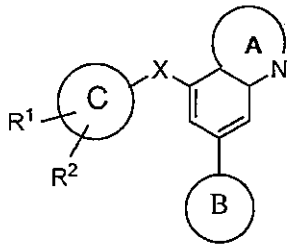
CLAIMS

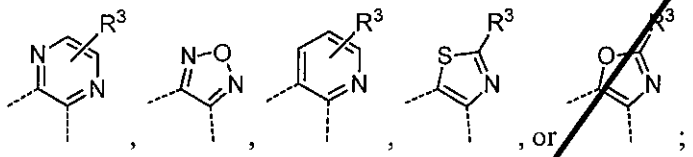
What is claimed is:

1. A compound having the formula:



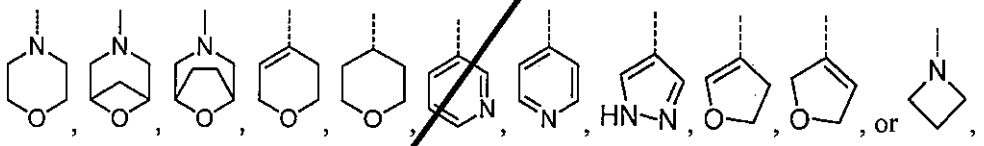
(I), wherein

Ring A is a ring system selected from



;

Ring B is a ring system selected from



wherein Ring B is optionally substituted with up to 4 fluorine atoms, up to two OH or up to two C_{1-4}alkyl which is optionally substituted with up to 3 fluorine atoms, up to two OH, or up to two OC_{1-2}alkyl groups;

Ring C is a cyclohexane or a cyclobutane ring;

X is –NH-, -O-, or -OC_{1-2}alkyl-;

each of R^1 and R^2 is, independently, hydrogen, -C(O)NHR^4, -C(O)OR^4, -NHC(O)R^4, -NHC(O)OR^4, -NHC(O)NHR^4, -NHS(O)$_2$R^4, -C_{0-4}alkyl-NHR^4, or -OR^4, wherein R^1 and R^2 cannot simultaneously be hydrogen, and wherein R^1 and R^2 and the intervening carbon atom can form a dioxane or dioxolane ring;

R^3 is hydrogen, -C_{1-4}alkyl, fluoro, chloro, -OC_{1-2}alkyl, -C(O)H, -C(O)OH, -C(O)OC_{1-2}alkyl, -CN, -C(O)NHC_{1-2}alkyl, or -C(O)NH_2, wherein each of said R^3 alkyl is optionally substituted with up to 3 fluorine atoms, up to two OH, or up to two OC_{1-2}alkyl groups;

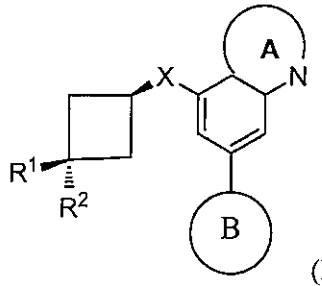
R^4 is hydrogen, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-5}cycloalkyl, phenyl, a 5-10-membered monocyclic or bicyclic heteroaryl ring selected from pyrrole, imidazole,

pyrazole, triazole, thiazole, isothiazole, oxazole, pyridine, pyrimidine, pyrimidinone, pyrazine, pyridazine, or quinoline, or a 4-10-membered monocyclic or bicyclic heterocyclyl ring selected from oxetane, tetrahydrofuran, tetrahydropyran, dihydroisoxazole, pyrimidine-2,4(1H,3H)-dione, dihydrofuropyrimidine, dihydropyranopyrimidine, dihydropyrrolopyrimidine, tetrahydropteridine, or tetrahydropyridopyrimidine, wherein each of said R^4 groups is optionally substituted with up to four Br, Cl, F, or C_{1-4}alkyl, up to three CN, NO_2, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, $C(O)OC_{1-4}$ alkyl, $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-$C(O)NH_2$, $C(O)NHC_{1-4}$ alkyl, $C(O)N(C_{1-4}$ alkyl$)_2$, $C(O)NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl), CH_2OR^5, C_{0-4} alkyl-$C(O)R^5$, C_{0-4} alkyl-$C(O)N(R^5)_2$, C_{0-4} alkyl-$C(O)OR^5$, C_{0-4} alkyl-$NHC(O)R^5$, C_{0-4} alkyl-$N(R^5)_2$, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, pyrrolidine or piperazine, a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, oxadiazole or tetrazole, or up to two OR^5, wherein each of said optional R^4 substituents is optionally substituted with up to four fluorine atoms, up to two C_{1-4}alkyl groups, up to two OH groups, up to two OC_{1-4}alkyl groups, up to two SC_{1-4}alkyl groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and

each R^5 is, independently, hydrogen, C_{1-4}alkyl, a 5-6-membered heteroaryl selected from imidazole, triazole, thiazole, pyridine, or pyrimidine, a 4-6-membered heterocyclyl selected from oxetane, tetrahydrofuran, or tetrahydropyran, and each R^5 group is optionally substituted with chloro, up to three fluorine atoms, up to two C_{1-2}alkyl, CH_2OH, CN, up to two OH, up to two OC_{1-2}alkyl, a spirooxetane, pyrrolidine, or triazole, or two R^5 groups together with the intervening nitrogen atom form a morpholine ring, azetidine ring, pyrrolidine ring, piperidine ring, or piperazine ring.

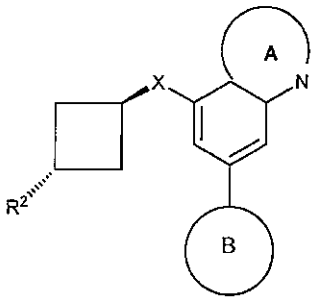
2. The compound of claim 1, wherein Ring C is cyclobutane.

3. The compound of claim 2, having the following formula:



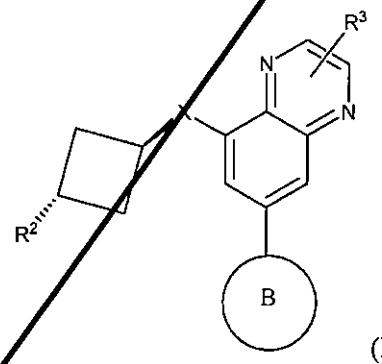
(II).

4. The compound of claim 3, having the following formula:



(II-A).

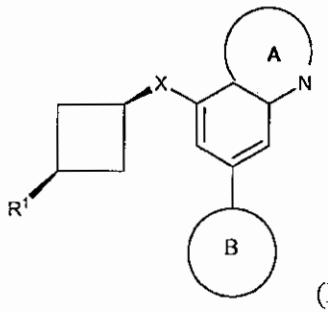
5. The compound of claim 4, having the following formula:



(II-A-1).

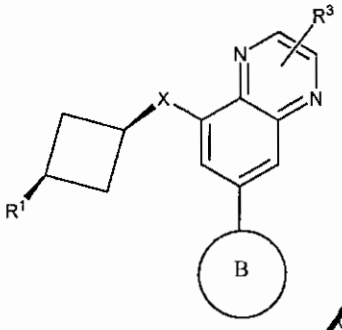
6. The compound of claim 4 or 5, wherein R^2 is $-C_{0-4}$ alkyl-NHR^4.

7. The compound of claim 3, having the following formula:



(**II-B**).

8. The compound of claim 7, having the following formula:

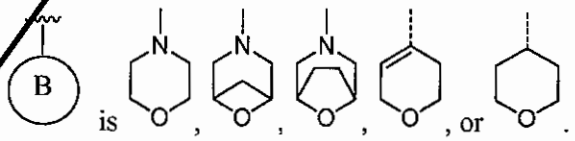


(**II-B-1**).

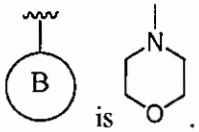
9. The compound of claim 7 or 8, wherein R^1 is -C_{0-4} alkyl-NHR^4.

