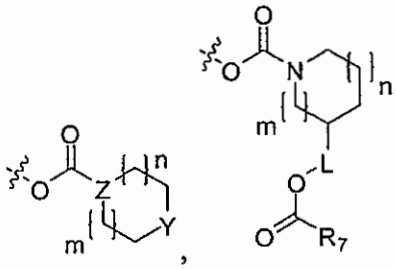
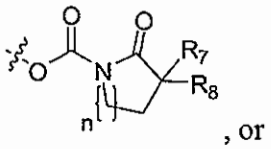
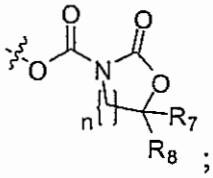


, or

;

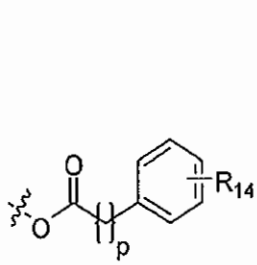
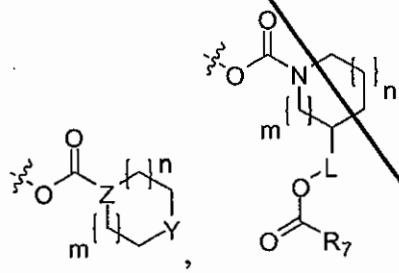
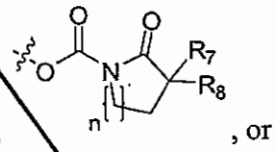
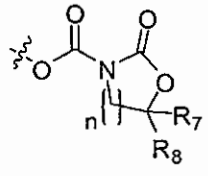
one of the remaining R-groups of R_1, R_2, R_3, R_4, and R_5 is halogen, $-CF_3$, C_1-C_8 alkyl, phenyl, $-OR_6$, or $-C(O)OR_6$; and each remaining R-group of R_1, R_2, R_3, R_4, and R_5 is hydrogen.

21. The compound of claim 1, wherein R_3 is $-OR_6$, -O-L-$OC(O)R_6$, -O-L-$OC(O)OR_6$, $-OC(O)R_6$, -OC(O)-L-$OC(O)R_6$, $-OC(O)OR_6$, -OC(O)O-L-$C(O)R_7$, -$OC(O)NR_6R_7$, -OC(O)N(R_6)-L-$OC(O)R_7$, -OC(O)N(-L-$OC(O)R_7$)(-L-$OC(O)R_8$),




, or

;

one of the remaining R-groups of R_1, R_2, R_3, R_4, and R_5 is halogen, $-CF_3$, C_1-C_8 alkyl, phenyl, $-OR_6$, or $-C(O)OR_6$; and each remaining R-group of R_1, R_2, R_3, R_4, and R_5 is hydrogen.

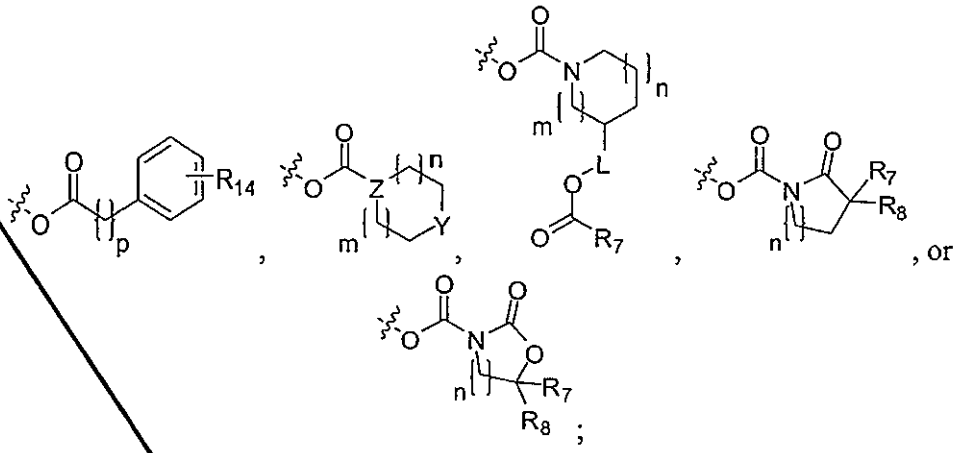
22. The compound of claim 1, wherein R_1 is $-OR_6$, -O-L-$OC(O)R_6$, -O-L-$OC(O)OR_6$, $-OC(O)R_6$, -OC(O)-L-$OC(O)R_6$, $-OC(O)OR_6$, -OC(O)O-L-$C(O)R_7$, -$OC(O)NR_6R_7$, -OC(O)N(R_6)-L-$OC(O)R_7$, -OC(O)N(-L-$OC(O)R_7$)(-L-$OC(O)R_8$),




, or

;

and R_2, R_3, R_4, and R_5 are each hydrogen.

23. The compound of claim 1, wherein R_3 is $-OR_6$, -O-L-$OC(O)R_6$, -O-L-$OC(O)OR_6$, $-OC(O)R_6$, -OC(O)-L-$OC(O)R_6$, $-OC(O)OR_6$,

-OC(O)O-L-C(O)R_7, -OC(O)NR_6R_7, -OC(O)N(R_6)-L-OC(O)R_7, -OC(O)N(-L-OC(O)R_7)(-L-OC(O)R_8),



and R_1, R_2, R_4, and R_5 are each hydrogen.

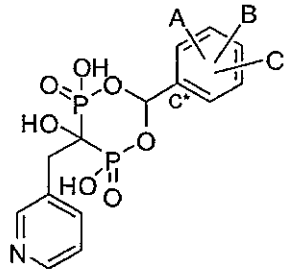
24. The compound of claim 22, wherein R_1 is -OC(O)OR_{16}, -OC(O)R_{16} or -OC(O)N$R_{16}R_{17}$ and R_{16} and R_{17} are each independently C_1-C_4 alkyl.

25. The compound of claim 23, wherein R_3 is -OC(O)OR_{16}, -OC(O)R_{16} or -OC(O)N$R_{16}R_{17}$ and R_{16} and R_{17} are each independently C_1-C_4 alkyl.

26. The compound of claim 1, wherein R_1 is -OC(O)OCH_3, -OC(O)OCH_2CH_3 or -OC(O)$OCH(CH_3)_2$; and
R_2, R_3, R_4 and R_5 are each independently hydrogen, halogen, -CF_3, C_1-C_8 alkyl, optionally substituted phenyl, -OR_6, or -C(O)OR_6.

27. The compound of claim 1, wherein R_3 is -OC(O)OCH_3 or -OC(O)$OCH(CH_3)_2$; and
R_1, R_2, R_4 and R_5 are each independently hydrogen, halogen, or -CF_3.

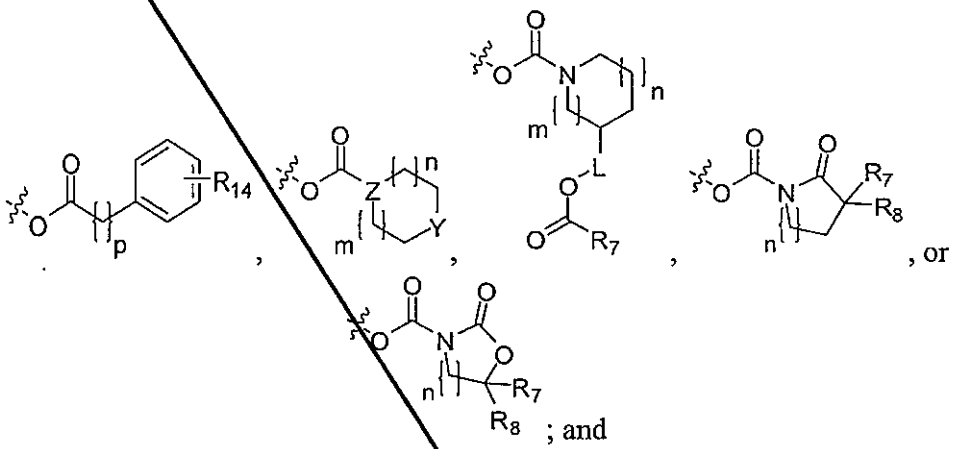
28. A compound of Formula II,



(II)

or a pharmaceutically acceptable salt or hydrate thereof,

wherein A is $-OR_6$, $-CO_2R_6$, -L-OC(O)R_6, -O-L-OC(O)R_6, -O-L-OC(O)OR_6, -OC(O)R_6, -OC(O)-L-OC(O)R_6, -OC(O)OR_6, -OC(O)O-L-C(O)R_7, -OC(O)O-L-C(O)OR_7, -C(O)NR_6R_7, -CNR_6R_7, -OC(O)NR_6R_7, -OC(O)N(R_6)-L-OC(O)R_7, -OC(O)N(-L-OC(O)R_7)(-L-OC(O)R_8),



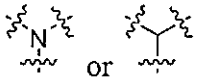
; and

B and C are each independently hydrogen, halogen, $-CF_3$, -CN, C_1-C_8 alkyl, phenyl, $-OR_6$, or -C(O)OR_6, or B and C when taken together form an optionally substituted 4- to 8-membered carbocyclic or heterocyclic ring, wherein the ring is saturated, unsaturated or aromatic;

wherein m and n are each independently an integer from 0 to 2;

Y is $-CH_2-$, -O-, $-NR_7-$, or -S-;

p is an integer from 1 to 3;

Z is  ;

each R_6 is independently hydrogen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_2-C_8 alkenyl, C_2-C_8 haloalkenyl, C_2-C_8 alkynyl, C_2-C_8 haloalkynyl, an optionally

substituted 4-8 membered saturated carbocyclic or heterocyclic ring, optionally substituted aryl, optionally substituted heteroaryl, -L-optionally substituted aryl or -L-optionally substituted heteroaryl;

L is C_1-C_8 alkyl;

R_{14} is hydrogen, halogen, C_1-C_8 alkyl, or C_1-C_8 alkoxyl;

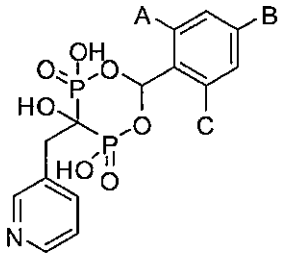
R_7 and R_8 are each independently hydrogen or C_1-C_8 alkyl; or

R_8 and R_7 taken together form an optionally substituted 4- to 8-membered carbocyclic or heterocyclic ring, wherein the ring is saturated, unsaturated or aromatic.

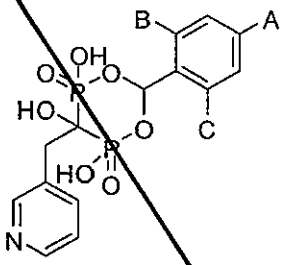
29. The compound of claim 28, wherein A is in the *ortho* or *para* position relative to C*.

