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(54) Title: INDAZOLE COMPOUNDS

(57) Abstract: The present invention relates to indazole compounds which are useful in the treatment of proliferative disorders such as cancer.

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INDAZOLE COMPOUNDS

FIELD OF THE INVENTION

The present invention relates to indazole compounds that may be useful as anti proliferative agents. More particularly, the present invention relates to substituted indazole compounds, methods for their preparation, pharmaceutical compositions containing these compounds and uses of these compounds in the treatment of proliferative disorders. These compounds may be useful as medicaments for the treatment of a number of proliferative disorders including tumours and cancers.

BACKGROUND OF THE INVENTION

Proliferative disorders such as cancer are characterised by the uncontrolled growth of cells within the body. As such proliferative disorders generally involve an abnormality in the control of cell growth and/or division leading to the formation of tumour and ultimately death. Without wishing to be bound by theory it is thought that this is caused by the pathways that regulate cell growth and division being altered in cancer cells. The alteration is such that the effects of these normal regulatory mechanisms in controlling cell growth and division either fails or is bypassed.

The uncontrolled cell growth and/or division ultimately proves fatal for the patient as successive rounds of mutations on the part of the cell then typically lead to the cancer cells having a selective advantage over normal healthy cells in the body of the patient leading to the cancer cells predominating in the cell mass of the patient. The cancer cells then typically metastasize to colonize other tissues or parts of the body other than the part of origin of the cancer cell leading to secondary tumours which eventually lead to organ failure and the death of the patient. It is the difficulty in controlling the rapid cell growth and division that is characteristic of cancer cells that make it hard to come up with effective chemotherapeutic strategies that do not at the same time harm healthy tissue.

A number of traditional treatments for proliferative disorders such as cancer seek to take advantage of their higher proliferative capacity and thus their higher sensitivity to DNA damage. Treatments that have been utilised include ionizing radiation (γ-rays, X-rays and the like) as well as cytotoxic agents such as bleomycin, cis-platin, vinblastine, cyclophosphamide, 5'-fluorouracil and methotrexate. These treatments all rely on causing damage to DNA and destabilisation of the chromosomal structure eventually leading to death of the cancer cells.

The problem with many of these approaches is that they are non-selective for cancer cells and healthy cells can and often will be adversely affected by the treatment. This is hardly surprising given that the cellular mechanisms targeted by these strategies occur in healthy cells as well as in cancer cells (although typically at slower rates) and merely serves to highlight the difficulty in achieving successful treatment of the cancer in the patient without causing irreparable harm to the healthy cells. As such with many of these treatments there can be devastating side effects which can not only significantly reduce the short term quality of life of the patient but may also have long term detriments on the health of the patient should they survive the cancer attack.

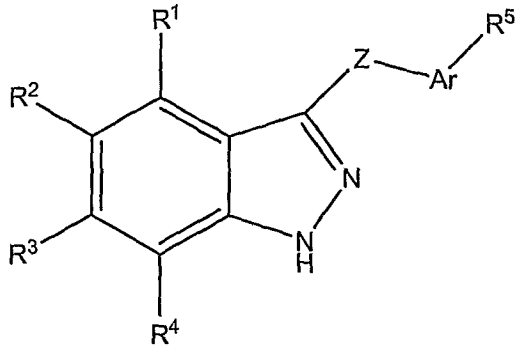
Whilst some of the above problems have substantially been overcome by the development of selective anti-cancer agents (such as tamoxifen) the effectiveness of all chemotherapeutic agents is subject to the development of drug resistance by the cancer cells in the patient. The development of drug resistance in the cancer cells of a patient tend to be class specific and therefore if the cancer cells of a patient develop drug resistance to a class of chemotherapeutics then all compounds within that class are typically rendered ineffective in the further treatment of that patient. As such in improving clinical outcomes for patients the identification of alternative chemotherapeutic agents is essential in providing the oncologist with an arsenal of drugs that may be used in any given situation.

The development of different classes of therapeutic agents is therefore important as it can help avoid the development of drug resistance and can also be used in combination therapies. Such combination therapies typically involve the use of chemotherapeutics with different properties and cellular targets which in turn tends to increase the overall effectiveness of any chosen chemotherapy regime and limits the possibility of drug resistance developing in the patient.

Accordingly, there is still a need to provide further anti-proliferative compounds that would be expected to have useful, improved pharmaceutical properties in the treatment of diseases such as cancer.

SUMMARY OF THE INVENTION

In one aspect the present invention provides a compound of the formula (I):



Formula (I)

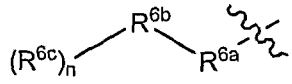
wherein

R^1, R^2, R^3 and R^4 are each independently selected from the group consisting of: H, halogen, nitro, cyano, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, aminoalkyl, acylamino, arylamino, sulfonylamino, sulfinylamino, -COOH, $-COR^6$, $-COOR^6$, $-CONHR^6$, $-NHCOR^6$, $-NHR^6$, $-NR^6R^8$, $-NHCOOR^6$, $-NHCONHR^6$, $-NHCON(OH)R^6$, $-NHCSN(OH)R^6$ $-NHSO_2NR^6$, $-NHSO_2R^6$, alkoxycarbonyl, alkylaminocarbonyl, sulfonyl, alkylsulfonyl, alkylsulfinyl, arylsulfonyl, arylsulfinyl, aminosulfonyl, $-SR^6$, $-R^7S(O)R^9$, $-R^7S(O)_2R^9$, $-R^7C(O)N(R^8)R^9$, $-R^7SO_2N(R^8)R^9$, $-R^7N(R^8)C(O)R^9$, $-R^7N(R^8)SO_2R^9$, $-R^7N(R^8)C(O)N(R^8)R^9$, $-R^7N(R^8)SO_2N(R^8)R^9$, and acyl, each of which may be optionally substituted;

R^5 is selected from the group consisting of: H, halogen, nitro, cyano, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy,

arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, aminoalkyl, acylamino, arylamino, sulfonylamino, sulfinylamino, -COOH, -COR^6, -$COOR^6$, -$CONHR^6$, -$NHCOR^6$, -$NHCOOR^6$, -$NHCONHR^6$, -$NHCSN(OH)R^6$ alkoxycarbonyl, alkylaminocarbonyl, sulfonyl, alkylsulfonyl, alkylsulfinyl, arylsulfonyl, arylsulfinyl, aminosulfonyl, -SR^6, -R^7R^9, -$R^7S(O)R^9$, -$R^7S(O)_2R^9$, -$R^7C(O)N(R^8)R^9$, -$R^7SO_2N(R^8)R^9$, -$R^7N(R^8)C(O)R^9$, -$R^7N(R^8)SO_2R^9$, -$R^7N(R^8)C(O)N(R^8)R^9$, -$R^7N(R^8)SO_2N(R^8)R^9$, and acyl, each of which may be optionally substituted;

each R^6 is independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, and acyl, each of which may be optionally substituted; or R^6 is a group of the formula:



R^{6a} is selected from the group consisting of a bond, alkyl, heteroalkyl and aryl, each of which may be optionally substituted;

R^{6b} is selected from the group consisting of a bond, alkyl, -CO-, cycloalkyl, aryl and heteroaryl, each of which may be optionally substituted;

R^{6c} is selected from the group consisting of H, alkyl, chloro, bromo, iodo, hydroxy, alkoxy, CH_3CONH- and heteroaryl;

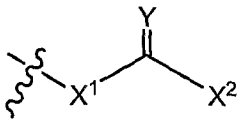
n is an integer from the group consisting of 0, 1, 2, 3, 4, and 5;

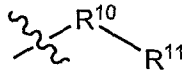
each R^7 is a bond or is selected from the group consisting of alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl and acyl, each of which may be optionally substituted;

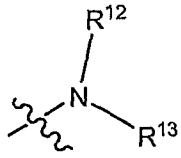
each R^8 is selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, and acyl, each of which may be optionally substituted;

each R^9 is independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted, or

R^9 is selected from the group consisting of







wherein X^1 is selected from the group consisting of $-N(R^6)$, -O- and –S-;

wherein Y is selected from the group consisting of O and S;

wherein X^2 is selected from the group consisting of $-OR^{14}$, $-SR^{14}$ and $-NR^{15}R^{16}$;

R^{10} is selected from the group consisting of alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted;

R^{11} is selected from the group consisting of H, halogen, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy,

heteroaryloxy, amino, alkylamino, and aminoalkyl, NH_2CO-, $(R^6)_2NCO$-, aminoalkyl and acyl, each of which may be optionally substituted;

R^{12} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted;

R^{13} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted; or

R^{12} and R^{13} together with the nitrogen to which they are attached form an optionally substituted heterocycloalkyl group;

R^{14} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted;

R^{15} and R^{16} are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl,

heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted, or

R^{15} and R^{16} together with the nitrogen to which they are attached form an optionally substituted heterocycloalkyl group;

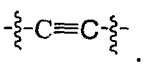
Z is a single bond or is selected from the group consisting of $-CH_2-$, $-CH_2CH_2-$, -CH=CH-, C_3-C_6 alkylene, C_3-C_6 alkenylene, C_2-C_6 alkynylene and C_3-C_6 cycloalkyl, each of which may be optionally substituted;

Ar is selected from the group consisting of aryl and heteroaryl, each of which may be optionally substituted;

or a pharmaceutically acceptable salt, N-oxide or prodrug thereof.

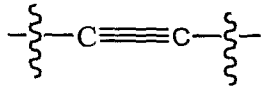
As with any group of structurally related compounds which possess a particular utility, certain groups are preferred for the compounds of the Formula (I) in their end use application.

In one embodiment Z is selected from the group consisting of:

-CH=CH- and  .

In a one specific embodiment Z is the group -CH=CH-. This group is typically in the E configuration.

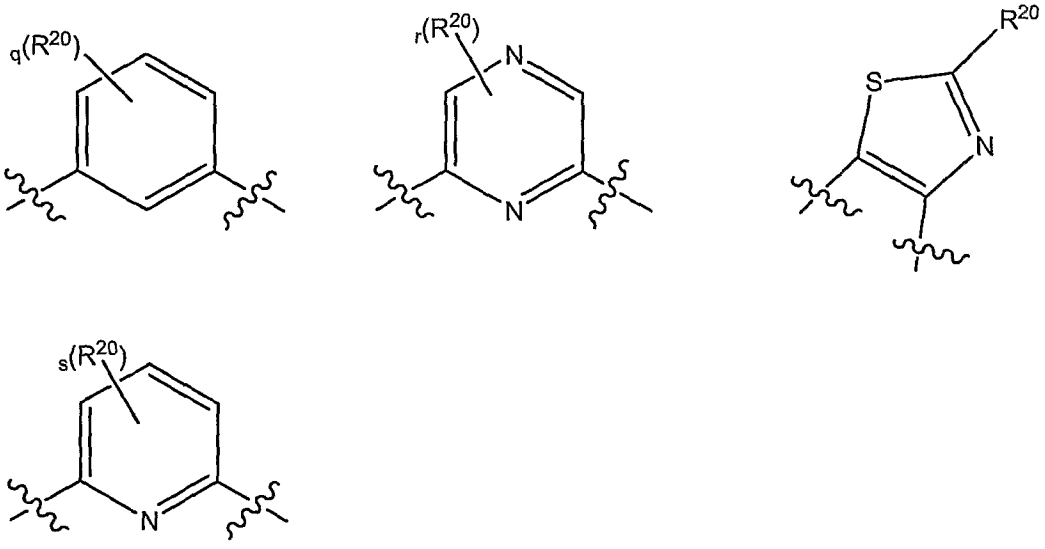
In another specific embodiment Z is a group of formula:

 .

In one embodiment Ar is selected from the group consisting of monocyclic aryl, monocyclic heteroaryl, bicyclic aryl and bicyclic heteroaryl, each of which may be optionally substituted.

In another embodiment Ar is selected from the group consisting of phenyl, pyrazine, thiazole, and pyridyl, each of which may be optionally substituted.

In yet an even further embodiment Ar is selected from the group consisting of:



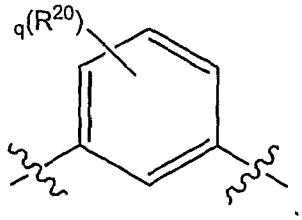
wherein each R^{20} is independently selected from the group consisting of H, halogen, nitro, cyano, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, aminoalkyl, acylamino, arylamino, sulfonylamino, sulfinylamino, -COOH, alkoxycarbonyl, alkylaminocarbonyl, sulfonyl, alkylsulfonyl, alkylsulfinyl, arylsulfonyl, arylsulfinyl, aminosulfonyl and acyl, each of which may be optionally substituted;

q is an integer selected from the group consisting of 0, 1, 2, 3, and 4;

r is an integer selected from the group consisting of 0, 1, and 2;

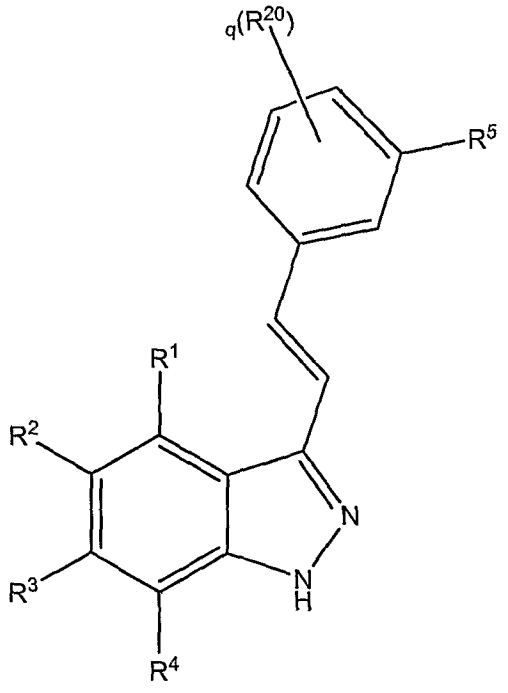
s is an integer selected from the group consisting of 0, 1, 2, and 3.

In a specific embodiment Ar is a group of formula:

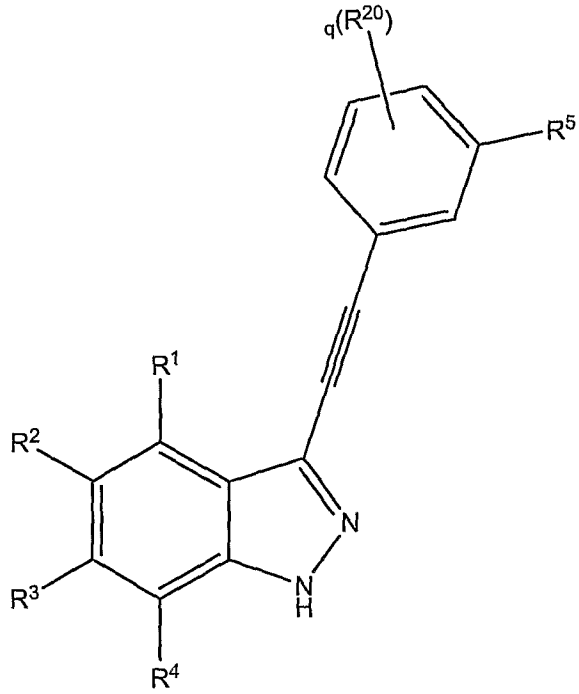


In one form of this embodiment q is 1 and R^{20} is selected from the group consisting of chloro, bromo, iodo, methyl, ethyl, propyl, hydroxy, alkoxy and nitro.

Accordingly in one embodiment the compounds are of formula (IIa) or (IIb):



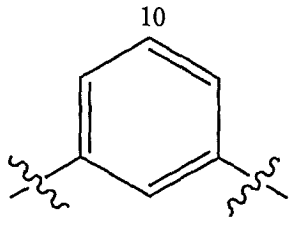
Formula (IIa)



Formula (IIb)

wherein R^1, R^2, R^3, R^4, R^5, R^{20} and q are as defined above.

In another embodiment Ar is a group of formula:



In one embodiment R^1 is selected from the group consisting of H, methyl, ethyl, propyl and butyl.

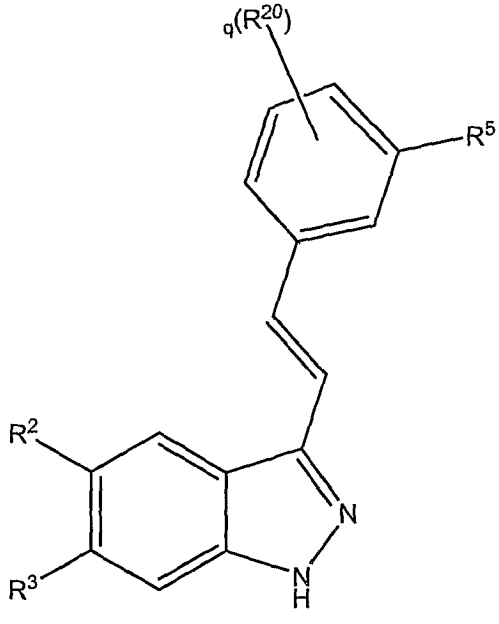
In one specific embodiment R^1 is H.

In another specific embodiment R^1 is methyl.

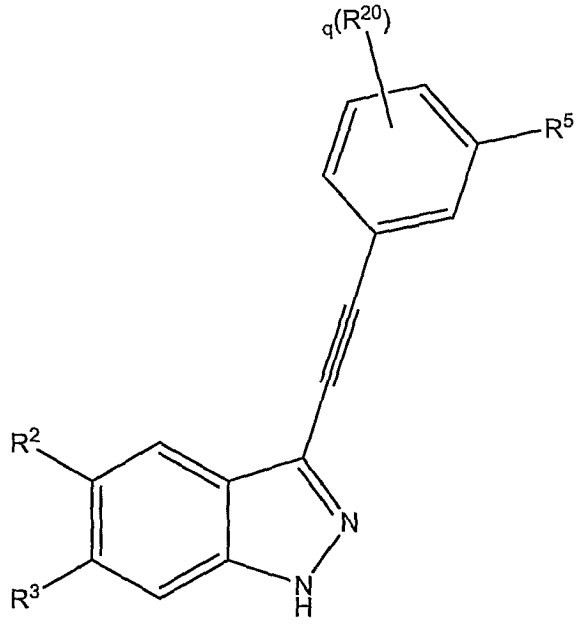
In one embodiment R^4 is selected from the group consisting of H, methyl, ethyl, propyl and butyl.

In one specific embodiment R^4 is H.

In one embodiment of the invention R^1 and R^4 are both H providing compounds of formula (IIIa) and (IIIb):



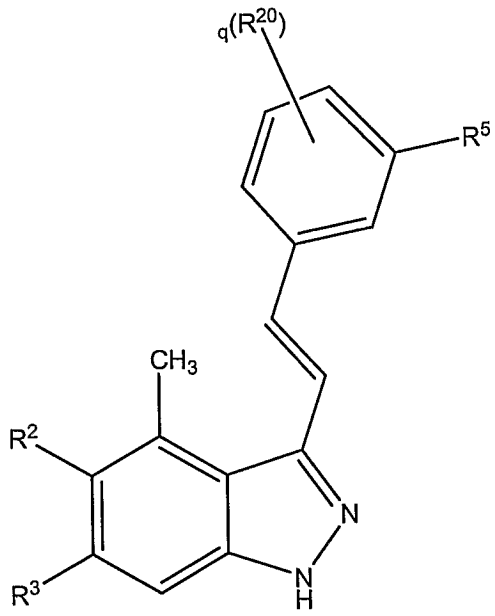
Formula (IIIa)



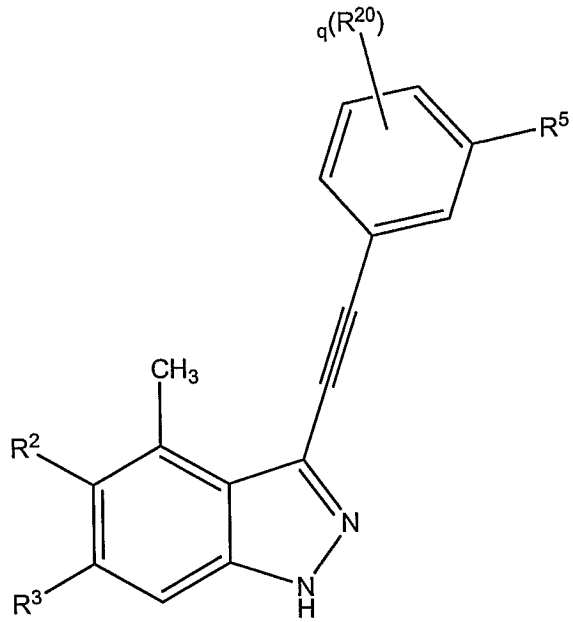
Formula (IIIb)

wherein R^2, R^3, R^5, R^{20} and q are as defined above.

In another embodiment of the invention R^1 is methyl and R^4 is H leading to compounds of formula (IIIc) and (IIId):



Formula (IIIc)

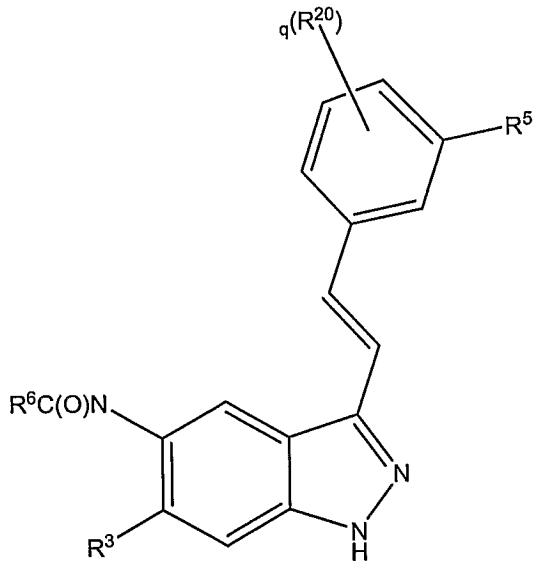


Formula (IIId)

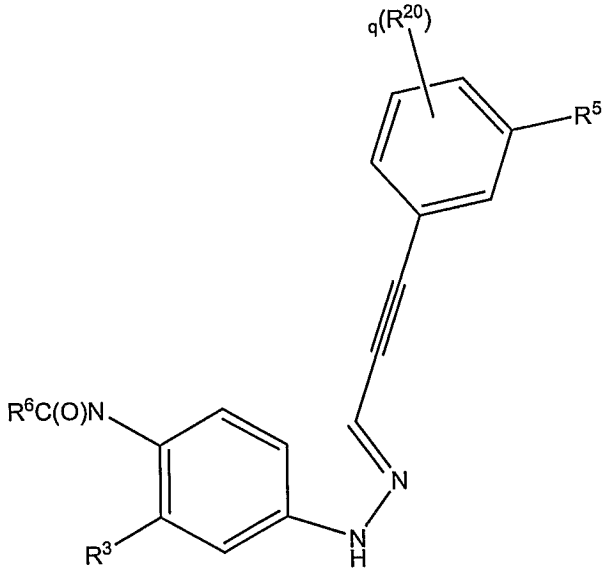
wherein R^2, R^3, R^5, R^{20} and q are as defined above.

In one embodiment R^2 is selected from the group consisting of: halogen, nitro, amino, cyano, -NHCOR^6, -NHR^6, -NR^{6}R^8, -NHCOOR^6, -NHCONHR^6, -NHCON(OH)R^6, -$NHSO_2NR^6$,and -$NHSO_2R^6$, each of which may be optionally substituted.

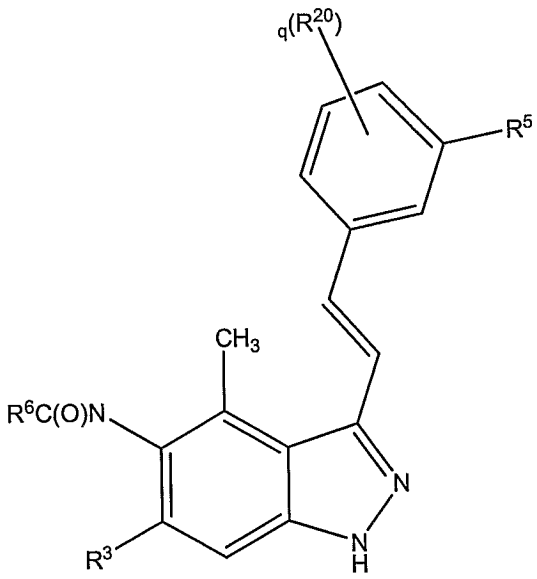
In one specific embodiment R^2 is $-NHCOR^6$ thus providing compounds of formula (IVa) to (IVd):



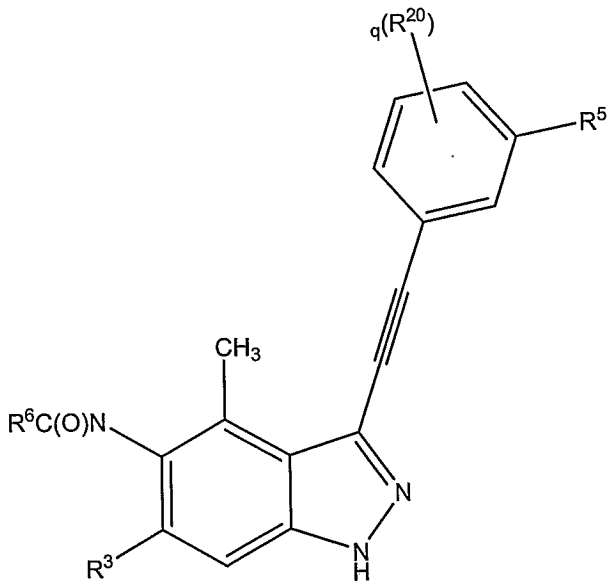
Formula (IVa)



Formula (IVb)



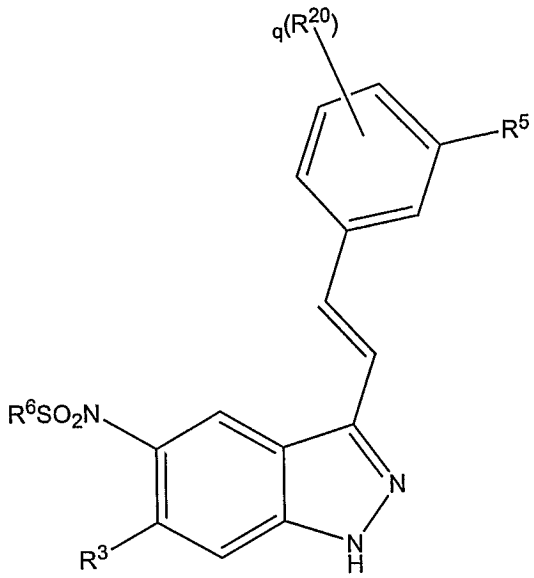
Formula (IVc)



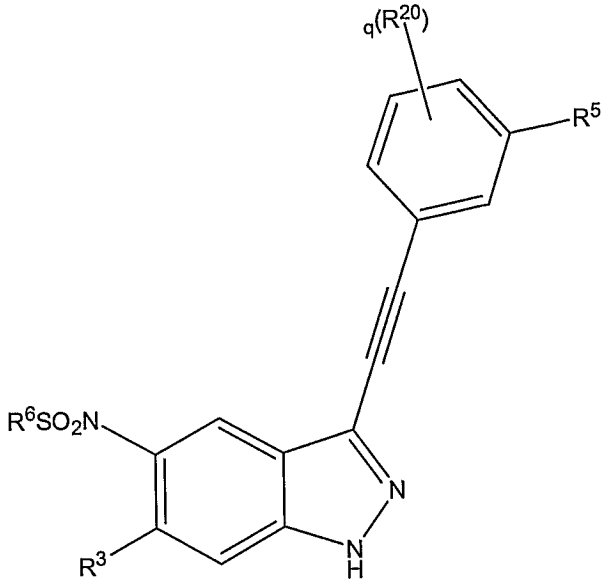
Formula (IVd)

wherein R^3, R^5, R^6, R^{20} and q are as defined above.

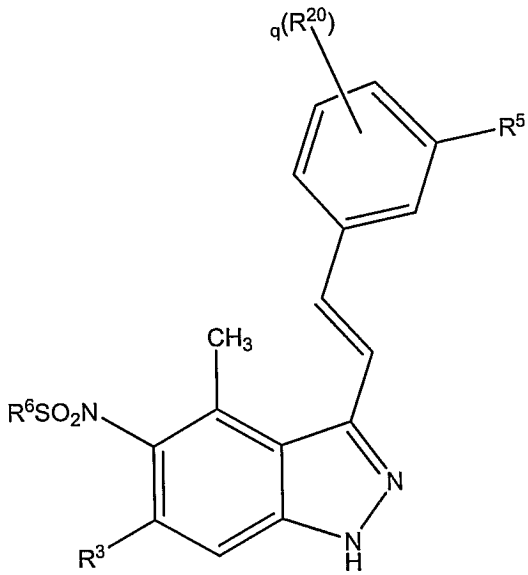
In another specific embodiment R^2 is $-NHSO_2R^6$, this provides compounds of formual (Va) to (Vd):



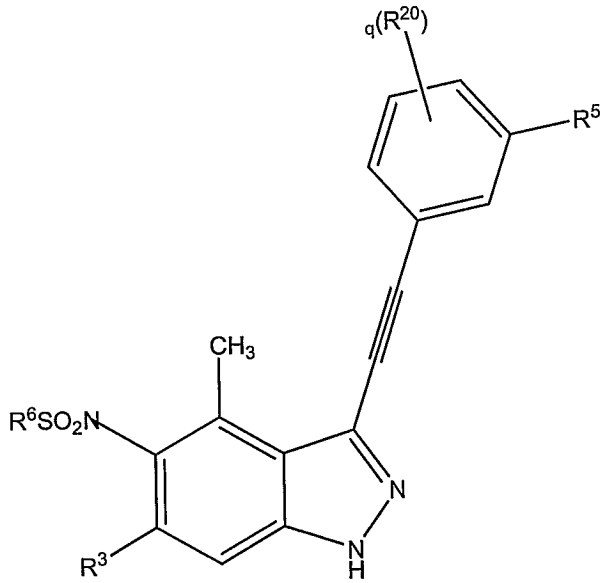
Formula (Va)



Formula (Vb)



Formula (Vc)



Formula (Vd)

wherein R^3, R^5, R^6, R^{20} and q are as defined above.