10. The compound of any one of claims 2-9, wherein X is –O- or -OC_{1-4} alkyl-.

11. The compound of any one of claims 2-10 wherein



12. The compound of claim 11 wherein



13. The compound of any one of claims 2-12, wherein R^3 is hydrogen.

14. The compound of any one of claims 2-13, wherein

R^4 is hydrogen, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-5}cycloalkyl, phenyl, wherein each of said R^4 groups is optionally substituted with up to four Br, Cl, F, or C_{1-4}alkyl, up to three CN, NO_2, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, $C(O)OC_{1-4}$alkyl, $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-$C(O)NH_2$, $C(O)NHC_{1-4}$ alkyl, $C(O)N(C_{1-4}$ alkyl$)_2$, $C(O)NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl), CH_2OR^5, C_{0-4} alkyl-$C(O)R^5$, C_{0-4} alkyl-$C(O)N(R^5)_2$,

C_{0-4} alkyl-$C(O)OR^5$, C_{0-4} alkyl-$NHC(O)R^5$, C_{0-4} alkyl-$N(R^5)_2$, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, pyrrolidine or piperazine, a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, oxadiazole or tetrazole, or up to two OR^5, wherein each of said optional R^4 substituents is optionally substituted with up to four fluorine atoms, up to two C_{1-4}alkyl groups, up to two OH groups, up to two OC_{1-4}alkyl groups, up to two

SC_{1-4}alkyl groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and

each R^5 is, independently, hydrogen, C_{1-4}alkyl, a 5-6-membered heteroaryl selected from imidazole, triazole, thiazole, pyridine, or pyrimidine, a 4-6-membered heterocyclyl selected from oxetane, tetrahydrofuran, or tetrahydropyran, and each R^5 group is optionally substituted with chloro, up to three fluorine atoms, up to two C_{1-2}alkyl, CH_2OH, CN, up to two OH, up to two OC_{1-2}alkyl, a spirooxetane, pyrrolidine, or triazole, or two R^5 groups together with the intervening nitrogen atom form a morpholine ring, azetidine ring, pyrrolidine ring, piperidine ring, or piperazine ring.

15. The compound of any one of claims 2-13, wherein

R^4 is a 5-10-membered monocyclic or bicyclic heteroaryl ring selected from pyrrole, imidazole, pyrazole, triazole, thiazole, isothiazole, oxazole, pyridine, pyrimidine, pyrimidinone, pyrazine, pyridazine, or quinoline, wherein each of said R^4 groups is optionally substituted with up to four Br, Cl, F, or C_{1-4}alkyl, up to three CN, NO_2, C_{2-4}alkenyl,

C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, $C(O)OC_{1-4}$ alkyl, $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-$C(O)NH_2$, $C(O)NHC_{1-4}$ alkyl, $C(O)N(C_{1-4}$ alkyl$)_2$, $C(O)NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl), CH_2OR^5, C_{0-4} alkyl-$C(O)R^5$, C_{0-4} alkyl-$C(O)N(R^5)_2$, C_{0-4} alkyl-$C(O)OR^5$, C_{0-4} alkyl-$NHC(O)R^5$, C_{0-4} alkyl-$N(R^5)_2$, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, pyrrolidine or piperazine, a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, oxadiazole or tetrazole, or up to two OR^5, wherein each of said optional R^4 substituents is optionally substituted with up to four fluorine atoms, up to two C_{1-4}alkyl groups, up to two OH groups, up to two OC_{1-4}alkyl groups, up to two SC_{1-4}alkyl groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and

each R^5 is, independently, hydrogen, C_{1-4}alkyl, a 5-6-membered heteroaryl selected from imidazole, triazole, thiazole, pyridine, or pyrimidine, a 4-6-membered heterocyclyl selected from oxetane, tetrahydrofuran, or tetrahydropyran, and each R^5 group is optionally substituted with chloro, up to three fluorine atoms, up to two C_{1-2}alkyl, CH_2OH, CN, up to two OH, up to two OC_{1-2}alkyl, a spirooxetane, pyrrolidine, or triazole, or two R^5 groups together with the intervening nitrogen atom form a morpholine ring, azetidine ring, pyrrolidine ring, piperidine ring, or piperazine ring.

16. The compound of any one of claims 2-13, wherein

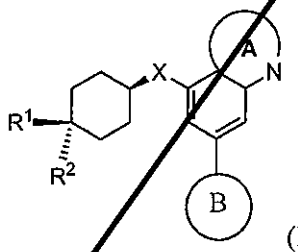
R^4 is a 4-10-membered monocyclic or bicyclic heterocyclyl ring selected from oxetane, tetrahydrofuran, tetrahydropyran, dihydroisoxazole, pyrimidine-2,4(1H,3H)-dione, dihydrofuropyrimidine, dihydropyranopyrimidine, dihydropyrrolopyrimidine, tetrahydropteridine, or tetrahydropyridopyrimidine, wherein each of said R^4 groups is optionally substituted with up to four Br, Cl, F, or C_{1-4}alkyl, up to three CN, NO_2, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, $C(O)OC_{1-4}$ alkyl, $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-$C(O)NH_2$, $C(O)NHC_{1-4}$ alkyl, $C(O)N(C_{1-4}$ alkyl$)_2$, $C(O)NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl), CH_2OR^5, C_{0-4} alkyl-$C(O)R^5$, C_{0-4} alkyl-$C(O)N(R^5)_2$, C_{0-4} alkyl-$C(O)OR^5$, C_{0-4} alkyl-$NHC(O)R^5$, C_{0-4} alkyl-$N(R^5)_2$, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine,

pyrrolidine or piperazine, a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, oxadiazole or tetrazole, or up to two OR^5, wherein each of said optional R^4 substituents is optionally substituted with up to four fluorine atoms, up to two C_{1-4}alkyl groups, up to two OH groups, up to two OC_{1-4}alkyl groups, up to two SC_{1-4}alkyl groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{1-4}$ alkyl-C_{3-5} cycloalkyl; and

each R^5 is, independently, hydrogen, C_{1-4}alkyl, a 5-6-membered heteroaryl selected from imidazole, triazole, thiazole, pyridine, or pyrimidine, a 4-6-membered heterocyclyl selected from oxetane, tetrahydrofuran, or tetrahydropyran, and each R^5 group is optionally substituted with chloro, up to three fluorine atoms, up to two C_{1-2}alkyl, CH_2OH, CN, up to two OH, up to two OC_{1-2}alkyl, a spirooxetane, pyrrolidine, or triazole, or two R^5 groups together with the intervening nitrogen atom form a morpholine ring, azetidine ring, pyrrolidine ring, piperidine ring, or piperazine ring.

17. The compound of claim 1, wherein Ring C is cyclohexane.

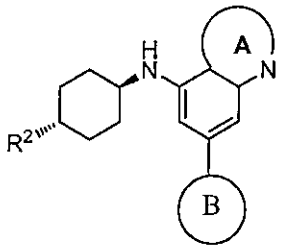
18. The compound of claim 17, having the following formula:



(III).

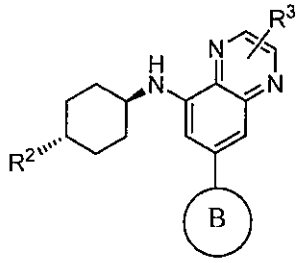
19. The compound of claim 17 or 18, wherein X is –NH-.

20. The compound of any one of claims 17-19, having the following formula:

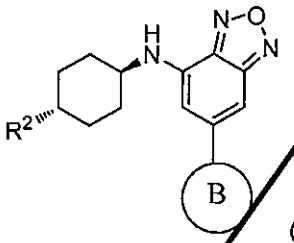


(III-A).

21. The compound of claim 20, having the following formula:



(**III-A-1**) or



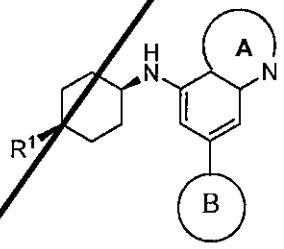
(**III-A-2**).

22. The compound of claim 20 or 21, wherein R^2 is $-C_{0-4}$ alkyl-NHR^4 or $-OR^4$.

23. The compound of claim 22, wherein R^2 is $-NHR^4$.

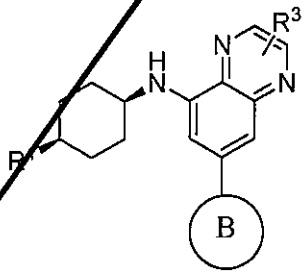
24. The compound of claim 22, wherein R^2 is $-OR^4$.

25. The compound of claim 17-19, having the following formula:

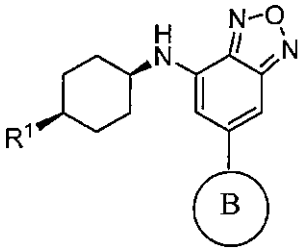


(**III-B**).

26. The compound of claim 25 having the following formula:



(**III-B-1**) or



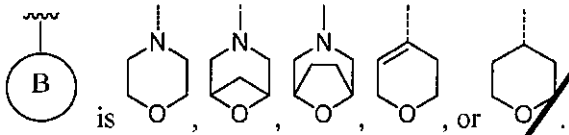
(**III-B-2**).

27. The compound of claim 25 or 26, wherein R^1 is $-C_{0-4}$ alkyl-NHR^4 or $-OR^4$.

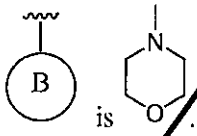
28. The compound of claim 27, wherein R^1 is -NHR^4.