30. The compound of claim 28, wherein A is in the *meta* position relative to C*.

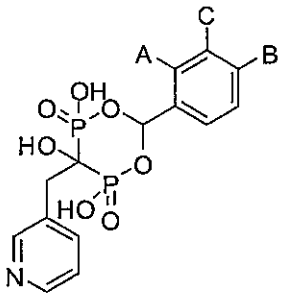
31. The compound of claim 28, wherein the compound is a compound or a pharmaceutically acceptable salt or hydrate of a compound of Formula IIa, IIb, IIc, IId, or IIe:



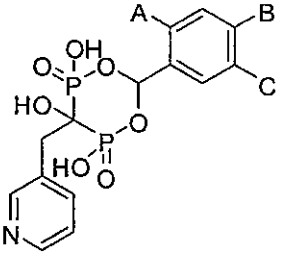
(IIa)



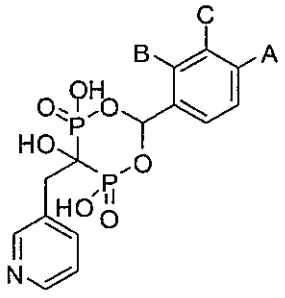
(IIb)



(IIc)



(IId)



(IIe).

32. The compound of claim 28, wherein A is $-OC(O)NR_6R_7$, $-OC(O)R_6$, or $-OC(O)OR_6$.

33. The compound of claim 32, wherein R_6 and R_7 are each independently hydrogen or C_1-C_8 alkyl.

34. The compound of claim 33, wherein B and C are each independently hydrogen, cyano, halogen, or $-OC(O)R_6$.

35. The compound of claim 34, wherein B and C are each independently halogen.

36. The compound of claim 36, wherein B and C are each fluoro.

37. The compound of claim 4, wherein R_6 is hydrogen, methyl, ethyl, propyl, isopropyl, *tert*-butyl, $-CH_2CH(CH_3)_2$, pentyl, $-CH_2C(CH_3)_3$, heptyl, $-CH(CH_3)(CH_2)_5CH_3$, $-CH=C(CH_3)_2$, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, benzyl or tetrahydro-2H-pyranyl.

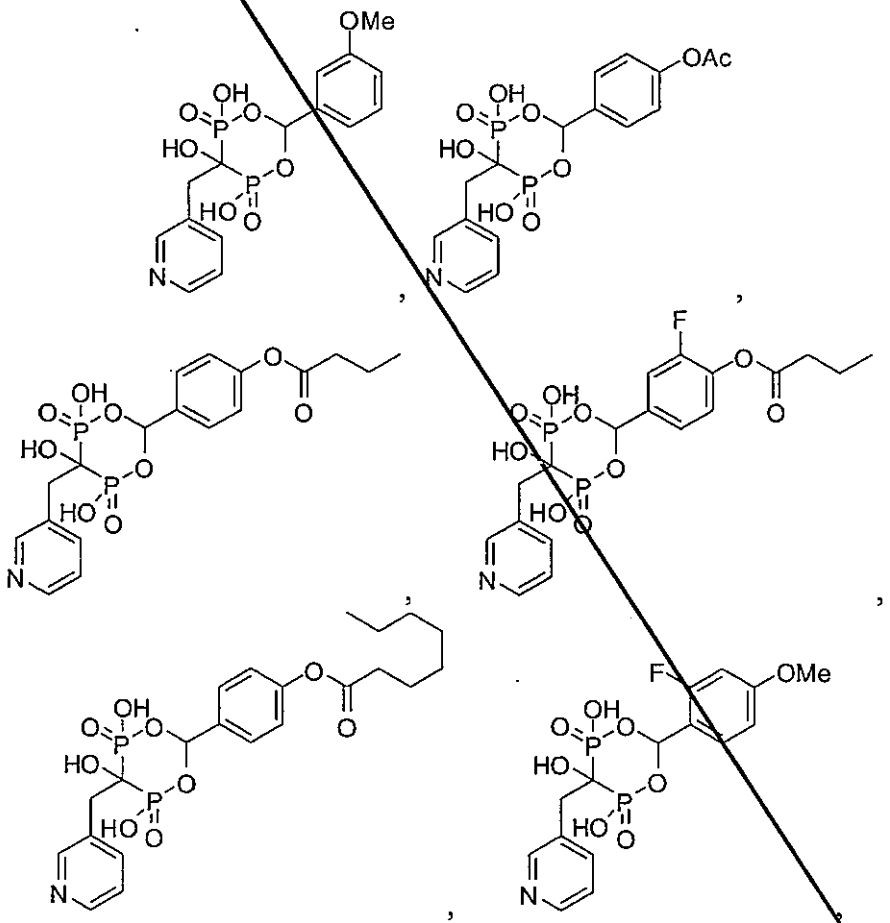
38. The compound of claim 1, wherein R_6 is hydrogen, methyl, ethyl, propyl, isopropyl, *tert*-butyl, $-CH_2CH(CH_3)_2$, pentyl, $-CH_2C(CH_3)_3$, heptyl, $-CH(CH_3)(CH_2)_5CH_3$, $-CH=C(CH_3)_2$, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, benzyl, or tetrahydro-2H-pyranyl; and R_7 and R_8 are each independently hydrogen, methyl, ethyl, propyl, isopropyl, *tert*-butyl.

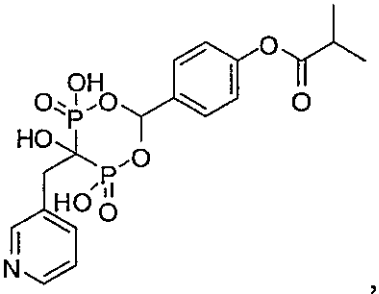
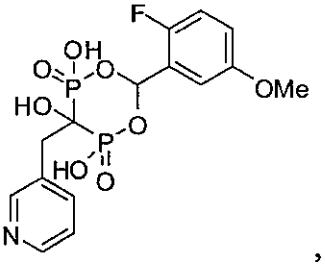
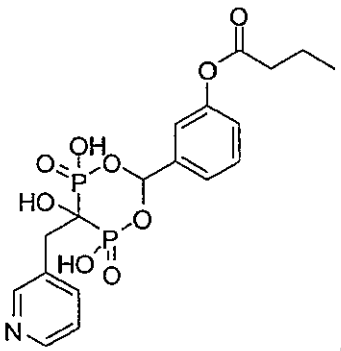
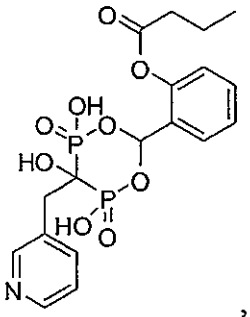
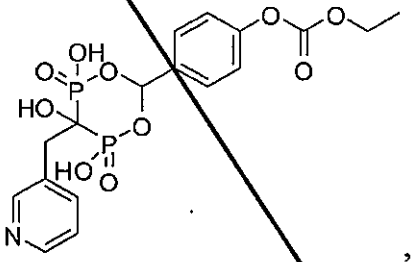
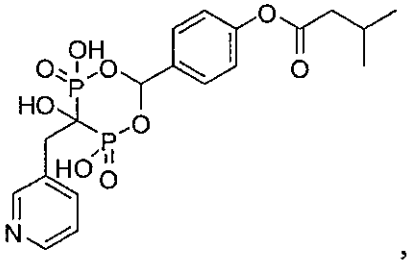
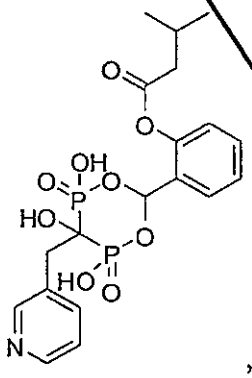
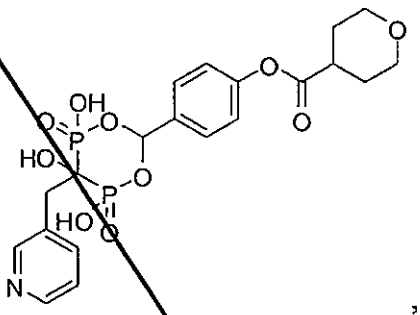
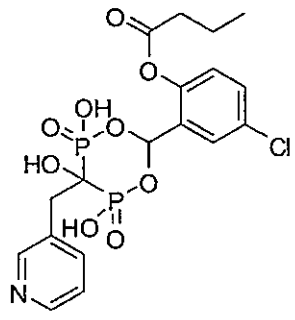
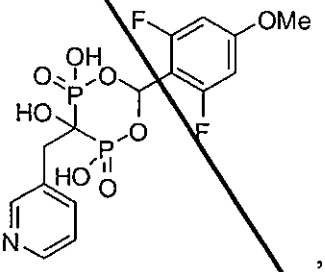
39. The compound of claim 1, wherein L is C_1-C_3 alkyl.