In another specific embodiment R^2 is $-NHR^6$.

In another specific embodiment R^2 is $-NHSO_2R^6$.

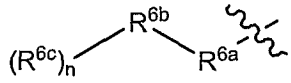
In another specific embodiment R^2 is -NHCON(OH)R^6.

In another specific embodiment R^2 is nitro.

In another specific embodiment R^2 is amino.

In another specific embodiment R^2 is chloro.

In one embodiment R^6 is selected from the group consisting of alkyl, alkenyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, and heteroarylalkyl, each of which may be optionally substituted; or R^6 is a group of the formula:



wherein:

R^{6a} is selected from the group consisting of a bond, alkyl, heteroalkyl and aryl, each of which may be optionally substituted;

R^{6b} is selected from the group consisting of a bond, alkyl, -CO-, cycloalkyl, aryl and heteroaryl, each of which may be optionally substituted;

R^{6c} is selected from the group consisting of H, alkyl, chloro, bromo, iodo hydroxy, alkoxy, CH_3CONH- and heteroaryl;

n is an integer selected from the group consisting of 0, 1, 2, 3, 4, and 5.

In another embodiment R^6 is selected from the group consisting of cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl and heteroarylalkyl, each of which may be optionally substituted.

In another specific embodiment R^6 is a group of the formula:

$A(CH_2)_t$-

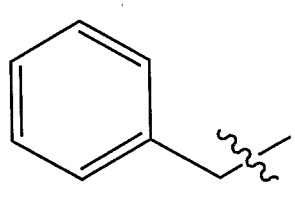
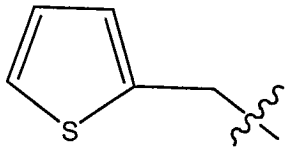
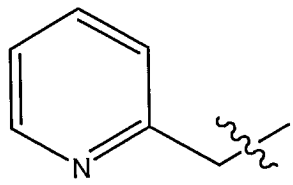
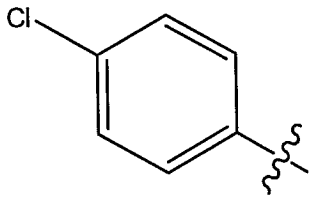
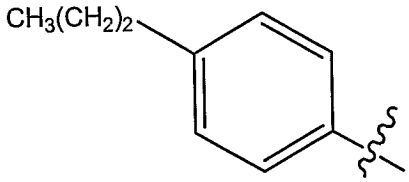
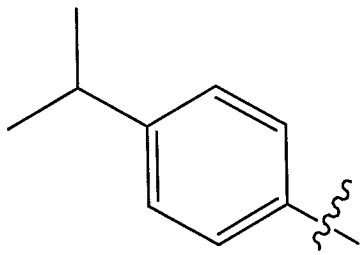
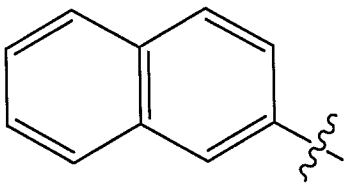
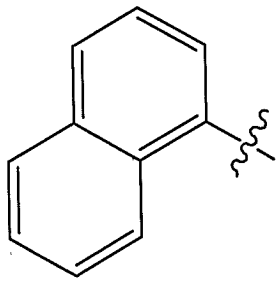
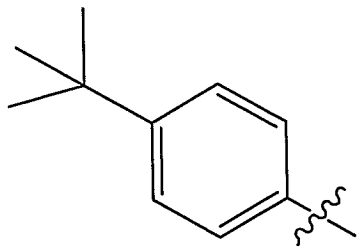
wherein A is selected from the group consisting of aryl, heteroaryl, cycloalkyl and heterocycloalkyl, each of which may be optionally substituted;

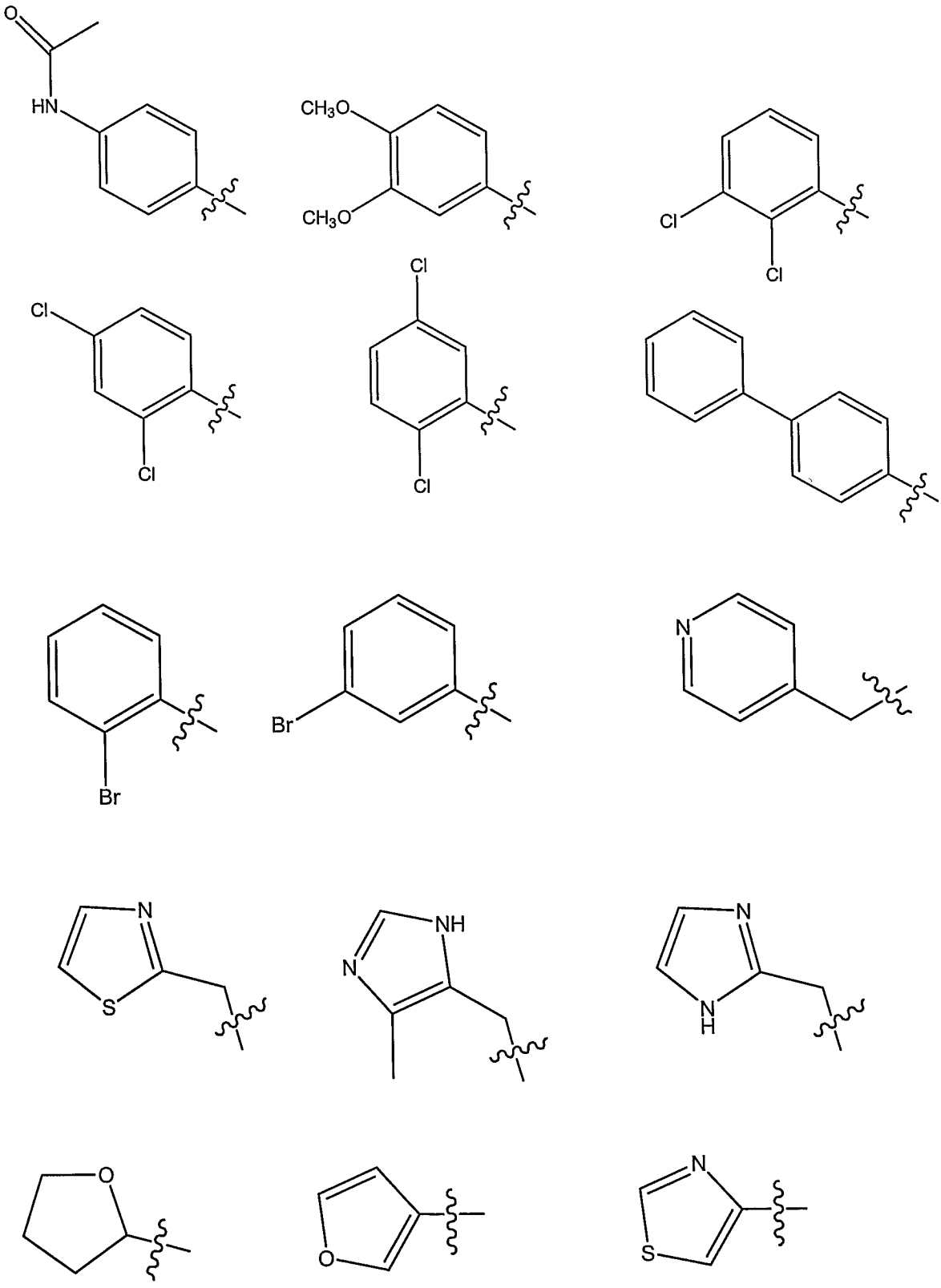
t is an integer selected from the group consisting of O, 1, 2, and 3.

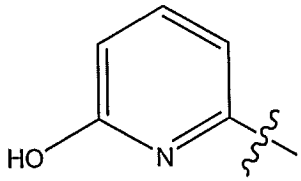
In one form of this embodiment A is aryl or heteroaryl, each of which may be optionally substituted;

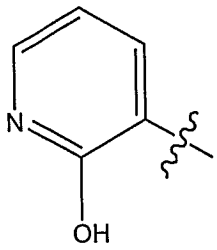
In one form of this embodiment t is o. In another form of this embodiment t is 1.

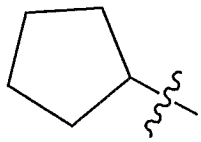
Suitable examples of R^6 are selected from the group consisting of:

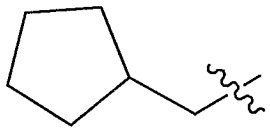










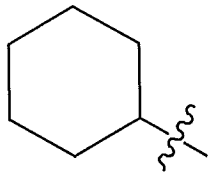

O
HN
CH3O
CH3O
Cl
Cl
Cl
Cl
Cl
Cl
Br
Br
N
N
S
NH
N
N
N
H
O
O
N
S

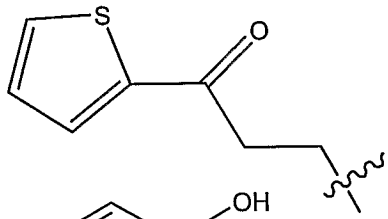


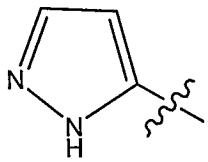


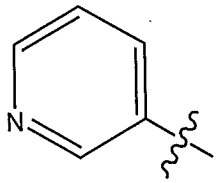


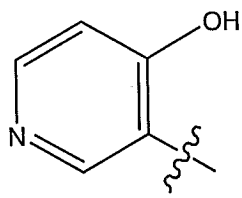


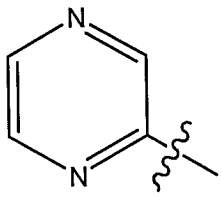


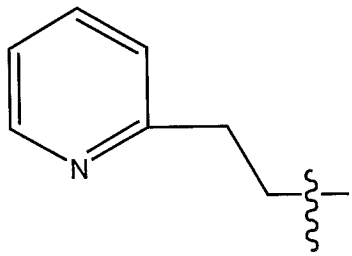


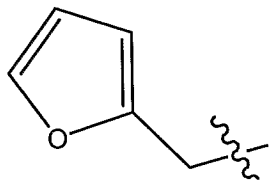


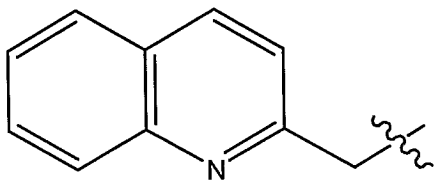


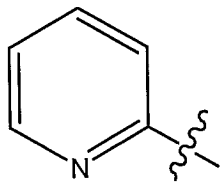




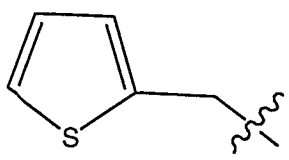








In one specific embodiment R^6 is a group of the formula:

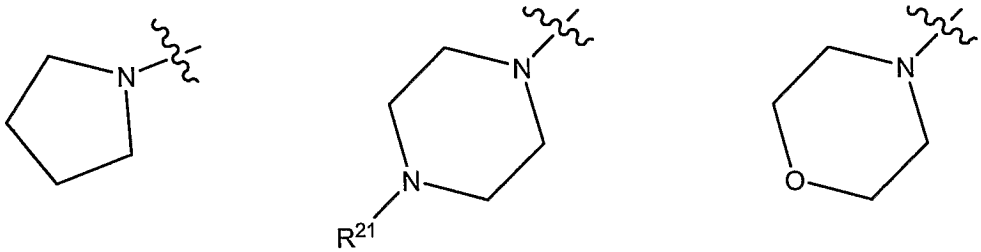


In one embodiment R^3 is selected from the group consisting of H, alkyl, heterocycloalkyl, halogen, alkylsulfanyl, alkylsulfinyl and alkylsulfonyl, each of which may be optionally substituted. Exemplary values of R^3 within the scope of this embodiment include H, methyl, ethyl, propyl, butyl, pentyl, hexyl, chloro, bromo, iodo, fluoromethansulfanyl, ethansulfanyl, methansulfinyl, ethansulfinyl, methansulfonyl, and ethansulfonyl.

In another embodiment R^3 is optionally substituted heterocycloalkyl. In one form of this embodiment the heterocycloalkyl group is a monocyclic heterocycloalkyl group.

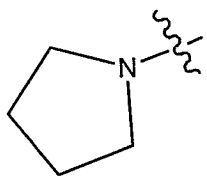
In another embodiment the R^3 is selected from the group consisting of pyrrolidyl, tetrahydrofuryl, tetrahydrothiofuranyl, piperidyl, piperazyl, tetrahydropyranyl, morphilino, 1,3-diazapane, 1,4-diazapane, 1,4-oxazepane, and 1,4-oxathiapane, each of which may be optionally substituted.

In another embodiment R^3 is selected from the group consisting of:

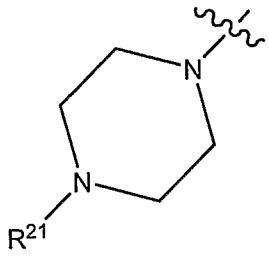


wherein R^{21} is selected from the group consisting of H, methyl, ethyl, propyl, butyl, pentyl and hexyl.

In one specific embodiment R^3 is a group of formula:

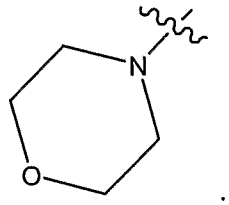


In another embodiment R^3 is a group of formula:



wherein R^{21} is selected from the group consisting of H, methyl, ethyl, propyl, butyl, pentyl and hexyl. In one specific form of this embodiment R^{21} is H or methyl.

In another specific embodiment R^3 is a group of formula:



In one embodiment R^5 is selected from the group consisting of: H, nitro, alkyl, heteroalkyl, heterocycloalkylalkyl, hydroxyalkyl, alkoxy, amino, $-R^7R^9$, $-R^7N(R^8)C(O)R^9$, each of which may be optionally substituted.

In one embodiment R^5 is $-R^7R^9$.

In another embodiment R^5 is $-R^7N(R^8)C(O)R^9$.

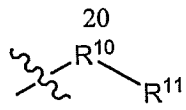
In one embodiment R^7 is a bond or alkyl.

In one specific embodiment R^7 is a bond. When R^7 is a bond then in the embodiments of R^5 given above R^5 is $-R^9$ or $-N(R^8)C(O)R^9$.

In another specific embodiment R^7 is methyl. When R^7 is a methyl then in the embodiments of R^5 given above R^5 is $-CH_2R^9$ or $-CH_2N(R^8)C(O)R^9$.

In one embodiment R^8 is H.

In one embodiment R^9 is a group of formula:



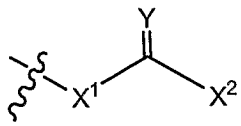
wherein R^{10} is selected from the group consisting of alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted;

R^{11} is selected from the group consisting of H, halogen, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, NH_2CO-, $(R^6)_2NCO$-, aminoalkyl and acyl, each of which may be optionally substituted.

In one embodiment R^{10} is selected from the group consisting of heterocycloalkyl, and arylalkyl.

In one embodiment R^{11} is selected from the group consisting of H, halogen, alkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, arylalkyl, hydroxyalkyl, alkoxyaryl, NH_2CO-, $(R^6)_2NCO$-, and acyl, each of which may be optionally substituted.

In another embodiment R^9 is a group of formula



wherein X^1 is selected from the group consisting of $-N(R^6)$, -O- and –S-;

wherein Y is selected from the group consisting of O and S;

wherein X^2 is selected from the group consisting of $-OR^{14}$, $-SR^{14}$ and $-NR^{15}R^{16}$;

R^{14} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted;

R^{15} and R^{16} are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted, or

R^{15} and R^{16} together with the nitrogen to which they are attached form an optionally substituted heterocycloalkyl group.

In one form of this embodiment X^1 is NH.

In another form of this embodiment Y is O.

In another form of this embodiment Y is S.

In another form of this embodiment X^2 is $-OR^{14}$.

In a one specific form of this embodiment R^{14} is selected from the group consisting of alkyl, alkenyl, cycloalkyl, heteroalkyl, heteroarylalkyl and heterocycloalkylalkyl, each of which may be optionally substituted.

In another form of this embodiment X^2 is $NR^{15}R^{16}$.

In another form of this embodiment X^2 is NHR^{16}.

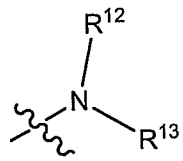
In another form of this embodiment R^{15} is selected from the group consisting of H, alkyl and hydroxy.

In another form of this embodiment R^{15} is selected from the group consisting of H, methyl and hydroxy.

In another embodiment R^{16} is selected from the group consisting of alkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, heteroarylalkyl, arylalkyl, cycloalkyl, heterocycloalkylalkyl and heteroarylalkyl, each of which may be optionally substituted.

In another embodiment R^{15} and R^{16}, together with the nitrogen atom to which they are attached form an optionally substituted heterocycloalkyl group.

In another embodiment R^9 is:



wherein R^{12} and R^{13} are as defined above.

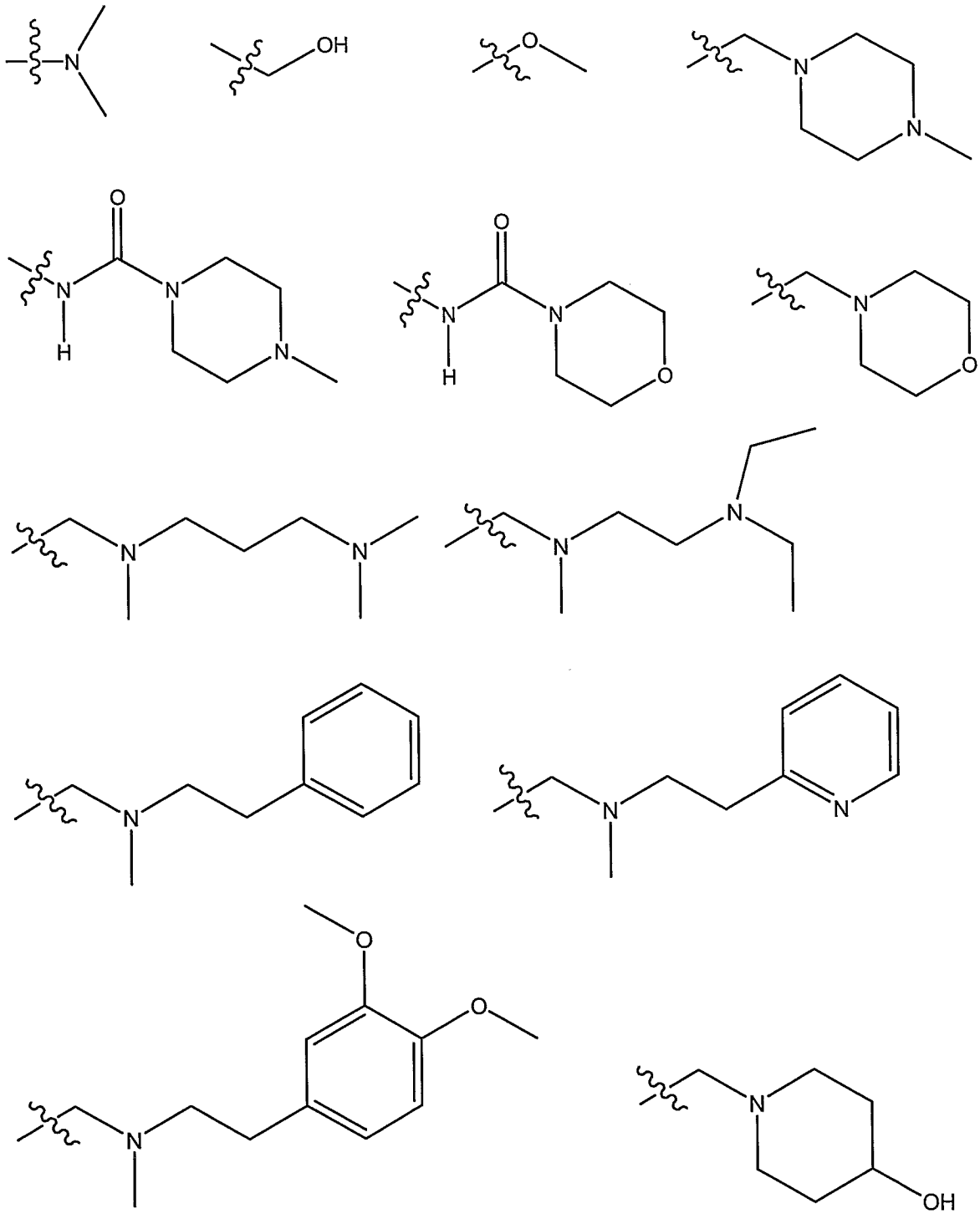
In one form of this embodiment R^{12} is selected from the group consisting of H, alkyl, heteroalkyl, arylalkyl, and heteroarylalkyl. Specific values of R^{12} include, H, methyl, ethyl, 2-hydroxy-ethyl, propyl, isopropyl, and benzyl.

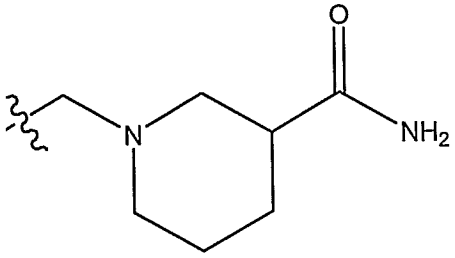
In one form of this embodiment R^{13} is selected from the group consisting of H, alkyl, heteroalkyl, arylalkyl, and heteroarylalkyl. Specific values of R^{13} include H, methyl, ethyl, 2-dimethyl-amino-ethyl, 2-di-ethyl-amino-ethyl, 2-phenyl-ethyl, propyl, 3-dimethyl-amino-propyl, benzyl, and 3-pyridin-3-yl-methyl.

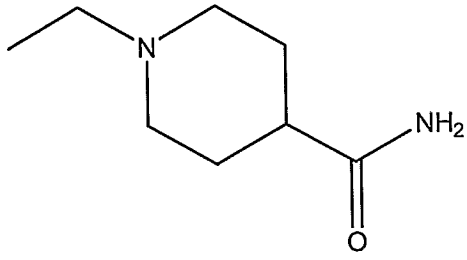
In one embodiment R^{12} and R^{13} along with the nitrogen atom to which they are attached form an optionally substituted heterocycloalkyl group. Examples of optionally substituted heterocycloalkyl groups include optionally substituted piperazine, optionally

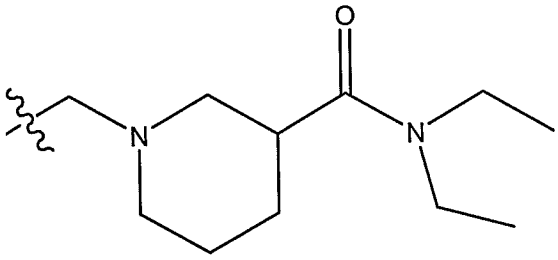
substituted, morpholine, optionally substituted piperidine, and optionally substituted thiomorpholine.

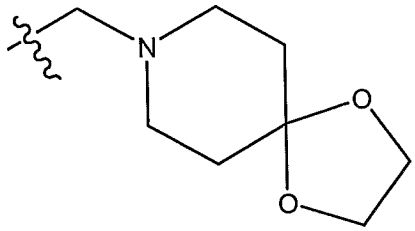
Exemplary values of R^5 include the following:

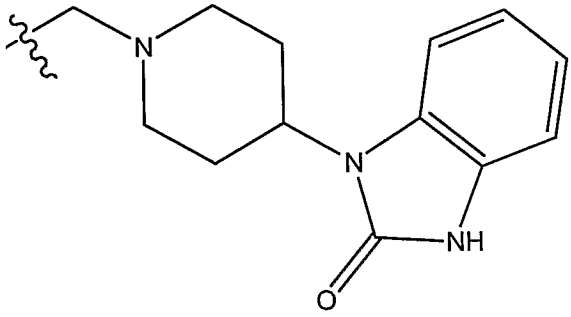


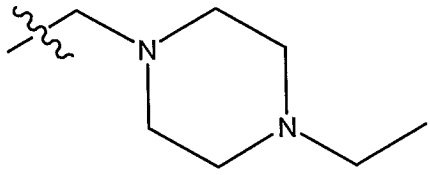


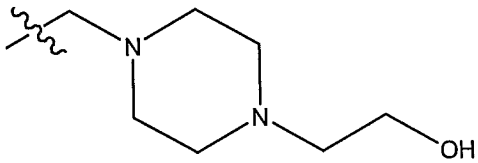


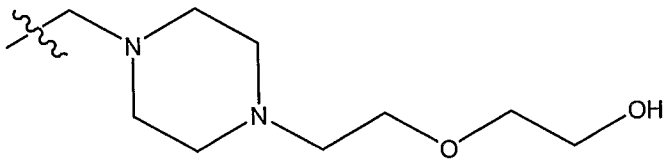


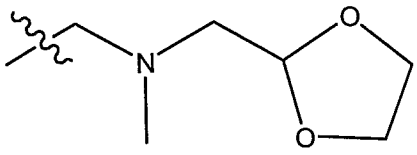


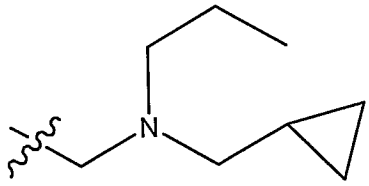


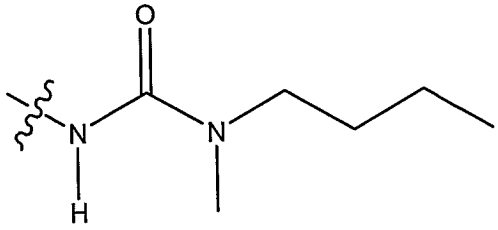


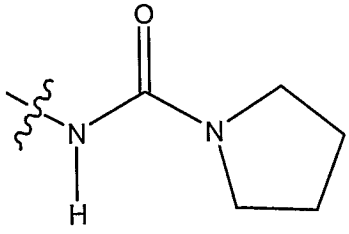


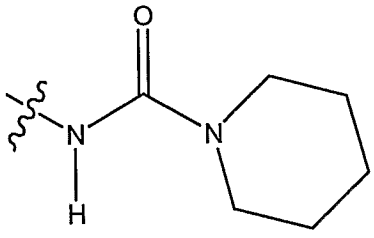


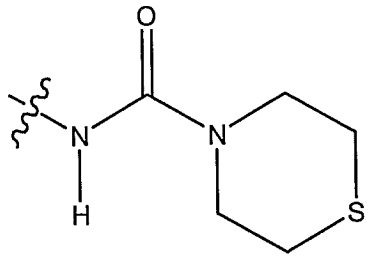


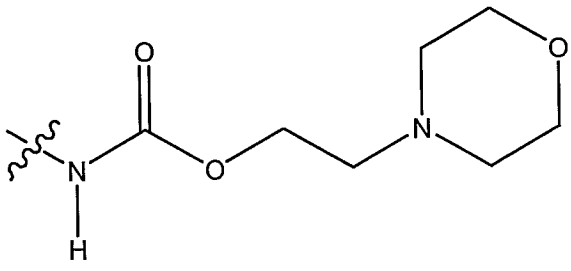


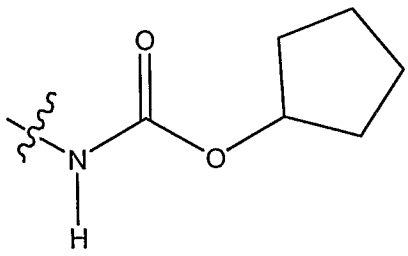


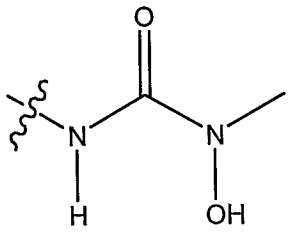


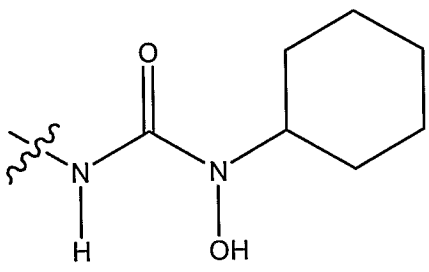


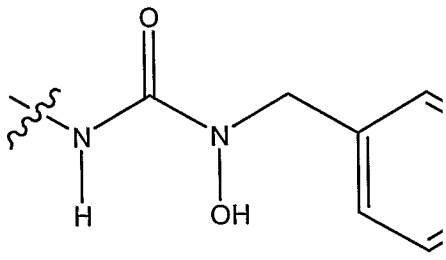


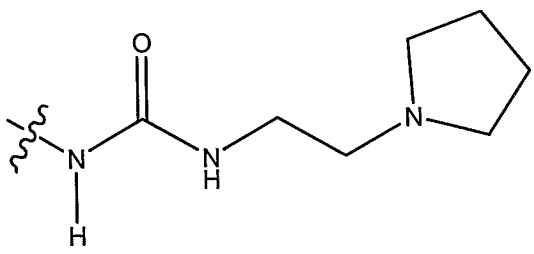


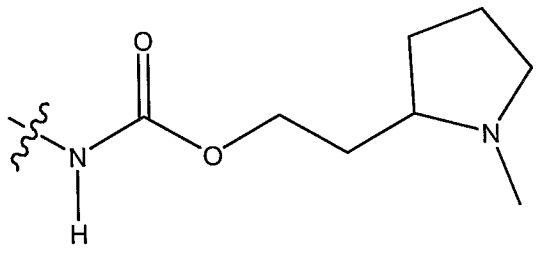


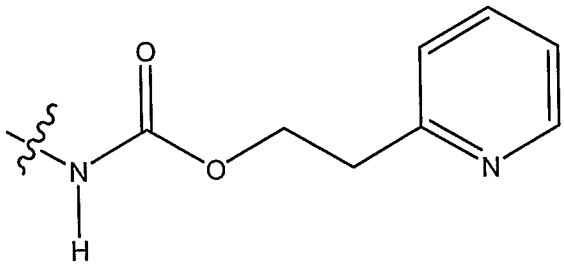




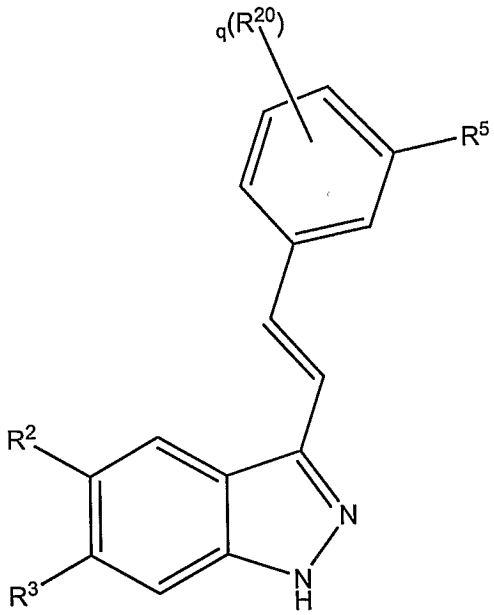




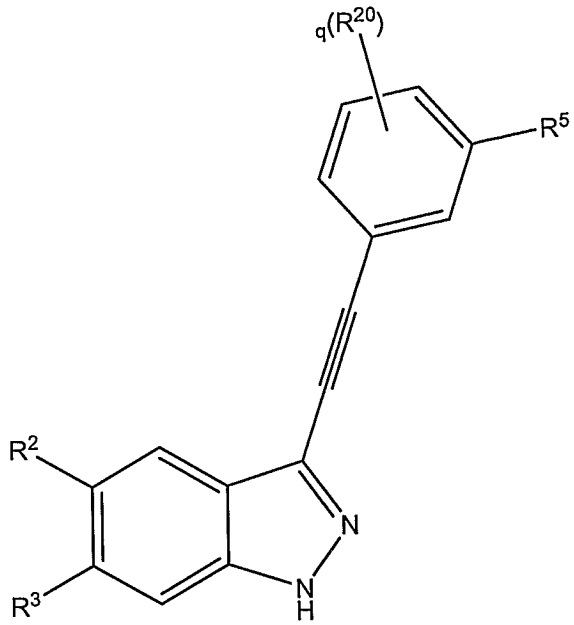




In one embodiment of the compounds of the invention the compounds are of the formula (VIa) or (VIb):