29. The compound of claim 27, wherein R^1 is -OR^4.

30. The compound of any one of claims 17-29 wherein

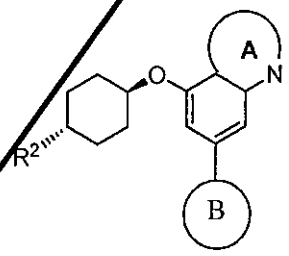


31. The compound of claim 30 wherein



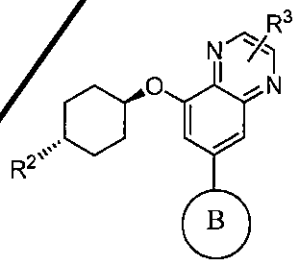
32. The compound of claim 17 or 18, wherein X is –O-.

33. The compound of claim 17, 18 or 32, having the following formula:

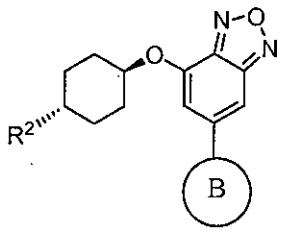


(III-C).

34. The compound of claim 33, having the following formula:



(III-C-1) or



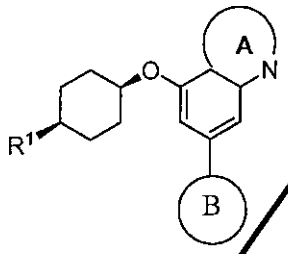
(III-C-2).

35. The compound of claim 33 or 34, wherein is R^2 is -C_{0-4} alkyl-NHR^4 or -OR^4.

36. The compound of claim 35, wherein is R^2 is -NHR^4.

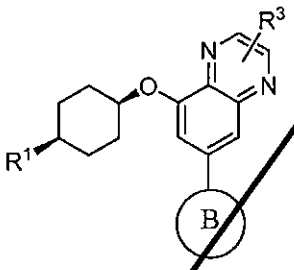
37. The compound of claim 35, wherein is R^2 is -OR^4.

38. The compound of claim 17, 18 or 32, having the following formula:

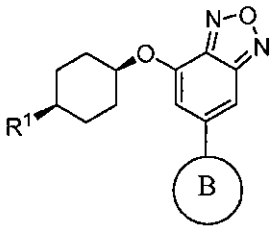


(III-D).

39. The compound according to claim 38 having the following formula:



(III-D-1) or



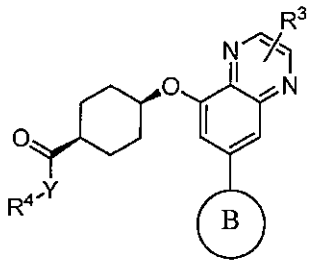
(III-D-2).

40. The compound of claim 38 or 39, wherein is R^1 is -C_{0-4} alkyl-NHR^4 or -OR^4.

41. The compound of claim 40, wherein is R^1 is -NHR^4.

42. The compound of claim 40, wherein is R^1 is -OR^4.

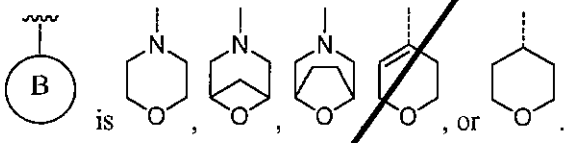
43. The compound of claim 38 or 39 having the following formula:



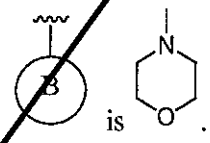
(**III-D-3**), wherein

Y is –O- or –NH-.

44. The compound of any one of claims 32-43 wherein



45. The compound of claim 44 wherein



46. The compound of any one of claims 17-45, wherein R^3 is hydrogen, C_{1-4}alkyl, OC_{1-2}alkyl, or $C(O)NH_2$, or C(O)H, wherein each of said R^3 alkyl is optionally substituted with OH.

47. The compound of claim 46, wherein R^3 is hydrogen.

48. The compound of any one of claims 17-47, wherein

R^4 is hydrogen, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-5}cycloalkyl, phenyl, wherein each of said R^4 groups is optionally substituted with up to four Br, Cl, F, or C_{1-4}alkyl, up to three CN, NO_2, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, $C(O)OC_{1-4}$ alkyl,

$C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-$C(O)NH_2$, $C(O)NHC_{1-4}$ alkyl, $C(O)N(C_{1-4}$ alkyl$)_2$, $C(O)NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl), CH_2OR^5, C_{0-4} alkyl-$C(O)R^5$, C_{0-4} alkyl-$C(O)N(R^5)_2$,
C_{0-4} alkyl-$C(O)OR^5$, C_{0-4} alkyl-$NHC(O)R^5$, C_{0-4} alkyl-$N(R^5)_2$, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, pyrrolidine or piperazine, a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, oxadiazole or tetrazole, or up to two OR^5, wherein each of said optional R^4 substituents is optionally substituted with up to four fluorine atoms, up to two C_{1-4}alkyl groups, up to two OH groups, up to two OC_{1-4}alkyl groups, up to two
SC_{1-4}alkyl groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and
each R^5 is, independently, hydrogen, C_{1-4}alkyl, a 5-6-membered heteroaryl selected from imidazole, triazole, thiazole, pyridine, or pyrimidine, a 4-6-membered heterocyclyl selected from oxetane, tetrahydrofuran, or tetrahydropyran, and each R^5 group is optionally substituted with chloro, up to three fluorine atoms, up to two C_{1-2}alkyl, CH_2OH, CN, up to two OH, up to two OC_{1-2}alkyl, a spirooxetane, pyrrolidine, or triazole, or two R^5 groups together with the intervening nitrogen atom form a morpholine ring, azetidine ring, pyrrolidine ring, piperidine ring, or piperazine ring.

49. The compound of any one of claims 17-47, wherein

R^4 is a 5-10-membered monocyclic or bicyclic heteroaryl ring selected from pyrrole, imidazole, pyrazole, triazole, thiazole, isothiazole, oxazole, pyridine, pyrimidine, pyrimidinone, pyrazine, pyridazine, or quinoline, wherein each of said R^4 groups is optionally substituted with up to four Br, Cl, F, or C_{1-4}alkyl, up to three CN, NO_2, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, $C(O)OC_{1-4}$ alkyl, $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-$C(O)NH_2$, $C(O)NHC_{1-4}$ alkyl, $C(O)N(C_{1-4}$ alkyl$)_2$,
$C(O)NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl), CH_2OR^5, C_{0-4} alkyl-$C(O)R^5$, C_{0-4} alkyl-$C(O)N(R^5)_2$, C_{0-4} alkyl-$C(O)OR^5$, C_{0-4} alkyl-$NHC(O)R^5$, C_{0-4} alkyl-$N(R^5)_2$, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, pyrrolidine or piperazine, a heteroaryl ring system selected from

furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, oxadiazole or tetrazole, or up to two OR^5, wherein each of said optional R^4 substituents is optionally substituted with up to four fluorine atoms, up to two C_{1-4}alkyl groups, up to two OH groups, up to two OC_{1-4}alkyl groups, up to two
SC_{1-4}alkyl groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and
each R^5 is, independently, hydrogen, C_{1-4}alkyl, a 5-6-membered heteroaryl selected from imidazole, triazole, thiazole, pyridine, or pyrimidine, a 4-6-membered heterocyclyl selected from oxetane, tetrahydrofuran, or tetrahydropyran, and each R^5 group is optionally substituted with chloro, up to three fluorine atoms, up to two C_{1-2}alkyl, CH_2OH, CN, up to two OH, up to two OC_{1-2}alkyl, a spirooxetane, pyrrolidine, or triazole, or two R^5 groups together with the intervening nitrogen atom form a morpholine ring, azetidine ring, pyrrolidine ring, piperidine ring, or piperazine ring.

50. The compound of claim 49, wherein

R^4 is pyridine or pyrimidine, which is optionally substituted with up to four Br, Cl, F, or C_{1-4}alkyl, up to three CN, NO_2, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, $C(O)OC_{1-4}$ alkyl, $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-$C(O)NH_2$, $C(O)NHC_{1-4}$ alkyl, $C(O)N(C_{1-4}$ alkyl$)_2$, $C(O)NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl), CH_2OR^5, C_{0-4} alkyl-$C(O)R^5$, C_{0-4} alkyl-$C(O)N(R^5)_2$,
C_{0-4} alkyl-$C(O)OR^5$, C_{0-4} alkyl-$NHC(O)R^5$, C_{0-4} alkyl-$N(R^5)_2$, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, pyrrolidine or piperazine, a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, oxadiazole or tetrazole, or up to two OR^5, wherein each of said optional R^4 substituents is optionally substituted with up to four fluorine atoms, up to two C_{1-4}alkyl groups, up to two OH groups, up to two OC_{1-4}alkyl groups, up to two
SC_{1-4}alkyl groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and
each R^5 is, independently, hydrogen, C_{1-4}alkyl, a 5-6-membered heteroaryl selected from imidazole, triazole, thiazole, pyridine, or pyrimidine, a 4-6-membered heterocyclyl

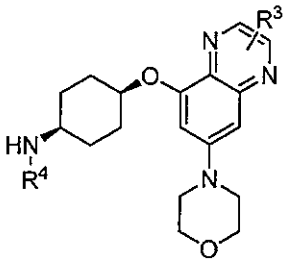
selected from oxetane, tetrahydrofuran, or tetrahydropyran, and each R^5 group is optionally substituted with chloro, up to three fluorine atoms, up to two C_{1-2}alkyl, CH_2OH, CN, up to two OH, up to two OC_{1-2}alkyl, a spirooxetane, pyrrolidine, or triazole, or two R^5 groups together with the intervening nitrogen atom form a morpholine ring, azetidine ring, pyrrolidine ring, piperidine ring, or piperazine ring.