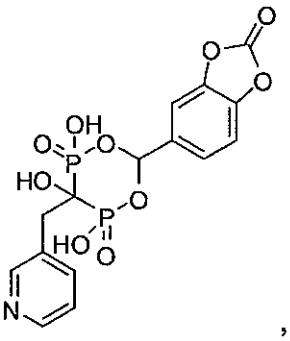
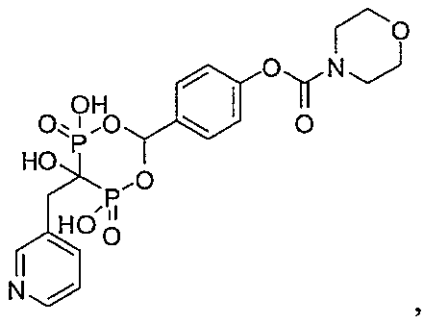
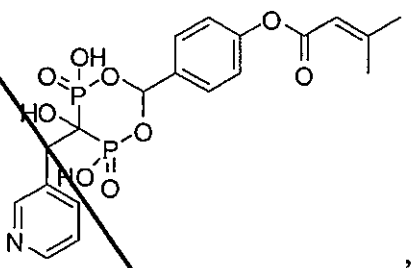
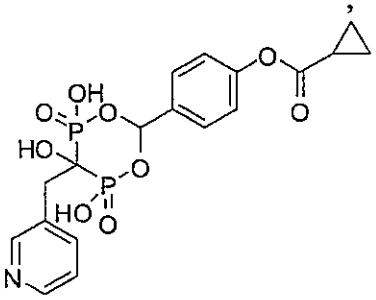
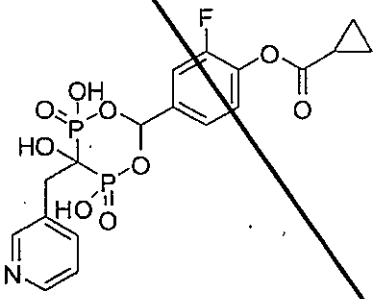
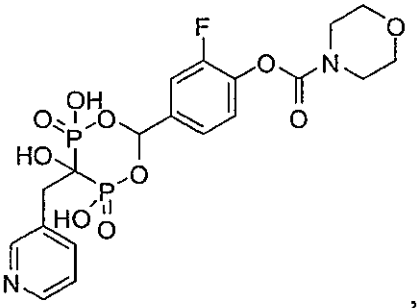
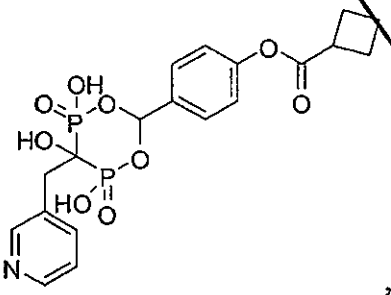
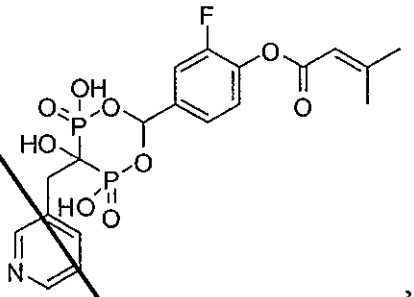
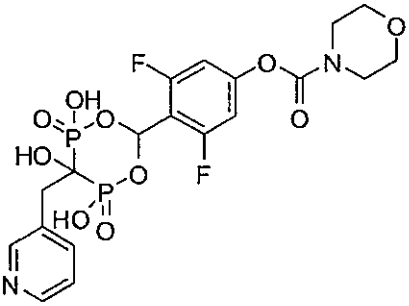
40. The compound of claim 1, wherein R_2, R_3, R_4 and R_5 are each hydrogen and R_1 is $-OC(O)OR_6$ or $-OC(O)OR_6$.