Formula (VIa)



Formula (VIb)

wherein:

R^2 is selected from the group consisting of: halogen, nitro, amino, cyano, -$NHCOR^6$, -NHR^6, -NR^6R^8, -$NHCOOR^6$, -$NHCONHR^6$, -$NHCON(OH)R^6$, -$NHSO_2NR^6$,and -$NHSO_2R^6$, each of which may be optionally substituted;

R^3 is selected from the group consisting of H, alkyl, heterocycloalkyl, halogen, alkylsulfanyl, alkylsulfinyl and alkylsulfonyl, each of which may be optionally substituted;

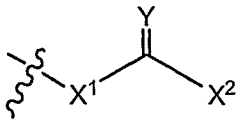
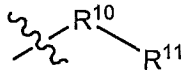
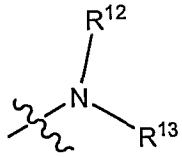
R^5 is selected from the group consisting of: nitro, alkyl, heteroalkyl, heterocycloalkylalkyl, hydroxyalkyl, alkoxy, amino, -R^7R^9, -$R^7N(R^8)C(O)R^9$, each of which may be optionally substituted;

R^6 is selected from the group consisting of cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl and heteroarylalkyl, each of which may be optionally substituted;

R^7 is a bond or alkyl;

R^8 is a H or alkyl;

R^9 is selected from the group consisting of

wherein X^1 is selected from the group consisting of $-N(R^6)$, -O- and –S-;

wherein Y is selected from the group consisting of O and S;

wherein X^2 is selected from the group consisting of $-OR^{14}$, $-SR^{14}$ and $-NR^{15}R^{16}$;

R^{10} is selected from the group consisting of alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted;

R^{11} is selected from the group consisting of H, halogen, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, NH_2CO-, $(R^6)_2NCO$-, aminoalkyl and acyl, each of which may be optionally substituted;

R^{12} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy,

heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted;

R^{13} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted; or

R^{12} and R^{13} together with the nitrogen to which they are attached form an optionally substituted heterocycloalkyl group;

R^{14} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted;

R^{15} and R^{16} are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted, or

R^{15} and R^{16} together with the nitrogen to which they are attached form an optionally substituted heterocycloalkyl group;

R^{20} is selected from the group consisting of H, halogen, nitro, cyano, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, aminoalkyl, acylamino, arylamino, sulfonylamino, sulfinylamino, -COOH, alkoxycarbonyl, alkylaminocarbonyl, sulfonyl, alkylsulfonyl, alkylsulfinyl, arylsulfonyl, arylsulfinyl, aminosulfonyl and acyl, each of which may be optionally substituted;

q is an integer selected from the group consisting of 0, 1, 2, 3, and 4;

or a pharmaceutically acceptable salt or prodrug thereof.

In different embodiments the values of the variables given for the compounds of formula (Via) and (Vlb) may vary as for the corresponding variables on earlier formula defined above.

Many if not all of the variables discussed above may be optionally substituted. If the variable is optionally substituted then the optional substituent may be selected from the group consisting of: halogen, =O, =S, -CN, $-NO_2$, $-CF_3$, $-OCF_3$, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkoxyheteroaryl, alkenyloxy, alkynyloxy, cycloalkyloxy, cycloalkenyloxy, heterocycloalkyloxy, heterocycloalkenyloxy, aryloxy, heteroaryloxy, arylalkyl, heteroarylalkyl, arylalkyloxy, -amino, alkylamino, acylamino, aminoalkyl, arylamino, sulfonyl, alkylsulfonyl, arylsulfonyl, aminosulfonyl, aminoalkyl, alkoxyalky, -COOH, $-COR^6$, $-C(O)OR^6$, -SH, $-SR^6$, $-OR^6$ and acyl.

In one embodiment the substituents are selected from the group consisting of: halogen, =O, =S, -CN, $-NO_2$, alkyl, alkenyl, heteroalkyl, haloalkyl, alkynyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, hydroxy, hydroxyalkyl, alkoxy, alkylamino, aminoalkyl, acylamino, phenoxy, alkoxyalkyl, benzyloxy, alkylsulfonyl, arylsulfonyl, aminosulfonyl, $-C(O)OR^6$, COOH, SH, and acyl.

In addition to compounds of Formula I, the embodiments disclosed are also directed to pharmaceutically acceptable salts, pharmaceutically acceptable prodrugs, pharmaceutically acceptable N-oxides and pharmaceutically active metabolites of such compounds, and pharmaceutically acceptable salts of such metabolites.

The invention also relates to pharmaceutical compositions including a compound of the invention with a pharmaceutically acceptable carrier, diluent or excipient.

In yet a further aspect the present invention provides a use of a compound of formula I in the preparation of a medicament for the treatment of a disorder caused by, associated with or accompanied by disruptions of cell proliferation. In a preferred embodiment the disorder is a proliferative disorder, most preferably cancer.

In yet a further aspect the invention provides a method of treatment of a disorder caused by, associated with or accompanied by disruptions of cell proliferation in a patient the method including administration of a therapeutically effective amount of a compound of formula I. In a preferred embodiment the disorder is a proliferative disorder preferably cancer.

In a preferred embodiment the cancer is a bone cancer including Ewing's sarcoma, osteosarcoma, chondrosarcoma and the like, brain and CNS tumours including acoustic neuroma, neuroblastomas, glioma and other brain tumours, spinal cord tumours, breast cancers, colorectal cancers, advanced colorectal adenocarcinomas, endocrine cancers including adenocortical carcinoma, pancreatic cancer, pituitary cancer, thyroid cancer, parathyroid cancer, thymus cancer, multiple endocrine neoplasma, gastrointestinal cancers including stomach cancer, oesophageal cancer, small intestine cancer, Liver cancer, extra hepatic bile duct cancer, gastrointestinal carcinoid tumour, gall bladder cancer, genitourinary cancers including testicular cancer, penile cancer, prostrate cancer, gynaecological cancers including cervical cancer, ovarian cancer, vaginal cancer, uterus/endometrium cancer, vulva cancer, gestational trophoblastic cancer, fallopian tube cancer, uterine sarcoma, head and neck cancers including oral cavity cancer, lip cancer, salivary gland cancer, larynx cancer, hypopharynx cancer, orthopharynx cancer, nasal cancer, paranasal cancer, nasopharynx cancer, leukaemia's including childhood leukaemia, acute lymphocytic leukaemia, acute myeloid leukaemia, chronic lymphocytic leukaemia, chronic myeloid leukaemia, hairy cell leukaemia, acute promyelocytic leukaemia, plasma cell leukaemia, myelomas, haematological disorders including myelodysplastic syndromes, myeloproliferative disorders, aplastic anaemia, Fanconi

anaemia, Waldenstroms Macroglobulinemia, lung cancers including small cell lung cancer, non-small cell lung cancer, lymphomas including Hodgkin's disease, non-Hodgkin's lymphoma, cutaneous T-cell lymphoma, peripheral T-cell lymphoma, B-cell lymphoma, Burkitt's lymphoma, AIDS related Lymphoma, eye cancers including retinoblastoma, intraocular melanoma, skin cancers including melanoma, non-melanoma skin cancer, merkel cell cancer, soft tissue sarcomas such as childhood soft tissue sarcoma, adult soft tissue sarcoma, Kaposi's sarcoma, urinary system cancers including kidney cancer, Wilms tumour, bladder cancer, urethral cancer, and transitional cell cancer.

In another preferred embodiment the cancer is bladder cancer, breast cancer, cervical cancer, colorectal cancer, colon cancer, gastric cancer, neuroblastoma, ovarian cancer, pancreatic cancer, leukaemia, lymphoma, prostate cancer and lung cancer.

In yet a further preferred embodiment the cancer is B-cell lymphoma (e.g. Burkitt's lymphoma), leukaemia's (e.g. acute promyelocytic leukaemia), cutaneous T-cell lymphoma (CTCL) and peripheral T-cell lymphoma.

In an even further embodiment the cancer is a solid tumor or a hematologic malignancy.

The invention also provides agents for the treatment of a disorder caused by, associated with or accompanied by disruptions of cell proliferation and/or angiogenesis including a compound of formula (I) as disclosed herein. The agent is preferably an anti-cancer agent.

DETAILED DESCRIPTION OF THE INVENTION

In this specification a number of terms are used which are well known to a skilled addressee. Nevertheless for the purposes of clarity a number of terms will be defined.

As used herein, the term unsubstituted means that there is no substituent or that the only substituents are hydrogen.

The term "optionally substituted" as used throughout the specification denotes that the group may or may not be further substituted or fused (so as to form a condensed polycyclic system), with one or more non-hydrogen substituent groups. Preferably the substituent groups are one or more groups independently selected from the group consisting of halogen, =O, =S, -CN, $-NO_2$, $-CF_3$, $-OCF_3$, alkyl, alkenyl, alkynyl, haloalkyl,

haloalkenyl, haloalkynyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkenyl, heterocycloalkylalkenyl, arylalkenyl, heteroarylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, arylheteroalkyl, heteroarylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxycycloalkyl, alkoxyheterocycloalkyl, alkoxyaryl, alkoxyheteroaryl, alkoxycarbonyl, alkylaminocarbonyl, alkenyloxy, alkynyloxy, cycloalkyloxy, cycloalkenyloxy, heterocycloalkyloxy, heterocycloalkenyloxy, aryloxy, phenoxy, benzyloxy, heteroaryloxy, arylalkyloxy, arylalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyloxy, amino, alkylamino, acylamino, aminoalkyl, arylamino, sulfonylamino, sulfinylamino, sulfonyl, alkylsulfonyl, arylsulfonyl, aminosulfonyl, sulfinyl, alkylsulfinyl, arylsulfinyl, aminosulfinylaminoalkyl, -COOH, $-COR^6$, $-C(O)OR^6$, $CONHR^6$, $NHCOR^6$, $NHCOOR^6$, $NHCONHR^6$, $C(=NOH)R^6$, -SH, $-SR^6$, $-OR^6$ and acyl.

"Alkyl" as a group or part of a group refers to a straight or branched aliphatic hydrocarbon group, preferably a C_1–C_{14} alkyl, more preferably C_1-C_{10} alkyl, most preferably C_1-C_6 unless otherwise noted. Examples of suitable straight and branched C_1-C_6 alkyl substituents include methyl, ethyl, n-propyl, 2-propyl, n-butyl, sec-butyl, t-butyl, hexyl, and the like. When alkyl is used as a bridging group it is typically (but not exclusively) referred to as alkylene. A similar convention applies to other bridging groups.

"Alkylamino" includes both monoalkylamino and dialkylamino, unless specified. "Monoalkylamino" means a –NH-Alkyl group, in which alkyl is as defined above. "Dialkylamino" means a $-N(alkyl)_2$ group, in which each alkyl may be the same or different and are each as defined herein for alkyl. The alkyl group is preferably a C_1-C_6 alkyl group.

"Alkylamino" includes both monoalkylamino and dialkylamino, unless specified. "Monoalkylamino" means a –NH-Alkyl group in which alkyl is as defined above. "Dialkylamino" means a $-N(alkyl)_2$ group in which each alkyl may be the same or different and are each as defined herein for alkyl. The alkyl group is preferably a C_1-C_6 alkyl group.

"Arylamino" includes both mono-arylamino and di-arylamino unless specified. Mono-arylamino means a group of formula aryl NH-, in which aryl is as defined herein. di-arylamino means a group of formula $(aryl)_2N$- where each aryl may be the same or different and are each as defined herein for aryl.

"Acyl" means an alkyl-CO- group in which the alkyl group is as described herein. Examples of acyl include acetyl and benzoyl. The alkyl group is preferably a C_1-C_6 alkyl group.

"Alkenyl" as a group or part of a group denotes an aliphatic hydrocarbon group containing at least one carbon-carbon double bond and which may be straight or branched preferably having 2-14 carbon atoms, more preferably 2-12 carbon atoms, most preferably 2-6 carbon atoms, in the normal chain. The group may contain a plurality of double bonds in the normal chain and the orientation about each is independently E or Z. Exemplary alkenyl groups include, but are not limited to, ethenyl, propenyl, butenyl, pentenyl, hexenyl, heptenyl, octenyl and nonenyl.

"Alkoxy" refers to an –O-alkyl group in which alkyl is defined herein. Preferably the alkoxy is a C_1-C_6alkoxy. Examples include, but are not limited to, methoxy and ethoxy.

"Alkenyloxy" refers to an -O- alkenyl group in which alkenyl is as defined herein. Preferred alkenyloxy groups are C_1-C_6 alkenyloxy groups.

"Alkynyloxy" refers to an –O-alkynyl group in which alkynyl is as defined herein. Preferred alkynyloxy groups are C_1-C_6 alkynyloxy groups.

"Alkoxycarbonyl" refers to an –C(O)-O-alkyl group in which alkyl is as defined herein. The alkyl group is preferably a C_1-C_6 alkyl group. Examples include, but not limited to, methoxycarbonyl and ethoxycarbonyl.

"Alkylsulfinyl" means a –S(O)-alkyl group in which alkyl is as defined above. The alkyl group is preferably a C_1-C_6 alkyl group. Exemplary alkylsulfinyl groups include, but not limited to, methylsulfinyl and ethylsulfinyl.

"Alkylsulfonyl" refers to a $-S(O)_2$-alkyl group in which alkyl is as defined above. The alkyl group is preferably a C_1-C_6 alkyl group. Examples include, but not limited to methylsulfonyl and ethylsulfonyl.

"Alkynyl" as a group or part of a group means an aliphatic hydrocarbon group containing a carbon-carbon triple bond and which may be straight or branched preferably having from 2-14 carbon atoms, more preferably 2-12 carbon atoms, more preferably 2-6

carbon atoms in the normal chain. Exemplary structures include, but are not limited to, ethynyl and propynyl.

"Alkylaminocarbonyl" refers to an alkylamino-carbonyl group in which alkylamino is as defined above.

"Cycloalkyl" refers to a saturated or partially saturated, monocyclic or fused or spiro polycyclic, carbocycle preferably containing from 3 to 9 carbons per ring, such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and the like, unless otherwise specified. It includes monocyclic systems such as cyclopropyl and cyclohexyl, bicyclic systems such as decalin, and polycyclic systems such as adamantane.

"Cycloalkenyl" means a non-aromatic monocyclic or multicyclic ring system containing at least one carbon-carbon double bond and preferably having from 5-10 carbon atoms per ring. Exemplary monocyclic cycloalkenyl rings include cyclopentenyl, cyclohexenyl or cycloheptenyl. The cycloalkenyl group may be substituted by one or more substituent groups.

The above discussion of alkyl and cycloalkyl substituents also applies to the alkyl portions of other substituents, such as without limitation, alkoxy, alkyl amines, alkyl ketones, arylalkyl, heteroarylalkyl, alkylsulfonyl and alkyl ester substituents and the like.

"Cycloalkylalkyl" means a cycloalkyl-alkyl- group in which the cycloalkyl and alkyl moieties are as previously described. Exemplary monocycloalkylalkyl groups include cyclopropylmethyl, cyclopentylmethyl, cyclohexylmethyl and cycloheptylmethyl.

"Halogen" represents chlorine, fluorine, bromine or iodine.

"Heterocycloalkyl" refers to a saturated or partially saturated monocyclic, bicyclic, or polycyclic ring containing at least one heteroatom selected from nitrogen, sulfur, oxygen, preferably from 1 to 3 heteroatoms in at least one ring. Each ring is preferably from 3 to 10 membered, more preferably 4 to 7 membered. Examples of suitable heterocycloalkyl substituents include pyrrolidyl, tetrahydrofuryl, tetrahydrothiofuranyl, piperidyl, piperazyl, tetrahydropyranyl, morphilino, 1,3-diazapane, 1,4-diazapane, 1,4-oxazepane, and 1,4-oxathiapane.

"Heterocycloalkenyl" refers to a heterocycloalkyl as described above but containing at least one double bond.

"Heterocycloalkylalkyl" refers to a heterocycloalkyl-alkyl group in which the heterocycloalkyl and alkyl moieties are as previously described. Exemplary heterocycloalkylalkyl groups include (2-tetrahydrofuryl)methyl, (2-tetrahydrothiofuranyl)methyl.

"Heteroalkyl" refers to a straight- or branched-chain alkyl group preferably having from 2 to 14 carbons, more preferably 2 to 10 atoms in the chain, one or more of which is a heteroatom selected from S, O, and N. Exemplary heteroalkyls include alkyl ethers, secondary and tertiary alkyl amines, alkyl sulfides, and the like.

"Aryl" as a group or part of a group denotes (i) an optionally substituted monocyclic, or fused polycyclic, aromatic carbocycle (ring structure having ring atoms that are all carbon) preferably having from 5 to 12 atoms per ring. Examples of aryl groups include phenyl, naphthyl, and the like; (ii) an optionally substituted partially saturated bicyclic aromatic carbocyclic moiety in which a phenyl and a C_{5-7} cycloalkyl or C_{5-7} cycloalkenyl group are fused together to form a cyclic structure, such as tetrahydronaphthyl, indenyl or indanyl.

"Arylalkenyl" means an aryl-alkenyl- group in which the aryl and alkenyl are as previously described. Exemplary arylalkenyl groups include phenylallyl.

"Arylalkyl" means an aryl-alkyl- group in which the aryl and alkyl moieties are as previously described. Preferred arylalkyl groups contain a C_{1-5} alkyl moiety. Exemplary arylalkyl groups include benzyl, phenethyl and naphthelenemethyl.

"Heteroaryl" either alone or part of a group refers to groups containing an aromatic ring (preferably a 5 or 6 membered aromatic ring) having one or more heteroatoms as ring atoms in the aromatic ring with the remainder of the ring atoms being carbon atoms. Suitable heteroatoms include nitrogen, oxygen and sulphur. Examples of heteroaryl include thiophene, benzothiophene, benzofuran, benzimidazole, benzoxazole, benzothiazole, benzisothiazole, naphtho[2,3-b]thiophene, furan, isoindolizine, xantholene, phenoxatine, pyrrole, imidazole, pyrazole, pyridine, pyrazine, pyrimidine, pyridazine, indole, isoindole, 1H-indazole, purine, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, cinnoline, carbazole, phenanthridine, acridine, phenazine, thiazole,

isothiazole, phenothiazine, oxazole, isooxazole, furazane, phenoxazine, 2-,3- or4- pyridyl, 2-, 3-, 4-, 5-, or 8- quinolyl, 1-, 3-, 4-, or 5- isoquinolinyl 1-, 2-, or 3- indolyl, and 2-, or 3- thienyl.

"Heteroarylalkyl" means a heteroaryl-alkyl group in which the heteroaryl and alkyl moieties are as previously described. Preferred heteroarylalkyl groups contain a lower alkyl moiety. Exemplary heteroarylalkyl groups include pyridylmethyl.

"Lower alkyl" as a group means unless otherwise specified, an aliphatic hydrocarbon group which may be straight or branched having 1 to 6 carbon atoms in the chain, more preferably 1 to 4 carbons such as methyl, ethyl, propyl (n-propyl or isopropyl) or butyl (n-butyl, isobutyl or tertiary-butyl).

It is understood that included in the family of compounds of Formula (I) are isomeric forms including diastereoisomers, enantiomers, tautomers, and geometrical isomers in "E" or "Z" configurational isomer or a mixture of E and Z isomers. It is also understood that some isomeric forms such as diastereomers, enantiomers, and geometrical isomers can be separated by physical and/or chemical methods and by those skilled in the art.

Some of the compounds of the disclosed embodiments may exist as single stereoisomers, racemates, and/or mixtures of enantiomers and/or diastereomers. All such single stereoisomers, racemates and mixtures thereof are intended to be within the scope of the subject matter described and claimed.

Additionally, Formula (I) is intended to cover, where applicable, solvated as well as unsolvated forms of the compounds. Thus, each formula includes compounds having the indicated structure, including the hydrated as well as the non-hydrated forms.

In addition to compounds of the Formula (I), the agents of the various embodiments include pharmaceutically acceptable salts, prodrugs, N-oxides and active metabolites of such compounds, and pharmaceutically acceptable salts of such metabolites.

The term "pharmaceutically acceptable salts" refers to salts that retain the desired biological activity of the above-identified compounds, and include pharmaceutically acceptable acid addition salts and base addition salts. Suitable

pharmaceutically acceptable acid addition salts of compounds of Formula (I) may be prepared from an inorganic acid or from an organic acid. Examples of such inorganic acids are hydrochloric, sulfuric, and phosphoric acid. Appropriate organic acids may be selected from aliphatic, cycloaliphatic, aromatic, heterocyclic carboxylic and sulfonic classes of organic acids, examples of which are formic, acetic, propionic, succinic, glycolic, gluconic, lactic, malic, tartaric, citric, fumaric, maleic, alkyl sulfonic, arylsulfonic. Suitable pharmaceutically acceptable base addition salts of compounds of Formula (I) include metallic salts made from lithium, sodium, potassium, magnesium, calcium, aluminium, and zinc, and organic salts made from organic bases such as choline, diethanolamine, morpholine. Other examples of organic salts are: ammonium salts, quaternary salts such as tetramethylammonium salt; amino acid addition salts such as salts with glycine and arginine. Additional information on pharmaceutically acceptable salts can be found in Remington's Pharmaceutical Sciences, 19th Edition, Mack Publishing Co., Easton, PA 1995. In the case of agents that are solids, it is understood by those skilled in the art that the inventive compounds, agents and salts may exist in different crystalline or polymorphic forms, all of which are intended to be within the scope of the present invention and specified formulae.

"Prodrug" means a compound which is convertible *in vivo* by metabolic means (e.g. by hydrolysis, reduction or oxidation) to a compound of formula (I). For example an ester prodrug of a compound of formula (I) containing a hydroxyl group may be convertible by hydrolysis *in vivo* to the parent molecule. Suitable esters of compounds of formula (I) containing a hydroxyl group, are for example acetates, citrates, lactates, tartrates, malonates, oxalates, salicylates, propionates, succinates, fumarates, maleates, methylene-bis-β-hydroxynaphthoates, gestisates, isethionates, di-*p*-toluoyltartrates, methanesulphonates, ethanesulphonates, benzenesulphonates, *p*-toluenesulphonates, cyclohexylsulphamates and quinates. As another example an ester prodrug of a compound of formula (I) containing a carboxy group may be convertible by hydrolysis in vivo to the parent molecule. (Examples of ester prodrugs are those described by F.J. Leinweber, Drug Metab. Res.,18:379, 1987).

The term "therapeutically effective amount" or "effective amount" is an amount sufficient to effect beneficial or desired clinical results. An effective amount can be administered in one or more administrations. An effective amount is typically sufficient to palliate, ameliorate, stabilize, reverse, slow or delay the progression of the disease state.

The indazole compounds may be suitable for prevention or treatment of a disorder caused by, associated with or accompanied by disruptions of cell proliferation and/or angiogenesis when used either alone or together with a pharmaceutically acceptable carrier, diluent or excipient. An example of such a disorder is cancer.

Administration of compounds within Formula (I) to humans can be by any of the accepted modes for enteral administration such as oral or rectal, or by parenteral administration such as subcutaneous, intramuscular, intravenous and intradermal routes. Injection can be bolus or via constant or intermittent infusion. The active compound is typically included in a pharmaceutically acceptable carrier or diluent and in an amount sufficient to deliver to the patient a therapeutically effective dose. In various embodiments the inhibitor compound may be selectively toxic or more toxic to rapidly proliferating cells, e.g. cancerous tumors, than to normal cells.

As used herein the term 'cancer' is a general term intended to encompass the vast number of conditions that are characterised by uncontrolled abnormal growth of cells.

It is anticipated that the compounds of the invention will be useful in treating various cancers including but not limited to bone cancers including Ewing's sarcoma, osteosarcoma, chondrosarcoma and the like, brain and CNS tumours including acoustic neuroma, neuroblastomas, glioma and other brain tumours, spinal cord tumours, breast cancers, colorectal cancers, advanced colorectal adenocarcinomas, endocrine cancers including adenocortical carcinoma, pancreatic cancer, pituitary cancer, thyroid cancer, parathyroid cancer, thymus cancer, multiple endocrine neoplasma, gastrointestinal cancers including stomach cancer, oesophageal cancer, small intestine cancer, Liver cancer, extra hepatic bile duct cancer, gastrointestinal carcinoid tumour, gall bladder cancer, genitourinary cancers including testicular cancer, penile cancer, prostrate cancer, gynaecological cancers including cervical cancer, ovarian cancer, vaginal cancer, uterus/endometrium cancer, vulva cancer, gestational trophoblastic cancer, fallopian tube cancer, uterine sarcoma, head and neck cancers including oral cavity cancer, lip cancer, salivary gland cancer, larynx cancer, hypopharynx cancer, orthopharynx cancer, nasal cancer, paranasal cancer, nasopharynx cancer, leukaemia's including childhood leukaemia, acute lymphocytic leukaemia, acute myeloid leukaemia, chronic lymphocytic leukaemia, chronic myeloid leukaemia, hairy cell leukaemia, acute promyelocytic leukaemia, plasma cell leukaemia, myelomas, haematological disorders including myelodysplastic syndromes, myeloproliferative disorders, aplastic anaemia, Fanconi anaemia, Waldenstroms Macroglobulinemia, lung cancers including small cell lung

cancer, non-small cell lung cancer, lymphomas including Hodgkin's disease, non-Hodgkin's lymphoma, cutaneous T-cell lymphoma, peripheral T-cell lymphoma, B-cell lymphoma, Burkitt's lymphoma, AIDS related Lymphoma, eye cancers including retinoblastoma, intraocular melanoma, skin cancers including melanoma, non-melanoma skin cancer, merkel cell cancer, soft tissue sarcomas such as childhood soft tissue sarcoma, adult soft tissue sarcoma, Kaposi's sarcoma, urinary system cancers including kidney cancer, Wilms tumour, bladder cancer, urethral cancer, and transitional cell cancer.

Exemplary cancers that may be treated by compounds of this invention include but are not limited to bladder cancer, breast cancer, cervical cancer, colorectal cancer, colon cancer, gastric cancer, neuroblastoma, ovarian cancer, pancreatic cancer, leukaemia, lymphoma, prostate cancer and lung cancer.

Exemplary cancers that may be treated by compounds of this invention include but are not limited to colon cancer, colorectal cancer, pancreatic cancer and cervical cancer.

Exemplary cancers that may be treated by compounds of the present inventions include but are not limited to B-cell lymphoma (e.g. Burkitt's lymphoma), leukaemia's (e.g. acute promyelocytic leukaemia), cutaneous T-cell lymphoma (CTCL) and peripheral T-cell lymphoma.

Exemplary cancers that may be treated by compounds of the present invention include solid tumors and hematologic malignancies.

In using the compounds of the invention they can be administered in any form or mode which makes the compound bioavailable. One skilled in the art of preparing formulations can readily select the proper form and mode of administration depending upon the particular characteristics of the compound selected, the condition to be treated, the stage of the condition to be treated and other relevant circumstances. We refer the reader to Remingtons Pharmaceutical Sciences, 19th edition, Mach Publishing Co. (1995) for further information.