51. The compound of any one of claims 17-47, wherein

R^4 is a 4-10-membered monocyclic or bicyclic heterocyclyl ring selected from oxetane, tetrahydrofuran, tetrahydropyran, dihydroisoxazole, pyrimidine-2,4(1H,3H)-dione, dihydrofuropyrimidine, dihydropyranopyrimidine, dihydropyrrolopyrimidine, tetrahydropteridine, or tetrahydropyridopyrimidine, wherein each of said R^4 groups is optionally substituted with up to four Br, Cl, F, or C_{1-4}alkyl, up to three CN, NO_2, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, $C(O)OC_{1-4}$ alkyl, $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-$C(O)NH_2$, $C(O)NHC_{1-4}$ alkyl, $C(O)N(C_{1-4}$ alkyl$)_2$, $C(O)NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl), CH_2OR^5, C_{0-4} alkyl-$C(O)R^5$, C_{0-4} alkyl-$C(O)N(R^5)_2$, C_{0-4} alkyl-$C(O)OR^5$, C_{0-4} alkyl-$NHC(O)R^5$, C_{0-4} alkyl-$N(R^5)_2$, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, pyrrolidine or piperazine, a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, oxadiazole or tetrazole, or up to two OR^5, wherein each of said optional R^4 substituents is optionally substituted with up to four fluorine atoms, up to two C_{1-4}alkyl groups, up to two OH groups, up to two OC_{1-4}alkyl groups, up to two
SC_{1-4}alkyl groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and

each R^5 is, independently, hydrogen, C_{1-4}alkyl, a 5-6-membered heteroaryl selected from imidazole, triazole, thiazole, pyridine, or pyrimidine, a 4-6-membered heterocyclyl selected from oxetane, tetrahydrofuran, or tetrahydropyran, and each R^5 group is optionally substituted with chloro, up to three fluorine atoms, up to two C_{1-2}alkyl, CH_2OH, CN, up to two OH, up to two OC_{1-2}alkyl, a spirooxetane, pyrrolidine, or triazole, or two R^5 groups together with the intervening nitrogen atom form a morpholine ring, azetidine ring, pyrrolidine ring, piperidine ring, or piperazine ring.

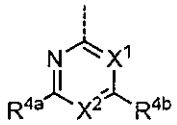
52. The compound of claim 32 having the formula:



(**IV**), wherein

R^3 is hydrogen, -C_{1-4}alkyl, fluoro, chloro, -OC_{1-2}alkyl, or -$C(O)NH_2$, -C(O)H, or -CN, wherein each of said R^3 alkyl is optionally substituted with OH or up to 3 fluorine atoms;

R^4 is



X^1 is N, CH, CF, CCl, or CC_{1-2} alkyl optionally substituted with up to 3 fluorine atoms;

X^2 is N or CR^{4c}, wherein X^1 and X^2 cannot simultaneously be N;

each of R^{4a}, R^{4b}, and R^{4c} is, independently, hydrogen, F, Cl, Br, CN, NO_2, C_{1-4} alkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C(O)C_{1-4} alkyl, C(O)OC_{0-4} alkyl-C_{3-5} cycloalkyl, $C(O)NH_2$, C(O)NHC_{1-4} alkyl, C(O)$N(C_{1-4}$ alkyl$)_2$, C(O)$NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl), a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, or piperazine, or a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, or tetrazole, or R^{4c}, R^{4a}, and the intervening atoms form a dihydrofuran, a dihydropyran, or a tetrahydropiperidine heterocyclic ring system;

wherein each of said R^{4a}, R^{4b}, or R^{4c} heterocyclic or heteroaryl ring systems is optionally substituted with up to four fluorine atoms, up to two C_{1-4} alkyl, up to two OH groups, a C(O)C_{1-4} alkyl, a C(O)OC_{1-4} alkyl, or a C(O)OC_{0-4} alkyl-C_{3-5} cycloalkyl; and

wherein each of said R^{4a}, R^{4b}, or R^{4c} alkyl or cycloalkyl is optionally substituted with up to 2 non-geminal OH groups or up to 3 fluorine atoms.

53. The compound of claim 52, wherein R^3 is hydrogen, -C_{1-4}alkyl, -OC_{1-2}alkyl, or -$C(O)NH_2$, or -C(O)H, wherein each of said R^3 alkyl is optionally substituted with OH.

54. The compound of claim 52 or 53, wherein R^3 is hydrogen.

55. The compound of any one of claims 52-54, wherein each of X^1 and X^2 is, independently, CH or N, wherein X^1 and X^2 cannot simultaneously be N.

56. The compound of any one of claims 52-55, wherein each of R^{4a} and R^{4b} is, independently, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, or piperazine,

wherein each of said R^{4a} or R^{4b} heterocyclic or heteroaryl ring systems is optionally substituted with up to four fluorine atoms, up to two C_{1-4} alkyl, up to two OH groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and

wherein each of said R^{4a} or R^{4b} alkyl or cycloalkyl is optionally substituted with up to 2 non-geminal OH groups or up to 3 fluorine atoms.

57. The compound of any one of claims 52-55, wherein each of R^{4a} and R^{4b} is, independently, a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, or tetrazole,

wherein each of said R^{4a} or R^{4b} heterocyclic or heteroaryl ring systems is optionally substituted with up to four fluorine atoms, up to two C_{1-4} alkyl, up to two OH groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and

wherein each of said R^{4a} or R^{4b} alkyl or cycloalkyl is optionally substituted with up to 2 non-geminal OH groups or up to 3 fluorine atoms.

58. The compound of any one of claims 52-55, wherein each of R^{4a} and R^{4b} is, independently, hydrogen, F, Cl, Br, CN, NO_2, C_{1-4} alkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, $C(O)OC_{1-4}$ alkyl, $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl, $C(O)NH_2$, $C(O)NHC_{1-4}$ alkyl, $C(O)N(C_{1-4}$ alkyl$)_2$, or $C(O)NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl),

wherein each of said R^{4a} or R^{4b} heterocyclic or heteroaryl ring systems is optionally substituted with up to four fluorine atoms, up to two C_{1-4} alkyl, up to two OH groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and

wherein each of said R^{4a} or R^{4b} alkyl or cycloalkyl is optionally substituted with up to 2 non-geminal OH groups or up to 3 fluorine atoms.

59. A compound selected from the list of compounds in Table 1.

60. A compound selected from the list of compounds in Table 2.

61. A pharmaceutical composition comprising a compound of any one of claims 1-60 and a pharmaceutically acceptable excipient.

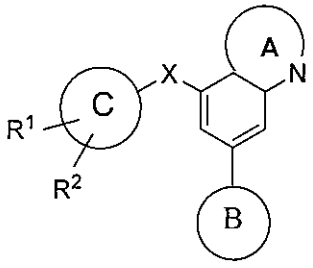
62. A method of sensitizing a cell to a therapeutic agent or a disease state that induces a DNA lesion comprising the step of contacting the cell with the compound of any one of claims 1-60, or a pharmaceutical composition comprising said compound.

63. A method of potentiating a therapeutic regimen for the treatment of cancer in a patient comprising the step of administering to said patient an effective amount of the compound of any one of claims 1-60, or a pharmaceutical composition comprising said compound.

64. A method of treating cancer or inhibiting cancer cell growth in a patient comprising administering to said patient an effective amount of the compound of any one of claims 1-60, or a pharmaceutical composition comprising said compound, either alone or in combination with one or more additional therapeutic agent.

