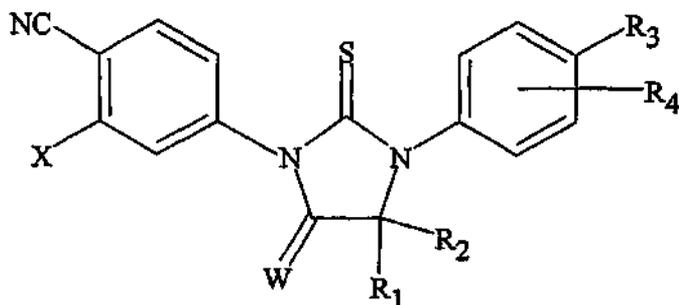


CLAIMS

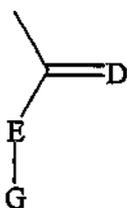
Claim 1. A compound having the formula



wherein X is selected from the group consisting of trifluoromethyl and iodo,

wherein W is selected from the group consisting of O and NR₅,

wherein R₅ is selected from the group consisting of H, methyl, and



wherein D is S or O and E is N or O and G is alkyl, aryl, substituted alkyl or substituted aryl; or
D is S or O and E-G together are C₁-C₄ lower alkyl,

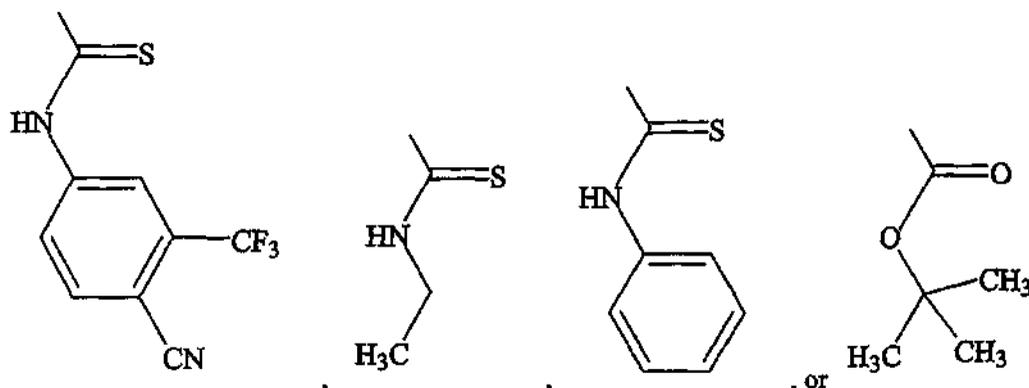
wherein R₁ and R₂ together comprise eight or fewer carbon atoms and are selected from the group consisting of alkyl, substituted alkyl including haloalkyl, and, together with the carbon to which they are linked, a cycloalkyl or substituted cycloalkyl group,

wherein R₃ is selected from the group consisting of hydrogen, halogen, methyl, C₁-C₄ alkoxy, formyl, haloacetoxy, trifluoromethyl, cyano, nitro, hydroxyl, phenyl, amino, methylcarbamoyl, methoxycarbonyl, acetamido, methanesulfonamino, methanesulfonyl, 4-methanesulfonyl-1-piperazinyl, piperazinyl, and C₁-C₆ alkyl or alkenyl optionally substituted with hydroxyl, methoxycarbonyl, cyano, amino, amido, nitro, carbamoyl, or substituted carbamoyl including methylcarbamoyl, dimethylcarbamoyl, and hydroxyethylcarbamoyl,

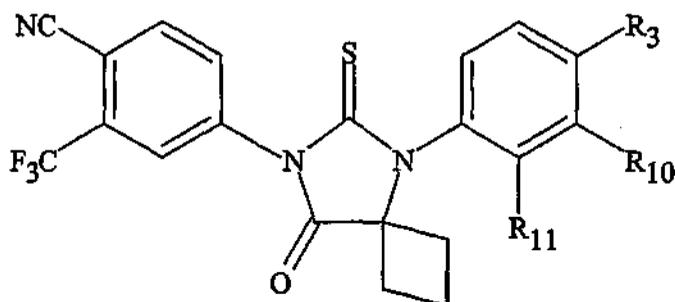
wherein R₄ is selected from the group consisting of hydrogen, halogen, alkyl, and haloalkyl,

wherein R₃ is not methylaminomethyl or dimethylaminomethyl.