The compounds of the present invention can be administered alone or in the form of a pharmaceutical composition in combination with a pharmaceutically acceptable carrier, diluent or excipient. The compounds of the invention, while effective themselves,

are typically formulated and administered in the form of their pharmaceutically acceptable salts as these forms are typically more stable, more easily crystallised and have increased solubility.

The compounds are, however, typically used in the form of pharmaceutical compositions which are formulated depending on the desired mode of administration. As such in a further embodiment the present invention provides a pharmaceutical composition including a compound of Formula (I) and a pharmaceutically acceptable carrier, diluent or excipient. The compositions are prepared in manners well known in the art.

The invention in other embodiments provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. In such a pack or kit can be found a container having a unit dosage of the agent (s). The kits can include a composition comprising an effective agent either as concentrates (including lyophilized compositions), which can be diluted further prior to use or they can be provided at the concentration of use, where the vials may include one or more dosages. Conveniently, in the kits, single dosages can be provided in sterile vials so that the physician can employ the vials directly, where the vials will have the desired amount and concentration of agent(s). Associated with such container(s) can be various written materials such as instructions for use, or a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

The compounds of the invention may be used or administered in combination with one or more additional drug (s) that are chemotherapeutic drugs and/or procedures (e.g. surgery, radiotherapy) for the treatment of the disorder/diseases mentioned. The components can be administered in the same formulation or in separate formulations. If administered in separate formulations the compounds of the invention may be administered sequentially or simultaneously with the other drug(s).

In addition to being able to be administered in combination with one or more additional drugs that include chemotherapeutic drugs, the compounds of the invention may be used in a combination therapy. When this is done the compounds are typically administered in combination with each other. Thus one or more of the compounds of the invention may be administered either simultaneously (as a combined preparation) or

sequentially in order to achieve a desired effect. This is especially desirable where the therapeutic profile of each compound is different such that the combined effect of the two drugs provides an improved therapeutic result.

Pharmaceutical compositions of this invention for parenteral injection comprise pharmaceutically acceptable sterile aqueous or nonaqueous solutions, dispersions, suspensions or emulsions as well as sterile powders for reconstitution into sterile injectable solutions or dispersions just prior to use. Examples of suitable aqueous and nonaqueous carriers, diluents, solvents or vehicles include water, ethanol, polyols (such as glycerol, propylene glycol, polyethylene glycol, and the like), and suitable mixtures thereof, vegetable oils (such as olive oil), and injectable organic esters such as ethyl oleate. Proper fluidity can be maintained, for example, by the use of coating materials such as lecithin, by the maintenance of the required particle size in the case of dispersions, and by the use of surfactants.

These compositions may also contain adjuvants such as preservative, wetting agents, emulsifying agents, and dispersing agents. Prevention of the action of micro-organisms may be ensured by the inclusion of various antibacterial and antifungal agents, for example, paraben, chlorobutanol, phenol sorbic acid, and the like. It may also be desirable to include isotonic agents such as sugars, sodium chloride, and the like. Prolonged absorption of the injectable pharmaceutical form may be brought about by the inclusion of agents that delay absorption such as aluminium monostearate and gelatin.

If desired, and for more effective distribution, the compounds can be incorporated into slow release or targeted delivery systems such as polymer matrices, liposomes, and microspheres.

The injectable formulations can be sterilized, for example, by filtration through a bacterial-retaining filter, or by incorporating sterilizing agents in the form of sterile solid compositions that can be dissolved or dispersed in sterile water or other sterile injectable medium just prior to use.

Solid dosage forms for oral administration include capsules, tablets, pills, powders, and granules. In such solid dosage forms, the active compound is mixed with at least one inert, pharmaceutically acceptable excipient or carrier such as sodium citrate or dicalcium phosphate and/or a) fillers or extenders such as starches, lactose, sucrose, glucose, mannitol, and silicic acid, b) binders such as, for example,

carboxymethylcellulose, alginates, gelatin, polyvinylpyrrolidone, sucrose, and acacia, c) humectants such as glycerol, d) disintegrating agents such as agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates, and sodium carbonate, e) solution retarding agents such as paraffin, f) absorption accelerators such as quaternary ammonium compounds, g) wetting agents such as, for example, cetyl alcohol and glycerol monostearate, h) absorbents such as kaolin and bentonite clay, and i) lubricants such as talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, and mixtures thereof. In the case of capsules, tablets and pills, the dosage form may also comprise buffering agents.

Solid compositions of a similar type may also be employed as fillers in soft and hard-filled gelatin capsules using such excipients as lactose or milk sugar as well as high molecular weight polyethylene glycols and the like.

The solid dosage forms of tablets, dragees, capsules, pills, and granules can be prepared with coatings and shells such as enteric coatings and other coatings well known in the pharmaceutical formulating art. They may optionally contain opacifying agents and can also be of a composition that they release the active ingredient(s) only, or preferentially, in a certain part of the intestinal tract, optionally, in a delayed manner. Examples of embedding compositions which can be used include polymeric substances and waxes.

If desired, and for more effective distribution, the compounds can be incorporated into slow release or targeted delivery systems such as polymer matrices, liposomes, and microspheres.

The active compounds can also be in microencapsulated form, if appropriate, with one or more of the above-mentioned excipients.

Liquid dosage forms for oral administration include pharmaceutically acceptable emulsions, solutions, suspensions, syrups and elixirs. In addition to the active compounds, the liquid dosage forms may contain inert diluents commonly used in the art such as, for example, water or other solvents, solubilizing agents and emulsifiers such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, dimethyl formamide, oils (in particular, cottonseed, groundnut, corn, germ, olive, castor, and sesame oils), glycerol,

tetrahydrofurfuryl alcohol, polyethylene glycols and fatty acid esters of sorbitan, and mixtures thereof.

Besides inert diluents, the oral compositions can also include adjuvants such as wetting agents, emulsifying and suspending agents, sweetening, flavoring, and perfuming agents.

Suspensions, in addition to the active compounds, may contain suspending agents as, for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline cellulose, aluminium metahydroxide, bentonite, agar-agar, and tragacanth, and mixtures thereof.

Compositions for rectal or vaginal administration are preferably suppositories which can be prepared by mixing the compounds of this invention with suitable non-irritating excipients or carriers such as cocoa butter, polyethylene glycol or a suppository wax which are solid at room temperature but liquid at body temperature and therefore melt in the rectum or vaginal cavity and release the active compound.

Dosage forms for topical administration of a compound of this invention include powders, patches, sprays, ointments and inhalants. The active compound is mixed under sterile conditions with a pharmaceutically acceptable carrier and any needed preservatives, buffers, or propellants which may be required.

The amount of compound administered will preferably treat and reduce or alleviate the condition. A therapeutically effective amount can be readily determined by an attending diagnostician by the use of conventional techniques and by observing results obtained under analogous circumstances. In determining the therapeutically effective amount a number of factors are to be considered including but not limited to, the species of animal, its size, age and general health, the specific condition involved, the severity of the condition, the response of the patient to treatment, the particular compound administered, the mode of administration, the bioavailability of the preparation administered, the dose regime selected, the use of other medications and other relevant circumstances.

A preferred dosage will be a range from about 0.01 to 300 mg per kilogram of body weight per day. A more preferred dosage will be in the range from 0.1 to 100 mg per kilogram of body weight per day, more preferably from 0.2 to 80 mg per kilogram of body

weight per day, even more preferably 0.2 to 50 mg per kilogram of body weight per day. A suitable dose can be administered in multiple sub-doses per day.

As discussed above, the compounds of the embodiments disclosed may be useful for treating proliferative diseases. Examples of such cell proliferative diseases or conditions include cancer (include any metastases), psoriasis, and smooth muscle cell proliferative disorders such as restenosis. The inventive compounds may be particularly useful for treating tumors such as breast cancer, colon cancer, lung cancer, ovarian cancer, prostate cancer, head and/or neck cancer, or renal, gastric, pancreatic cancer and brain cancer as well as hematologic malignancies such as lymphoma and leukaemia's. In addition, the inventive compounds may be useful for treating a proliferative disease that is refractory to the treatment with other chemotherapeutics; and for treating hyperproliferative condition such as leukaemia's, psoriasis and restenosis. In other embodiments, compounds in this invention can be used to treat pre-cancer conditions including myeloid dysplasia, endometrial dysplasia and cervical dysplasia. In yet another embodiments, compounds in this invention can be used to treat myeloproliferative disorders including chronic idiopathic myelofibrosis, polycythemia vera, essential thrombocythemia, chronic myeloid leukemia.

SYNTHESIS

The agents of the various embodiments may be prepared using the reaction routes and synthesis schemes as described below, employing the techniques available in the art using starting materials that are readily available. The preparation of particular compounds of the embodiments is described in detail in the following examples, but the artisan will recognize that the chemical reactions described may be readily adapted to prepare a number of other agents of the various embodiments. For example, the synthesis of non-exemplified compounds may be successfully performed by modifications apparent to those skilled in the art, e.g. by appropriately protecting interfering groups, by changing to other suitable reagents known in the art, or by making routine modifications of reaction conditions. A list of suitable protecting groups in organic synthesis can be found in T.W. Greene's Protective Groups in Organic Synthesis, John Wiley & Sons, 1981. Alternatively, other reactions disclosed herein or known in the art will be recognized as having applicability for preparing other compounds of the various embodiments.

Reagents useful for synthesizing compounds may be obtained or prepared according to techniques known in the art.

In the examples described below, unless otherwise indicated, all temperatures in the following description are in degrees Celsius and all parts and percentages are by weight, unless indicated otherwise.

Various starting materials and other reagents were purchased from commercial suppliers, such as Aldrich Chemical Company or Lancaster Synthesis Ltd., and used without further purification, unless otherwise indicated. Tetrahydrofuran (THF) and N,N-dimethylformamide (DMF) were purchased from Aldrich in SureSeal bottles and used as received. All solvents were purified by using standard methods in the art, unless otherwise indicated.

The reactions set forth below were performed under a positive pressure of nitrogen, argon or with a drying tube, at ambient temperature (unless otherwise stated), in anhydrous solvents, and the reaction flasks are fitted with rubber septa for the introduction of substrates and reagents via syringe. Glassware was oven-dried and/or heat-dried. Analytical thin-layer chromatography was performed on glass-backed silica gel 60 F 254 plates (E Merck (0.25 mm)) and eluted with the appropriate solvent ratios (v/v). The reactions were assayed by TLC and terminated as judged by the consumption of starting material.

The TLC plates were visualized by UV absorption or with a p-anisaldehyde spray reagent or a phosphomolybdic acid reagent (Aldrich Chemical, 20wt% in ethanol) which was activated with heat, or by staining in iodine chamber. Work-ups were typically done by doubling the reaction volume with the reaction solvent or extraction solvent and then washing with the indicated aqueous solutions using 25% by volume of the extraction volume (unless otherwise indicated). Product solutions were dried over anhydrous sodium sulfate prior to filtration, and evaporation of the solvents was under reduced pressure on a rotary evaporator and noted as solvents removed in vacuo. Flash column chromatography [Still et al, J. Org. Chem., 43, 2923 (1978)] was conducted using E Merck-grade flash silica gel (47-61 mm) and a silica gel:crude material ratio of about 20:1 to 50:1, unless otherwise stated. Hydrogenolysis was done at the pressure indicated or at ambient pressure.

1H NMR spectra was recorded on a Bruker instrument operating at 400 MHz, and ^{13}C-NMR spectra was recorded operating at 100 MHz. NMR spectra are obtained as $CDCl_3$ solutions (reported in ppm), using chloroform as the reference standard (7.25 ppm and 77.00 ppm) or CD_3OD (3.4 and 4.8 ppm and 49.3 ppm), or an internal

tetramethylsilane standard (0.00 ppm) when appropriate. Other NMR solvents were used as needed. When peak multiplicities are reported, the following abbreviations are used: s = singlet, d = doublet, t = triplet, m = multiplet, br = broadened, dd = doublet of doublets, dt = doublet of triplets. Coupling constants, when given, are reported in Hertz.

Mass spectra were obtained using LC/MS either in ESI or APCI. All melting points are uncorrected.

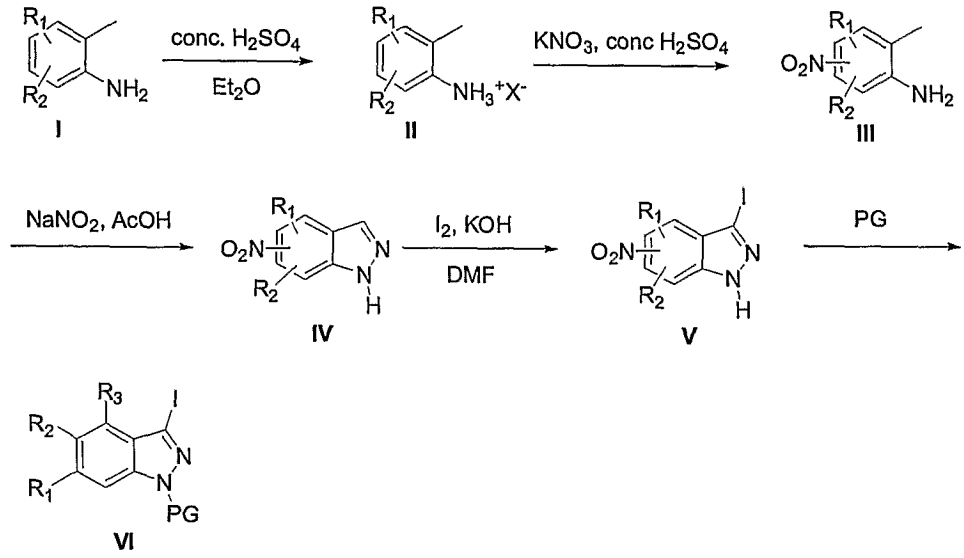
All final products had greater than 90% purity (by HPLC at wavelengths of 220 nm and 254 nm).

The following examples are intended to illustrate the embodiments disclosed and are not to be construed as being limitations thereto. Additional compounds, other than those described below, may be prepared using the following described reaction scheme or appropriate variations or modifications thereof.

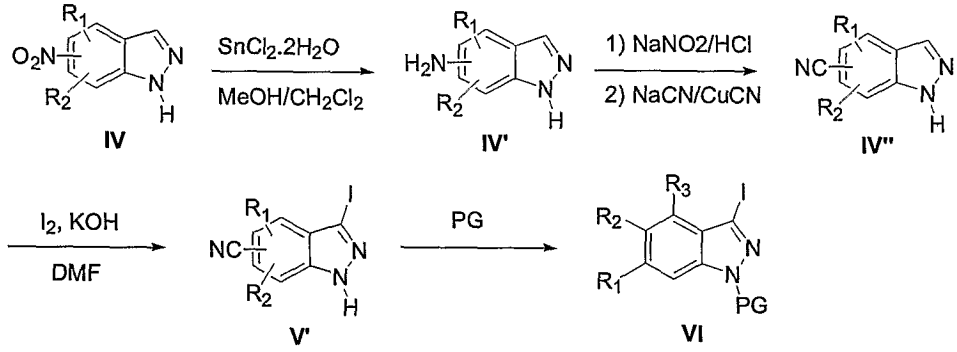
The target compounds of this invention may be prepared as illustrated by Scheme I-VII and by general methods known to those skilled in the art.

Scheme I

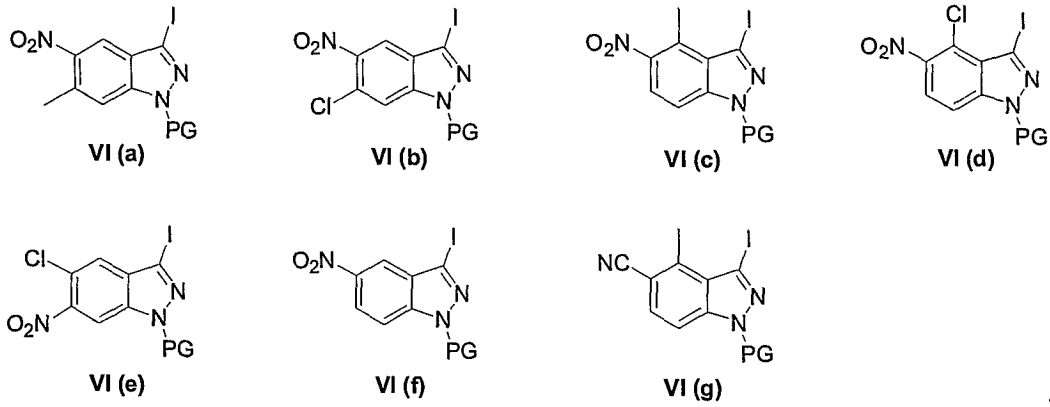
Scheme Ia



Scheme Ib



where several intermediates (VI) were synthesized as follows:

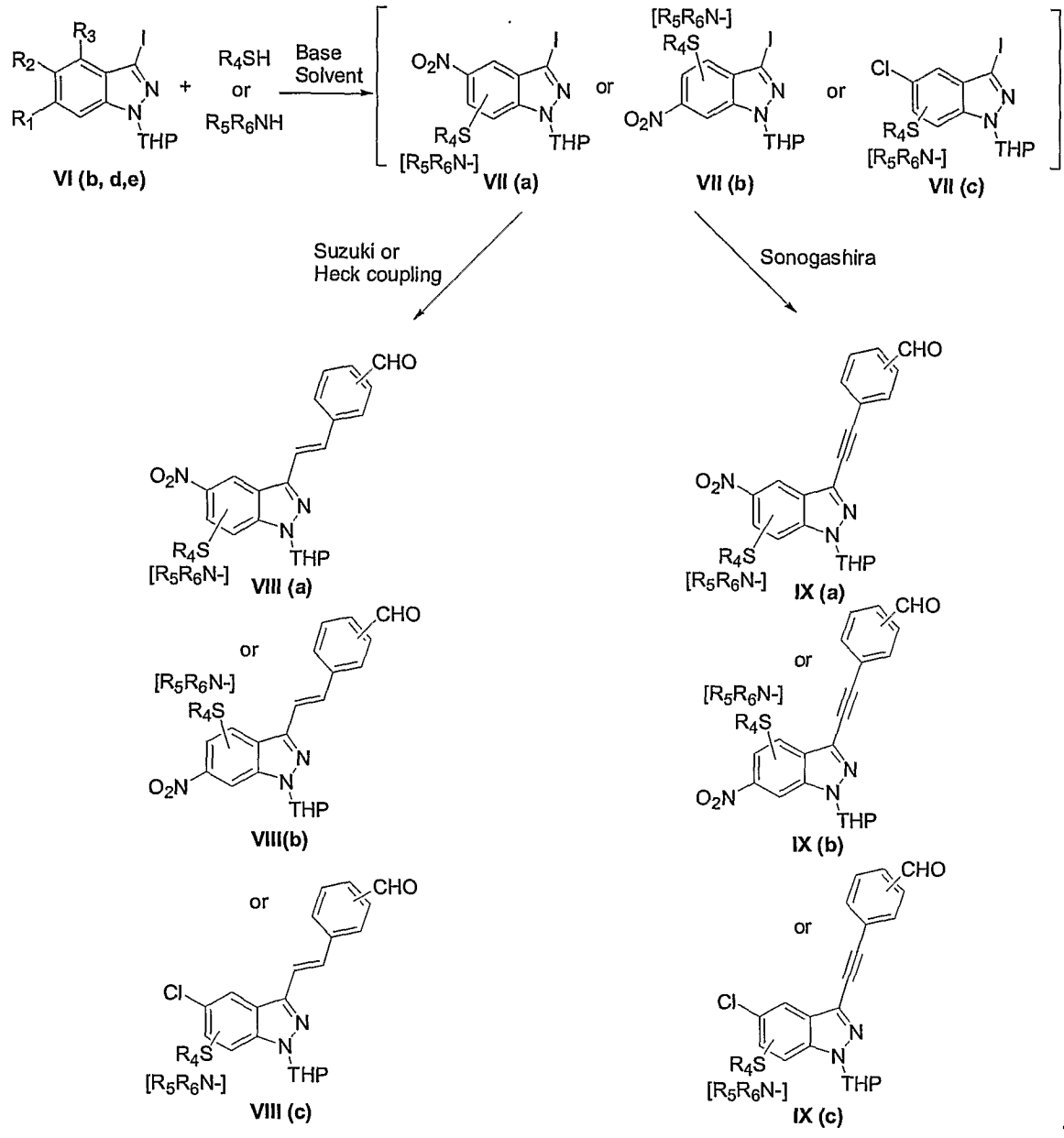


Intermediates (**VI**) can be synthesized by the synthetic route shown in Scheme Ia and Ib. The reaction of substituted aniline (**I**) with concentrated sulfuric acid in diethyl ether gave the aniline sulfate (**II**). The nitro group was introduced to the aromatic ring by treatment of (**II**) to an ice-cold solution of potassium nitrate in concentrated sulfuric acid to produce (**III**). Treatment of (**III**) with aqueous sodium nitrite and followed by heating with acetic acid to give cyclized product (**IV**). Successive addition of iodine and potassium pellets to a stirring solution of (**IV**) in a suitable solvent (eg. *N*,*N*-dimethylformamide) gave (**V**).

Scheme Ia: Successive addition of iodine and potassium pellets to a stirring solution of (**IV**) in a suitable solvent (eg. *N*,*N*-dimethylformamide) gave (**V**). (**VI**) was obtained by typical protection procedure, for example reaction of (**V**) with 3,4-dihydropyran under the catalysis of a suitable acid (eg. *p*-toluenesulfonic acid monohydrate) in a suitable solvent (eg. acetonitrile).

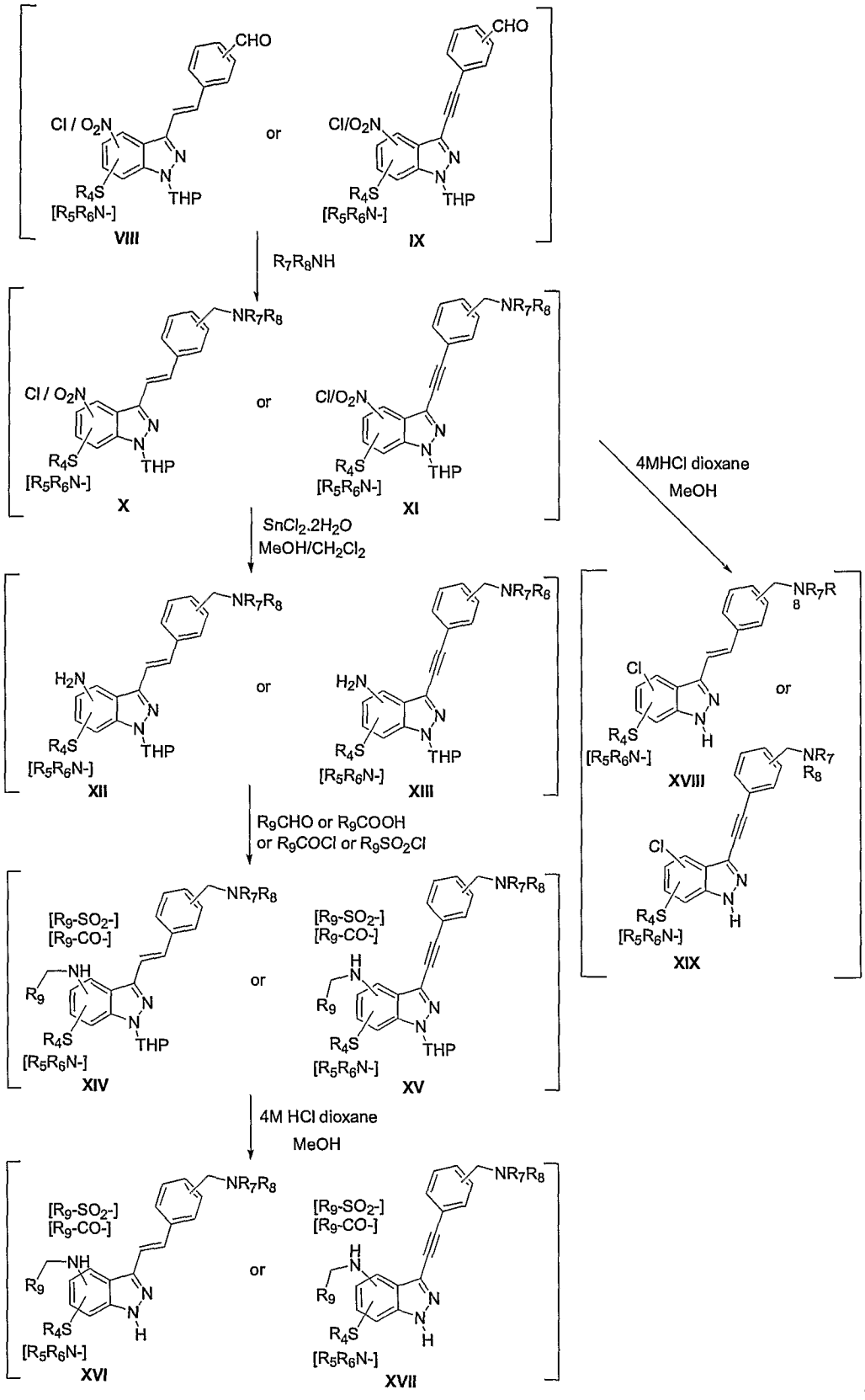
Scheme Ib: The nitro indazole derivatives (**IV**) was reduced by appropriate reducing agent (e.g. tin (II) chloride) and the resulting amine (**IV'**) was converted to the cyano compound using a modified Sandmeyer's reaction to produce the corresponding (**IV''**). Successive addition of iodine and potassium pellets to a stirring solution of (**IV''**) in a suitable solvent (eg. *N*,*N*-dimethylformamide) gave (**V'**). (**VI**) was obtained by typical protection procedure, for example reaction of (**V'**) with 3,4-dihydropyran under the catalysis of a suitable acid (eg. *p*-toluenesulfonic acid monohydrate) in a suitable solvent (eg. acetonitrile).

Scheme II



Scheme II illustrates the synthetic sequences that yield indazole derivatives containing alkenyl group (**VIII**) and alkynyl group (**IX**). (**VI**) underwent a displacement reaction using a suitable base (e.g. potassium carbonate) in an appropriate solvent (e.g. *N,N*-dimethylformamide) to produce various intermediates (**VII**) of various functionalities on the indazoles. Suitable coupling of the indazole ring by displacement of the iodide produced (**VIII**) and (**IX**). For example, in the presence of a suitable Pd(O) or Pd(II) catalysts, the alkenyl side chain was coupled to indazole by known methods (e.g. Heck or Suzuki coupling) to produce (**VIII**). Similarly, in the presence of a suitable Pd(O) or Pd(II) catalysts, the alkynyl side chain was coupled to indazole by known method (e.g. Sonogashira coupling) to produce (**IX**).

Scheme III

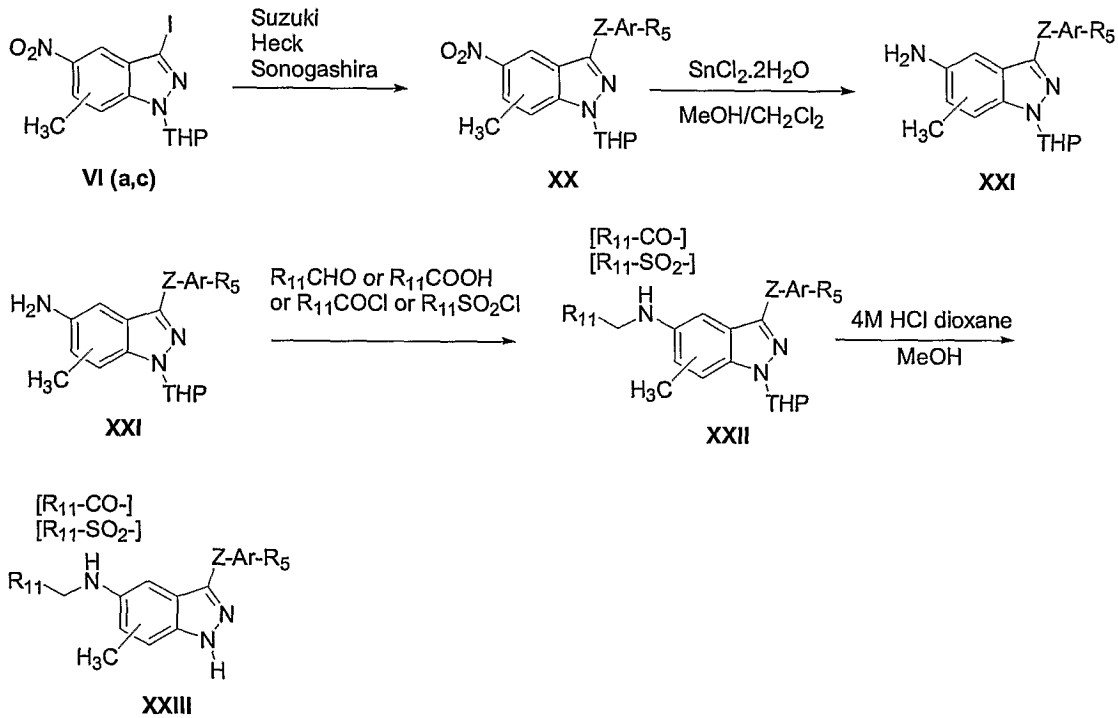


Scheme III illustrates several synthetic routes that yield the target compounds. When (**VIII**) or (**IX**) was reacted with an appropriate amine under reduction conditions

($NaBH(OAc)_3/CH_3COOH$), (**X**) or (**XI**) were obtained respectively and can be transformed to corresponding (**XVIII**) and (**XVIX**) by a typical deprotection procedure, for example stirring in 4M hydrochloric acid in dioxane.

Specifically, for example, the nitro indazole derivatives (**X**) or (**XI**) can be reduced by appropriate reducing agent (eg. tin (II) chloride) and the resulting amine (**XII**) or (**XIII**) can be coupled with appropriate starting materials to produce the corresponding (**XIV**) or (**XV**) respectively. For example, coupling between amine and acid chloride using a suitable base (e.g. pyridine) gave the corresponding amide. These can be further transformed to corresponding (**XVI**) or (**XVII**) by a typical deprotection procedure as described in the previous paragraph.