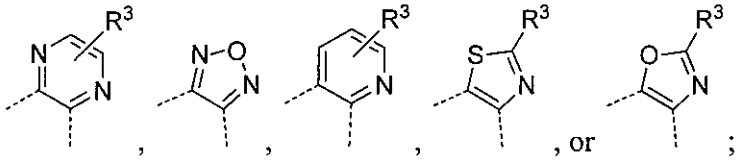
Claims

1. A compound having the formula:

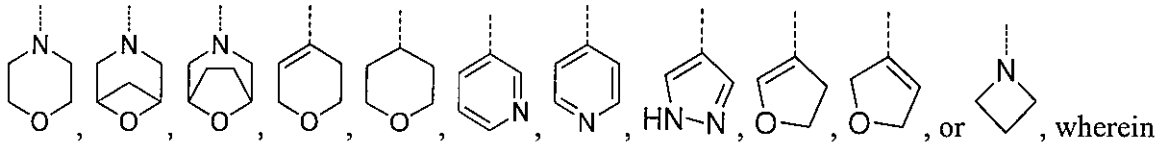


(**I**), wherein

Ring A is a ring system selected from



Ring B is a ring system selected from



Ring B is optionally substituted with up to 4 fluorine atoms, up to two OH or up to two C_{1-4}alkyl which is optionally substituted with up to 3 fluorine atoms, up to two OH, or up to two OC_{1-2}alkyl groups;

Ring C is a cyclohexane or a cyclobutane ring;

X is –NH-, -O-, or -OC_{1-4} alkyl-;

each of R^1 and R^2 is, independently, hydrogen, -C(O)NHR^4, -C(O)OR^4, -NHC(O)R^4, -NHC(O)OR^4, -NHC(O)NHR^4, -$NHS(O)_2R^4$, -C_{0-4} alkyl-NHR^4, or -OR^4, wherein R^1 and R^2 cannot simultaneously be hydrogen, and wherein R^1 and R^2 and the intervening carbon atom can form a dioxane or dioxolane ring;

R^3 is hydrogen, -C_{1-4}alkyl, fluoro, chloro, -OC_{1-2}alkyl, -C(O)H, -C(O)OH, -$C(O)OC_{1-2}$alkyl, -CN, -$C(O)NHC_{1-2}$alkyl, or -$C(O)NH_2$, wherein each of said R^3 alkyl is optionally substituted with up to 3 fluorine atoms, up to two OH, or up to two OC_{1-2}alkyl groups;

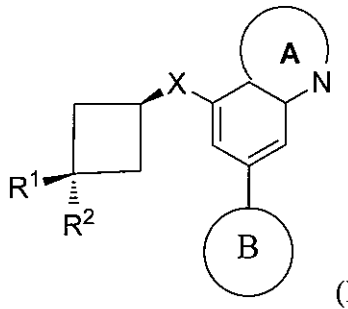
R^4 is hydrogen, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-5}cycloalkyl, phenyl, a 5-10-membered monocyclic or bicyclic heteroaryl ring selected from pyrrole, imidazole, pyrazole, triazole,

thiazole, isothiazole, oxazole, pyridine, pyrimidine, pyrimidinone, pyrazine, pyridazine, or quinoline, or a 4-10-membered monocyclic or bicyclic heterocyclyl ring selected from oxetane, tetrahydrofuran, tetrahydropyran, dihydroisoxazole, pyrimidine-2,4(1H,3H)-dione, dihydrofuropyrimidine, dihydropyranopyrimidine, dihydropyrrolopyrimidine, tetrahydropteridine, or tetrahydropyridopyrimidine, wherein each of said R^4 groups is optionally substituted with up to four Br, Cl, F, or C_{1-4}alkyl, up to three CN, NO_2, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, $C(O)OC_{1-4}$ alkyl, $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-$C(O)NH_2$, $C(O)NHC_{1-4}$ alkyl, $C(O)N(C_{1-4}$ alkyl$)_2$, $C(O)NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl), CH_2OR^5, C_{0-4} alkyl-$C(O)R^5$, C_{0-4} alkyl-$C(O)N(R^5)_2$, C_{0-4} alkyl-$C(O)OR^5$, C_{0-4} alkyl-$NHC(O)R^5$, C_{0-4} alkyl-$N(R^5)_2$, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, pyrrolidine or piperazine, a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, oxadiazole or tetrazole, or up to two OR^5, wherein each of said optional R^4 substituents is optionally substituted with up to four fluorine atoms, up to two C_{1-4}alkyl groups, up to two OH groups, up to two OC_{1-4}alkyl groups, up to two SC_{1-4}alkyl groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and

each R^5 is, independently, hydrogen, C_{1-4}alkyl, a 5-6-membered heteroaryl selected from imidazole, triazole, thiazole, pyridine, or pyrimidine, a 4-6-membered heterocyclyl selected from oxetane, tetrahydrofuran, or tetrahydropyran, and each R^5 group is optionally substituted with chloro, up to three fluorine atoms, up to two C_{1-2}alkyl, CH_2OH, CN, up to two OH, up to two OC_{1-2}alkyl, a spirooxetane, pyrrolidine, or triazole, or two R^5 groups together with the intervening nitrogen atom form a morpholine ring, azetidine ring, pyrrolidine ring, piperidine ring, or piperazine ring.

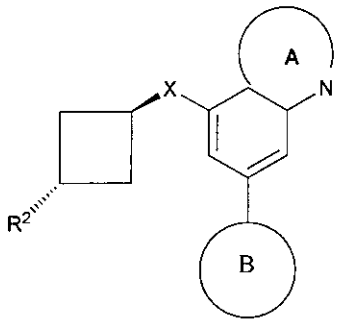
2. The compound of claim 1, wherein Ring C is cyclobutane.

3. The compound of claim 2, having the following formula:



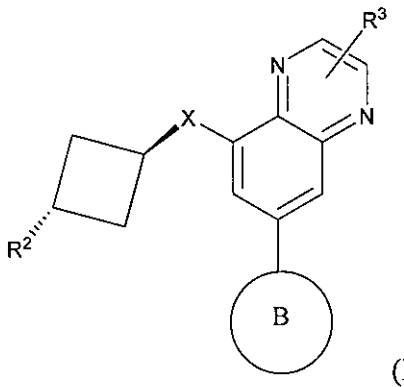
(II).

4. The compound of claim 3, having the following formula:



(II-A).

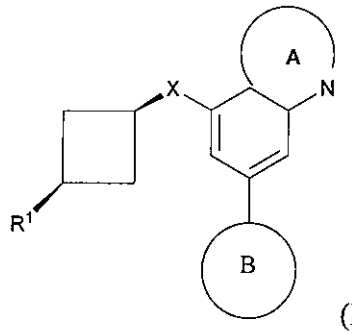
5. The compound of claim 4, having the following formula:



(II-A-1).

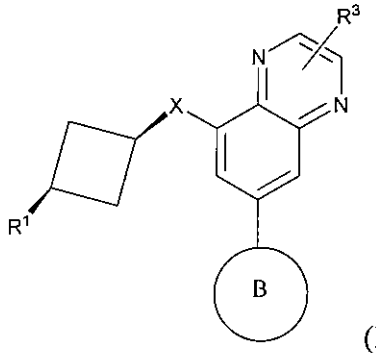
6. The compound of claim 4 or 5, wherein R^2 is $-C_{0-4}$ alkyl-NHR^4.

7. The compound of claim 3, having the following formula:



(II-B).

8. The compound of claim 7, having the following formula:

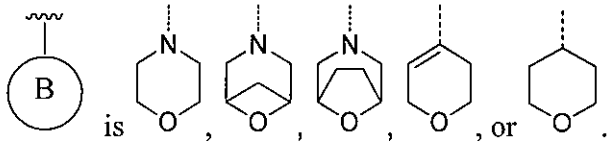


(II-B-1).

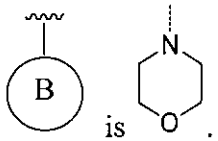
9. The compound of claim 7 or 8, wherein R^1 is $-C_{0-4}$ alkyl-NHR^4.

10. The compound of any one of claims 2-9, wherein X is –O- or $-OC_{1-4}$ alkyl-.

11. The compound of any one of claims 2-10 wherein



12. The compound of claim 11 wherein



13. The compound of any one of claims 2-12, wherein R^3 is hydrogen.

14. The compound of any one of claims 2-13, wherein

R^4 is hydrogen, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-5}cycloalkyl, phenyl, wherein each of said R^4 groups is optionally substituted with up to four Br, Cl, F, or C_{1-4}alkyl, up to three CN, NO_2, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, $C(O)OC_{1-4}$ alkyl, $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-$C(O)NH_2$, $C(O)NHC_{1-4}$ alkyl, $C(O)N(C_{1-4}$ alkyl$)_2$, $C(O)NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl), CH_2OR^5, C_{0-4} alkyl-$C(O)R^5$, C_{0-4} alkyl-$C(O)N(R^5)_2$, C_{0-4} alkyl-$C(O)OR^5$, C_{0-4} alkyl-$NHC(O)R^5$, C_{0-4} alkyl-$N(R^5)_2$, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, pyrrolidine or piperazine, a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, oxadiazole or tetrazole, or up to two OR^5, wherein each of said optional R^4 substituents is optionally substituted with up to four fluorine atoms, up to two C_{1-4}alkyl groups, up to two OH groups, up to two OC_{1-4}alkyl groups, up to two SC_{1-4}alkyl groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and each R^5 is, independently, hydrogen, C_{1-4}alkyl, a 5-6-membered heteroaryl selected from imidazole, triazole, thiazole, pyridine, or pyrimidine, a 4-6-membered heterocyclyl selected from oxetane, tetrahydrofuran, or tetrahydropyran, and each R^5 group is optionally substituted with chloro, up to three fluorine atoms, up to two C_{1-2}alkyl, CH_2OH, CN, up to two OH, up to two OC_{1-2}alkyl, a spirooxetane, pyrrolidine, or triazole, or two R^5 groups together with the intervening nitrogen atom form a morpholine ring, azetidine ring, pyrrolidine ring, piperidine ring, or piperazine ring.