41. The compound of claim 40, wherein R_1 is $-OC(O)OR_6$ and R_6 is C_1-C_8 alkyl.

42. The compound or a pharmaceutically acceptable salt or hydrate of the compound of claim 1, wherein the compound is:




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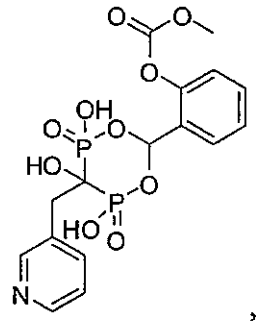
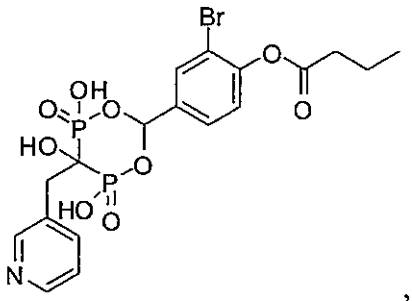
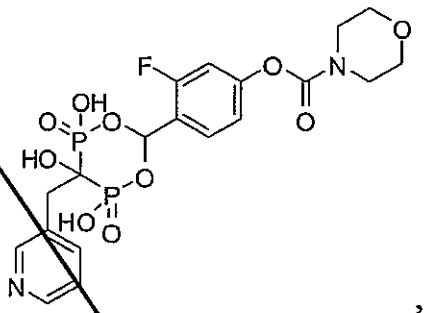
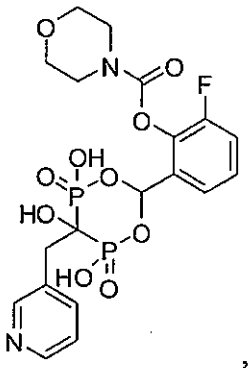
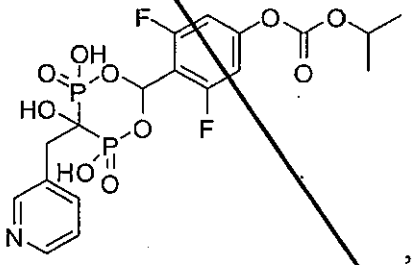
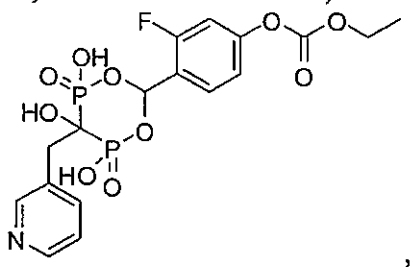
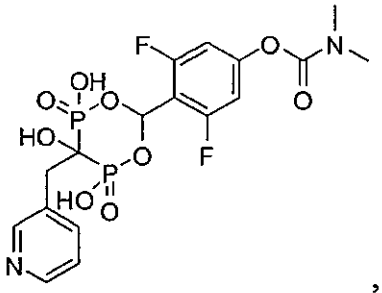
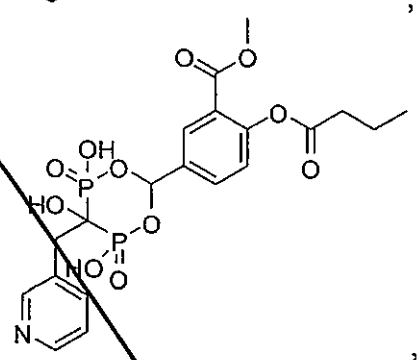
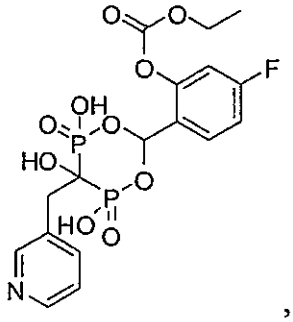
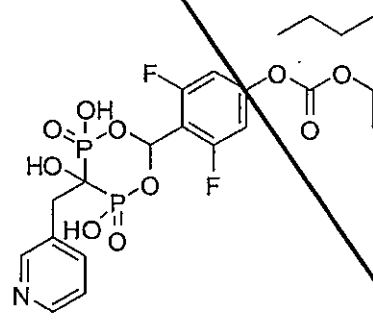
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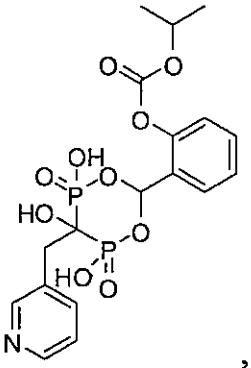
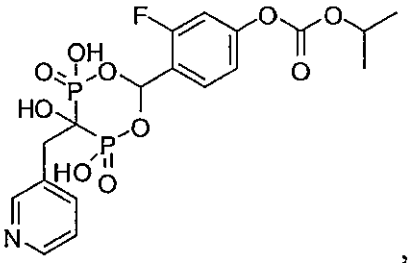
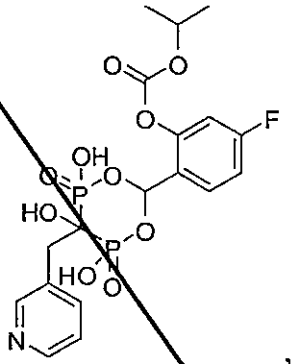
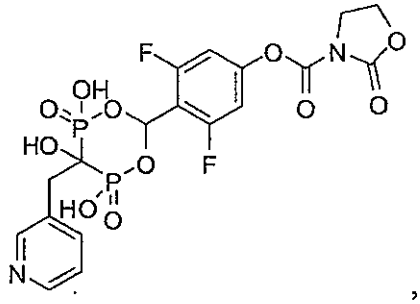
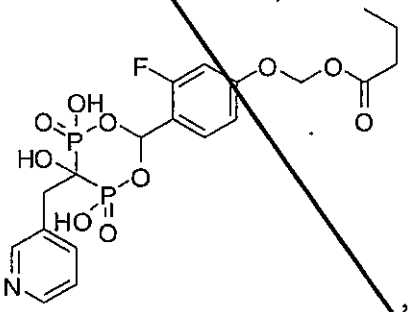
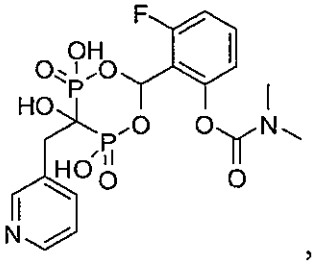
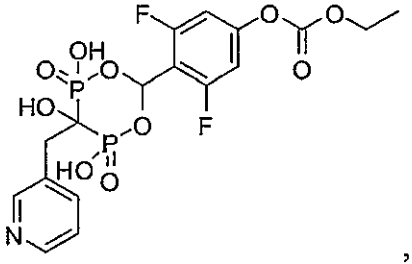
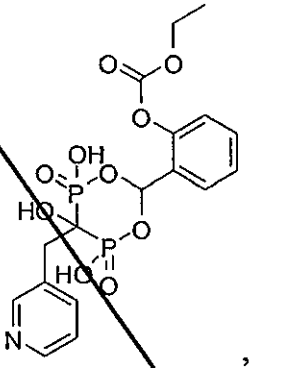
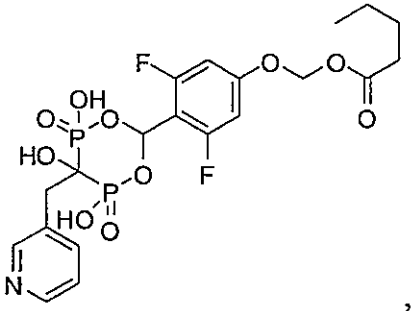
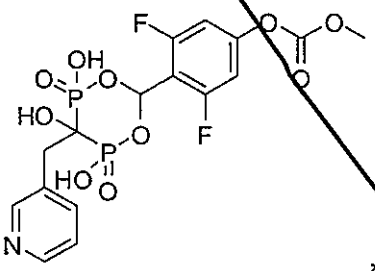
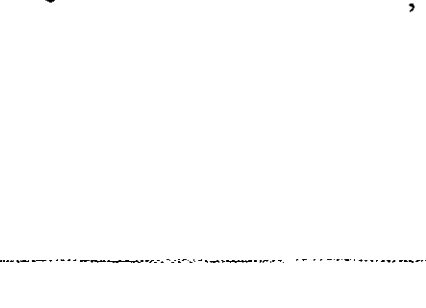
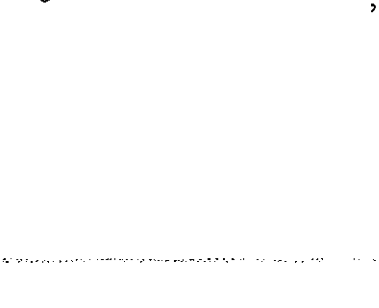
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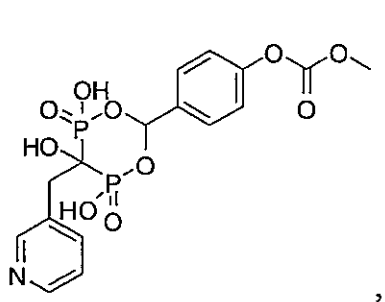
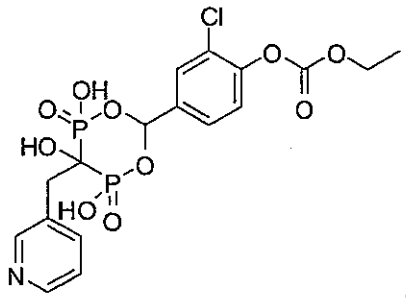
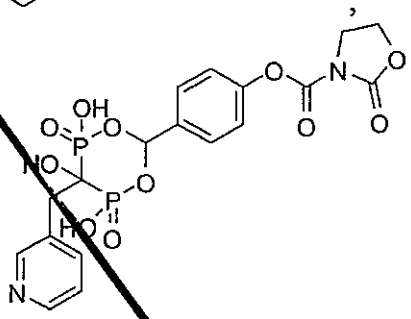
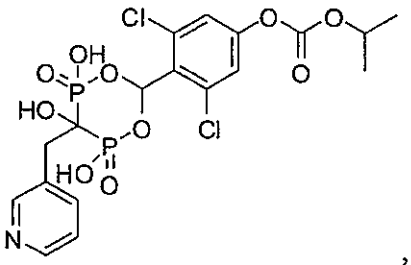
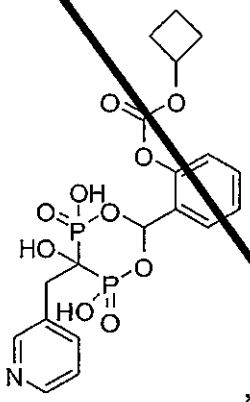
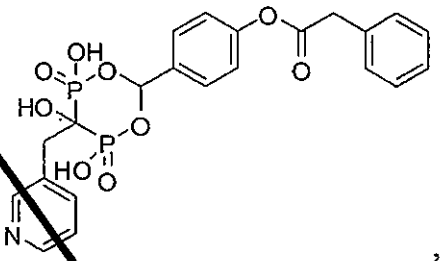
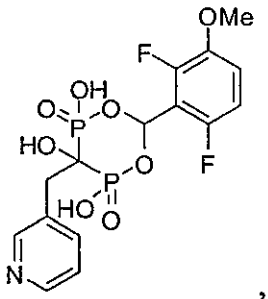
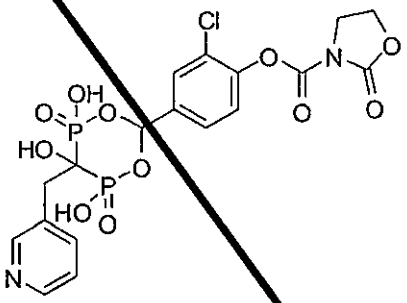
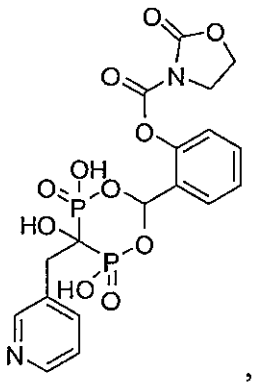
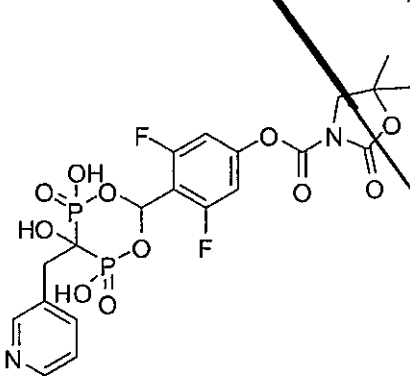
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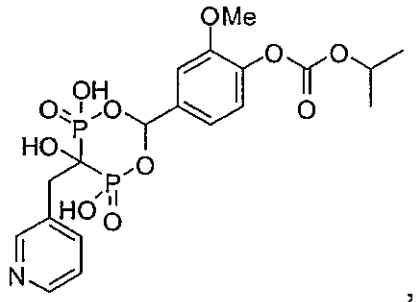
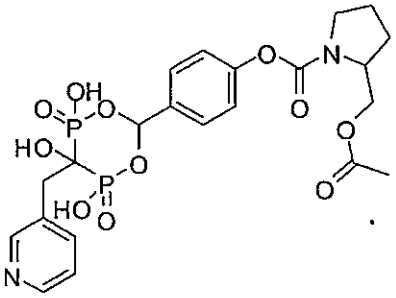
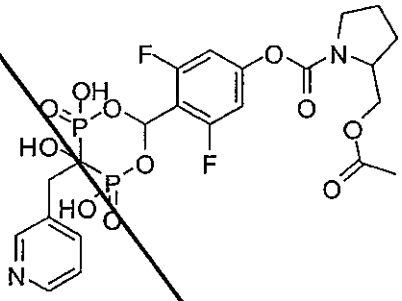
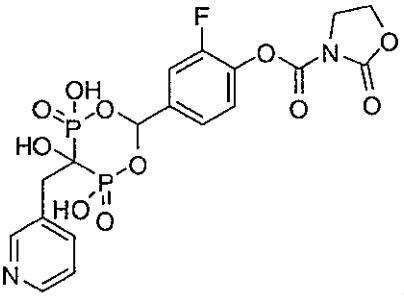
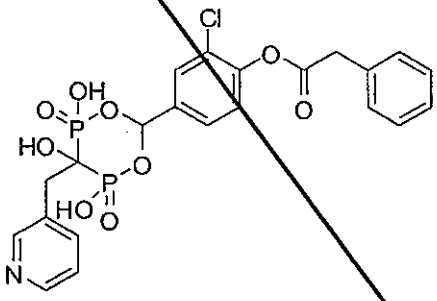
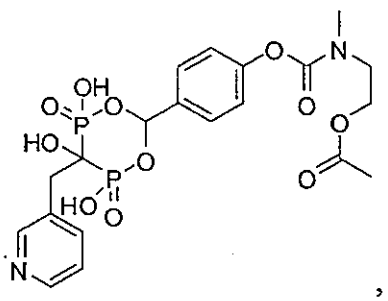
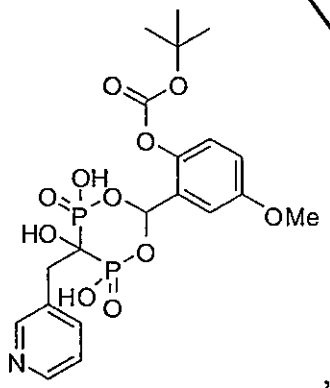
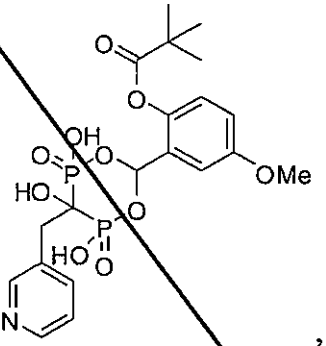
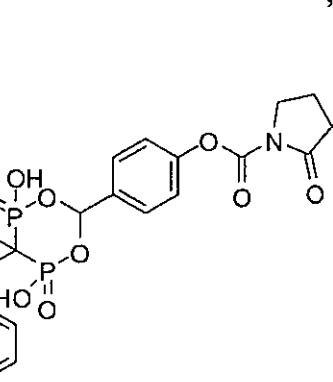
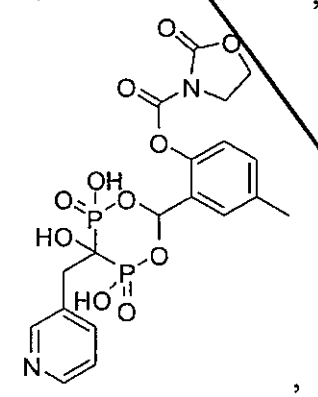
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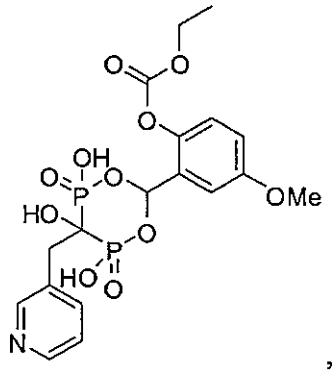
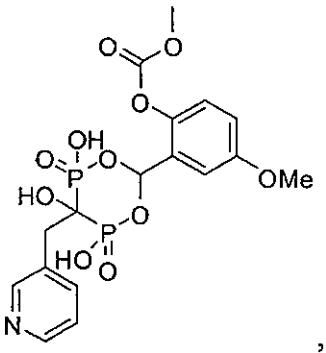
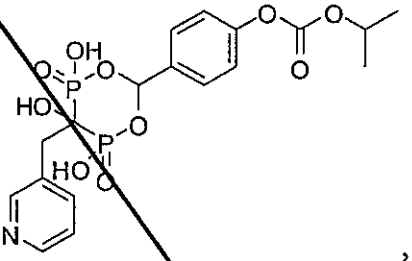
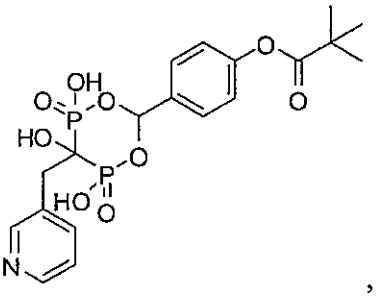
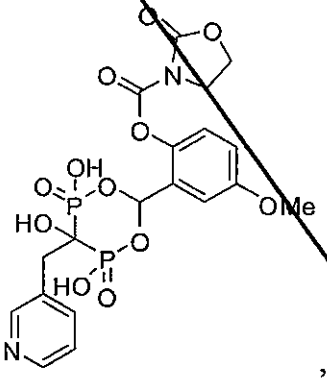
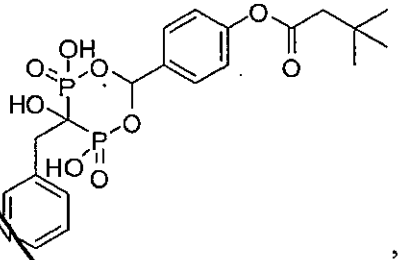
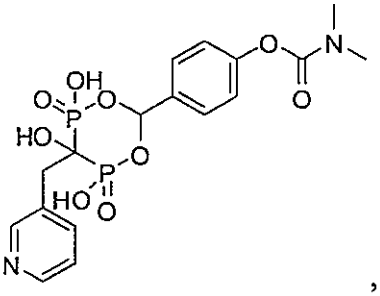
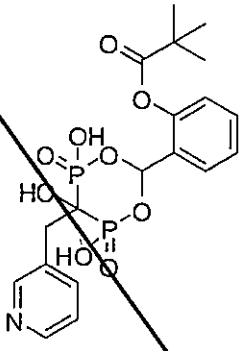