Scheme IV



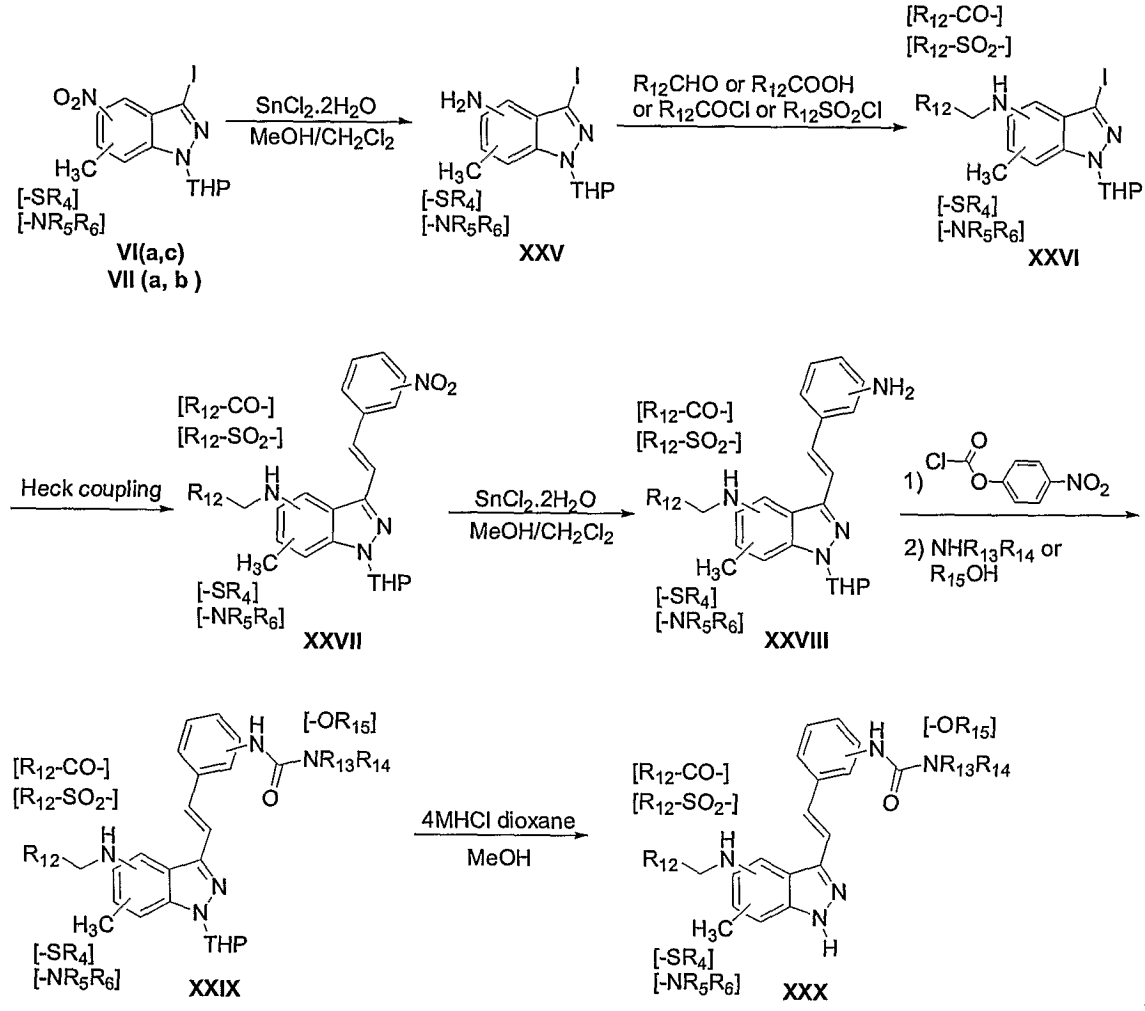
VI (a,c) XX XXI

XXI XXII

XXIII

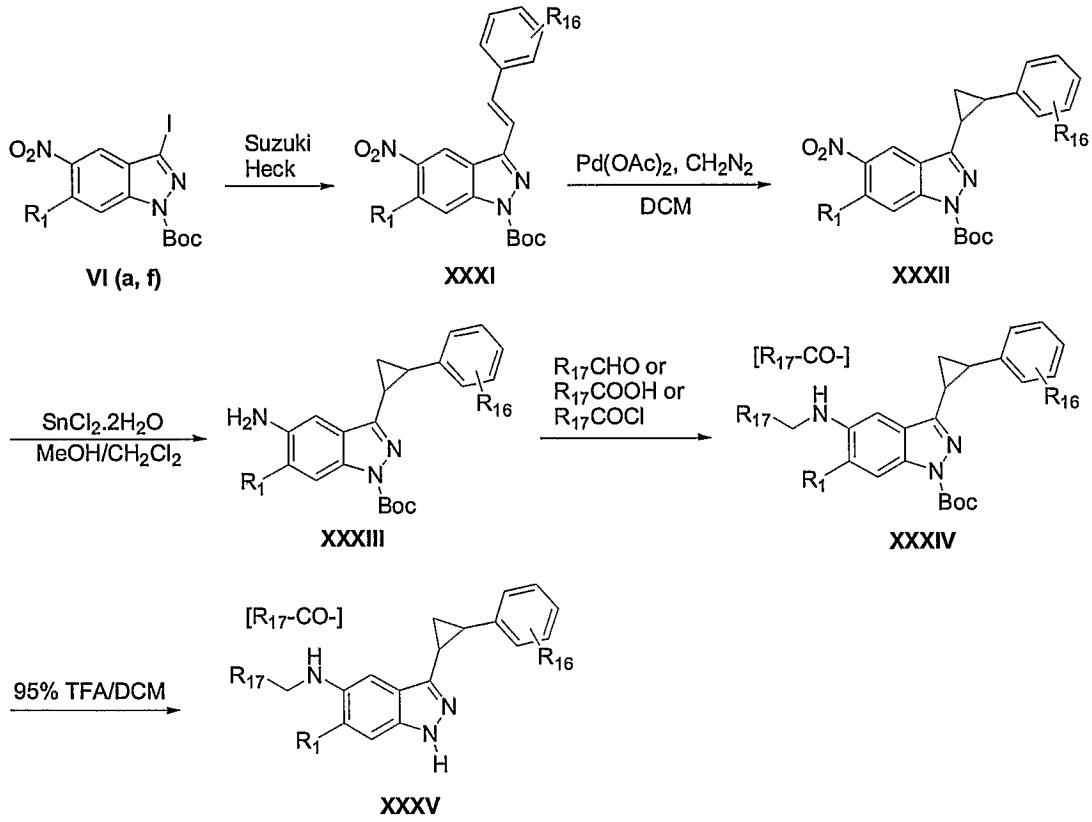
Scheme IV illustrates the synthetic routes of target compounds with heteroaryl side chain. Z-A-R_5 can be coupled to (**VI**) by known methods (e.g. Suzuki, Heck or Sonogashira coupling) to produce (**XX**). The nitro indazole derivatives (**XX**) can be reduced by appropriate reducing agent (e.g. tin (II) chloride) and the resulting amine (**XXI**) can be coupled with appropriate starting materials to produce the corresponding (**XXII**). For example, coupling between amine and acid chloride using a suitable base (e.g. pyridine) gave the corresponding amide. These can be further transformed to corresponding (**XXIII**) by a typical deprotection procedure as described above.

Scheme V



Specifically, target compounds with alkenyl and carbamate moieties can be synthesized by the synthetic route as illustrated in Scheme V. The nitro group of (**VI**) or (**VII**) can be reduced by appropriate reducing agent (e.g. tin (II) chloride) and the resulting amine (**XXV**) can be coupled with appropriate starting materials to produce the corresponding (**XXVI**). The alkenyl side chain was coupled to (**XXVI**) by known method (e.g. Heck coupling) in the presence of a suitable Pd(O) or Pd(II) catalysts to produce (**XXVII**). The nitro group of (**XXVII**) can be reduced by appropriate reducing agent (e.g. tin (II) chloride) and the resulting aniline (**XXVIII**) can be coupled with appropriate starting materials to produce the corresponding carbamate (**XXIX**) using a suitable reagent (e.g. 4-nitrophenylchloroformate). These can be further transformed to corresponding (**XXX**) by a typical deprotection procedure as described in the previous paragraph.

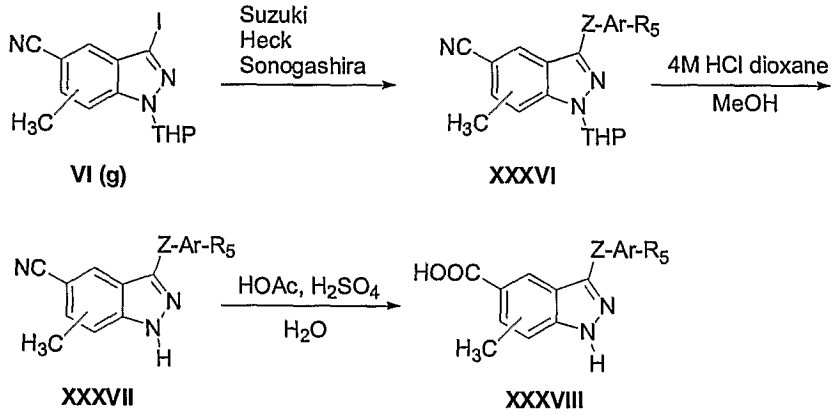
Scheme VI



VI (a, f) XXXI XXXII XXXIII XXXIV XXXV

Alternatively, another class of target compounds consisting cyclopropyl indazoles can be synthesized by the synthetic route as illustrated in Scheme VI. The alkenyl side chain was coupled to indazole by known methods (e.g. Heck or Suzuki coupling) in the presence of a suitable Pd(O) or Pd(II) catalysts to produce (**XXXI**). Treatment of the alkenyl indazole with diazomethane in a suitable solvent (e.g. diethyl ether) gave the corresponding cyclized propyl indazole (**XXXII**). The nitro group of (**XXXII**) was reduced by appropriate reducing agent (e.g. tin (II) chloride) and the resulting aniline (**XXXIII**) can be coupled with appropriate starting materials to produce the corresponding (**XXXIV**) using appropriate starting materials. These can be further transformed to corresponding (**XXXV**) by a typical deprotection procedure, for example using 95% trifluoroacetic acid in dichloromethane.

Scheme VII



Scheme VII illustrates the synthetic routes to target compounds with cyano and acid moiety. Z-Ar-R_5 can be coupled to (**VI**) by known methods (e.g. Suzuki, Heck or Sonogashira coupling) to produce (**XXXVI**). These were further transformed to corresponding (**XXVII**) by a typical deprotection procedure as described above. The nitrile was converted to the corresponding acid in acidic conditions yielding to (**XXXVIII**).

The following preparation and examples are given to enable those skilled in the art to more clearly understand and to practice the subject matter hereof. They should not be considered as limiting the scope of the disclosure, but merely as being illustrative and representative thereof.

Example 1 (Compound 125)

Preparation of *N*-{6-(4-Methyl-piperazin-1-yl)-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1*H*-indazol-5-yl}-methanesulfonamide

Step 1 Displacement of chloro

To a pre-stirred solution of 6-chloro-3-iodo-5-nitro-1-tetrahydro-pyran-2-yl)-1*H*-indazole (**VI b**) (2.0 g, 4.9 mmol), *N*-methyl piperazine (2.45 g, 24.53 mmol), and diisopropyl ethyl amine (1.26 g, 9.8 mmol) in DMSO (20 mL) was heated to 95°C for overnight and then cooled to room temperature. Deionized water (200 mL) was added and the reaction mixture was allowed to stir for 15 minutes. The product 3-Iodo-6-(4-methyl-piperazin-1-yl)-5-nitro-1-(tetrahydro-pyran-2-yl)-1H-indazole precipitated out which was filtered under suction pump and washed with deionized water (200 mL) and hexane (20

mL). The pale yellow solid was obtained and dried under vacuum (1.3 g, 60% yield). MS (m/z): 472 $(MH)^+$.

Step 2 NO_2 reduction

To a pre-stirred solution of 3-Iodo-6-(4-methyl-piperazin-1-yl)-5-nitro-1-(tetrahydro-pyran-2-yl)-1H-indazole (1.5 g, 3.18 mmol) in (1:1MeOH/CH_2Cl_2 (20 mL) was added $SnCl_2.2H_2O$ (4.30g, 19.09 mmol) and the resulting mixture was stirred overnight and then cooled to 0 °C. Saturated Na_2CO_3 (20 mL) was carefully added and the reaction mixture was allowed to stir for 60 minutes. The aqueous layer was extracted with CH_2Cl_2 (100 mL) twice. The combined organic layer was washed with brine, dried (sodium sulfate), filtered and concentrated in *vacuo*. The product 3-iodo-6-(4-methyl-piperazin-1-yl)-1-(tetrahydro-pyran-2-yl)-1H-indazol-5-ylamine was purified by column (CH_2Cl_2/MeOH) (1.05 g, 72 % yield). MS (m/z): 442 $(MH)^+$.

Step 3 Sulfonamide synthesis

Methane sulfonyl chloride (0.544 g. 4.75 mmol) was added to a pre-stirred solution of 3-iodo-6-(4-methyl-piperazin-1-yl)-1-(tetrahydro-pyran-2-yl)-1*H*-indazol-5-ylamine (1.4 g, 3.17 mmol) and pyridine (0.63 g, 7.93 mmol) in CH_2Cl_2 (20 mL). The resulting solution was at room temperature for 2 hours and then cooled to room temperature. Saturated sodium hydrogen carbonate solution was added and the reaction mixture was allowed to stir for 15 minutes. The aqueous layer was extracted with dichloromethane (50mL) twice. The combined organic layer was washed with brine, dried (sodium sulfate), filtered and concentrated in *vacuo*. The product *N*-[3-iodo-6-(4-methyl-piperazin-1-yl)-1-(tetrahydro-pyran-2-yl)-1*H*-indazol-5-yl]-methanesulfonamide was purified by column (CH_2Cl_2/Acetone). The product was obtained as pale yellow solid (1.5 g, 91 % yield). MS (m/z): 520 $(MH)^+$.

Step 4 Heck Coupling

To a solution of *N*-[3-Iodo-6-(4-methyl-piperazin-1-yl)-1-(tetrahydro-pyran-2-yl)-1*H*-indazol-5-yl]-methanesulfonamide (0.91g, 1.75 mmol) in dry DMF (10 mL) at ambient temperature was added 3-vinyl-benzaldehyde (0.35 g, 2.63 mmol) and DIEA (0.68 g, 5.26 mmol), followed by addition of $Pd(OAc)_2$ (0.0196g, 0.0876 mmol) and P(*o*-toly)$_3$ (0.159 g, 0.526 mmol). The resulting mixture was stirred at 105 °C for 6 hours. The reaction mixture was cooled to 0 °C and quenched with sat. $NaHCO_3$ (10mL). The product was extracted with CH_2Cl_2 thrice and the combined organic extracts were washed with H_2O followed by brine, dried over Na_2SO_4 and concentrated under reduced pressure to furnish a solid, which was purified by column (CH_2Cl_2/acetone) to obtain 3-{2-[6-(4-Methyl-

piperazin-1-yl)-5-nitro-1-(tetrahydro-pyran-2-yl)-1H-indazol-3-yl]-vinyl}-benzaldehyde (0.37 g, 40 % yield) . MS (m/z): 476 $(MH)^+$.

Step 5 Reductive amination:

To a solution of 3-{2-[6-(4-Methyl-piperazin-1-yl)-5-nitro-1-(tetrahydro-pyran-2-yl)-1H-indazol-3-yl]-vinyl}-benzaldehyde (0.060g, 0.114 mmol) in dry CH_2Cl_2 (5 mL) at ambient temperature was added morpholine (0.0198 g, 0.228 mmol) followed by addition of $Na(OAc)_3BH$ (0.048g, 0.229 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was cooled to 0 °C and quenched with sat. $NaHCO_3$ (10mL). The product was extracted with CH_2Cl_2 thrice and the combined organic extracts were washed with H_2O followed by brine, dried over Na_2SO_4 and concentrated under reduced pressure to furnish a solid, which was purified by column (CH_2Cl_2/Acetone) to obtain N-[6-(4-Methyl-piperazin-1-yl)-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1-(tetrahydro-pyran-2-yl)-1H-indazol-5-yl]-methanesulfonamide (0.034 g, 50 % yield). MS (m/z): 596 $(MH)^+$.

Step 6 THP deprotection

To a solution of N-[6-(4-Methyl-piperazin-1-yl)-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1-(tetrahydro-pyran-2-yl)-1H-indazol-5-yl]-methanesulfonamide 30 mg in MeOH (2 mL) was added 4M HCl/dioxane (2 mL) and stirred for 2 hours. The precipitated product was filtered and washed with CH_2Cl_2 to obtain N-{6-(4-Methyl-piperazin-1-yl)-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1H-indazol-5-yl}-methanesulfonamide as solid (0.020 g, 80%). MS (m/z): 511 $(MH)^+$.

Example 2 (Compound 13)

Preparation of [(6-Methyl-3-(2-pyrazin-2-yl-vinyl)-1*H*-indazol-5-yl]-pyridin-2-yl-methylamine

Step 1 Heck coupling

An oven-dried 2-necked round bottom flask was evacuated and purged with N_2 prior to the addition of DMF (20 mL), $Pd(OAc)_2$ (56 mg, 0.25 mmol) and P(*o*-toly)$_3$ (152 mg, 0.5 mmol). The system was evacuated and purged twice with N_2. The reaction was then stirred for 5 mins. Following that, triethylamine (2.1 mL, 15 mmol), 3-iodo-6-methyl-5-nitro-1-(tetrahydro-pyran-2-yl)-1*H*-indazole (**VI a**) (1.97 g, 5.0 mmol)and 2-vinyl-pyrazine (1.0 mL, 10 mmol) were added sequentially. The reaction mixture was stirred at 140 °C for 4h. The mixture was cooled to room temperature and water (40 mL) was

added to precipitate out a dark brown solid. The solid was filtered and washed with MeOH to obtain an orange solid (1g, 55 %) MS (m/z): 366 $(MH)^+$.

Step 2 NO_2 reduction

6-Methyl-5-nitro-3-(2-pyrazin-2-yl-vinyl)-1-(tetrahydro-pyran-2-yl)-1*H*-indazole (500 mg, 1.37 mmol) was reduced to 6-methyl-3-(2-pyrazin-2-yl-vinyl)-1-(tetrahydro-pyran-2-yl)-1*H*-indazol-5-ylamine (350 mg, 76 %) using the procedure described in step 2 of Example 1 MS (m/z): 336 $(MH)^+$.

Step 3 Reductive amination

[6-Methyl-3-(2-pyrazin-2-yl-vinyl)-1-(tetrahydro-pyran-2-yl)-1H-indazol-5-yl]-pyridin-2-ylmethyl-amine was prepared using the procedure described in step 4 of Example 1 by using appropriate starting materials (80 mg, 84%). MS (m/z): 427 $(MH)^+$.

Step 4 THP deprotection

The titled compound was prepared by THP deprotection of [6-methyl-3-(2-pyrazin-2-yl-vinyl)-1-(tetrahydro-pyran-2-yl)-1H-indazol-5-yl]-pyridin-2-ylmethyl-amine (80 mg, 0.188 mmol) using the procedure described in step 5 of Example 1. It was obtained as a dark red solid (0.020 g, 31 %). HPLC: 92 %; t_R = (LC/PDA: Xterra 1S column, 4.6 x 20mm 3.5µ column; 2.0 ml/min, gradient 5-95% B over 6 min, Solvent A: H_2O with 0.1% TFA; Solvent B: acetonitrile with 0.1 TFA; UV 254): 1.60 min; MS (m/z): 343 $(MH)^+$. ^1H NMR (MeOD, 400 MHz): δ 2.55(s, 3H), 5.09 (s, 2H), 7.02 (s, 1H), 7.47 (s, 1H), 7.60 (d, 1H, J = 16.4 Hz), 8.00 (m, 1H), 8.13 (d, 1H, J = 16.4 Hz), 8.25 (d, 1H, J = 8.0 Hz), 8.60 (d, 1H, J = 2.7 Hz), 8.65 (dt, 1H, J_1 = 1.5 Hz, J_2 = 8.0 Hz), 8.74 (m, 1H), 8.79 (m, 1H), 9.03 (d, 1H, J = 1.4 Hz).

Example 3 (Compound 182)

Preparation of 4-methyl-piperazine-1-carboxylic acid {3-[2-(5-acetylamino-6-pyrrolidin-1-yl-1*H*-indazol-3-yl)-vinyl]-phenyl}-amide

Step 1 Displacement with pyrrolidine

3-Iodo-5-nitro-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazole was prepared from 6-chloro-3-iodo-5-nitro-1-(tetrahydro-pyran-2-yl)-1*H*-indazole (**VI b**) (1.07 g, 2.63 mmol) and pyrrolidine (1.10 mL, 13.1 mmol) according to step 1 of Example 1. (850 mg, 73 %) MS (m/z): 443 $(MH)^+$.

Step 2 Reduction of NO_2

3-Iodo-5-nitro-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazole (1.00 g, 2.26 mmol) was reduced to 3-iodo-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazol-5-ylamine using the procedure described in step 2 of Example 1. (700 mg, 75 %) MS (m/z): 413 $(MH)^+$.

Step 3 Acylation

N-[3-Iodo-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1H-indazol-5-yl]-acetamide was prepared from 3-iodo-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazol-5-ylamine (420 mg, 1.02 mmol) using the procedure described in step 3 of Example 1. The crude mixture was passed through a short plug of Si and flush with CH_2Cl_2 and 50 % ethyl acetate-hexane mixture to yield a pale orange solid (300 mg, 65 %). MS (m/z): 455 $(MH)^+$.

Step 4 Heck coupling

N-[3-[2-(3-Nitro-phenyl)-vinyl]-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazol-5-yl]-acetamide was prepared by Heck coupling of *N*-[3-iodo-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1H-indazol-5-yl]-acetamide (300 mg, 0.661 mmol) and 1-nitro-3-vinyl-benzene (0.184 mL, 1.32 mmol) using the procedure described in step 1 of Example 2. The mixture was diluted with CH_2Cl_2 (20 mL) and washed twice with DI water (20 mL x 2). The combined organic layer was dried and concentrated under reduced pressure. MeOH was added to the residue to precipitate out the desired product as a yellow solid (150 mg, 48 %). MS (m/z): 476 $(MH)^+$.

Step 5 Reduction of NO_2

N-[3-[2-(3-Nitro-phenyl)-vinyl]-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazol-5-yl]-acetamide (100 mg, 0.211 mmol) was reduced to *N*-[3-[2-(3-amino-phenyl)-vinyl]-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1H-indazol-5-yl]-acetamide using the procedure described in step 2 of Example 1 (80 mg, 85 %). MS (m/z): 446 $(MH)^+$.

Step 6 Urea formation

To a solution of *N*-[3-[2-(3-amino-phenyl)-vinyl]-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazol-5-yl]-acetamide (50 mg, 0.112 mmol) in CH_2Cl_2 (2 mL), 4-nitrophenylchloroformate (42.2 mg, 0.225 mmol) and pyridine (45.3 µL, 0.56 mmol) were added and the reaction was stirred for 2h. *N*-Methylpiperazine (25 µL, 0.225 mmol) was then added and the reaction was stirred for another 1h. Water (4 mL) was then added to quench the reaction. The organic layer was washed thrice with water (2 mL x 2) and then dried with Na_2SO_4. CH_2Cl_2 was then removed under reduced pressure to afford the crude

product 4-methyl-piperazine-1-carboxylic acid (3-{2-[5-acetylamino-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazol-3-yl]-vinyl}-phenyl)-amide which was used for the next step (80 mg). MS (m/z): 572 $(MH)^+$.

Step 7 THP deprotection

The titled compound was prepared by THP deprotection of (4-methyl-piperazine-1-carboxylic acid (3-{2-[5-acetylamino-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazol-3-yl]-vinyl}-phenyl)-amide (80 mg, 0.140 mmol) using the procedure described in step 5 of Example 1. The mixture was then purified by reverse phase HPLC (Luna C_{18}, 21.2X150 mm, water/acetonitrile/0.1% TFA. HPLC: 98 %; t_R = (LC/PDA: Xterra 1S column, 4.6 x 20mm 3.5µ column; 2.0 ml/min, gradient 5-95% B over 6 min, Solvent A: H_2O with 0.1% TFA; Solvent B: acetonitrile with 0.1 TFA; UV 254): 1.45 min; MS (m/z): 488 $(MH)^+$. ^1H NMR (MeOD, 400 MHz): δ 2.07 (t, 4H, *J* = 6.0 Hz), 2.24 (s, 3H), 2.97 (s, 3H), 3.19 (bs, 2H), 3.41 (t, 4H, *J* = 6.0 Hz), 3.57(bs, 2H), 4.38 (bs, 2H), 7.18 (s, 1H), 7.32-7.33 (m, 3H), 7.39 (d, 1H, *J* = 16.7 Hz), 7.45 (d, 1H, *J* = 16.7 Hz), 7.67 (bs, 1H), 8.07 (s, 1H).

Example 4 (Compound 181)

Preparation of 5-Chloro-6-ethanesulfonyl-3-styryl-1*H*-indazole

Step 1 Displacement of Cl with thiol ether

To a pre-stirred solution of 5-chloro-3-iodo-6-nitro-1-(tetrahydro-pyran-2-yl)-1*H*-indazole (**VI e**) (1.230 g, 3.0 mmol) and potassium carbonate(0.900 g, 6.5 mmol) in *N*,*N*-dimethylformamide (15 mL) was added ethanethiol (400 µL, 5.4 mmol). The resulting solution was heated to 95°C for 20 hours and then cooled to room temperature. Deionized water (15 mL) was added and the reaction mixture was allowed to stir for 15 minutes. The aqueous layer was extracted with ethyl acetate (10 mL) twice. The combined organic layer was washed with brine, dried (sodium sulfate), filtered and concentrated in *vacuo*. The product 5-chloro-6-ethylsulfanyl-3-iodo-1-(tetrahydro-pyran-2-yl)-1*H*-indazole was precipitated using methanol and obtained as a yellow solid (0.987 g, 78% yield). MS (m/z): 422 $(MH)^+$.

Step2 Suzuki coupling

To a pre-stirred solution of 5-chloro-6-ethylsulfanyl-3-iodo-1-(tetrahydro-pyran-2-yl)-1*H*-indazole (0.200 g, 0.47 mmol) and *trans*-phenylvinylboronic acid (0.100 g, 0.68 mmol) in dry toluene (2 mL) was added catalytic amount of tetrakis(triphenylphosphine)palladium(0), followed by methanol (0.5 mL). Saturated

sodium hydrogen carbonate solution (2 mL) was added, and the resulting mixture was heated to 110°C for 4 hours and then cooled to room temperature. Deionized water (5 mL) was added and the reaction mixture was allowed to stir for 15 minutes. The aqueous layer was extracted with ethyl acetate (5 mL) twice. The combined organic layer was washed with brine, dried (sodium sulfate), filtered and concentrated in *vacuo*. The product 5-chloro-6-ethylsulfanyl-3-styryl-1-(tetrahydro-pyran-2-yl)-1*H*-indazole was precipitated using methanol and obtained as a yellow solid (0.155 g, 83 % yield). MS (m/z): 400 $(MH)^+$.

Step 3 Oxidation of thioether to sulfone

3-Chloroperoxybenzoic acid (0.100 g. 0.58 mmol) was added to a pre-stirred solution of 5-chloro-6-ethylsulfanyl-3-styryl-1-(tetrahydro-pyran-2-yl)-1*H*-indazole (0.100 g, 0.25 mmol) in acetonitrile (2 mL). The resulting solution was heated to 70°C for 20 hours and then cooled to room temperature. Saturated sodium hydrosulfide solution was added and the reaction mixture was allowed to stir for 15 minutes. The aqueous layer was extracted with dichloromethane (5 mL) twice. The combined organic layer was washed with brine, dried (sodium sulfate), filtered and concentrated in *vacuo*. The product 5-chloro-6-ethanesulfonyl-3-styryl-1-(tetrahydro-pyran-2-yl)-1*H*-indazole was obtained as a yellow solid (0.087 g, 81 % yield). MS (m/z): 431 $(MH)^+$.

Step 4 THP deprotection

The titled compound was prepared by THP deprotection of 5-chloro-6-ethanesulfonyl-3-styryl-1-(tetrahydro-pyran-2-yl)-1*H*-indazole (0.030 g, 0.07 mmol) using the procedure described in step 5 of Example 1. It was obtained as a yellow solid (0.021 g, 86%). HPLC: 93%; t_R = (LC/PDA: Xterra 1S column, 4.6 x 20mm 3.5µ column; 2.0 ml/min, gradient 5-95% B over 6 min, Solvent A: H_2O with 0.1% TFA; Solvent B: acetonitrile with 0.1 TFA; UV 254): 3.57 min; ^1H NMR (400 MHz, $CDCl_3$): δ 8.55 (s, 1H), 8.22 (s, 1H), 7.45 – 7.71 (m, 1H), 7.66 – 7.64 (m, 2H), 7.46 – 4.40 (m, 4H), 3.76 (q, J = 7.5 Hz, 2H), 1.32 (t, J = 7.5 Hz, 3H); MS (m/z): 347 $(MH)^+$.