15. The compound of any one of claims 2-13, wherein

R^4 is a 5-10-membered monocyclic or bicyclic heteroaryl ring selected from pyrrole, imidazole, pyrazole, triazole, thiazole, isothiazole, oxazole, pyridine, pyrimidine, pyrimidinone, pyrazine, pyridazine, or quinoline, wherein each of said R^4 groups is optionally substituted with up to four Br, Cl, F, or C_{1-4}alkyl, up to three CN, NO_2, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, $C(O)OC_{1-4}$ alkyl, $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl,

C_{0-4} alkyl-C(O)NH_2, C(O)NHC_{1-4} alkyl, C(O)$N(C_{1-4}$ alkyl$)_2$, C(O)$NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl), CH_2OR^5, C_{0-4} alkyl-C(O)R^5, C_{0-4} alkyl-C(O)$N(R^5)_2$, C_{0-4} alkyl-C(O)OR^5,

C_{0-4} alkyl-NHC(O)R^5, C_{0-4} alkyl-$N(R^5)_2$, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, pyrrolidine or piperazine, a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, oxadiazole or tetrazole, or up to two OR^5, wherein each of said optional R^4 substituents is optionally substituted with up to four fluorine atoms, up to two C_{1-4}alkyl groups, up to two OH groups, up to two OC_{1-4}alkyl groups, up to two SC_{1-4}alkyl groups, a C(O)C_{1-4} alkyl, a C(O)OC_{1-4} alkyl, or a C(O)OC_{0-4} alkyl-C_{3-5} cycloalkyl; and

each R^5 is, independently, hydrogen, C_{1-4}alkyl, a 5-6-membered heteroaryl selected from imidazole, triazole, thiazole, pyridine, or pyrimidine, a 4-6-membered heterocyclyl selected from oxetane, tetrahydrofuran, or tetrahydropyran, and each R^5 group is optionally substituted with chloro, up to three fluorine atoms, up to two C_{1-2}alkyl, CH_2OH, CN, up to two OH, up to two OC_{1-2}alkyl, a spirooxetane, pyrrolidine, or triazole, or two R^5 groups together with the intervening nitrogen atom form a morpholine ring, azetidine ring, pyrrolidine ring, piperidine ring, or piperazine ring.

16. The compound of any one of claims 2-13, wherein

R^4 is a 4-10-membered monocyclic or bicyclic heterocyclyl ring selected from oxetane, tetrahydrofuran, tetrahydropyran, dihydroisoxazole, pyrimidine-2,4(1H,3H)-dione, dihydrofuropyrimidine, dihydropyranopyrimidine, dihydropyrrolopyrimidine, tetrahydropteridine, or tetrahydropyridopyrimidine, wherein each of said R^4 groups is optionally substituted with up to four Br, Cl, F, or C_{1-4}alkyl, up to three CN, NO_2, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl,

C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, C(O)OC_{1-4} alkyl, C(O)OC_{0-4} alkyl-C_{3-5} cycloalkyl,

C_{0-4} alkyl-C(O)NH_2, C(O)NHC_{1-4} alkyl, C(O)$N(C_{1-4}$ alkyl$)_2$, C(O)$NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl), CH_2OR^5, C_{0-4} alkyl-C(O)R^5, C_{0-4} alkyl-C(O)$N(R^5)_2$, C_{0-4} alkyl-C(O)OR^5,

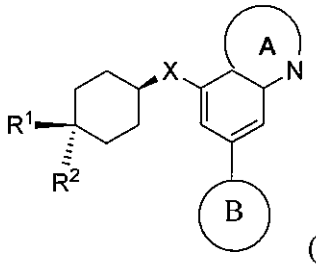
C_{0-4} alkyl-NHC(O)R^5, C_{0-4} alkyl-$N(R^5)_2$, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, pyrrolidine or piperazine, a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, oxadiazole or tetrazole, or up to two OR^5, wherein each of said optional R^4 substituents

is optionally substituted with up to four fluorine atoms, up to two C_{1-4}alkyl groups, up to two OH groups, up to two OC_{1-4}alkyl groups, up to two SC_{1-4}alkyl groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and

each R^5 is, independently, hydrogen, C_{1-4}alkyl, a 5-6-membered heteroaryl selected from imidazole, triazole, thiazole, pyridine, or pyrimidine, a 4-6-membered heterocyclyl selected from oxetane, tetrahydrofuran, or tetrahydropyran, and each R^5 group is optionally substituted with chloro, up to three fluorine atoms, up to two C_{1-2}alkyl, CH_2OH, CN, up to two OH, up to two OC_{1-2}alkyl, a spirooxetane, pyrrolidine, or triazole, or two R^5 groups together with the intervening nitrogen atom form a morpholine ring, azetidine ring, pyrrolidine ring, piperidine ring, or piperazine ring.

17. The compound of claim 1, wherein Ring C is cyclohexane.

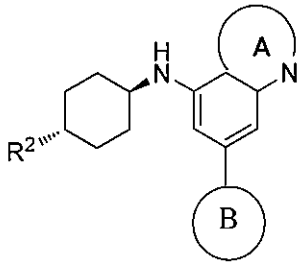
18. The compound of claim 17, having the following formula:



(III).

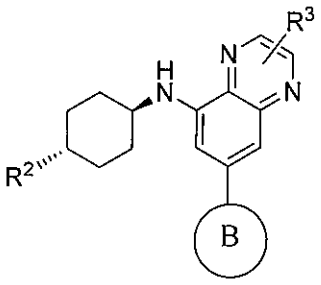
19. The compound of claim 17 or 18, wherein X is –NH-.

20. The compound of any one of claims 17-19, having the following formula:

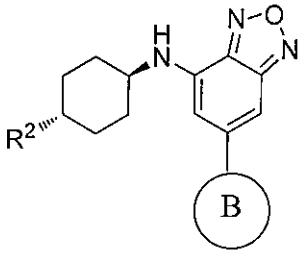


(III-A).

21. The compound of claim 20, having the following formula:



(III-A-1) or



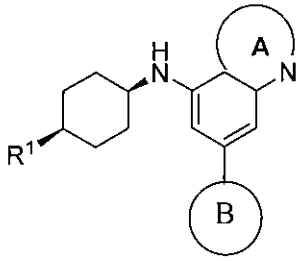
(III-A-2).

22. The compound of claim 20 or 21, wherein R^2 is -C_{0-4} alkyl-NHR^4 or -OR^4.

23. The compound of claim 22, wherein R^2 is -NHR^4.

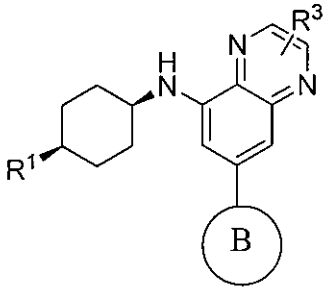
24. The compound of claim 22, wherein R^2 is -OR^4.

25. The compound of claim 17-19, having the following formula:

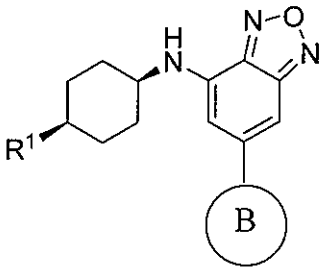


(III-B).

26. The compound of claim 25 having the following formula:



(III-B-1) or



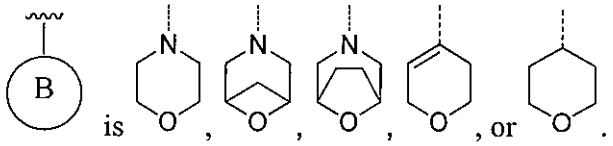
(III-B-2).

27. The compound of claim 25 or 26, wherein R^1 is -C_{0-4} alkyl-NHR^4 or -OR^4.

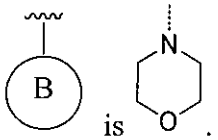
28. The compound of claim 27, wherein R^1 is $-NHR^4$.