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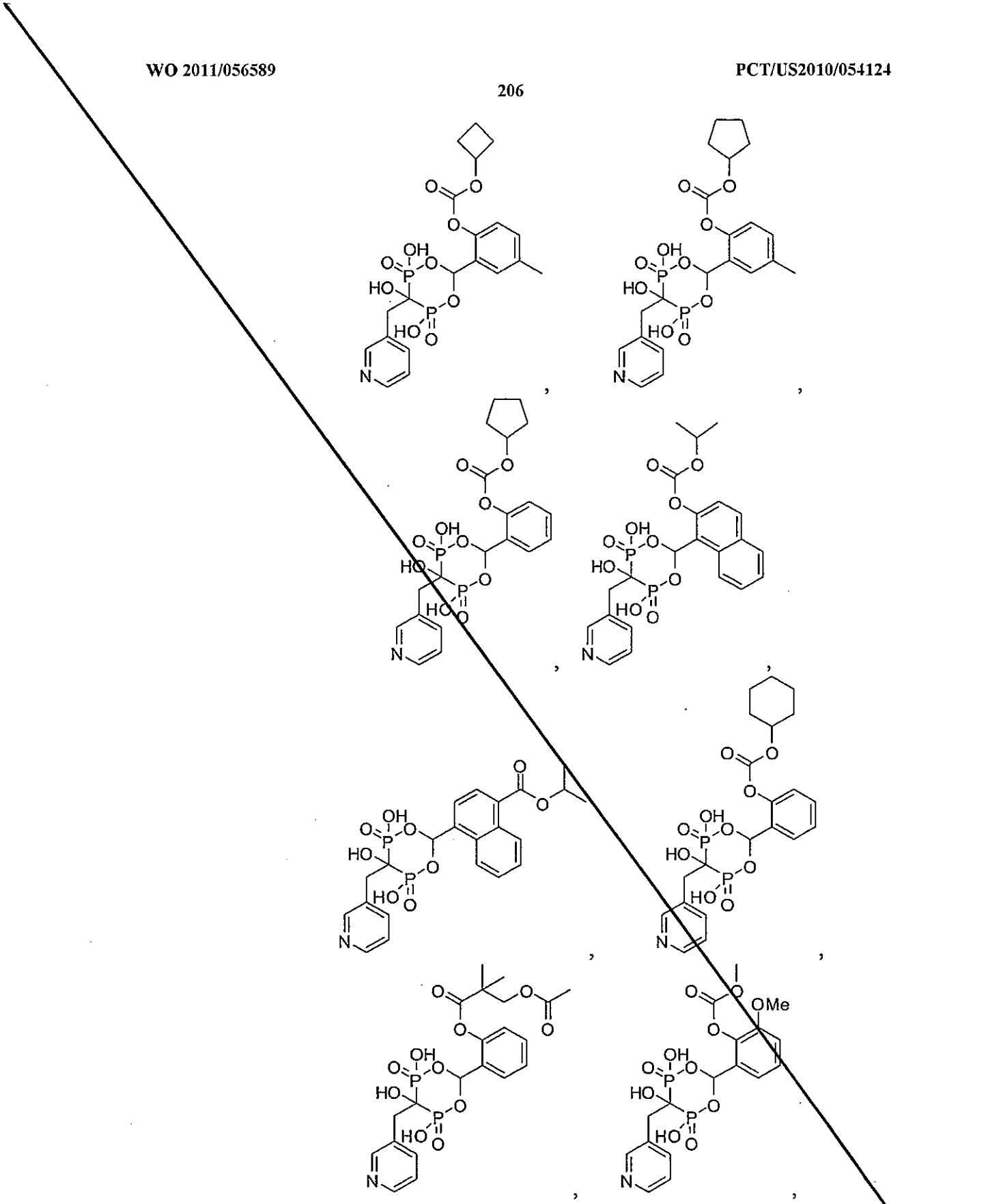

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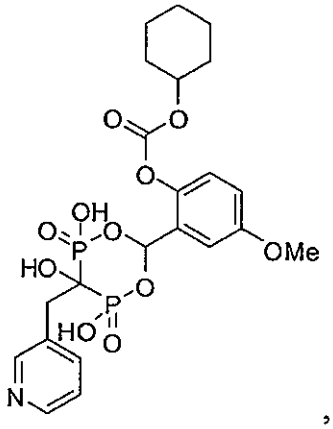
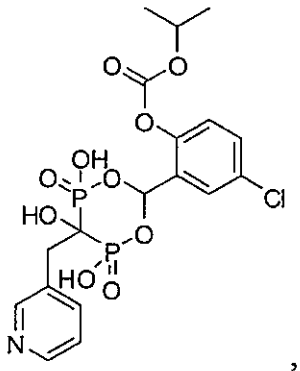
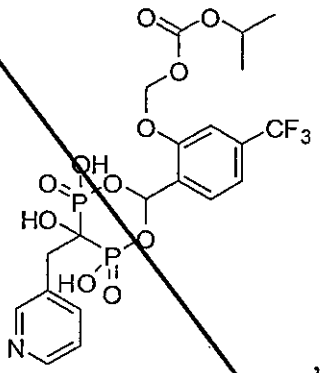
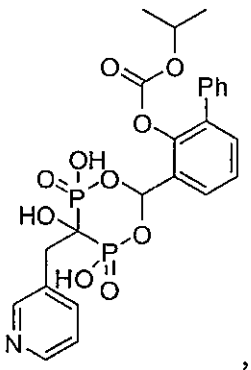
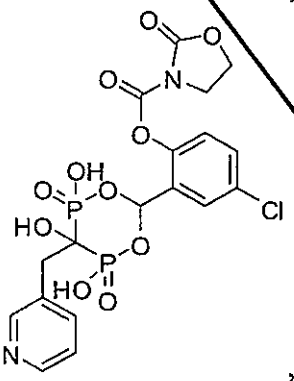
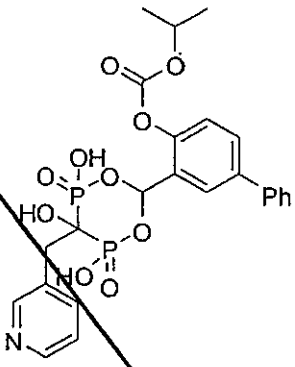
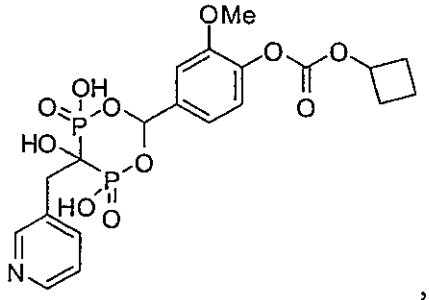
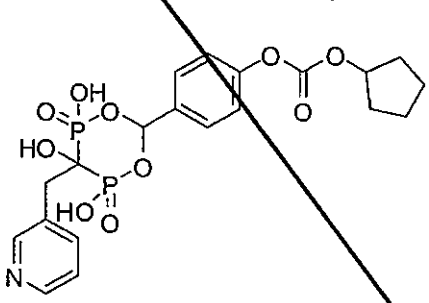
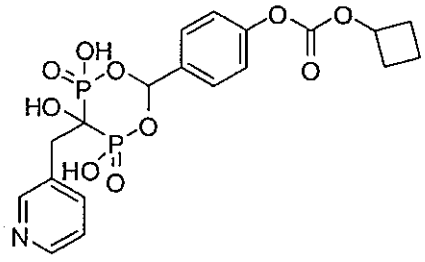
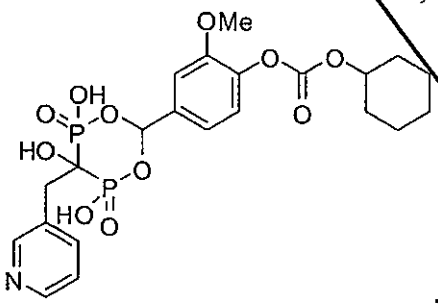

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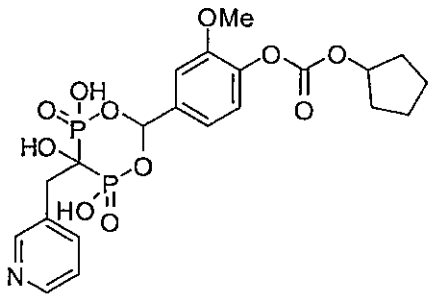
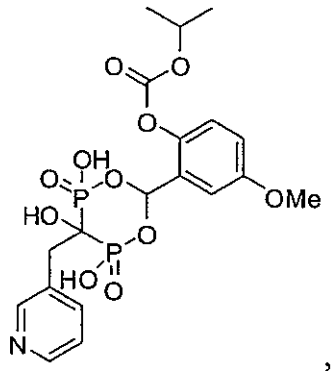
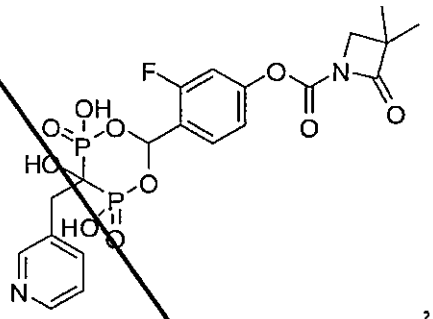
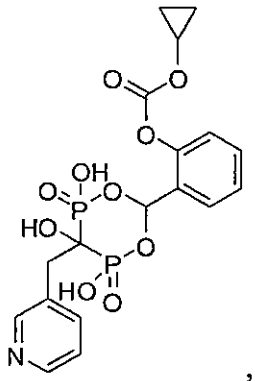
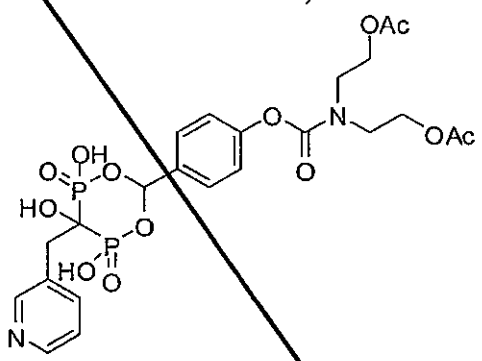
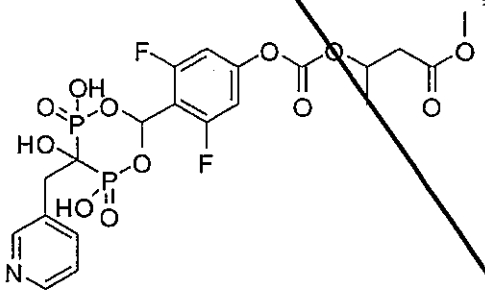
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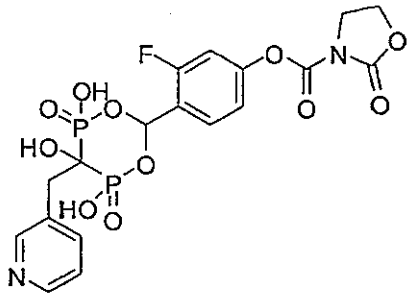
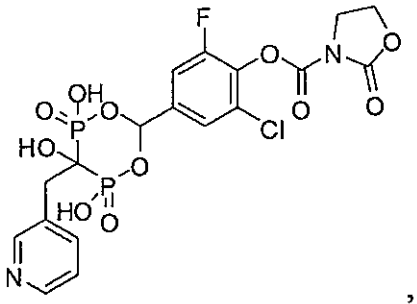
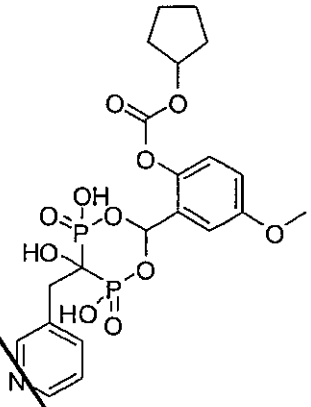
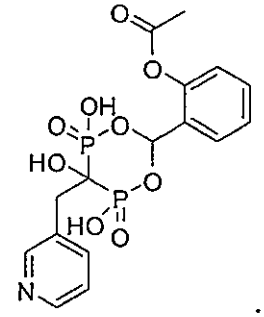
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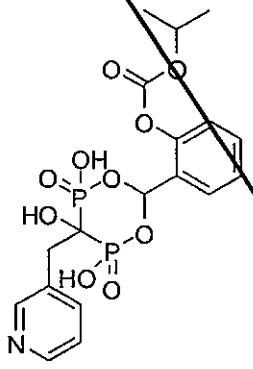