Claim 2. The compound of claim 1, wherein R₅ is



Claim 3. The compound of claim 1, having the formula



wherein R₃ is selected from the group consisting of hydroxy, methylcarbamoyl, methylcarbamoylpropyl, methylcarbamoylethyl, methylcarbamoylmethyl, methylsulfonocarbamoylpropyl, methylaminomethyl, dimethylaminomethyl, methylsulfonyloxymethyl, carbamoylmethyl, carbamoylethyl, carboxymethyl, methoxycarbonylmethyl, methanesulfonyl, 4-cyano-3-trifluoromethylphenylcarbamoylpropyl, carboxypropyl, 4-methanesulfonyl-1-piperazinyl, piperazinyl, methoxycarbonyl, 3-cyano-4-trifluoromethylphenylcarbamoyl, hydroxyethylcarbamoylethyl, and hydroxyethoxycarbonylethyl, and

wherein R₁₀ and R₁₁ are both H or, respectively, F and H, or H and F.

Claim 4. The compound of claim 3, wherein R₁₀ and R₁₁ are both H.

Claim 5. The compound of claim 3, wherein R₁₀ and R₁₁ are, respectively, F and H.

Claim 6. The compound of claim 3, wherein R₃ is methylcarbamoyl.

Claim 7. The compound of claim 3, wherein R3 is methylcarbamoyl and R10 and R11 are, respectively, F and H.

Claim 8. The compound of claim 1,

wherein R1 and R2 are independently methyl or, together with the carbon to which they are linked, a cycloalkyl group of 4 to 5 carbon atoms, and

R3 is selected from the group consisting of carbamoyl, alkylcarbamoyl, carbamoylalkyl, and alkylcarbamoylalkyl, and R4 is H or F.

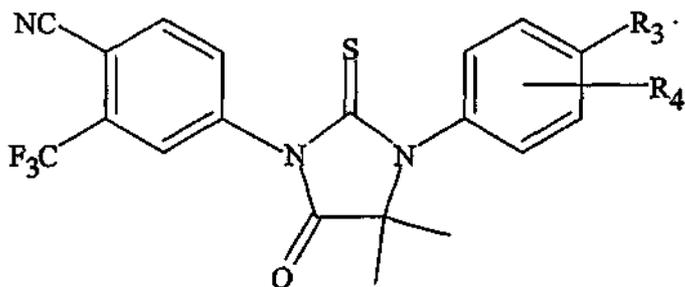
Claim 9. The compound of claim 8, wherein R4 is 3-fluoro.

Claim 10. The compound of claim 1,

wherein R1 and R2 are independently methyl or, together with the carbon to which they are linked, a cycloalkyl group of 4 to 5 carbon atoms,

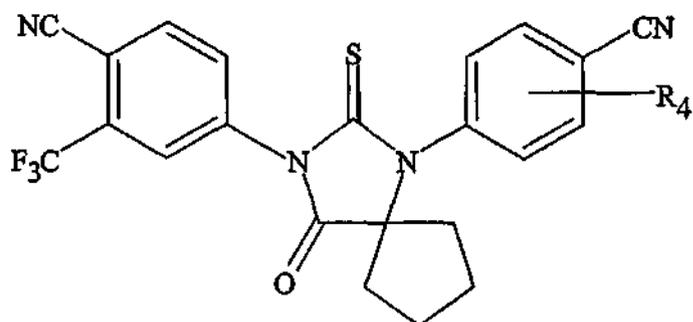
R3 is selected from the group consisting of cyano, hydroxy, methylcarbamoyl, methylcarbamoyl-substituted alkyl, methylsulfoncarbamoyl-substituted alkyl, methylaminomethyl, dimethylaminomethyl, methylsulfonyloxymethyl, methoxycarbonyl, acetamido, methanesulfonamido, carbamoyl-substituted alkyl, carboxymethyl, methoxycarbonylmethyl, methanesulfonyl, 4-cyano-3-trifluoromethylphenylcarbamoyl-substituted alkyl, carboxy-substituted alkyl, 4-(1,1-dimethylethoxy)carbonyl-1-piperazinyl, 4-methanesulfonyl-1-piperazinyl, piperazinyl, hydroxyethylcarbamoyl-substituted alkyl, hydroxyethoxycarbonyl-substituted alkyl, and 3-cyano-4-trifluoromethylphenylcarbamoyl, and R4 is F.