29. The compound of claim 27, wherein R^1 is $-OR^4$.

30. The compound of any one of claims 17-29 wherein

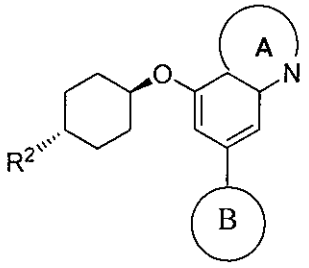


31. The compound of claim 30 wherein



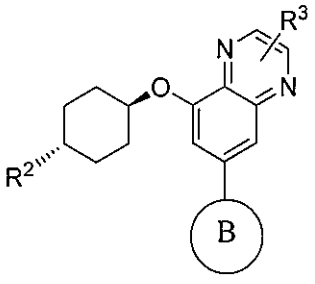
32. The compound of claim 17 or 18, wherein X is –O-.

33. The compound of claim 17, 18 or 32, having the following formula:

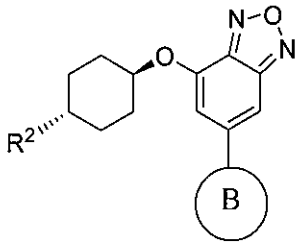


(III-C).

34. The compound of claim 33, having the following formula:



(III-C-1) or



(III-C-2).

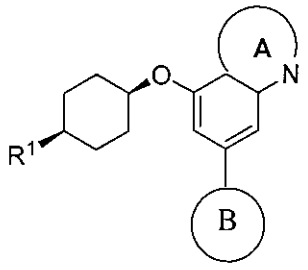
.

35. The compound of claim 33 or 34, wherein is R^2 is -C_{0-4} alkyl-NHR^4 or -OR^4.

36. The compound of claim 35, wherein is R^2 is -NHR^4.

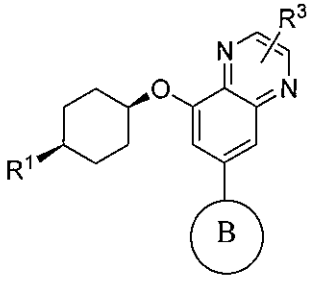
37. The compound of claim 35, wherein is R^2 is -OR^4.

38. The compound of claim 17, 18 or 32, having the following formula:

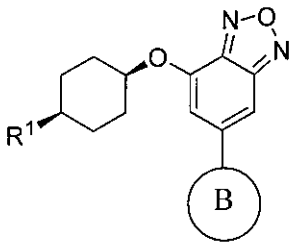


(III-D).

39. The compound according to claim 38 having the following formula:



(III-D-1) or



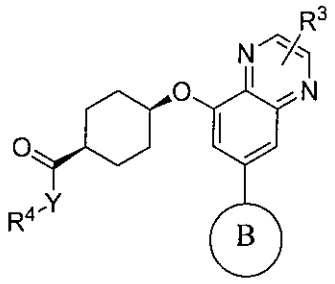
(III-D-2).

40. The compound of claim 38 or 39, wherein is R^1 is -C_{0-4} alkyl-NHR^4 or -OR^4.

41. The compound of claim 40, wherein is R^1 is -NHR^4.

42. The compound of claim 40, wherein is R^1 is -OR^4.

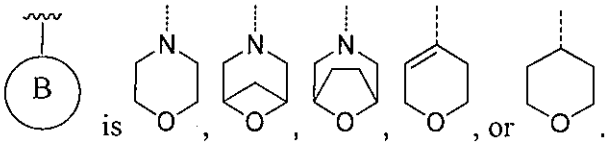
43. The compound of claim 38 or 39 having the following formula:



(**III-D-3**), wherein

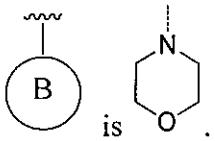
Y is –O- or –NH-.

44. The compound of any one of claims 32-43 wherein



is , , , , or .

45. The compound of claim 44 wherein



is .

46. The compound of any one of claims 17-45, wherein R^3 is hydrogen, C_{1-4}alkyl, OC_{1-2}alkyl, or $C(O)NH_2$, or C(O)H, wherein each of said R^3 alkyl is optionally substituted with OH.

47. The compound of claim 46, wherein R^3 is hydrogen.

48. The compound of any one of claims 17-47, wherein

R^4 is hydrogen, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-5}cycloalkyl, phenyl, wherein each of said R^4 groups is optionally substituted with up to four Br, Cl, F, or C_{1-4}alkyl, up to three CN, NO_2, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, $C(O)OC_{1-4}$ alkyl,

$C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-$C(O)NH_2$, $C(O)NHC_{1-4}$ alkyl, $C(O)N(C_{1-4}$ alkyl$)_2$, $C(O)NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl), CH_2OR^5, C_{0-4} alkyl-$C(O)R^5$, C_{0-4} alkyl-$C(O)N(R^5)_2$, C_{0-4} alkyl-$C(O)OR^5$, C_{0-4} alkyl-$NHC(O)R^5$, C_{0-4} alkyl-$N(R^5)_2$, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, pyrrolidine or piperazine, a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, oxadiazole or tetrazole, or up to two OR^5, wherein each of said optional R^4 substituents is optionally substituted with up to four fluorine atoms, up to two C_{1-4}alkyl groups, up to two OH groups, up to two OC_{1-4}alkyl groups, up to two SC_{1-4}alkyl groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and each R^5 is, independently, hydrogen, C_{1-4}alkyl, a 5-6-membered heteroaryl selected from imidazole, triazole, thiazole, pyridine, or pyrimidine, a 4-6-membered heterocyclyl selected from oxetane, tetrahydrofuran, or tetrahydropyran, and each R^5 group is optionally substituted with chloro, up to three fluorine atoms, up to two C_{1-2}alkyl, CH_2OH, CN, up to two OH, up to two OC_{1-2}alkyl, a spirooxetane, pyrrolidine, or triazole, or two R^5 groups together with the intervening nitrogen atom form a morpholine ring, azetidine ring, pyrrolidine ring, piperidine ring, or piperazine ring.

49. The compound of any one of claims 17-47, wherein

R^4 is a 5-10-membered monocyclic or bicyclic heteroaryl ring selected from pyrrole, imidazole, pyrazole, triazole, thiazole, isothiazole, oxazole, pyridine, pyrimidine, pyrimidinone, pyrazine, pyridazine, or quinoline, wherein each of said R^4 groups is optionally substituted with up to four Br, Cl, F, or C_{1-4}alkyl, up to three CN, NO_2, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, $C(O)OC_{1-4}$ alkyl, $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-$C(O)NH_2$, $C(O)NHC_{1-4}$ alkyl, $C(O)N(C_{1-4}$ alkyl$)_2$, $C(O)NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl), CH_2OR^5, C_{0-4} alkyl-$C(O)R^5$, C_{0-4} alkyl-$C(O)N(R^5)_2$, C_{0-4} alkyl-$C(O)OR^5$, C_{0-4} alkyl-$NHC(O)R^5$, C_{0-4} alkyl-$N(R^5)_2$, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, pyrrolidine or piperazine, a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, oxadiazole or tetrazole, or up to two OR^5, wherein each of said

optional R^4 substituents is optionally substituted with up to four fluorine atoms, up to two C_{1-4}alkyl groups, up to two OH groups, up to two OC_{1-4}alkyl groups, up to two SC_{1-4}alkyl groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and each R^5 is, independently, hydrogen, C_{1-4}alkyl, a 5-6-membered heteroaryl selected from imidazole, triazole, thiazole, pyridine, or pyrimidine, a 4-6-membered heterocyclyl selected from oxetane, tetrahydrofuran, or tetrahydropyran, and each R^5 group is optionally substituted with chloro, up to three fluorine atoms, up to two C_{1-2}alkyl, CH_2OH, CN, up to two OH, up to two OC_{1-2}alkyl, a spirooxetane, pyrrolidine, or triazole, or two R^5 groups together with the intervening nitrogen atom form a morpholine ring, azetidine ring, pyrrolidine ring, piperidine ring, or piperazine ring.