Example 5 (Compound 222)

Preparation of *N*-{3-[3-(4-Methyl-piperazin-1-ylmethyl)-phenylethynyl]-6-pyrrolidin-1-yl-1*H*-indazol-5-yl}-acetamide

Step 1 Sonogashira coupling

3-Iodo-5-nitro-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazole was prepared by the displacement reaction of (**VI b**) which was described in step 1 of Example 1. To a pre-stirred solution of 3-iodo-5-nitro-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-

indazole (1.200 g, 3.35 mmol) and trimethylsilaneacetylene (0.6 mL, 4.25 mmol) in acetonitrile (15 mL), $Pd(OAc)_2$ and triethylamine (1.4 mL, 10.10 mmol) were added. The resulting solution was heated to 70°C for 20 hours and then cooled to room temperature. The solution was filtered through filtering agent celite and concentrated in *vacuo*. The product 5-nitro-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-3-trimethylsilanylethynyl-1*H*-indazole was precipitated using methanol and obtained as a yellow solid (1.018 g, 74 % yield). MS (m/z): 413 $(MH)^+$.

Step 2 TMS deprotection

10% potassium hydroxide solution in ethanol (10 mL) was added to 5-nitro-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-3-trimethylsilanylethynyl-1*H*-indazole (1.018 g, 2.47 mmol) and the resulting solution was allowed to stir for 1 hour. Deionized water (10 mL) was added and the reaction mixture was allowed to stir another 15 min. The reaction mixture was concentrated to one-fourth its volume. The aqueous layer was extracted with ethyl acetate (10 mL) twice. The combined organic layer was washed with brine, dried (sodium sulfate), filtered and concentrated in *vacuo*. The product 3-ethynyl-5-nitro-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazole precipitated using methanol and was obtained as a yellow solid (0.801 g, 96 % yield). MS (m/z): 341 $(MH)^+$.

Step 3 NO_2 reduction

3-Ethynyl-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazol-5-ylamine was prepared by reduction of 3-ethynyl-5-nitro-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazole (0.150 g, 0.44 mmol) using the procedure described in step 2 of Example 1 (0.115g, 84%). MS (m/z): 311 $(MH)^+$.

Step 4 Acetylation

N-[3-Ethynyl-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazol-5-yl]-acetamide was prepared by acetylation of 3-ethynyl-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazol-5-ylamine (0.115g, 0.37 mmol) using the procedure described in step 3 of Example 1 by using appropriate starting materials (0.096g, 73%). MS (m/z): 353 $(MH)^+$.

Step 5 Reductive amination

1-(3-Iodo-benzyl)-4-methyl-piperazine was prepared by reductive amination of 3-iodobenzaldehyde (0.341 g, 1.47 mmol) using the procedure described in step 4 of Example 1 by using appropriate starting materials (0.389 g, 84%). MS (m/z): 317 $(MH)^+$.

Step 6 Sonogashira Coupling

N-[3-[3-(4-Methyl-piperazin-1-ylmethyl)-phenylethynyl]-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazol-5-yl]-acetamide was prepared by Sonogashira coupling of *N*-[3-Ethynyl-6-pyrrolidin-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazol-5-yl]-acetamide (0.059 g, 0.17 mmol) and 1-(3-Iodo-benzyl)-4-methyl-piperazine (0.060 g, 0.19 mmol) using the procedure described in step 1 of this example (0.062 g, 68%). MS (m/z): 541 $(MH)^+$.

Step 7 THP deprotection

The titled compound was prepared by THP deprotection of 5-chloro-6-ethanesulfonyl-3-styryl-1-(tetrahydro-pyran-2-yl)-1*H*-indazole (0.062 g, 0.11 mmol) using the procedure described in step 5 of Example 1. It was obtained as a yellow solid (0.041 g, 78%). HPLC: 96 %; t_R = (LC/PDA: Xterra 1S column, 4.6 x 20mm 3.5µ column; 2.0 ml/min, gradient 5-95% B over 6 min, Solvent A: H_2O with 0.1% TFA; Solvent B: acetonitrile with 0.1 TFA; UV 254): 1.32 min; MS (m/z): 457 $(MH)^+$.

Example 6 (Compound 4)

Preparation of N-{6-Methyl-3-[2-(3-nitro-phenyl)-cyclopropyl]-1H-indazol-5-yl}-2-phenyl-acetamide

Step 1 Reduction of NO_2

3-Iodo-5-nitro-6-methyl-1-yl-1-(tetrahydro-pyran-2-yl)-1*H*-indazole was reduced to 3-Iodo-6-methyl-1-(tetrahydro-pyran-2-yl)-1H-indazol-5-ylamine using the procedure described in step 2 of Example 1. MS (m/z): 358 $(MH)^+$.

Step 2 Acylation

N-[3-Iodo-6-methyl-1-(tetrahydro-pyran-2-yl)-1H-indazol-5-yl]-2-phenyl-acetamide was prepared from 3-Iodo-6-methyl-1-(tetrahydro-pyran-2-yl)-1H-indazol-5-ylamine using the procedure described in step 3 of Example 1. The crude mixture was passed through a short plug of Si and flush with CH_2Cl_2 and 50 % ethyl acetate-hexane mixture to yield a pale orange solid. MS (m/z): 476 $(MH)^+$.

Step 3 Heck coupling

N-[6-Methyl-3-[2-(3-nitro-phenyl)-vinyl]-1-(tetrahydro-pyran-2-yl)-1H-indazol-5-yl]-2-phenyl-acetamide was prepared by heck coupling of *N*-[3-Iodo-6-methyl-1-(tetrahydro-pyran-2-yl)-1H-indazol-5-yl]-2-phenyl-acetamide and 1-nitro-3-vinyl-benzene using the

procedure described in step 1 of Example 2 The mixture was diluted with CH_2Cl_2 (20 mL) and washed twice with DI water (20 mL x 2). The combined organic layer was dried and concentrated under reduced pressure. MeOH was added to the residue to precipitate out the desired product as a yellow solid. MS (m/z): 497 $(MH)^+$.

Step 4 Cyclopropanation

To an ice-cold solution of N-[6-Methyl-3-[2-(3-nitro-phenyl)-vinyl]-1-(tetrahydro-pyran-2-yl)-1H-indazol-5-yl]-2-phenyl-acetamide (0.270g, 0.554 mmol) and $Pd(OAc)_2$ (0.006g, 0.027 mmol) in a mixture of CH_2Cl_2 (10 mL) and 1,4-dioxane (2 mL) was added freshly prepared 1M CH_2N_2 in Et_2O (40 mL) drop-wise carefully. The resulting mixture was stirred at 0 °C for 1hour. The product was filtered through celite, and purified by column (EtOAc/hexane) to obtain N-[6-Methyl-3-[2-(3-nitro-phenyl)-cyclopropyl]-1-(tetrahydro-pyran-2-yl)-1H-indazol-5-yl]-2-phenyl-acetamide in 0.175 g, 63% yield . MS (m/z): 511 $(MH)^+$.

Step 5 THP deprotection

The titled compound was prepared by THP deprotection of N-[6-Methyl-3-[2-(3-nitro-phenyl)-cyclopropyl]-1-(tetrahydro-pyran-2-yl)-1H-indazol-5-yl]-2-phenyl-acetamide (0.175 g, 0.343 mmol) using the procedure described in step 5 of Example 1. It was obtained as a yellow solid (0.041 g, 78%). MS (m/z): 427 $(MH)^+$.

Example 7

Preparation of 4-Methyl-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1H-indazole-5-carboxylic acid (208)

Step 1 cyano formation

To a solution of 4-methyl-1H-indazol-5-ylamine (2g, 15.3mmol) cooled in ice (50g) was added concentrated hydrochloric acid (3.25ml) and then a solution of sodium nitrite (1g, 15mmol) in water (3ml). The mixture was stirred at 0 °C for 30 min then was added a solution of sodium cyanide (2.21g, 45mmol) and copper cyanide (1.5g, 16.7mmol) in water (5mL) and ethyl acetate (24mL) at 0 °C. The mixture was stirred at 0 °C for 30 min, 3 hrs at room temperature then heated at 50 °C briefly and cooled to room temperature. The mixture was filtrated through Celite. The layers were separated and the organic phase was washed with brine and dried. The crude was purified by flash chromatography (hexane/ethyl acetate:80/20) giving the 4-methyl-1H-indazole-5-carbonitrile in 38% yield. MS (m/z): 158 $(MH)^+$.

Step 2 Iodination and THP protection

3-Iodo-4-methyl-1-(tetrahydro-pyran-2-yl)-1H-indazole-5-carbonitrile was prepared using standard procedure as described in previous examples.

Step 3 Heck coupling

3-[2-(3-Formyl-phenyl)-vinyl]-4-methyl-1-(tetrahydro-pyran-2-yl)-1H-indazole-5-carbonitrile was prepared by Heck coupling of 3-iodo-4-methyl-1-(tetrahydro-pyran-2-yl)-1H-indazole-5-carbonitrile and 3-Vinyl-benzaldehyde using the procedure described in step 1 of Example 2. The mixture was diluted with CH_2Cl_2 (20 mL) and washed twice with DI water (20 mL x 2). The combined organic layer was dried and concentrated under reduced pressure. MeOH was added to the residue to precipitate the desired product as a yellow solid. MS (m/z): 378 $(MH)^+$.

Step 4 Reductive amination

4-Methyl-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1-(tetrahydro-pyran-2-yl)-1H-indazole-5-carbonitrile was prepared using the procedure described in step 4 of Example 1 by using appropriate starting materials. MS (m/z): 427 $(MH)^+$.

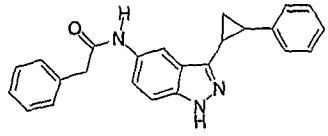
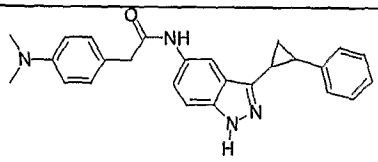
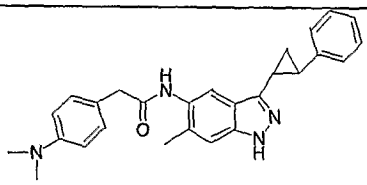
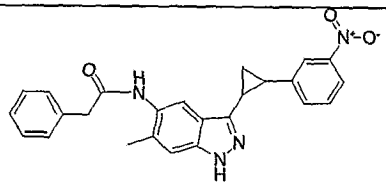
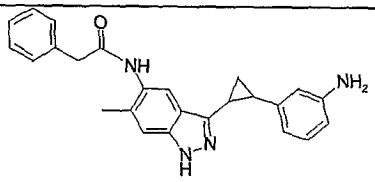
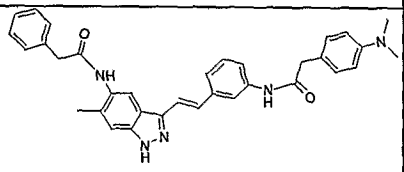
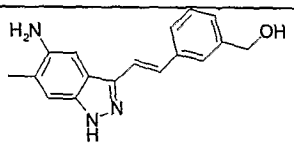
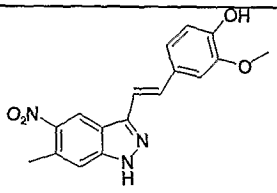
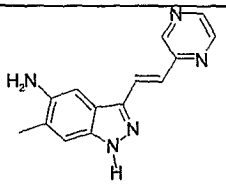
Step 5 THP deprotection

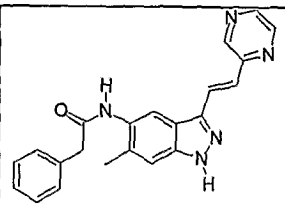
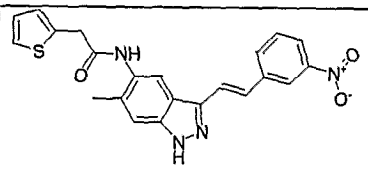
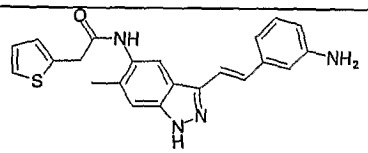
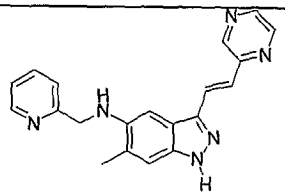
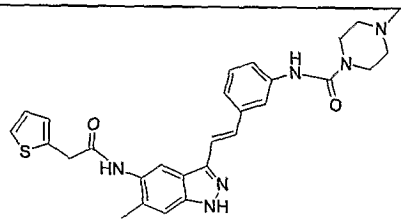
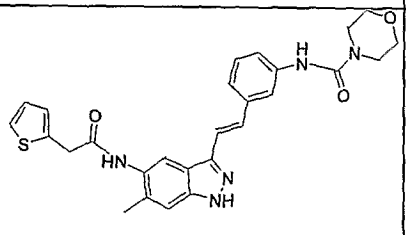
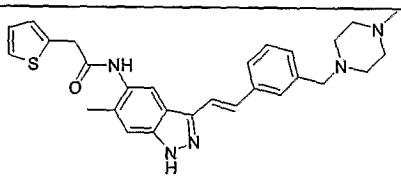
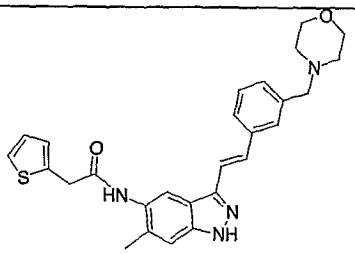
4-Methyl-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1H-indazole-5-carbonitrile was prepared by THP deprotection of 4-Methyl-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1-(tetrahydro-pyran-2-yl)-1H-indazole-5-carbonitrile (80 mg, 0.188 mmol) using the procedure described in step 5 of Example 1. MS (m/z): 359 $(MH)^+$.

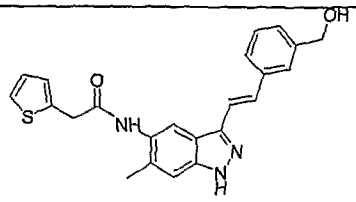
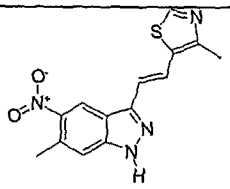
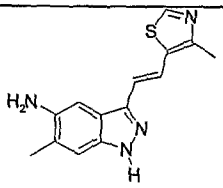
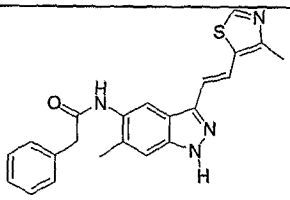
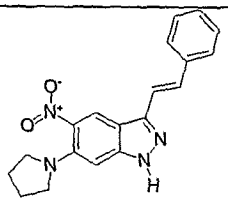
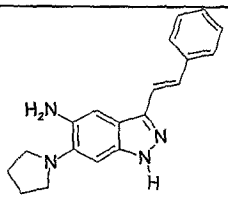
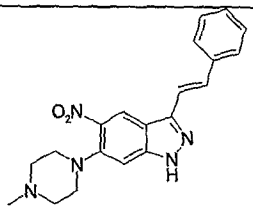
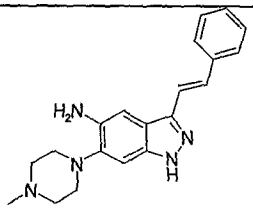
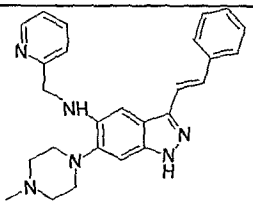
Step 6 Conversion to acid

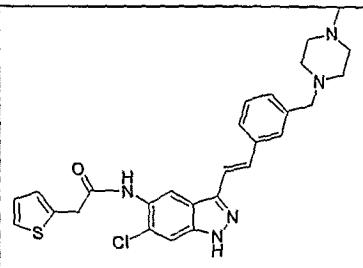
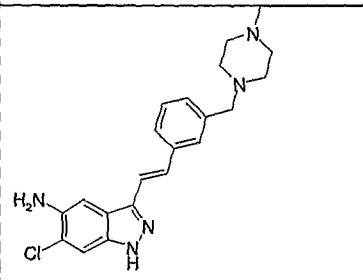
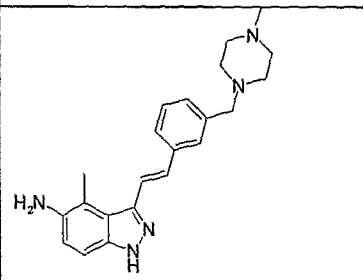
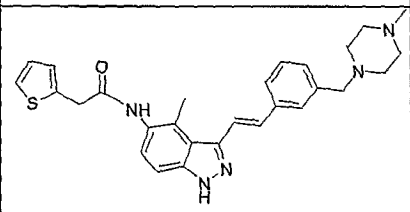
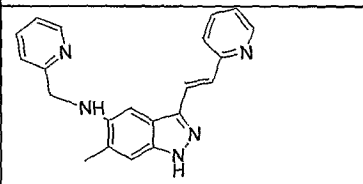
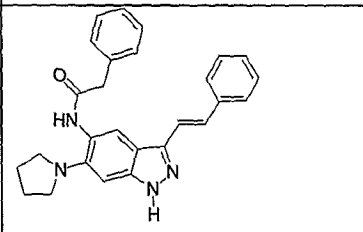
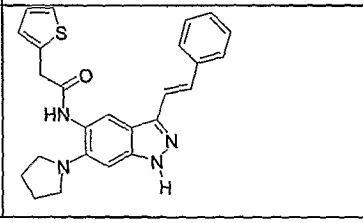
4-Methyl-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1H-indazole-5-carboxylic acid was prepared by heating 4-Methyl-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1H-indazole-5-carbonitrile in a mixture of acetic acid, sulfuric acid and water at 100 °C. The mixture was neutralized with sodium carbonate and the compound precipitated, then filtrated and washed with cold water. The compound was obtained in 71% yield. MS (m/z): 378 $(MH)^+$.

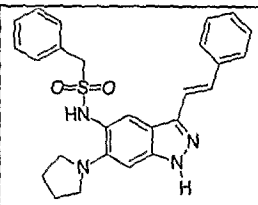
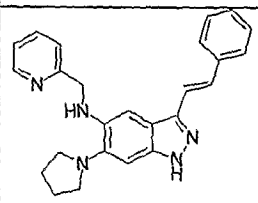
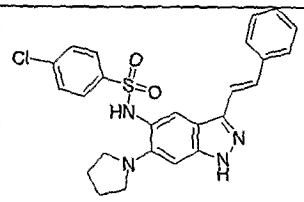
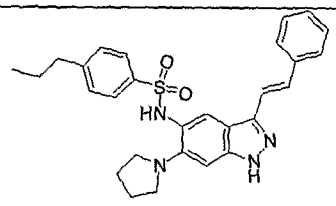
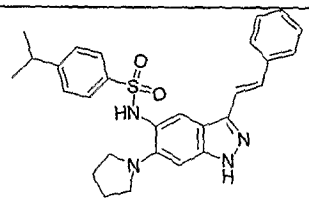
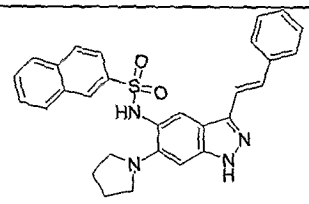
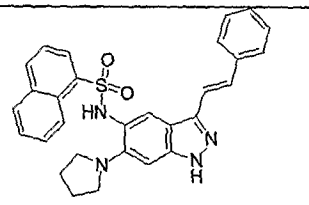
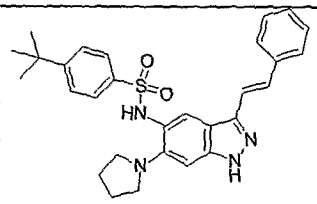
The following preferred compounds are representative examples prepared by methods disclosed or analogous to those disclosed in above Examples 1-7:

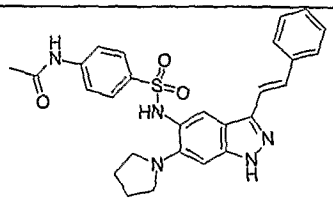
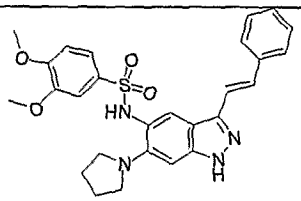
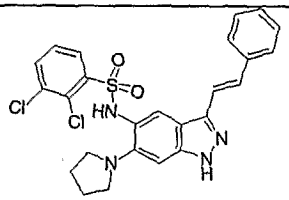
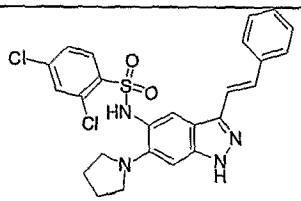
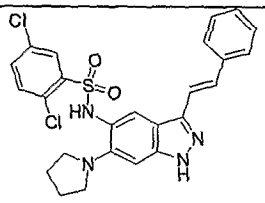
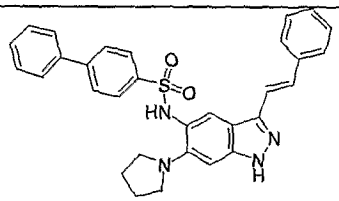
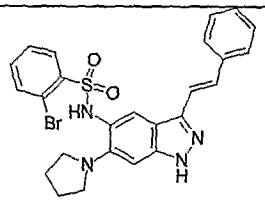
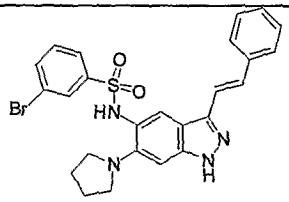
Cmpd No	Structures	Name	m/z [MH]+	Scheme
1		2-Phenyl-N-[3-(2-phenyl-cyclopropyl)-1H-indazol-5-yl]-acetamide	368	VI
2		2-(4-Dimethylamino-phenyl)-N-[3-(2-phenyl-cyclopropyl)-1H-indazol-5-yl]-acetamide	411	VI
3		2-(4-Dimethylamino-phenyl)-N-[6-methyl-3-(2-phenyl-cyclopropyl)-1H-indazol-5-yl]-acetamide	425	VI
4		N-{6-Methyl-3-[2-(3-nitro-phenyl)-cyclopropyl]-1H-indazol-5-yl}-2-phenyl-acetamide	427	VI
5		N-{3-[2-(3-Amino-phenyl)-cyclopropyl]-6-methyl-1H-indazol-5-yl}-2-phenyl-acetamide	397	VI
6		2-(4-Dimethylamino-phenyl)-N-{3-[2-(6-methyl-5-phenylacetylamino-1H-indazol-3-yl)-vinyl]-phenyl}-acetamide	544	III
7		{3-[2-(5-Amino-6-methyl-1H-indazol-3-yl)-vinyl]-phenyl}-methanol	280	III
8		2-Methoxy-4-[2-(6-methyl-5-nitro-1H-indazol-3-yl)-vinyl]-phenol	326	III
9		6-Methyl-3-(2-pyrazin-2-yl-vinyl)-1H-indazol-5-ylamine	252	IV

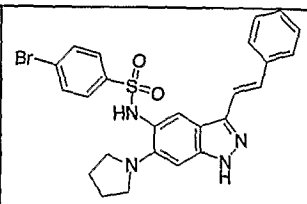
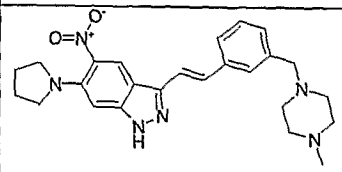
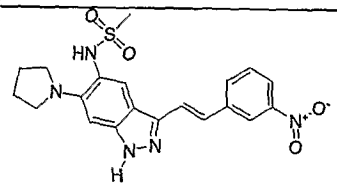
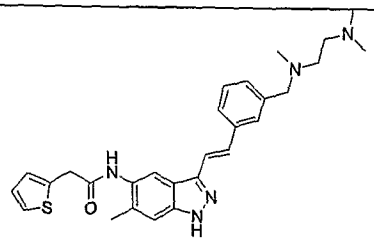
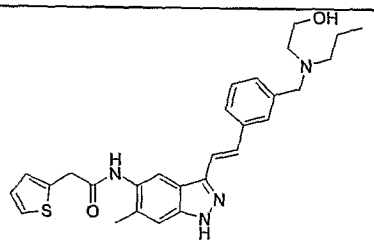
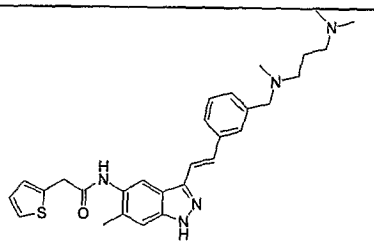
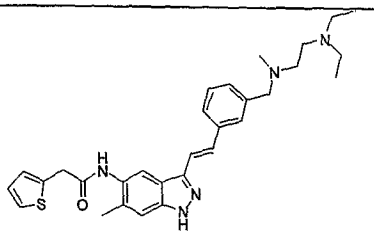
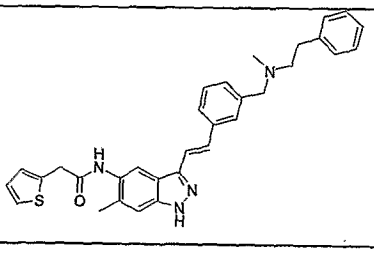
10		N-[6-Methyl-3-(2-pyrazin-2-yl-vinyl)-1H-indazol-5-yl]-2-phenyl-acetamide	370	IV
11		N-{6-Methyl-3-[2-(3-nitro-phenyl)-vinyl]-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide	419	V
12		N-{3-[2-(3-Amino-phenyl)-vinyl]-6-methyl-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide	389	V
13		[6-Methyl-3-(2-pyrazin-2-yl-vinyl)-1H-indazol-5-yl]-pyridin-2-ylmethyl-amine	343	IV
14		4-Methyl-piperazine-1-carboxylic acid (3-{2-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-amide	515	V
15		Morpholine-4-carboxylic acid (3-{2-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-amide	502	V
16		N-(6-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	486	III
17		N-{6-Methyl-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide	473	III

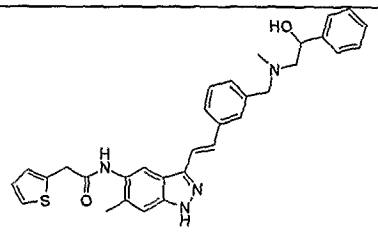
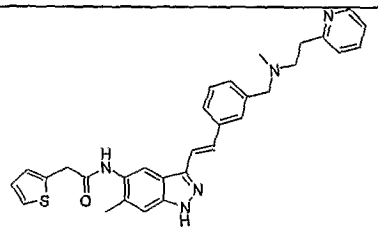
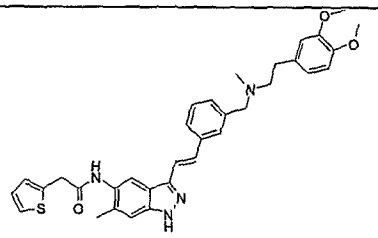
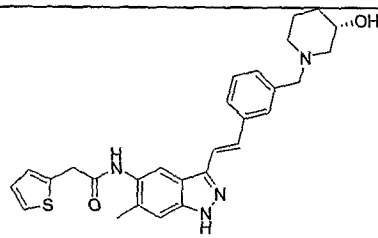
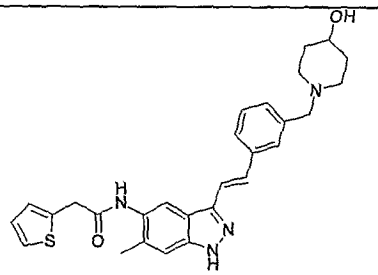
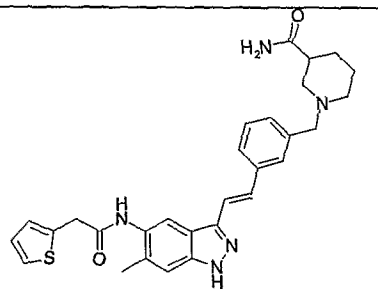
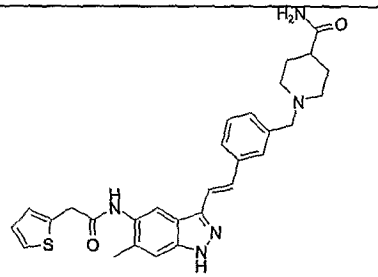
18		N-{3-[2-(3-Hydroxymethyl-phenyl)-vinyl]-6-methyl-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide	404	III
19		6-Methyl-3-[2-(4-methyl-thiazol-5-yl)-vinyl]-5-nitro-1H-indazole	301	IV
20		6-Methyl-3-[2-(4-methyl-thiazol-5-yl)-vinyl]-1H-indazol-5-ylamine	271	IV
21		N-{6-Methyl-3-[2-(4-methyl-thiazol-5-yl)-vinyl]-1H-indazol-5-yl}-2-phenyl-acetamide	389	IV
22		5-Nitro-6-pyrrolidin-1-yl-3-styryl-1H-indazole	335	III
23		6-Pyrrolidin-1-yl-3-styryl-1H-indazol-5-ylamine	305	III
24		6-(4-Methyl-piperazin-1-yl)-5-nitro-3-styryl-1H-indazole	364	III
25		6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-ylamine	334	III
26		[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-pyridin-2-ylmethyl-amine	425	III