Claim 11. The compound of claim 1, having the formula



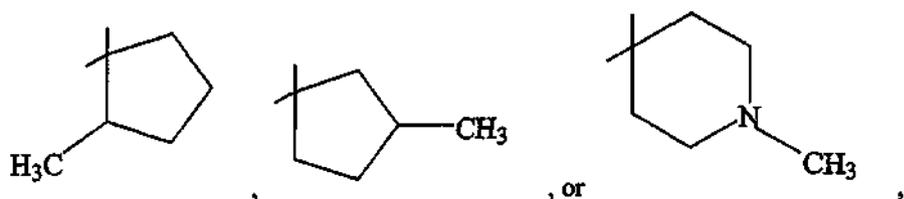
wherein R3 is selected from the group consisting of methylcarbonyl, methoxycarbonyl, acetamido, and methanesulfonamido, and R4 is selected from the group consisting of F and H.

Claim 12. The compound of claim 1, having the formula



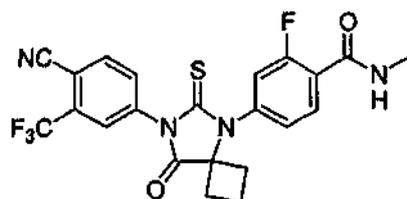
wherein R₄ is selected from the group consisting of F and H.

Claim 13. A compound according to claim 1, wherein R₁ and R₂ together with the carbon to which they are linked are



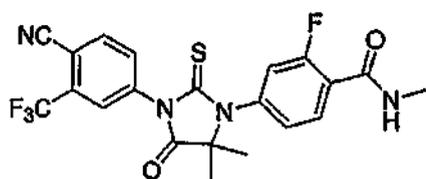
Claim 14. A compound selected from the compounds of Tier 1 and Tier 2.

Claim 15. The compound of claim 1, having the formula



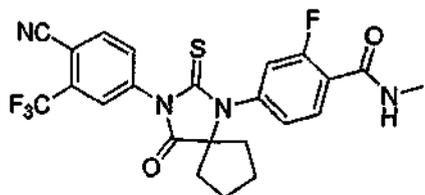
[RD162]

Claim 16. The compound of claim 1, having the formula



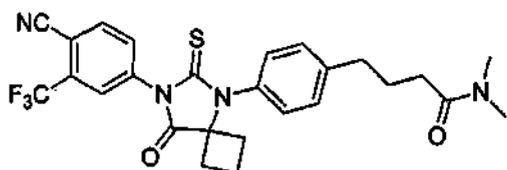
[RD162']

Claim 17. The compound of claim 1, having the formula



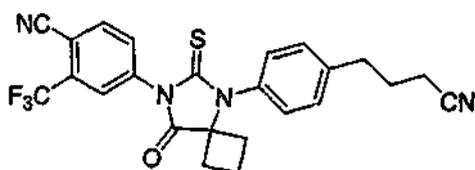
[RD162'']

Claim 18. The compound of claim 1, having the formula



[RD169]

Claim 19. The compound of claim 1, having the formula



[RD170]

Claim 20. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to any of claims 1-19 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

Claim 21. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

Claim 22. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to claim 9, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

23. A pharmaceutical composition as claimed in claim 20 or 21 or wherein said compound is in an amount equivalent to a dosage amount of from about 0.001 mg per kg body weight per day to about 100 mg per kg body weight per day for treatment of hyperproliferative disorder.

24. A pharmaceutical composition as claimed in claim 20 or 21 wherein said compound is in an amount equivalent to a dosage amount of from about 0.01 mg per kg body weight per day to about 100 mg per kg body weight per day.

25. A pharmaceutical composition as claimed in claim 20 or 21 wherein said compound is in an amount equivalent to a dosage amount of from about 0.1 mg per kg body weight per day to about 10 mg per kg body weight per day.