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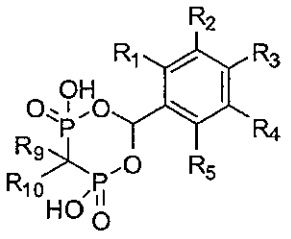
43. The compound or a pharmaceutically acceptable salt or hydrate of the compound of claim 1, wherein the compound is:



44. The compound of claim 43, wherein the compound is a *trans*-isomer.

45. The compound of claim 44, wherein the compound is a monosodium salt monohydrate.

46. A compound of Formula III,



(III)

or a pharmaceutically acceptable salt or hydrate thereof,

wherein R_1, R_2, R_3, R_4 and R_5 are each independently

a) hydrogen;

b) halogen, -CN, $-CF_3$, or $-NO_2$;

c) C_1-C_8 alkyl or C_1-C_8 haloalkyl;

d) C_2-C_8 alkenyl or C_2-C_8 haloalkenyl;

e) C_2-C_8 alkynyl or C_2-C_8 haloalkynyl;

f) optionally substituted aryl or optionally substituted heteroaryl;

g) $-C(O)R_6$;

h) $-C(O)OR_6$, or $-CO_2R_6$;

i) $-OR_6$, $-O$-L-$OC(O)R_6$, or $-O$-L-$OC(O)OR_6$;

j) $-OC(O)R_6$, or $-OC(O)$-L-$OC(O)R_6$;

k) $-OC(O)OR_6$, $-OC(O)O$-L-$C(O)R_7$, $-OC(O)O$-L-$C(O)OR_7$, or -L-$OC(O)R_6$;

l) $-C(O)NR_6R_7$, or $-CNR_6R_7$;

m) $-OC(O)NR_6R_7$, $-OC(O)N(R_6)$-L-$OC(O)R_7$, $-OC(O)O$-L-(R_6)-L-$C(O)R_7$, $-OC(O)$-$C(R_6)(R_7)$-L-$OC(O)R_8$, $-OC(O)N(-$L-$OC(O)R_7)(-$L-$OC(O)R_8)$;

n) $-SR_6$, or $-NR_6R_7$;

o) $-NR_6C(O)R_7$;

p) $-NR_6C(O)OR_7$;

q) $-NR_6C(O)NR_7$;

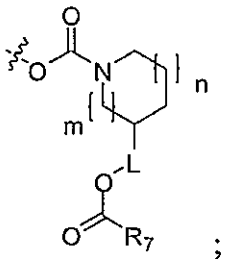
r) $-OSO_2R_6$;

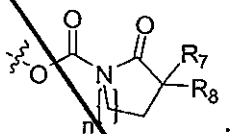
s) $-SO_2OR_6$;

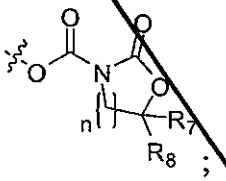
t) $-SO_2R_6$;

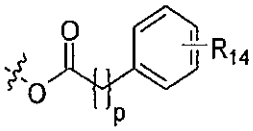
u) $-NR_6SO_2R_7$;

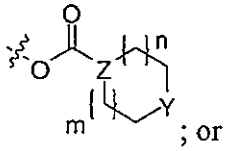
v) $-SO_2NR_6R_7$;

w)  ;

x)  ;

y)  ;

z)  ;

aa)  ; or

bb) R_1 and R_2, R_2 and R_3, R_3 and R_4, or R_4 and R_5 taken together form an optionally substituted 4- to 8-membered carbocyclic or heterocyclic ring, wherein the ring is saturated, unsaturated or aromatic;

wherein m and n are each independently an integer from 0 to 2;

Y is $-CH_2-$, -O-, $-NR_7-$, or -S-;

p is an integer from 1 to 3;

R_{14} is hydrogen, halogen, C_1-C_8 alkyl, or C_1-C_8 alkoxyl;

Z is  or ;

R_6 is independently hydrogen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_2-C_8 alkenyl, C_2-C_8 haloalkenyl, C_2-C_8 alkynyl, C_2-C_8 haloalkynyl, an optionally substituted 4-8 membered saturated carbocyclic or heterocyclic ring, optionally substituted aryl, optionally substituted heteroaryl, -L-optionally substituted aryl or -L-optionally substituted heteroaryl;

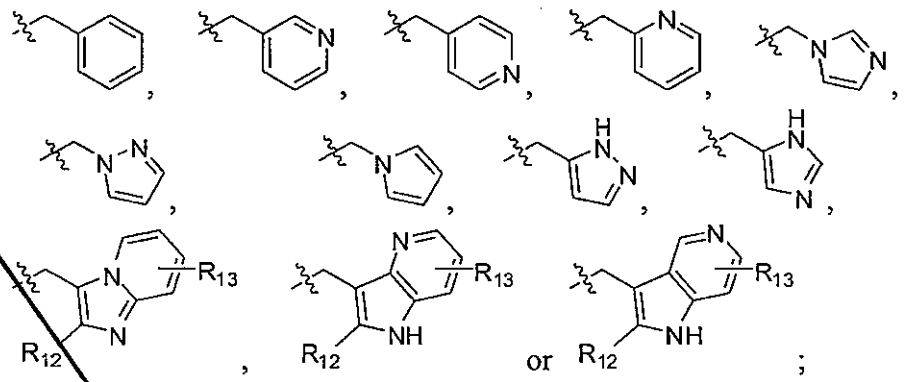
R_7 and R_8 are each independently hydrogen or C_1-C_8 alkyl; and L is C_1-C_8 alkyl; or

R_6 and R_7 taken together form an optionally substituted 4- to 8-membered carbocyclic or heterocyclic ring, wherein the ring is saturated, unsaturated or aromatic;

and R_9 and R_{10} are each independently hydrogen, halogen, oxygen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_2-C_8 alkenyl, C_2-C_8 haloalkenyl, C_2-C_8 alkynyl, C_2-C_8 haloalkynyl, optionally substituted aryl, optionally substituted heteroaryl, $-OR_6$, $-SR_6$, $-NR_6R_7$, -(C_1-C_8 alkyl)-NR_6R_7, -(C_1-C_8 haloalkyl)-NR_6R_7, -(C_2-C_8 alkenyl)-NR_6R_7, -(C_2-C_8 haloalkenyl)-NR_6R_7, -(C_2-C_8 alkynyl)-NR_6R_7, -(C_2-C_8 haloalkyl)-NR_6R_7, -L-R_{11}; or R_9 and R_{10} taken together form a monocyclic or bicyclic optionally substituted carbocyclic or heterocyclic ring, wherein the ring is saturated, unsaturated or aromatic;

wherein R_{11} is optionally substituted aryl or optionally substituted heteroaryl.

47. The compound of claim 46, wherein R_9 is hydrogen, oxygen, -F, -Cl, $-CH_3$, -OH, -SH, $-NH_2$, $-CH_2-R_{11}$, or -N-(C_1-C_8 alkyl); R_{10} is -Cl, $-CH_3$, -S-phenyl, -S(*p*-chlorophenyl), $-(CH_2)_qNH_2$, $-(CH_2)_qNR_6R_7$,

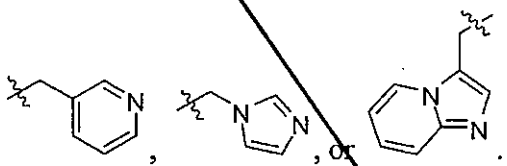


q is an integer from 0 to 8;

R_{12} is hydrogen, -OH, C_1-C_8 alkyl, $-CH_3$, or -F; and

R_{13} is hydrogen, -OH, C_1-C_8 alkyl, $-OCH_3$, $-OCH_2$-phenyl, $-CF_3$, $-NH_2$, -F, or -Br.