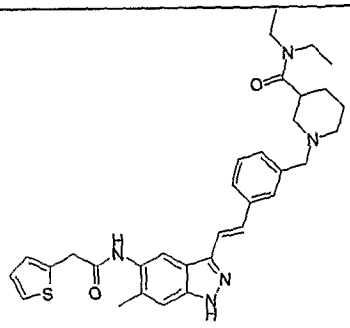
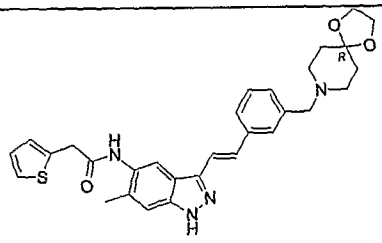
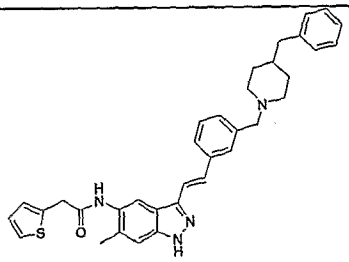
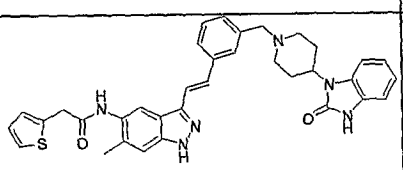
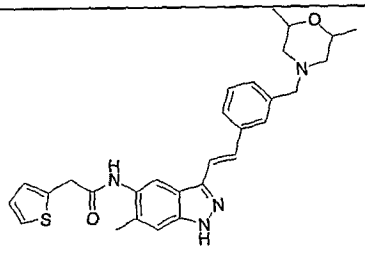
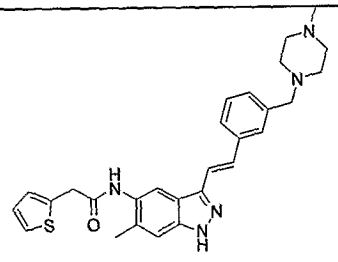
27		N-(6-Chloro-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	507	III
28		6-Chloro-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-ylamine	382	III
29		4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-ylamine	362	III
30		N-(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	486	III
31		[6-Methyl-3-(2-pyridin-2-yl-vinyl)-1H-indazol-5-yl]-pyridin-2-ylmethyl-amine	342	IV
32		2-Phenyl-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-acetamide	423	III
33		N-(6-Pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	429	III

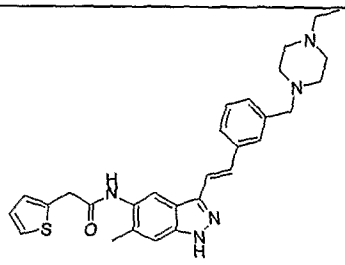
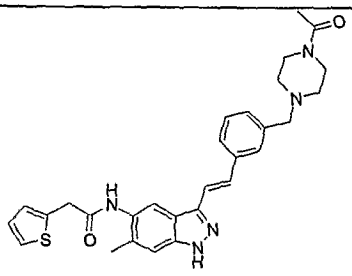
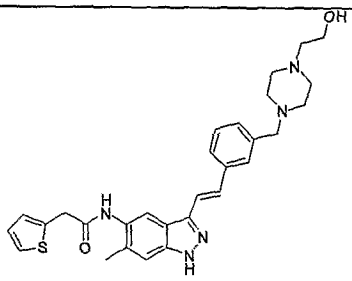
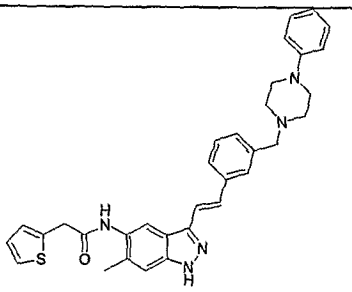
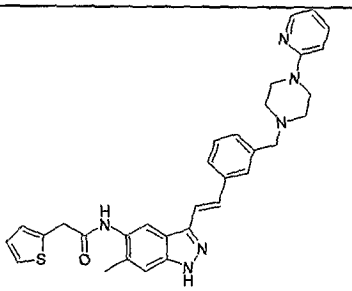
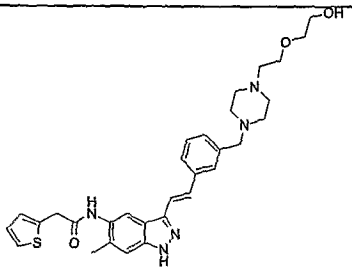
34		C-Phenyl-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-methanesulfonamide	459	III
35		Pyridin-2-ylmethyl-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-amine	396	III
36		4-Chloro-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide	479	III
37		4-Propyl-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide	487	III
38		4-Isopropyl-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide	487	III
39		Naphthalene-2-sulfonic acid (6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-amide	495	III
40		Naphthalene-1-sulfonic acid (6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-amide	495	III
41		4-tert-Butyl-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide	501	III

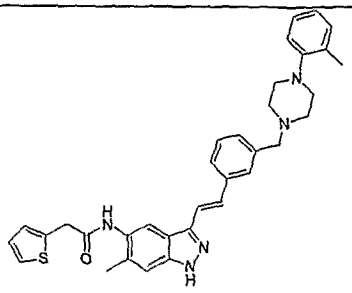
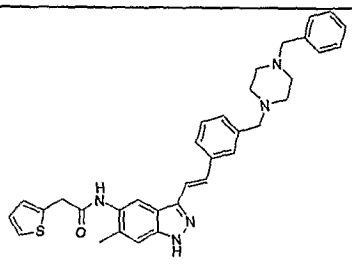
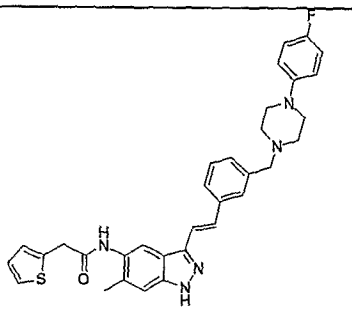
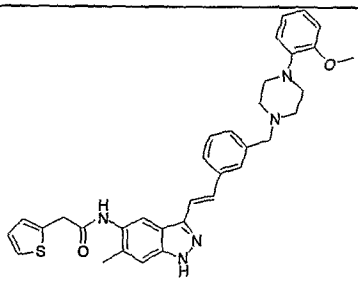
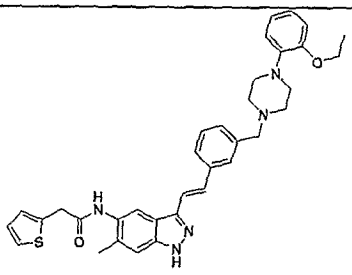
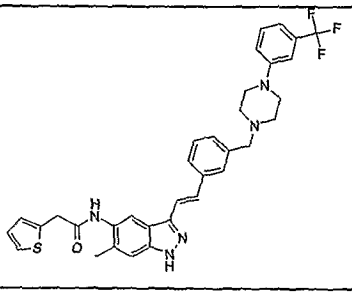
42		N-[4-(6-Pyrrolidin-1-yl-3-styryl-1H-indazol-5-ylsulfamoyl)-phenyl]-acetamide	502	III
43		3,4-Dimethoxy-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide	505	III
44		2,3-Dichloro-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide	513	III
45		2,4-Dichloro-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide	513	III
46		2,5-Dichloro-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide	513	III
47		Biphenyl-4-sulfonic acid (6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-amide	521	III
48		2-Bromo-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide	523	III
49		3-Bromo-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide	523	III

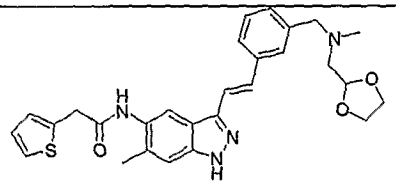
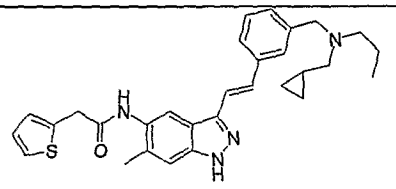
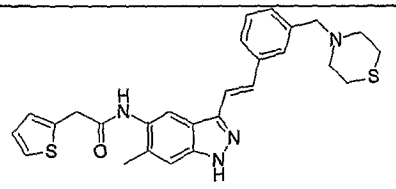
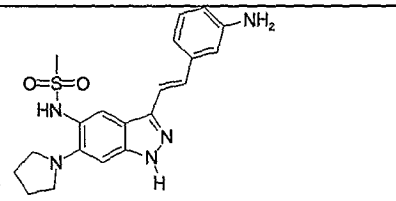
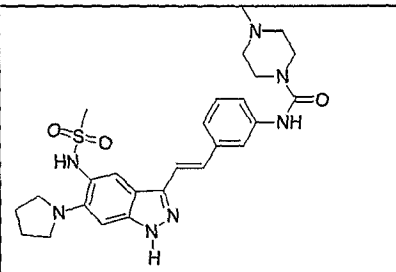
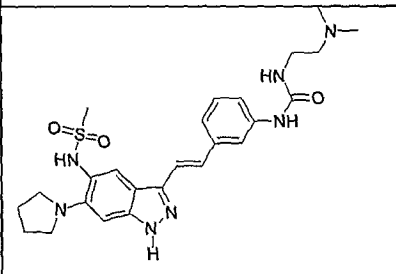
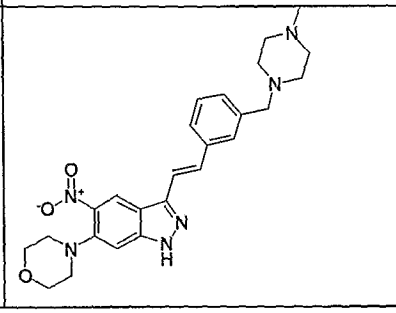
50		4-Bromo-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide	523	III
51		3-{2-[3-(4-Methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-5-nitro-6-pyrrolidin-1-yl-1H-indazole	447	III
52		N-{3-[2-(3-Nitro-phenyl)-vinyl]-6-pyrrolidin-1-yl-1H-indazol-5-yl}-methanesulfonamide	428	III
53		N-{3-[2-(3-{[(2-Dimethylamino-ethyl)-methyl-amino]-methyl}-phenyl)-vinyl]-6-methyl-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide	488	III
54		N-{3-[2-(3-{[(2-Hydroxy-ethyl)-propyl-amino]-methyl}-phenyl)-vinyl]-6-methyl-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide	489	III
55		N-{3-[2-(3-{[(3-Dimethylamino-propyl)-methyl-amino]-methyl}-phenyl)-vinyl]-6-methyl-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide	502	III
56		N-{3-[2-(3-{[(2-Diethylamino-ethyl)-methyl-amino]-methyl}-phenyl)-vinyl]-6-methyl-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide	516	III
57		N-[6-Methyl-3-(2-{3-[(methyl-phenethyl-amino)-methyl]-phenyl}-vinyl)-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide	521	III

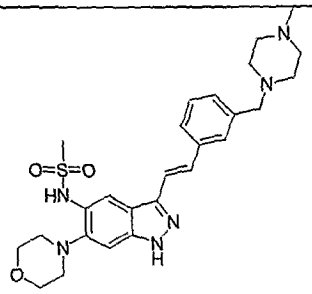
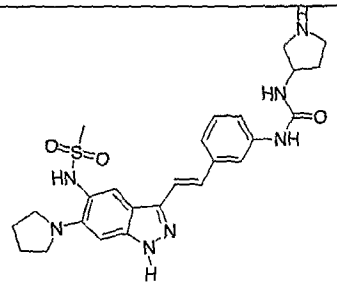
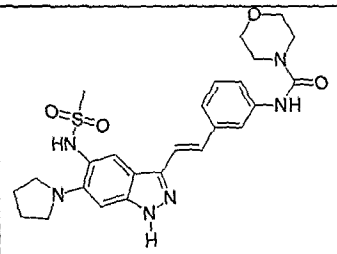
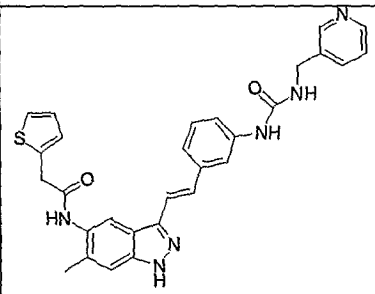
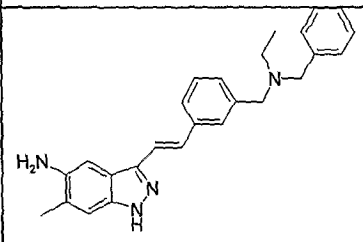
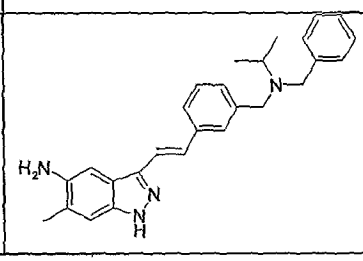
58		N-{3-[2-(3-{[(2-Hydroxy-2-phenyl-ethyl)-methyl-amino]-methyl}-phenyl)-vinyl]-6-methyl-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide	537	III
59		N-{6-Methyl-3-[2-(3-{[methyl-(2-pyridin-2-yl-ethyl)-amino]-methyl}-phenyl)-vinyl]-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide	522	III
60		N-(3-{2-[3-({[2-(3,4-Dimethoxy-phenyl)-ethyl]-methyl-amino}-methyl)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	581	III
61		N-(3-{2-[3-(3-Hydroxy-piperidin-1-ylmethyl)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	487	III
62		N-(3-{2-[3-(4-Hydroxy-piperidin-1-ylmethyl)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	487	III
63		1-(3-{2-[6-Methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-benzyl)-piperidine-3-carboxylic acid amide	514	III
64		1-(3-{2-[6-Methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-benzyl)-piperidine-4-carboxylic acid amide	514	III

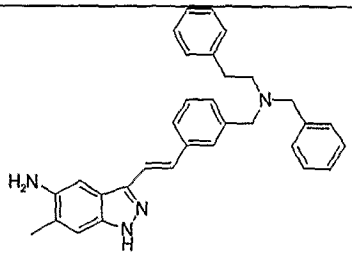
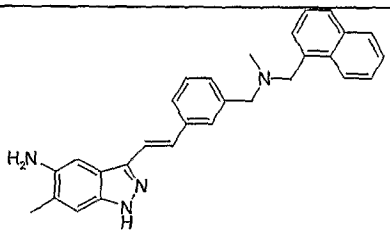
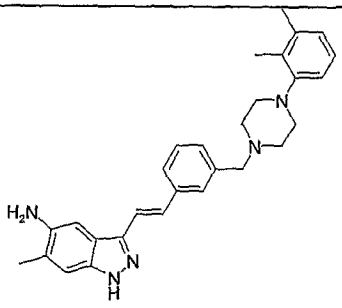
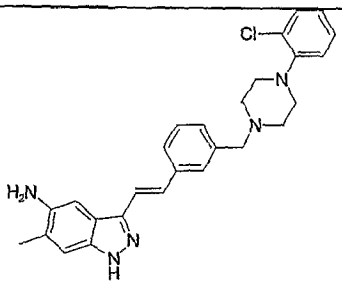
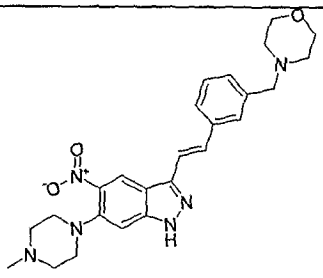
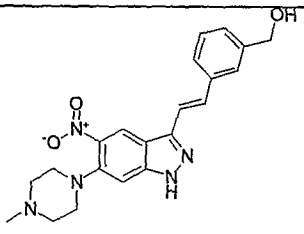
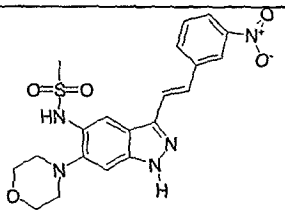
65		1-(3-{2-[6-Methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-benzyl)-piperidine-3-carboxylic acid diethylamide	570	III
66		N-(3-{2-[3-(1,4-Dioxa-8-aza-spiro[4.5]dec-8-ylmethyl)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	529	III
67		N-(3-{2-[3-(4-Benzyl-piperidin-1-ylmethyl)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	561	III
68		N-[6-Methyl-3-(2-{3-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-ylmethyl]-phenyl}-vinyl)-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide	603	III
69		N-(3-{2-[3-(2,6-Dimethyl-morpholin-4-ylmethyl)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	501	III
70		N-(6-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	486	III

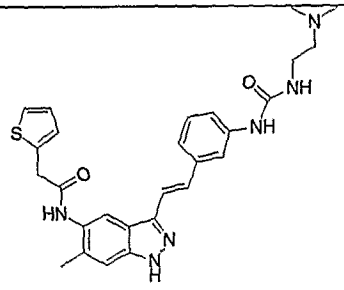
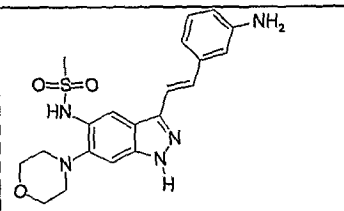
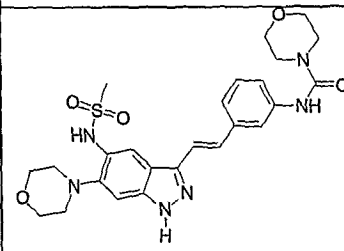
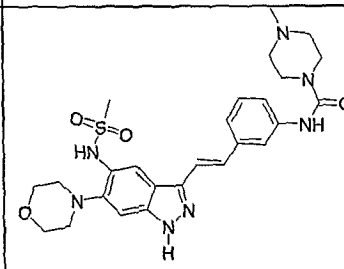
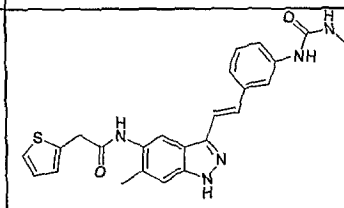
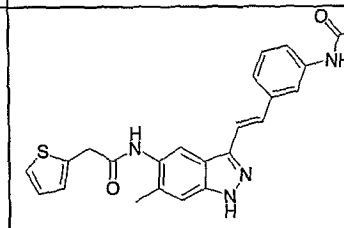
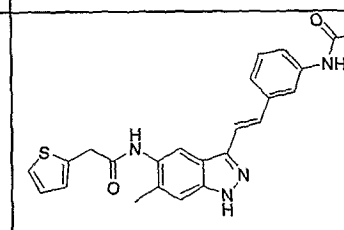
71		N-(3-{2-[3-(4-Ethyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	500	III
72		N-(3-{2-[3-(4-Acetyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	514	III
73		N-[3-(2-{3-[4-(2-Hydroxy-ethyl)-piperazin-1-ylmethyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide	516	III
74		N-(6-Methyl-3-{2-[3-(4-phenyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	548	III
75		N-(6-Methyl-3-{2-[3-(4-pyridin-2-yl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	549	III
76		N-{3-[2-(3-{4-[2-(2-Hydroxy-ethoxy)-ethyl]-piperazin-1-ylmethyl}-phenyl)-vinyl]-6-methyl-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide	560	III

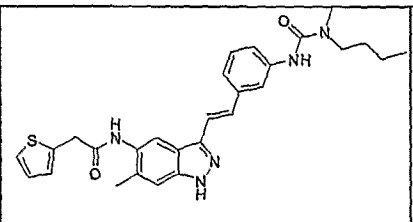
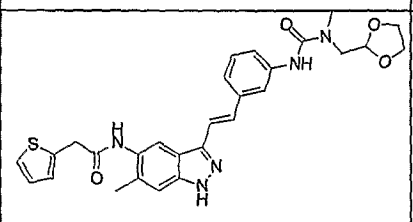
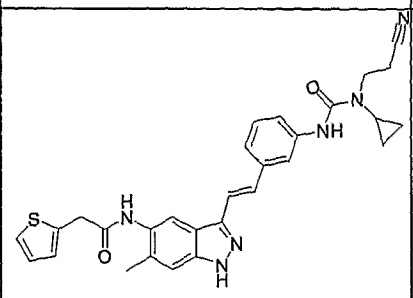
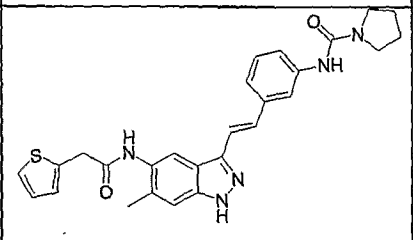
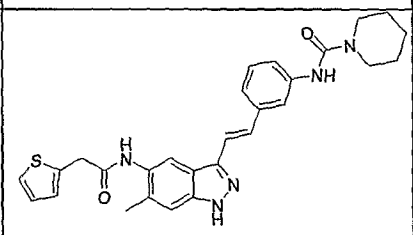
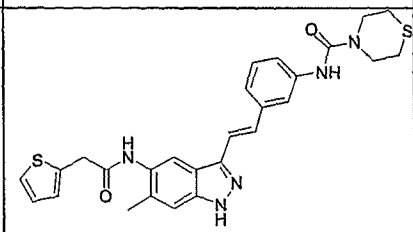
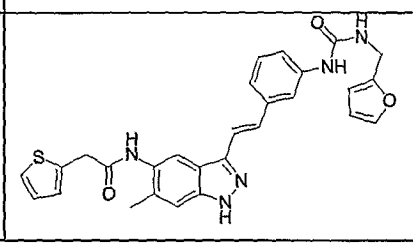
77		N-(6-Methyl-3-{2-[3-(4-o-tolyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	562	III
78		N-(3-{2-[3-(4-Benzyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	562	III
79		N-[3-(2-{3-[4-(4-Fluoro-phenyl)-piperazin-1-ylmethyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide	566	III
80		N-[3-(2-{3-[4-(2-Methoxy-phenyl)-piperazin-1-ylmethyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide	578	III
81		N-[3-(2-{3-[4-(2-Ethoxy-phenyl)-piperazin-1-ylmethyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide	592	III
82		N-[6-Methyl-3-(2-{3-[4-(3-trifluoromethyl-phenyl)-piperazin-1-ylmethyl]-phenyl}-vinyl)-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide	616	III

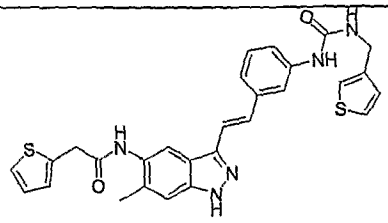
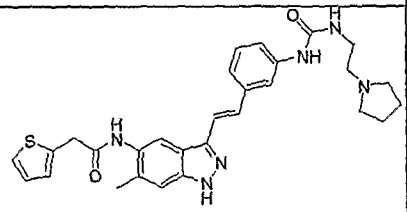
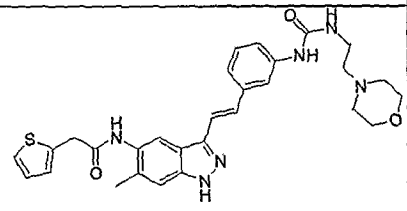
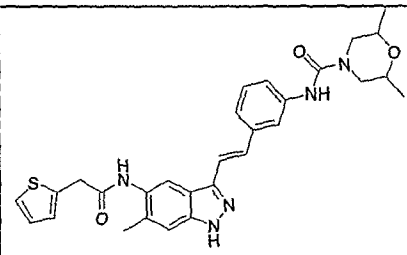
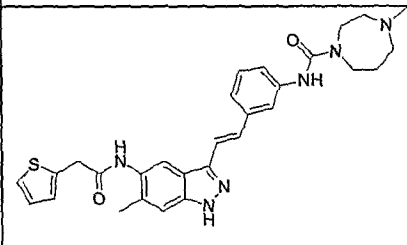
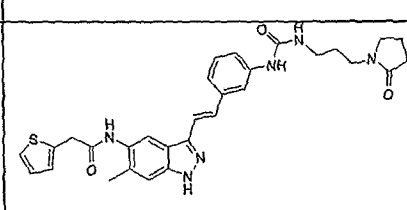
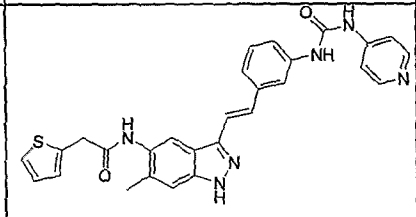
83		N-[3-(2-{3-[([1,3]Dioxolan-2-ylmethyl-methyl-amino)-methyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide	503	III
84		N-[3-(2-{3-[(Cyclopropylmethyl-propyl-amino)-methyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide	499	III
85		N-{6-Methyl-3-[2-(3-thiomorpholin-4-ylmethyl-phenyl)-vinyl]-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide	489	III
86		N-{3-[2-(3-Amino-phenyl)-vinyl]-6-pyrrolidin-1-yl-1H-indazol-5-yl}-methanesulfonamide	398	III
87		4-Methyl-piperazine-1-carboxylic acid {3-[2-(5-methanesulfonylamino-6-pyrrolidin-1-yl-1H-indazol-3-yl)-vinyl]-phenyl}-amide	524	V
88		N-[3-(2-{3-[3-(2-Dimethylamino-ethyl)-ureido]-phenyl}-vinyl)-6-pyrrolidin-1-yl-1H-indazol-5-yl]-methanesulfonamide	512	V
89		3-{2-[3-(4-Methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-6-morpholin-4-yl-5-nitro-1H-indazole	463	III

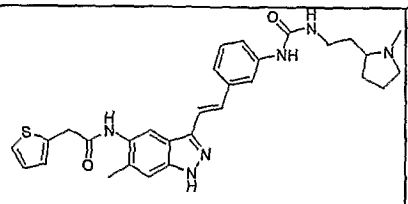
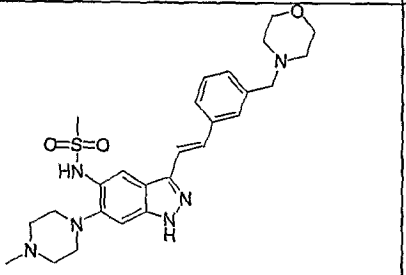
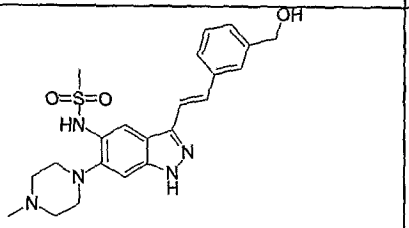
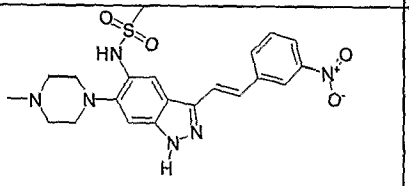
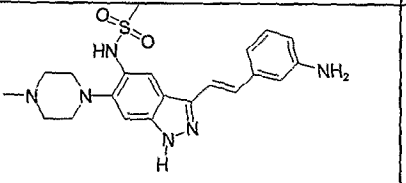
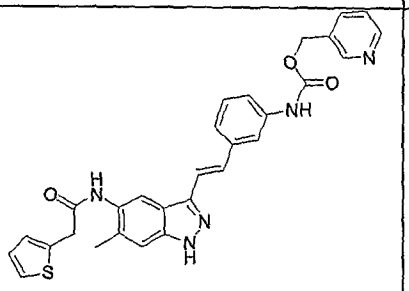
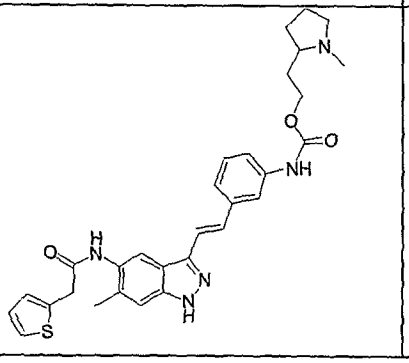
90		N-(3-{2-[3-(4-Methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-6-morpholin-4-yl-1H-indazol-5-yl)-methanesulfonamide	511	III
91		N-(6-Pyrrolidin-1-yl-3-{2-[3-(3-pyrrolidin-3-yl-ureido)-phenyl]-vinyl}-1H-indazol-5-yl)-methanesulfonamide	510	V
92		Morpholine-4-carboxylic acid {3-[2-(5-methanesulfonylamino-6-pyrrolidin-1-yl-1H-indazol-3-yl)-vinyl]-phenyl}-amide	511	V
93		N-(6-Methyl-3-{2-[3-(3-pyridin-3-ylmethyl-ureido)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	523	V
94		3-(2-{3-[(Benzyl-ethyl-amino)-methyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-ylamine	397	III
95		3-(2-{3-[(Benzyl-isopropyl-amino)-methyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-ylamine	411	III

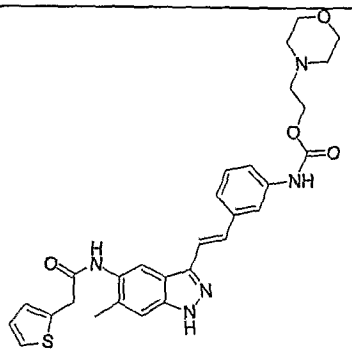
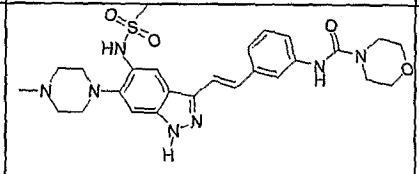
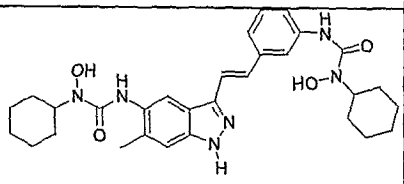
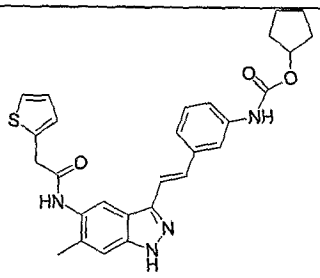
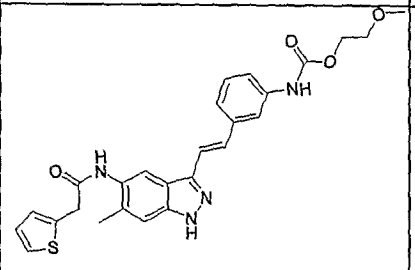
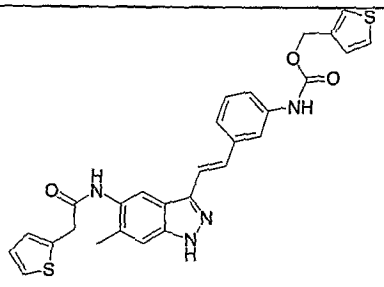
96		3-(2-{3-[(Benzyl-phenethyl-amino)-methyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-ylamine	474	III
97		6-Methyl-3-(2-{3-[(methyl-naphthalen-1-ylmethyl-amino)-methyl]-phenyl}-vinyl)-1H-indazol-5-ylamine	433	III
98		3-(2-{3-[4-(2,3-Dimethyl-phenyl)-piperazin-1-ylmethyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-ylamine	452	III
99		3-(2-{3-[4-(2-Chloro-phenyl)-piperazin-1-ylmethyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-ylamine	459	III
100		6-(4-Methyl-piperazin-1-yl)-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-5-nitro-1H-indazole	463	III
101		(3-{2-[6-(4-Methyl-piperazin-1-yl)-5-nitro-1H-indazol-3-yl]-vinyl}-phenyl)-methanol	394	III
102		N-{6-Morpholin-4-yl-3-[2-(3-nitro-phenyl)-vinyl]-1H-indazol-5-yl}-methanesulfonamide	444	III, V