26. A pharmaceutical composition as claimed in claim 20 or 21 wherein said compound is in an amount equivalent to a dosage amount of about 1 mg per kg body weight per day.

27. The pharmaceutical composition as claimed in claim 21, wherein the compound is in a form that can be administered as an intravenous injection, by injection into tissue, intraperitoneally, orally, or nasally.

28. The composition of claim 27, wherein the composition is administered orally

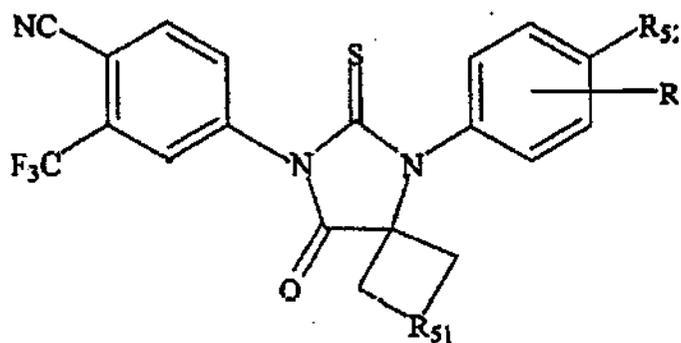
29. The pharmaceutical composition as claimed in claim 21, wherein the composition has a form selected from the group consisting of a solution, dispersion, suspension, powder, capsule, tablet, pill, time release capsule, time release tablet, and time release pill.

30. The pharmaceutical composition as claimed in claim 28, wherein the composition has a form selected from the group consisting of a capsule, tablet, and pill.

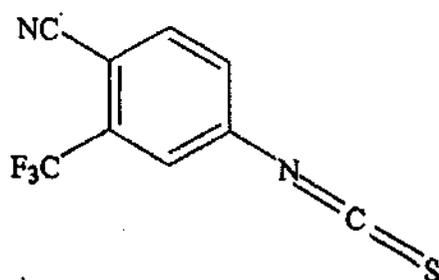
31. The pharmaceutical composition as claimed in claim 28, wherein the compound is selected from the group consisting of RD162', RD162", RD 169, or RD170, or a pharmaceutically acceptable salt thereof.

32. The pharmaceutical composition as claimed in claim 28, wherein the compound is N-methyl-4-[7-(4-cyano-3-trifluoromethylphenyl)-8-oxo-6-thioxo-5,7-diaza-spiro[3.4]oct-5-yl]-2-fluorobenzamide [RD162] or a pharmaceutically acceptable salt thereof.

33. A method of synthesizing a diaryl compound of formula:

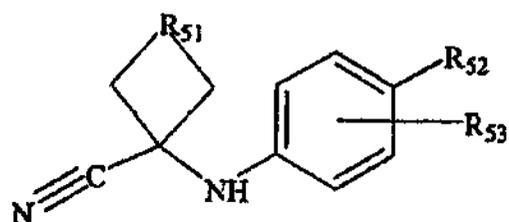


comprising mixing Compound I



Compound I

with Compound II

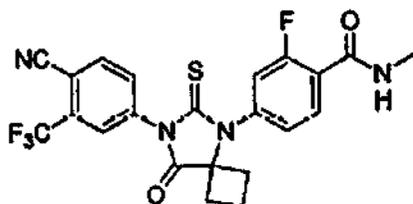


in a first polar solvent to form a mixture, heating the mixture, adding a second polar solvent, the same as or different from the first polar solvent, and an aqueous acid to the mixture, refluxing the mixture, cooling the mixture and combining with water, and separating the diaryl compound from the mixture, wherein R51 comprises an alkyl chain of from 1 to 4 carbon atoms, R52 is selected from the group consisting of cyano, hydroxy, methylcarbamoyl, methylcarbamoyl-substituted alkyl, methylsulfoncarbamoyl-substituted alkyl, methylaminomethyl, dimethylaminomethyl, methylsulfonyloxymethyl, methoxycarbonyl, 3-cyano-4-trifluoromethylphenylcarbamoyl, carbamoyl-substituted alkyl, carboxymethyl, methoxycarbonylmethyl, methanesulfonyl, 4-cyano-3-trifluoromethylphenylcarbamoyl-substituted alkyl, carboxy-substituted alkyl, 4-methanesulfonyl-1-piperazinyl, piperazinyl, hydroxyethylcarbamoyl-substituted alkyl, and

hydroxyethoxycarbonyl- substituted alkyl, and R53 is selected from the group consisting of F and H.