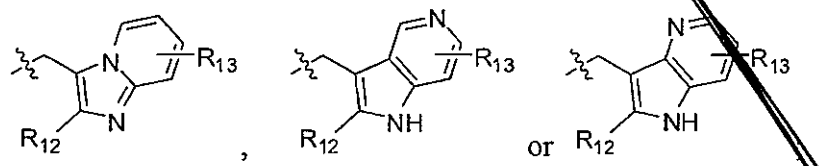
48. The compound of claim 47, wherein R_{10} is $-CH_2CH_2NH_2$, $-(CH_2)_3NH_2$, $-(CH_2)_2N(CH_3)((CH_2)_4CH_3)$,



49. The compound of claim 47, wherein R_9 is -OH.

50. The compound of claim 46, wherein R_9 is hydrogen, -F, or -Cl;

R_{10} is



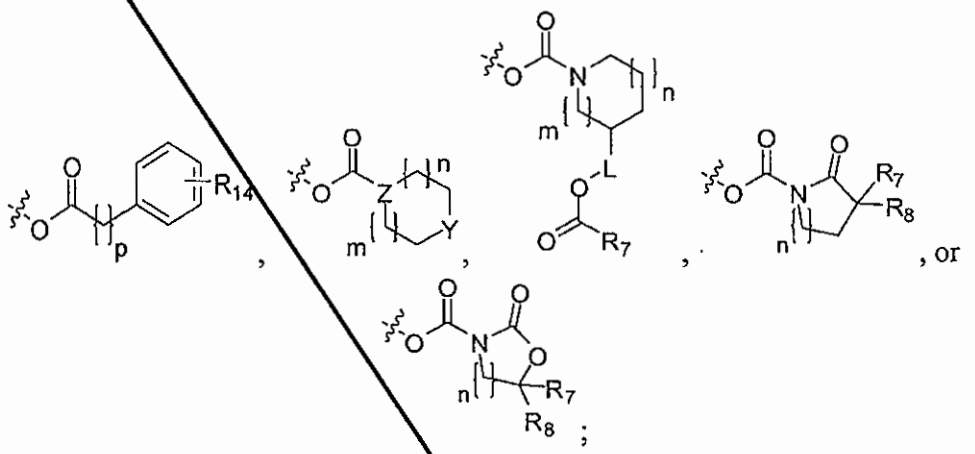
R_{12} is hydrogen, -OH, C_1-C_8 alkyl, $-OCH_3$, or -F; and

R_{13} is hydrogen, -OH, C_1-C_8 alkyl, or -F.

51. The compound of claim 50, wherein R_9 is hydrogen or -F; and R_{12} and R_{13} are each independently hydrogen, -OH, $-CH_3$, $-CH_2CH_3$, $-C(CH_3)_3$, or -F.

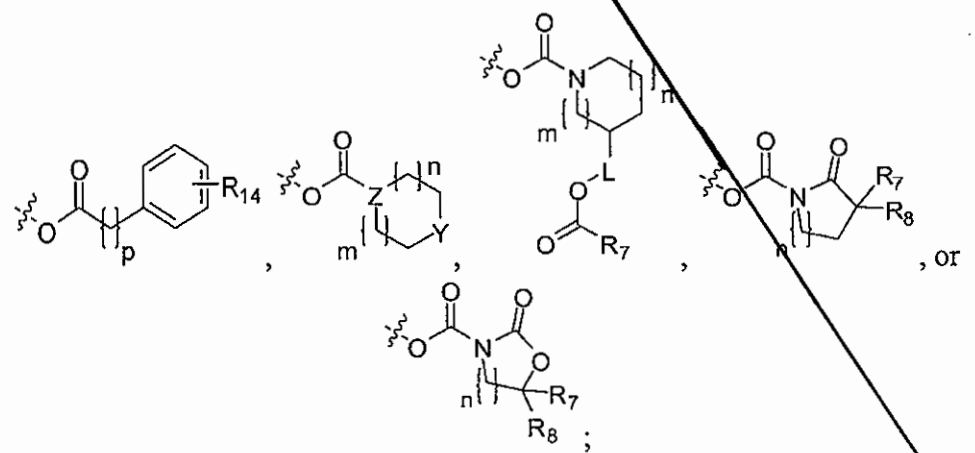
52. The compound of claim 50, wherein R_9 is hydrogen or -F; and R_{12} and R_{13} are each hydrogen.

53. The compound of claim 46, wherein R_1 and R_5 are each independently halogen; and R_3 is $-OR_6$, -O-L-OC(O)R_6, -O-L-OC(O)OR_6, -OC(O)R_6, -OC(O)-L-OC(O)R_6, -OC(O)OR_6, -OC(O)O-L-C(O)R_7, -OC(O)NR_6R_7, -OC(O)N(R_6)-L-OC(O)R_7, -OC(O)N(-L-OC(O)R_7)(-L-OC(O)R_8),



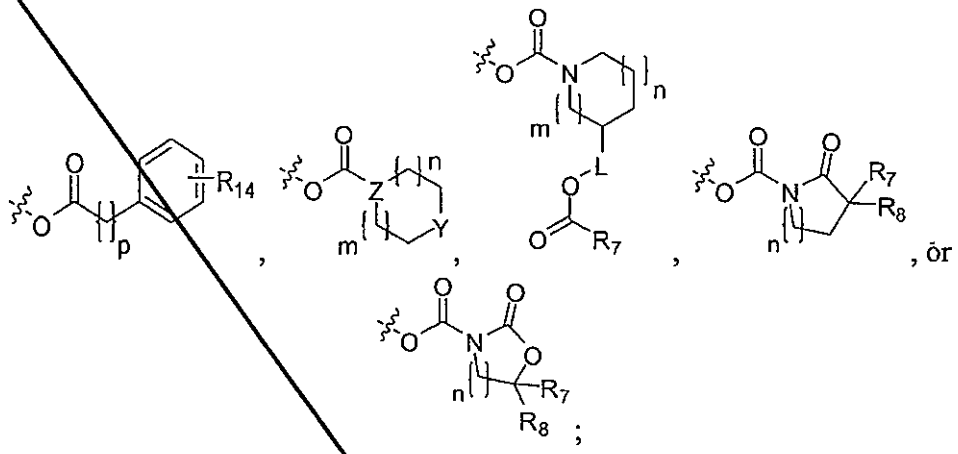
and R_2 and R_4 are each hydrogen.

54. The compound of claim 46, wherein R_1 is $-OR_6$, -O-L-OC(O)R_6, -O-L-OC(O)OR_6,-OC(O)R_6, -OC(O)-L-OC(O)R_6, -OC(O)OR_6, -OC(O)O-L-C(O)R_7, -OC(O)NR_6R_7, -OC(O)N(R_6)-L-OC(O)R_7, -OC(O)N(-L-OC(O)R_7)(-L-OC(O)R_8),



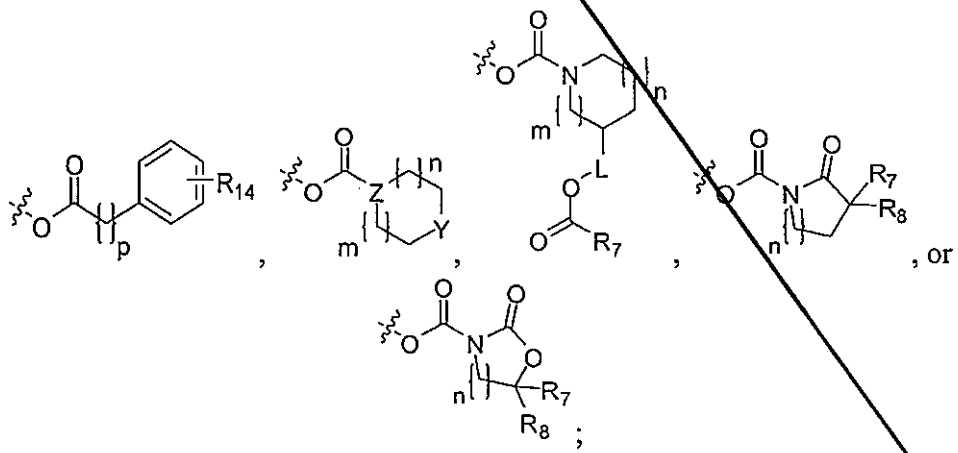
one of R_2, R_3, R_4 and R_5 is halogen, $-CF_3$, C_1-C_8 alkyl, phenyl, $-OR_6$, or $-C(O)OR_6$; and each remaining R-group of R_2, R_3, R_4 and is hydrogen.

55. The compound of claim 46, wherein R_3 is $-OR_6$, -O-L-$OC(O)R_6$, -O-L-$OC(O)OR_6$, $-OC(O)R_6$, -OC(O)-L-$OC(O)R_6$, $-OC(O)OR_6$, -OC(O)O-L-$C(O)R_7$, -$OC(O)NR_6R_7$, -OC(O)N(R_6)-L-$OC(O)R_7$, -OC(O)N(-L-$OC(O)R_7$)(-L-$OC(O)R_8$),



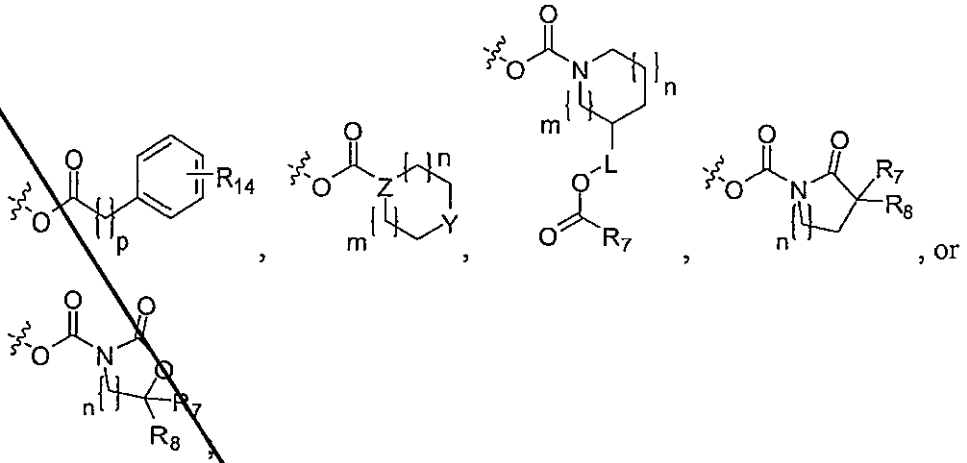
one of R_1, R_2, R_4 and R_5 is halogen, $-CF_3$, C_1-C_8 alkyl, phenyl, $-OR_6$, or $-C(O)OR_6$; and each remaining R-group of R_1, R_2, R_4 and R_5 is hydrogen.

56. The compound of claim 46, wherein R_1 is $-OR_6$, -O-L-$OC(O)R_6$, -O-L-$OC(O)OR_6$, $-OC(O)R_6$, -OC(O)-L-$OC(O)R_6$, $-OC(O)OR_6$, -OC(O)O-L-$C(O)R_7$, -$OC(O)NR_6R_7$, -OC(O)N(R_6)-L-$OC(O)R_7$, -OC(O)N(-L-$OC(O)R_7$)(-L-$OC(O)R_8$),



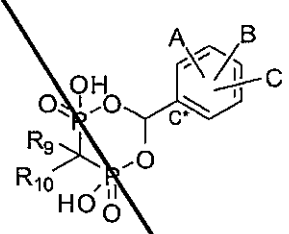
and R_2, R_3, R_4, and R_5 are each hydrogen.