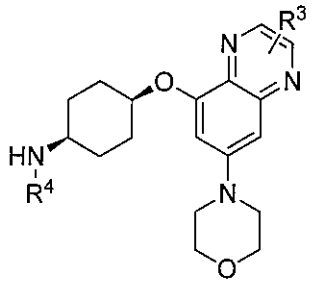
50. The compound of claim 49, wherein

R^4 is pyridine or pyrimidine, which is optionally substituted with up to four Br, Cl, F, or C_{1-4}alkyl, up to three CN, NO_2, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, $C(O)OC_{1-4}$ alkyl, $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-$C(O)NH_2$, $C(O)NHC_{1-4}$ alkyl, $C(O)N(C_{1-4}$ alkyl$)_2$, $C(O)NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl), CH_2OR^5, C_{0-4} alkyl-$C(O)R^5$, C_{0-4} alkyl-$C(O)N(R^5)_2$, C_{0-4} alkyl-$C(O)OR^5$, C_{0-4} alkyl-$NHC(O)R^5$, C_{0-4} alkyl-$N(R^5)_2$, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, pyrrolidine or piperazine, a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, oxadiazole or tetrazole, or up to two OR^5, wherein each of said optional R^4 substituents is optionally substituted with up to four fluorine atoms, up to two C_{1-4}alkyl groups, up to two OH groups, up to two OC_{1-4}alkyl groups, up to two SC_{1-4}alkyl groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and each R^5 is, independently, hydrogen, C_{1-4}alkyl, a 5-6-membered heteroaryl selected from imidazole, triazole, thiazole, pyridine, or pyrimidine, a 4-6-membered heterocyclyl selected from oxetane, tetrahydrofuran, or tetrahydropyran, and each R^5 group is optionally substituted with chloro, up to three fluorine atoms, up to two C_{1-2}alkyl, CH_2OH, CN, up to two OH, up to two OC_{1-2}alkyl, a spirooxetane, pyrrolidine, or triazole, or two R^5 groups together with the intervening nitrogen atom form a morpholine ring, azetidine ring, pyrrolidine ring, piperidine ring, or piperazine ring.

51. The compound of any one of claims 17-47, wherein

R^4 is a 4-10-membered monocyclic or bicyclic heterocyclyl ring selected from oxetane, tetrahydrofuran, tetrahydropyran, dihydroisoxazole, pyrimidine-2,4(1H,3H)-dione, dihydrofuropyrimidine, dihydropyranopyrimidine, dihydropyrrolopyrimidine, tetrahydropteridine, or tetrahydropyridopyrimidine, wherein each of said R^4 groups is optionally substituted with up to four Br, Cl, F, or C_{1-4}alkyl, up to three CN, NO_2, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, C(O)OC_{1-4} alkyl, C(O)OC_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-C(O)NH_2, C(O)NHC_{1-4} alkyl, C(O)N(C_{1-4} alkyl)$_2$, C(O)NH(C_{0-4} alkyl-C_{3-5} cycloalkyl), CH_2OR^5, C_{0-4} alkyl-C(O)R^5, C_{0-4} alkyl-C(O)N(R^5)$_2$, C_{0-4} alkyl-C(O)OR^5, C_{0-4} alkyl-NHC(O)R^5, C_{0-4} alkyl-N(R^5)$_2$, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, pyrrolidine or piperazine, a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, oxadiazole or tetrazole, or up to two OR^5, wherein each of said optional R^4 substituents is optionally substituted with up to four fluorine atoms, up to two C_{1-4}alkyl groups, up to two OH groups, up to two OC_{1-4}alkyl groups, up to two SC_{1-4}alkyl groups, a C(O)C_{1-4} alkyl, a C(O)OC_{1-4} alkyl, or a C(O)OC_{0-4} alkyl-C_{3-5} cycloalkyl; and each R^5 is, independently, hydrogen, C_{1-4}alkyl, a 5-6-membered heteroaryl selected from imidazole, triazole, thiazole, pyridine, or pyrimidine, a 4-6-membered heterocyclyl selected from oxetane, tetrahydrofuran, or tetrahydropyran, and each R^5 group is optionally substituted with chloro, up to three fluorine atoms, up to two C_{1-2}alkyl, CH_2OH, CN, up to two OH, up to two OC_{1-2}alkyl, a spirooxetane, pyrrolidine, or triazole, or two R^5 groups together with the intervening nitrogen atom form a morpholine ring, azetidine ring, pyrrolidine ring, piperidine ring, or piperazine ring.

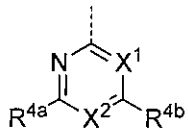
52. The compound of claim 32 having the formula:



(**IV**), wherein

R^3 is hydrogen, -C_{1-4}alkyl, fluoro, chloro, -OC_{1-2}alkyl, or -$C(O)NH_2$, -C(O)H, or -CN, wherein each of said R^3 alkyl is optionally substituted with OH or up to 3 fluorine atoms;

R^4 is



X^1 is N, CH, CF, CCl, or CC_{1-2} alkyl optionally substituted with up to 3 fluorine atoms;

X^2 is N or CR^{4c}, wherein X^1 and X^2 cannot simultaneously be N;

each of R^{4a}, R^{4b}, and R^{4c} is, independently, hydrogen, F, Cl, Br, CN, NO_2, C_{1-4} alkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, $C(O)OC_{1-4}$ alkyl, $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl, $C(O)NH_2$, $C(O)NHC_{1-4}$ alkyl, $C(O)N(C_{1-4}$ alkyl$)_2$, $C(O)NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl), a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, or piperazine, or a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, or tetrazole, or R^{4c}, R^{4a}, and the intervening atoms form a dihydrofuran, a dihydropyran, or a tetrahydropiperidine heterocyclic ring system;

wherein each of said R^{4a}, R^{4b}, or R^{4c} heterocyclic or heteroaryl ring systems is optionally substituted with up to four fluorine atoms, up to two C_{1-4} alkyl, up to two OH groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and

wherein each of said R^{4a}, R^{4b}, or R^{4c} alkyl or cycloalkyl is optionally substituted with up to 2 non-geminal OH groups or up to 3 fluorine atoms.

53. The compound of claim 52, wherein R^3 is hydrogen, -C_{1-4}alkyl,

$-OC_{1-2}$alkyl, or $-C(O)NH_2$, or -C(O)H, wherein each of said R^3 alkyl is optionally substituted with OH.

54. The compound of claim 52 or 53, wherein R^3 is hydrogen.

55. The compound of any one of claims 52-54, wherein each of X^1 and X^2 is, independently, CH or N, wherein X^1 and X^2 cannot simultaneously be N.

56. The compound of any one of claims 52-55, wherein each of R^{4a} and R^{4b} is, independently, a heterocyclic ring system selected from oxetane, azetidine, tetrahydrofuran, dihydropyran, tetrahydropyran, morpholine, piperidine, or piperazine,

wherein each of said R^{4a} or R^{4b} heterocyclic or heteroaryl ring systems is optionally substituted with up to four fluorine atoms, up to two C_{1-4} alkyl, up to two OH groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and

wherein each of said R^{4a} or R^{4b} alkyl or cycloalkyl is optionally substituted with up to 2 non-geminal OH groups or up to 3 fluorine atoms.

57. The compound of any one of claims 52-55, wherein each of R^{4a} and R^{4b} is, independently, a heteroaryl ring system selected from furan, oxazole, oxadiazole, pyrrole, pyrazole, triazole, or tetrazole,

wherein each of said R^{4a} or R^{4b} heterocyclic or heteroaryl ring systems is optionally substituted with up to four fluorine atoms, up to two C_{1-4} alkyl, up to two OH groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and

wherein each of said R^{4a} or R^{4b} alkyl or cycloalkyl is optionally substituted with up to 2 non-geminal OH groups or up to 3 fluorine atoms.

58. The compound of any one of claims 52-55, wherein each of R^{4a} and R^{4b} is, independently, hydrogen, F, Cl, Br, CN, NO_2, C_{1-4} alkyl, C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{0-4} alkyl-O-C_{1-4} alkyl, C_{0-4} alkyl-O-C_{0-4} alkyl-C_{3-5} cycloalkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, $C(O)OC_{1-4}$ alkyl, $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl, $C(O)NH_2$, $C(O)NHC_{1-4}$ alkyl, $C(O)N(C_{1-4}$ alkyl$)_2$, or $C(O)NH(C_{0-4}$ alkyl-C_{3-5} cycloalkyl),

wherein each of said R^{4a} or R^{4b} heterocyclic or heteroaryl ring systems is optionally substituted with up to four fluorine atoms, up to two C_{1-4} alkyl, up to two OH groups, a $C(O)C_{1-4}$ alkyl, a $C(O)OC_{1-4}$ alkyl, or a $C(O)OC_{0-4}$ alkyl-C_{3-5} cycloalkyl; and

wherein each of said R^{4a} or R^{4b} alkyl or cycloalkyl is optionally substituted with up to 2 non-geminal OH groups or up to 3 fluorine atoms.

59. A compound selected from the list of compounds in Table 1.

60. A compound selected from the list of compounds in Table 2.

61. A pharmaceutical composition comprising a compound of any one of claims 1-60 and a pharmaceutically acceptable excipient.

62. A compound of any one of claims 1-61, or a pharmaceutical composition comprising said compound for use in the sensitization of a cell to a therapeutic agent or a disease state that induces a DNA lesion.

63. A compound of any one of claims 1-60, or a pharmaceutical composition comprising said compound for use in the potentiation of a therapeutic regimen for the treatment of cancer in a patient.

64. A compound of any one of claims 1-60, or a pharmaceutical composition either alone or in combination with one or more additional therapeutic agent for use in the treatment of cancer or inhibiting cancer cell growth in a patient.