34. The method of claim 31, wherein R51 comprises an alkyl chain of from 1 to 2 carbon atoms, R52 is selected from the group consisting of carbamoyl and methylcarbamoyl, and R53 is F.

35. A method of synthesizing a compound of formula:



[RD 162]

comprising mixing 4-isothiocyanato-2-trifluoromethylbenzonitrile and N-methyl-4-(1-cyanocyclobutylamino)-2-fluorobenzamide in dimethylformamide to form a first mixture, heating the first mixture to form a second mixture, adding alcohol and acid to the second mixture to form a third mixture, refluxing the third mixture to form a fourth mixture, cooling the fourth mixture, combining the fourth mixture with water and extracting an organic layer; isolating the compound from the organic layer.

36. A method of synthesizing the compound of claim 16 [RD 162], comprising mixing N-Methyl-2-fluoro-4-(1,1-dimethyl-cyanomethyl)-aminobenzamide and 4- Isothiocyanato-2-trifluoromethylbenzonitrile in DMF and heating to form a first mixture; adding an alcohol and an acid to the first mixture to form a second mixture; refluxing the second mixture; cooling the second mixture, combining the second mixture with water and extracting an organic layer; isolating the compound from the organic layer.

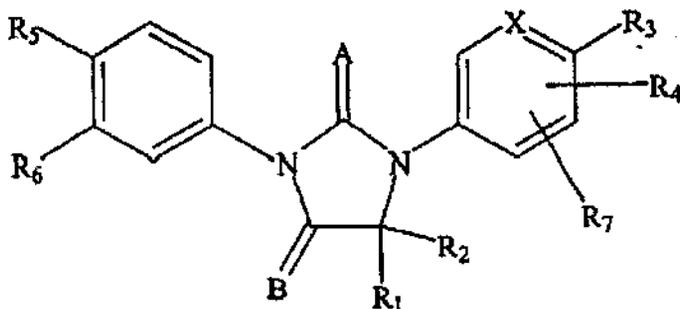
37. A method of synthesizing the compound of claim 17 [RD162"], comprising mixing N-Methyl-2-fluoro-4-(1-cyanocyclopentyl)aminobenzamide, 4-isothiocyanato-2- trifluoromethyl benzonitrile, and DMF and heating under reflux to form a first mixture; adding an alcohol and an acid to the first mixture to form a second mixture; refluxing the second mixture; cooling the second mixture;

combining the second mixture with water and extracting an organic layer; isolating the compound from the organic layer.

38. A method of synthesizing the compound of claim 18 [RD 169], comprising mixing N,N-Dimethyl 4-[4-(1-cyanocyclobutylamino)phenyl]butanamide, 4-isothiocyanato-2- trifluoromethyl benzonitrile, and DMF and heating under reflux to form a first mixture; adding an alcohol and an acid to the first mixture to form a second mixture; refluxing the second mixture; cooling the second mixture; combining the second mixture with water and extracting an organic layer; isolating the compound from the organic layer.