57. The compound of claim 46, wherein R_3 is $-OR_6$, -O-L-$OC(O)R_6$, -O-L-$OC(O)OR_6$, $-OC(O)R_6$, -OC(O)-L-$OC(O)R_6$, $-OC(O)OR_6$, -OC(O)O-L-$C(O)R_7$, $-OC(O)NR_6R_7$, -OC(O)N(R_6)-L-$OC(O)R_7$, -OC(O)N(-L-$OC(O)R_7$)(-L-$OC(O)R_8$),



and R_1, R_2, R_4, and R_5 are each hydrogen.

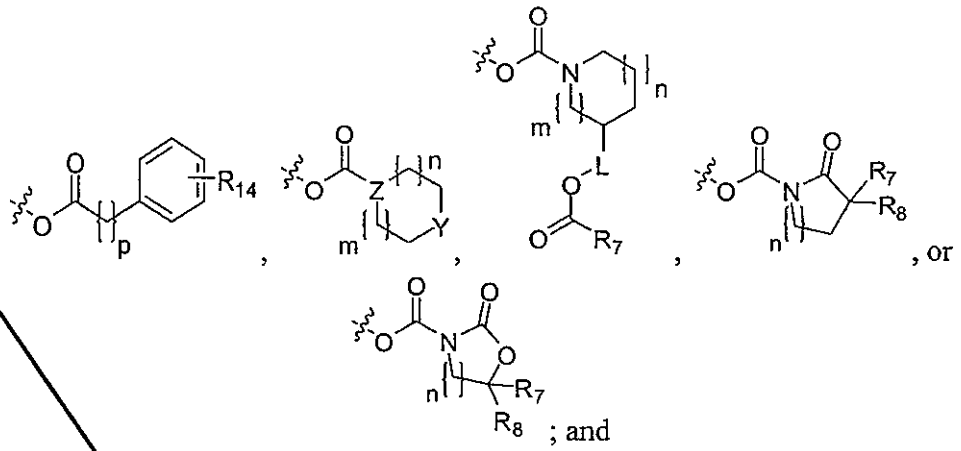
58. A compound of Formula IV,



(IV)

or a pharmaceutically acceptable salt or hydrate thereof,

wherein A is $-OR_6$, $-CO_2R_6$, -L-$OC(O)R_6$, -O-L-$OC(O)R_6$, -O-L-$OC(O)OR_6$, $-OC(O)R_6$, -OC(O)-L-$OC(O)R_6$, $-OC(O)OR_6$, -OC(O)O-L-$C(O)R_7$, -OC(O)O-L-$C(O)OR_7$, $-C(O)NR_6R_7$, $-CNR_6R_7$, $-OC(O)NR_6R_7$, -OC(O)N(R_6)-L-$OC(O)R_7$, -OC(O)N(-L-$OC(O)R_7$)(-L-$OC(O)R_8$),



; and

B and C are each independently hydrogen, halogen, $-CF_3$, -CN, C_1-C_8 alkyl, phenyl, $-OR_6$, or $-C(O)OR_6$, or B and C when taken together form an optionally substituted 4- to 8-membered carbocyclic or heterocyclic ring, wherein the ring is saturated, unsaturated or aromatic; and

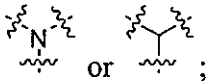
R_9 and R_{10} are each independently hydrogen, halogen, oxygen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_2-C_8 alkenyl, C_2-C_8 haloalkenyl, C_2-C_8 alkynyl, C_2-C_8 haloalkynyl, optionally substituted aryl, optionally substituted heteroaryl, $-OR_6$, $-SR_6$, $-NR_6R_7$, $-(C_1$-C_8 alkyl)-NR_6R_7, $-(C_1$-C_8 haloalkyl)-NR_6R_7, $-(C_2$-C_8 alkenyl)-NR_6R_7, $-(C_2$-C_8 haloalkenyl)-NR_6R_7, $-(C_2$-C_8 alkynyl)-NR_6R_7, $-(C_2$-C_8 haloalkyl)-NR_6R_7, -L-R_{11}; or R_9 and R_{10} taken together form a monocyclic or bicyclic optionally substituted carbocyclic or heterocyclic ring, wherein the ring is saturated, unsaturated or aromatic;

wherein R_{11} is optionally substituted aryl or optionally substituted heteroaryl;

m and n are each independently an integer from 0 to 2;

Y is $-CH_2-$, -O-, $-NR_7-$, or -S-;

p is an integer from 1 to 3;

Z is  ;

each R_6 is independently hydrogen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_2-C_8 alkenyl, C_2-C_8 haloalkenyl, C_2-C_8 alkynyl, C_2-C_8 haloalkynyl, an optionally

substituted 4-8 membered saturated carbocyclic or heterocyclic ring, optionally substituted aryl, optionally substituted heteroaryl, -L-optionally substituted aryl or -L-optionally substituted heteroaryl; L is C_1-C_8 alkyl; R_{14} is hydrogen, halogen, C_1-C_8 alkyl, or C_1-C_8 alkoxyl;

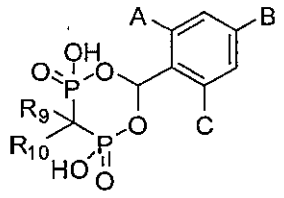
R_7 and R_8 are each independently hydrogen or C_1-C_8 alkyl; or

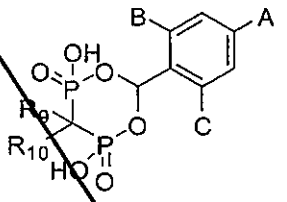
R_6 and R_7 taken together form an optionally substituted 4- to 8-membered carbocyclic or heterocyclic ring, wherein the ring is saturated, unsaturated or aromatic.

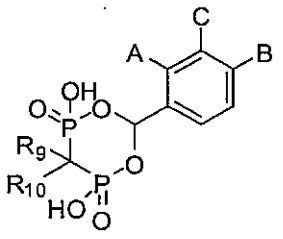
59. The compound of claim 58, wherein A is in the *ortho* or *para* position relative to C*.

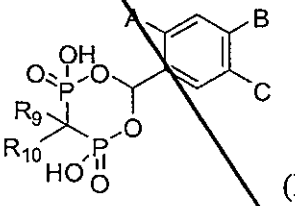
60. The compound of claim 58, wherein A is in the *meta* position relative to C*.

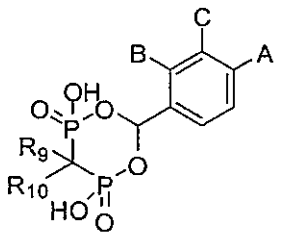
61. The compound of claim 58, wherein the compound is a compound or a pharmaceutically acceptable salt or hydrate of a compound of Formula IVa, IVb, IVc, IVd, or IVe:


(IVa)

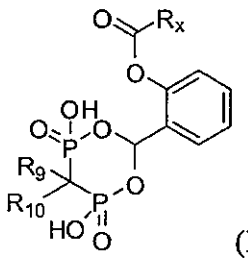

(IVb)


(IVc)


(IVd)

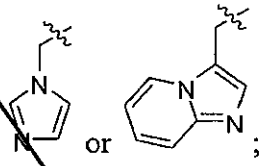

(IVe).

62. The compound or a pharmaceutically acceptable salt or hydrate of a compound of claim 61, wherein the compound or a pharmaceutically acceptable salt or hydrate of a compound of Fomula IVa is a compound or a pharmaceutically acceptable salt or hydrate of a compound of Fomula IVf,

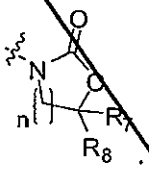


(IVf),

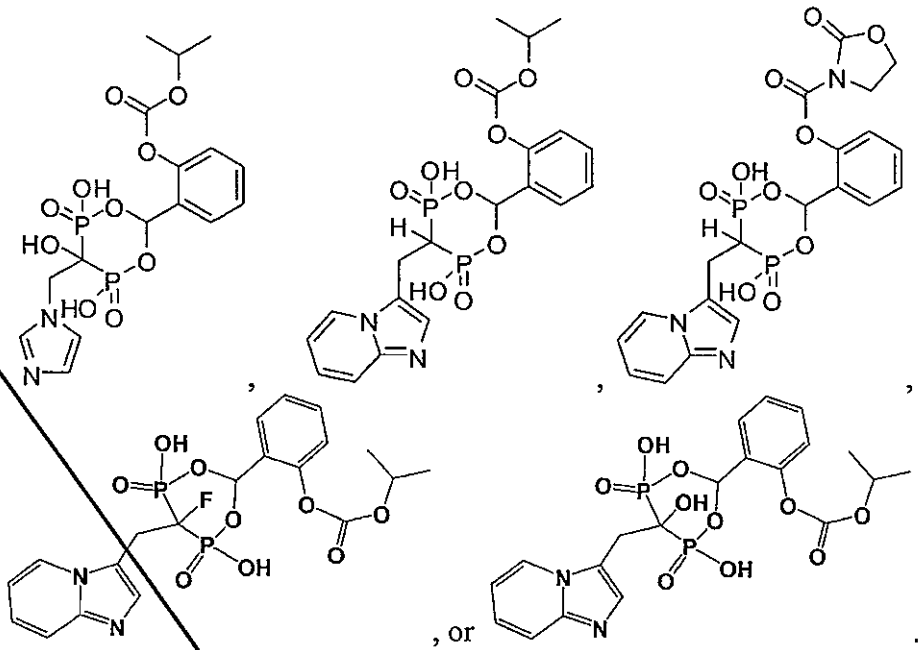
wherein R_9 is H, OH, or F; R_{10} is



and R_x is C_1-C_8 alkyl, C_1-C_8 alkoxyl or



63. The compound or a pharmaceutically acceptable salt or hydrate of a compound of claim 62, wherein the compound is



64. A pharmaceutical composition comprising a compound of claim 46 or a pharmaceutically acceptable salt or hydrate thereof and a pharmaceutically acceptable carrier.

65. The pharmaceutical composition of claim 64, wherein the composition further comprises at least one pharmaceutically active ingredient selected from the group consisting of: an anti-inflammatory, an immunomodulator, a chelator, a musculoskeletal anabolic agent, and a combination thereof.

66. A method of treating or preventing disorders associated with abnormal calcium and phosphate metabolism, the method comprising administering an effective amount of a compound of claim 46 or a pharmaceutically acceptable salt or hydrate thereof to a patient in need of such treatment.

67. The method of claim 66, wherein the disorder associated with abnormal calcium and phosphate metabolism is osteoporosis, rheumatoid arthritis, osteoarthritis, Paget's disease, alveolar bone loss, bone related cancer therapy, or an orthopedic disorder.

CLAIMS

1. An invention not claimed in any divisional application.