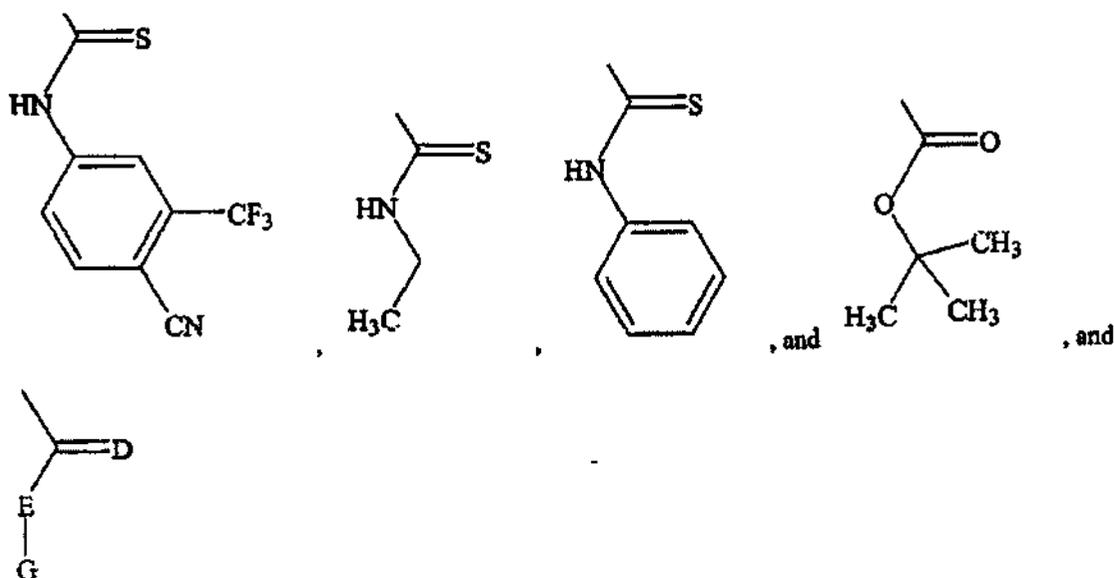
39. A method of synthesizing the compound of claim 19[RD170], comprising mixing DMSO, dichloromethane, and oxalyl chloride to form a first mixture, adding 4-(4-(7-(4-Cyano-3-(trifluoromethyl)phenyl)-8-oxo-6-thioxo-5,7-diazaspiro[3.4]octan-5-yl)phenyl)butanamide to the first mixture to form a second mixture; adding triethylamine to the second mixture to form a third mixture; warming the third mixture and quenching with aqueous NH_4Cl to form a fourth mixture; extracting an organic layer from the fourth mixture; isolating the compound from the organic layer.

40. A compound having the formula



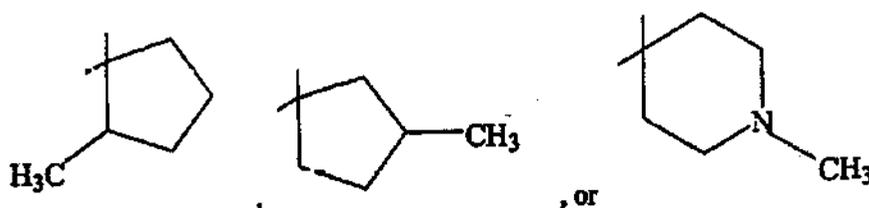
wherein R_5 is CN or NO_2 or SO_2R_n , wherein R_6 is CF_3 , alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, halogenated alkyl, halogenated alkenyl, halogenated alkynyl, halogen, wherein A is sulfur (S) or oxygen (O),

wherein B is O or S or NR_8 , wherein R_8 is selected from the group consisting of H, methyl, aryl, substituted aryl, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heterocyclic aromatic or non-aromatic, substituted heterocyclic aromatic or non-aromatic, cycloalkyl, substituted cycloalkyl, SO_2R_n , NR_nR_i , $(\text{CO})\text{OR}_{11}$, $(\text{CO})\text{NR}_{11}\text{R}_{12}$, $(\text{CO})\text{R}_{11}$, $(\text{CS})\text{R}_{11}$, $(\text{CS})\text{NR}_{11}\text{R}_{12}$, $(\text{CS})\text{OR}_{11}$,



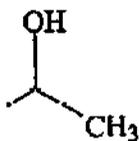
wherein D is S or O and E is N or O and G is alkyl, aryl, substituted alkyl or substituted aryl; or

D is S or O and E-G together are C1-C4 lower alkyl, wherein R1 and R2 are independently alkyl, haloalkyl, hydrogen, aryl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, halogenated alkenyl, halogenated alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heterocyclic aromatic or non-aromatic, substituted heterocyclic aromatic or non-aromatic, cycloalkyl, substituted cycloalkyl, or R₁ and R₂ are connected to form a cycle which can be heterocyclic, substituted heterocyclic, cycloalkyl, substituted cycloalkyl,



wherein X is carbon or nitrogen and can be at any position in the ring, and wherein R3, R4, and R7 are independently selected from the group consisting of hydrogen, halogen, methyl, methoxy, formyl, haloacetoxy, trifluoromethyl, cyano, nitro, hydroxyl, phenyl, amino, methylcarbamoyl, methylcarbamoyl-substituted alkyl, dimethylcarbamoyl-substituted alkyl,

methoxycarbonyl, acetamido, methanesulfonamino, carbamoyl-substituted alkyl, methanesulfonyl, 4-methanesulfonyl-1-piperazinyl, piperazinyl, hydroxyethylcarbamoyl-substituted alkyl, hydroxyl-substituted alkyl, hydroxyl-substituted alkenyl, carbamoyl-substituted alkenyl, methoxycarbonyl-



substituted alkyl, cyano-substituted alkyl,

, aryl, substituted aryl, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, halogenated alkenyl, halogenated alkynyl, SO_2R_{11} , $NR_{11}R_{12}$, $NR_{12}(CO)OR_{11}$, $NH(CO)NR_{11}R_{12}$, $NR_{12}(CO)R_{11}$, $O(CO)R_{11}$, $O(CO)OR_{11}$, $O(CS)R_{11}$, $NR_{12}(CS)R_{11}$, $NH(CS)NR_{11}R_{12}$, $NR_{12}(CS)OR_{11}$, arylalkyl, arylalkenyl, arylalkynyl, heterocyclic aromatic or non-aromatic, substituted heterocyclic aromatic or non-aromatic, cycloalkyl, substituted cycloalkyl, haloalkyl, methylsulfonocarbonyl-substituted alkyl, methylaminomethyl, dimethylaminomethyl, methylsulfonyloxymethyl, methoxycarbonyl, acetamido, methanesulfonamido, carbamoyl-substituted alkyl, carboxymethyl, methoxycarbonylmethyl, methanesulfonyl, 4-cyano-3-trifluoromethylphenylcarbamoyl-substituted alkyl, carboxy-substituted alkyl, 4-(1,1-dimethylethoxy)carbonyl-1-piperaziny, hydroxyethylcarbamoyl-substituted alkyl, hydroxyethoxycarbonyl-substituted alkyl, 3-cyano-4-trifluoromethylphenylcarbamoyl, wherein R_{11} and R_{12} are independently hydrogen, aryl, aralkyl, substituted aralkyl, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, halogenated alkyl, halogenated alkenyl, halogenated alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heterocyclic aromatic or non-aromatic, substituted heterocyclic aromatic or non-aromatic, cycloalkyl, or substituted cycloalkyl, or R_{11} and R_{12} can be connected to form a cycle which can be heterocyclic aromatic or non-aromatic, substituted heterocyclic aromatic, cycloalkyl, or substituted cycloalkyl.

41. The compound of claim 40, wherein the compound has substantial androgen receptor antagonist activity and no substantial agonist activity on hormone refractory prostate cancer cells.

42. A method comprising: providing at least one compound according to claim 40; measuring inhibition of androgen receptor activity for the compound and determining if the inhibition is above a first predetermined level, measuring stimulation of androgen receptor activity in hormone refractory cancer cells for the compound and determining if the stimulation is below a second predetermined level, selecting the compound if the inhibition is above the first predetermined level and the stimulation is below the second predetermined level.

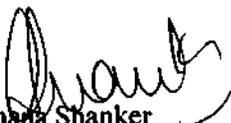
43. The method of claim 42, wherein the predetermined levels are those of bicalutamide.

44. The method of claim 42, wherein the step of measuring inhibition comprises measuring inhibitory concentration (IC50) in an AR response reporter system or a prostate specific antigen secreting system.

45. The method of claim 42, wherein the step of measuring stimulation comprises measuring fold induction by increasing concentrations in an AR response reporter system or a prostate specific antigen secreting system.

46. The method of claim 42, wherein the steps of measuring inhibition and/or stimulation comprise measuring an effect of the compound on tumor growth in an animal.

Dated this day 13th day of December 2007


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