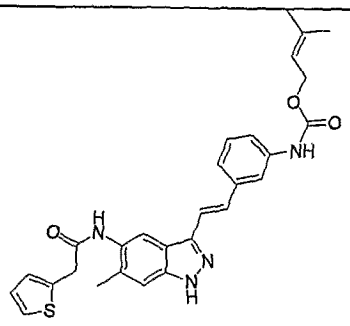
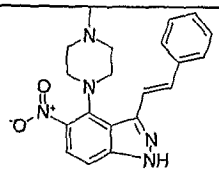
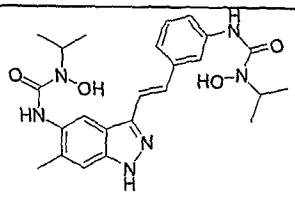
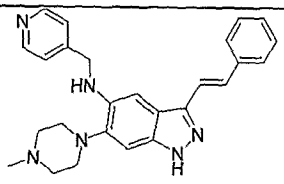
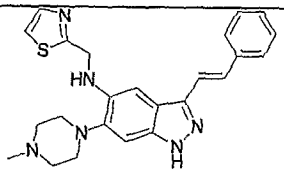
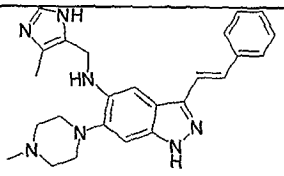
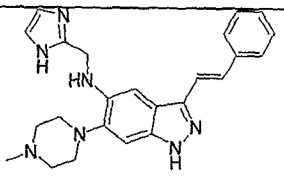
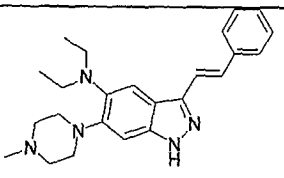
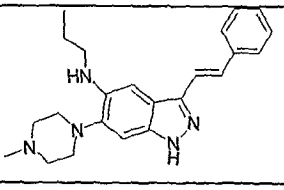
103		N-[3-(2-{3-[3-(2-Dimethylamino-ethyl)-ureido]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide	503	V
104		N-{3-[2-(3-Amino-phenyl)-vinyl]-6-morpholin-4-yl-1H-indazol-5-yl}-methanesulfonamide	414	III, V
105		Morpholine-4-carboxylic acid {3-[2-(5-methanesulfonylamino-6-morpholin-4-yl-1H-indazol-3-yl)-vinyl]-phenyl}-amide	527	III, V
106		4-Methyl-piperazine-1-carboxylic acid {3-[2-(5-methanesulfonylamino-6-morpholin-4-yl-1H-indazol-3-yl)-vinyl]-phenyl}-amide	540	III, V
107		N-[3-(2-{3-[3-(2-Methoxy-ethyl)-ureido]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide	490	V
108		N-(3-{2-[3-(3-Cyclopropyl-ureido)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	472	V
109		N-(3-{2-[3-(3-Cyclopentyl-ureido)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	500	V

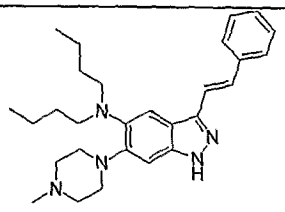
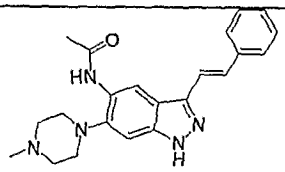
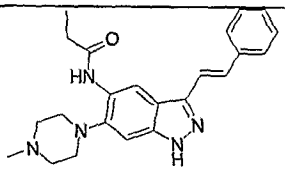
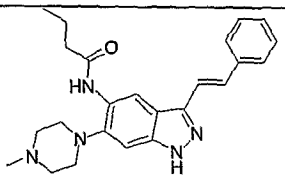
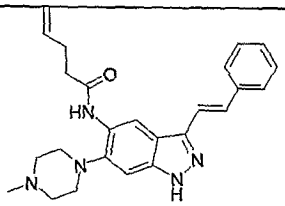
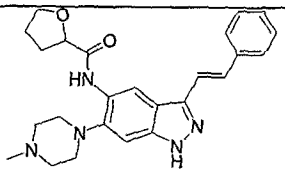
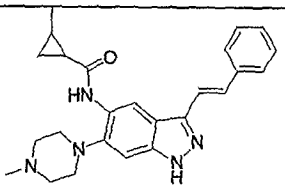
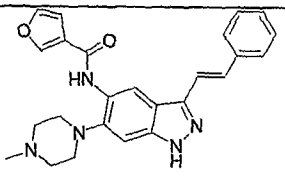
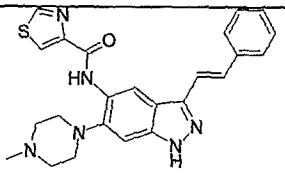
110		N-(3-{2-[3-(3-Butyl-3-methyl-ureido)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	502	V
111		N-(3-{2-[3-(3-[1,3]Dioxolan-2-ylmethyl-3-methyl-ureido)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	531	V
112		N-[3-(2-{3-[3-(2-Cyano-ethyl)-3-cyclopropyl-ureido]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide	525	V
113		Pyrrolidine-1-carboxylic acid (3-{2-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-amide	486	V
114		Piperidine-1-carboxylic acid (3-{2-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-amide	500	V
115		Thiomorpholine-4-carboxylic acid (3-{2-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-amide	518	V
116		N-(3-{2-[3-(3-Furan-2-ylmethyl-ureido)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	512	V

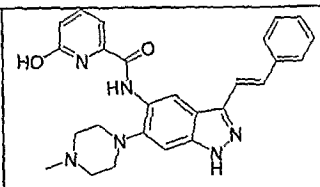
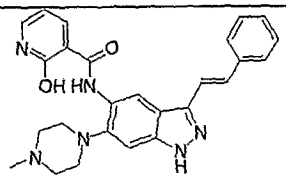
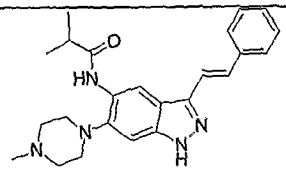
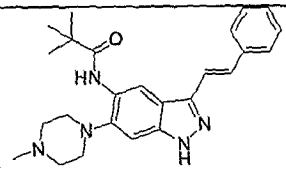
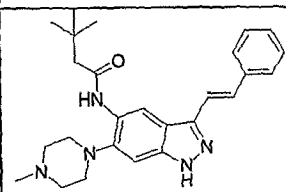
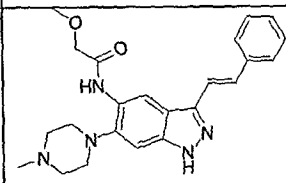
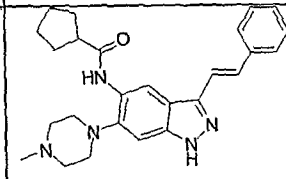
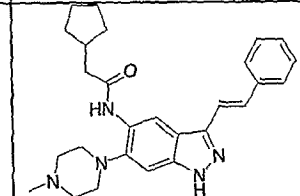
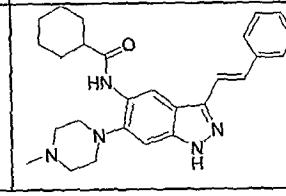
117		N-(6-Methyl-3-{2-[3-(3-thiophen-3-ylmethyl-ureido)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	528	V
118		N-[6-Methyl-3-(2-{3-[3-(2-pyrrolidin-1-yl-ethyl)-ureido]-phenyl}-vinyl)-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide	529	V
119		N-[6-Methyl-3-(2-{3-[3-(2-morpholin-4-yl-ethyl)-ureido]-phenyl}-vinyl)-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide	545	V
120		2,6-Dimethyl-morpholine-4-carboxylic acid (3-{2-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-amide	530	V
121		4-Methyl-[1,4]diazepane-1-carboxylic acid (3-{2-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-amide	529	V
122		N-{6-Methyl-3-[2-(3-{3-[3-(2-oxo-pyrrolidin-1-yl)-propyl]-ureido}-phenyl)-vinyl]-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide	557	V
123		N-(6-Methyl-3-{2-[3-(3-pyridin-4-yl-ureido)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	509	V

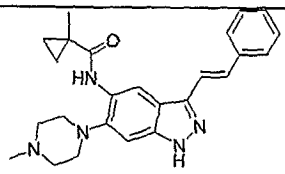
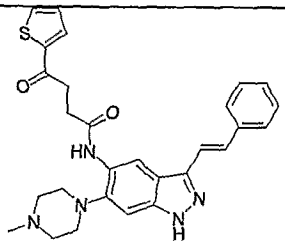
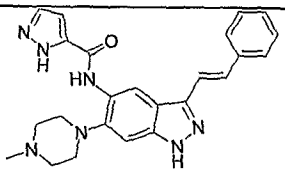
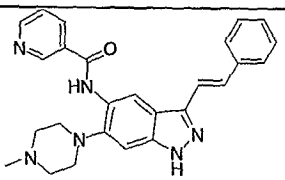
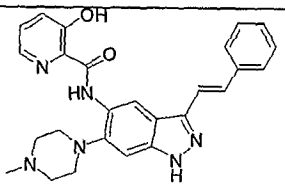
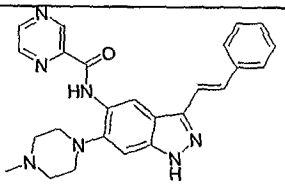
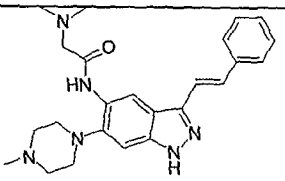
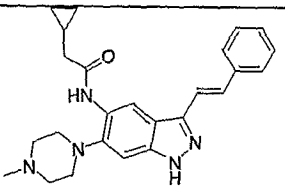
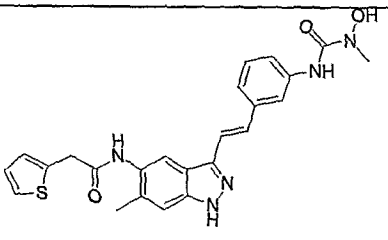
124		N-{6-Methyl-3-[2-(3-{3-[2-(1-methyl-pyrrolidin-2-yl)-ethyl]-ureido}-phenyl)-vinyl]-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide	543	V
125		N-{6-(4-Methyl-piperazin-1-yl)-3-[2-(3-*morpholin*-4-ylmethyl-phenyl)-vinyl]-1H-indazol-5-yl}-methanesulfonamide	511	III
126		N-[3-[2-(3-Hydroxymethyl-phenyl)-vinyl]-6-(4-methyl-piperazin-1-yl)-1H-indazol-5-yl]-methanesulfonamide	442	III
127		N-{6-(4-Methyl-piperazin-1-yl)-3-[2-(3-nitro-phenyl)-vinyl]-1H-indazol-5-yl}-methanesulfonamide	457	III
128		N-[3-[2-(3-Amino-phenyl)-vinyl]-6-(4-methyl-piperazin-1-yl)-1H-indazol-5-yl]-methanesulfonamide	427	III
129		(3-{2-[6-Methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-carbamic acid pyridin-3-ylmethyl ester	524	V
130		(3-{2-[6-Methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-carbamic acid 2-(1-methyl-pyrrolidin-2-yl)-ethyl ester	544	V

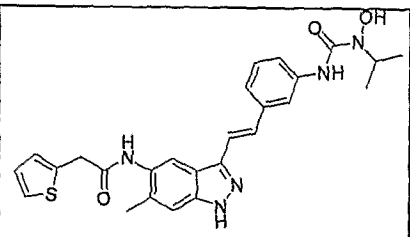
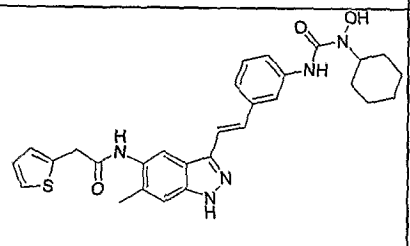
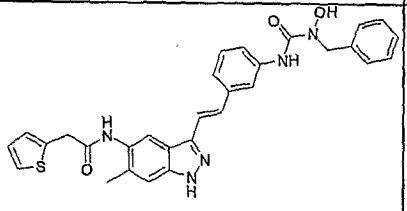
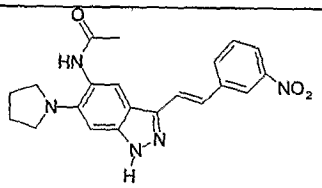
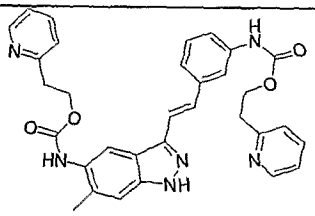
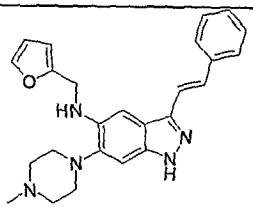
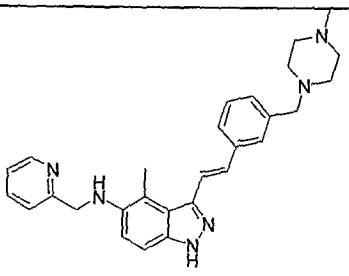
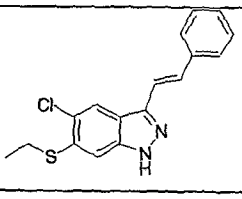
131		(3-{2-[6-Methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-carbamic acid 2-morpholin-4-yl-ethyl ester	546	V
132		Morpholine-4-carboxylic acid (3-{2-[5-methanesulfonylamino-6-(4-methyl-piperazin-1-yl)-1H-indazol-3-yl]-vinyl}-phenyl)-amide	540	V
133			547	V
134		(3-{2-[6-Methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-carbamic acid cyclopentyl ester	501	V
135		(3-{2-[6-Methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-carbamic acid 2-methoxy-ethyl ester	491	V
136		(3-{2-[6-Methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-carbamic acid thiophen-3-ylmethyl ester	529	V

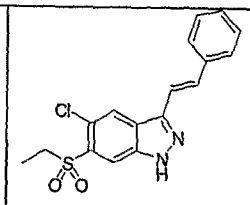
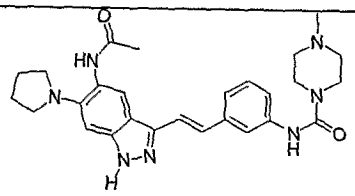
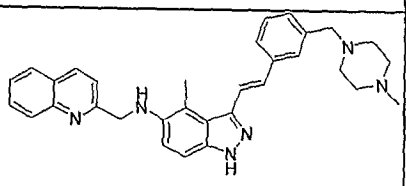
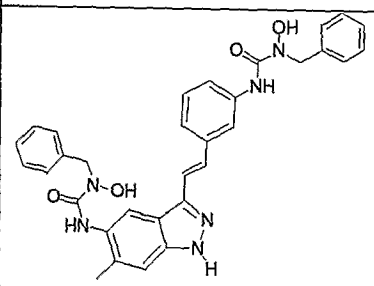
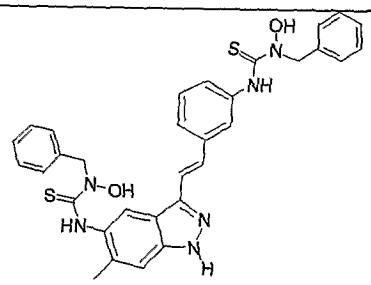
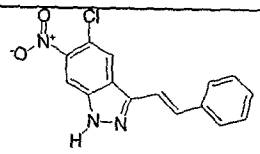
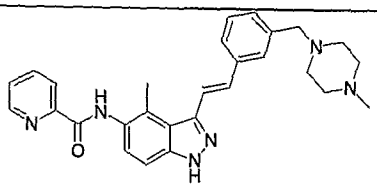
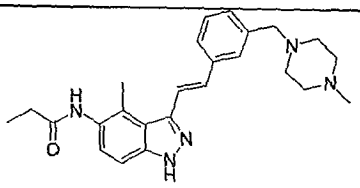
137		(3-{2-[6-Methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-carbamic acid 3-methyl-but-2-enyl ester	501	V
138		4-(4-Methyl-piperazin-1-yl)-5-nitro-3-styryl-1H-indazole	364	III
139			367	V
140		[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-pyridin-4-ylmethyl-amine	425	III
141		[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-thiazol-2-ylmethyl-amine	431	III
142		(5-Methyl-3H-imidazol-4-ylmethyl)-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amine	428	III
143		(1H-Imidazol-2-ylmethyl)-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amine	414	III
144		Diethyl-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amine	390	III
145		[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-propyl-amine	376	III

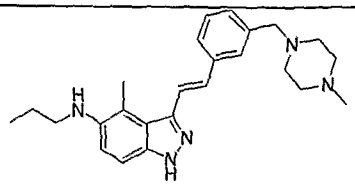
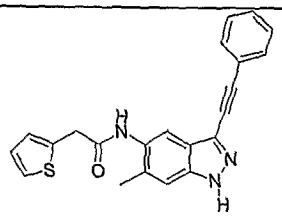
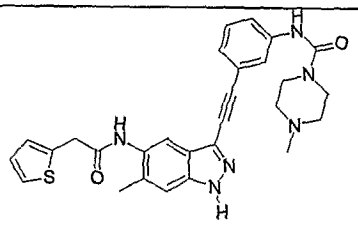
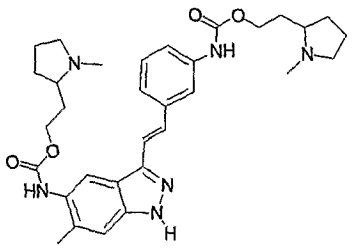
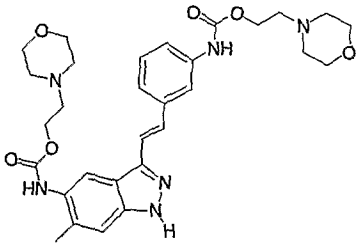
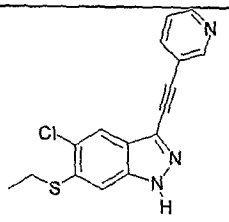
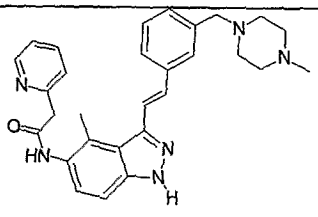
146		Dibutyl-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amine	446	III
147		N-[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-acetamide	376	III
148		N-[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-propionamide	390	III
149		N-[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-butyramide	404	III
150		Pent-4-enoic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide	416	III
151		Tetrahydro-furan-2-carboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide	432	III
152		2-Methyl-cyclopropanecarboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide	416	III
153		Furan-3-carboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide	428	III
154		Thiazole-4-carboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide	445	III

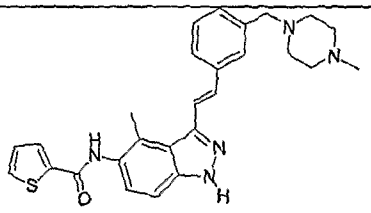
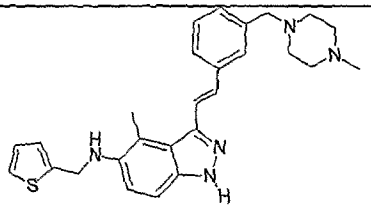
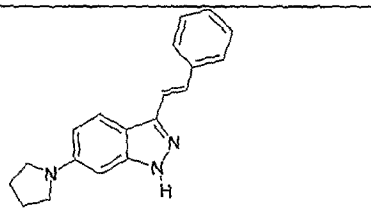
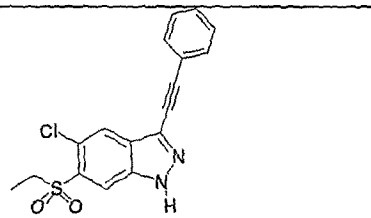
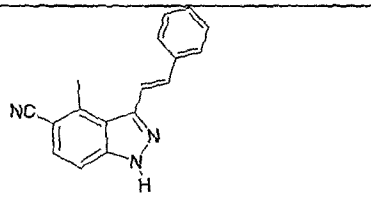
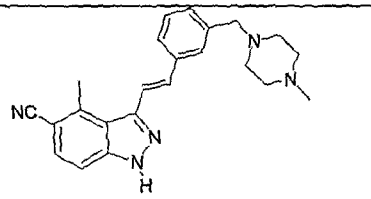
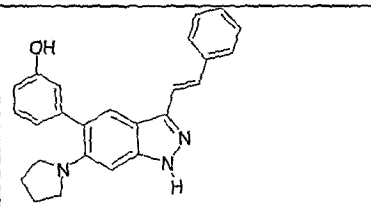
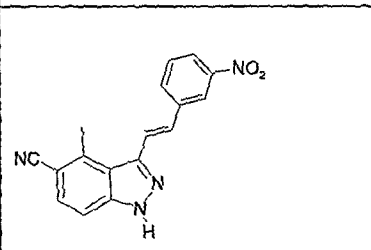
155		6-Hydroxy-pyridine-2-carboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide	455	III
156		2-Hydroxy-N-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-nicotinamide	455	III
157		N-[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-isobutyramide	404	III
158		2,2-Dimethyl-N-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-propionamide	418	III
159		3,3-Dimethyl-N-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-butyramide	432	III
160		2-Methoxy-N-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-acetamide	406	III
161		Cyclopentanecarboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide	430	III
162		2-Cyclopentyl-N-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-acetamide	444	III
163		Cyclohexanecarboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide	444	III

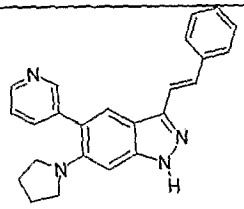
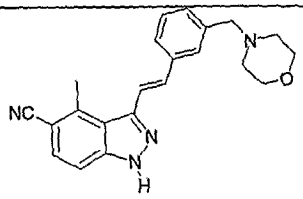
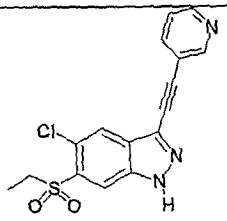
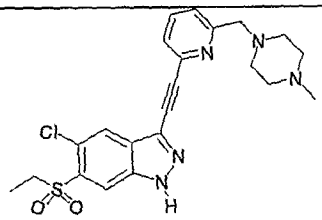
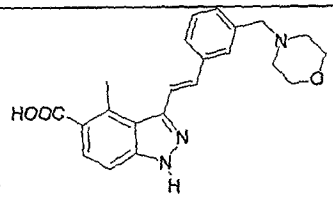
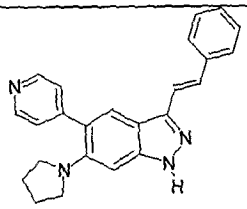
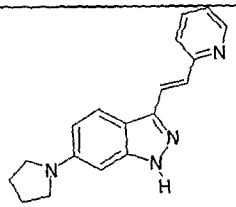
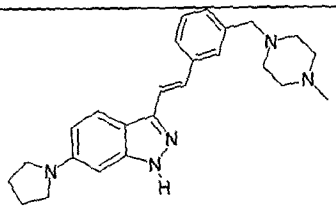
164		1-Methyl-cyclopropanecarboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide	416	III
165		N-[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-4-oxo-4-thiophen-2-yl-butyramide	500	III
166		2H-Pyrazole-3-carboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide	428	III
167		N-[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-nicotinamide	439	III
168		3-Hydroxy-pyridine-2-carboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide	455	III
169		Pyrazine-2-carboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide	440	III
170		2-Dimethylamino-N-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-acetamide	419	III
171		2-Cyclopropyl-N-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-acetamide	416	III
172			462	V

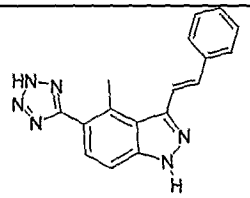
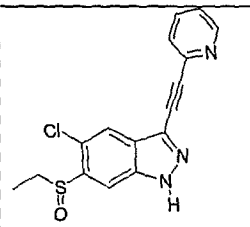
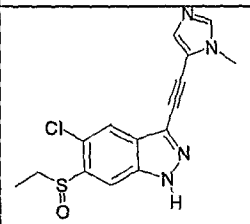
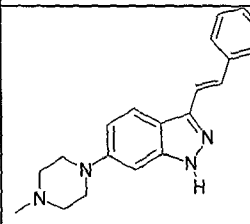
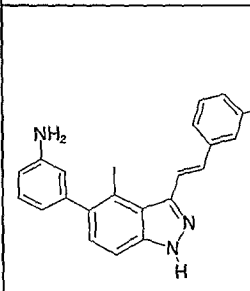
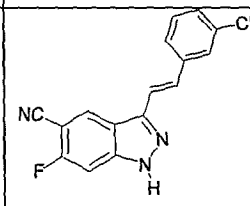
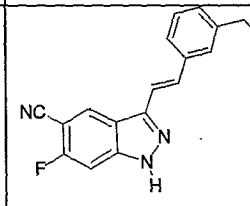
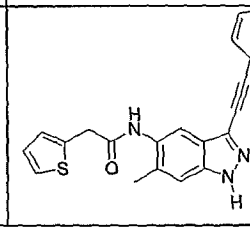
173			490	V
174			530	V
175			538	V
176		N-{3-[2-(3-Nitro-phenyl)-vinyl]-6-pyrrolidin-1-yl-1H-indazol-5-yl}-acetamide	392	III
177		(6-Methyl-3-{2-[3-(2-pyridin-2-yl-ethoxycarbonylamino)-phenyl]-vinyl}-1H-indazol-5-yl)-carbamic acid 2-pyridin-2-yl-ethyl ester		V
178		Furan-2-ylmethyl-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amine	414	III
179		(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-pyridin-2-ylmethyl-amine	453	III
180		5-Chloro-6-ethylsulfanyl-3-styryl-1H-indazole	315	III

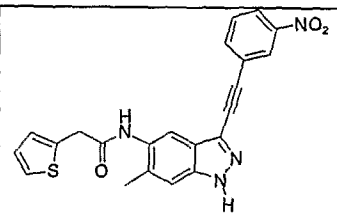
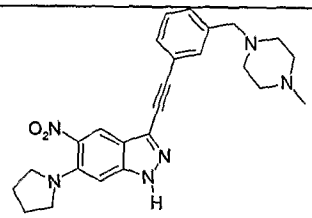
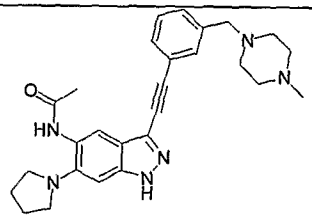
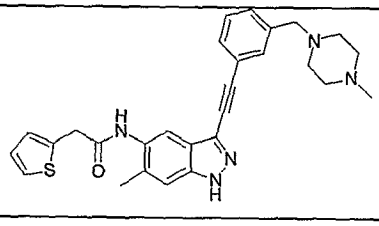
181		5-Chloro-6-ethanesulfonyl-3-styryl-1H-indazole	347	III
182		4-Methyl-piperazine-1-carboxylic acid {3-[2-(5-acetylamino-6-pyrrolidin-1-yl-1H-indazol-3-yl)-vinyl]-phenyl}-amide	488	V
183		(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-quinolin-2-ylmethyl-amine	503	III
184			563	V
185			595	V
186		5-Chloro-6-nitro-3-styryl-1H-indazole	301	III
187		Pyridine-2-carboxylic acid (4-methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-amide	467	III
188		N-(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-propionamide	418	III

189		(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-propyl-amine	404	III
190		N-(6-Methyl-3-phenylethynyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide	372	V
191		4-Methyl-piperazine-1-carboxylic acid {3-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-ylethynyl]-phenyl}-amide	514	V
192		[6-Methyl-3-(2-{3-[2-(1-methyl-pyrrolidin-2-yl)-ethoxycarbonylamino]-phenyl}-vinyl)-1H-indazol-5-yl]-carbamic acid 2-(1-methyl-pyrrolidin-2-yl)-ethyl ester	576	V
193		(6-Methyl-3-{2-[3-(2-morpholin-4-yl-ethoxycarbonylamino)-phenyl]-vinyl}-1H-indazol-5-yl)-carbamic acid 2-morpholin-4-yl-ethyl ester	579	V
194		5-Chloro-6-ethylsulfanyl-3-pyridin-3-ylethynyl-1H-indazole	315	III
195		N-(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-2-pyridin-2-yl-acetamide	482	III

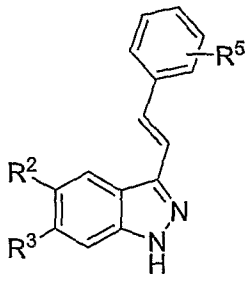
196		Thiophene-2-carboxylic acid (4-methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-amide	473	III
197		(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-thiophen-2-ylmethyl-amine	459	III
198		6-Pyrrolidin-1-yl-3-styryl-1H-indazole	290	III
199		5-Chloro-6-ethanesulfonyl-3-phenylethynyl-1H-indazole	346	III
200		4-Methyl-3-styryl-1H-indazole-5-carbonitrile	260	VII
201		4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazole-5-carbonitrile	372	VII
202		3-(6-Pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-phenol	382	III
203		4-Methyl-3-[2-(3-nitro-phenyl)-vinyl]-1H-indazole-5-carbonitrile	305	VII

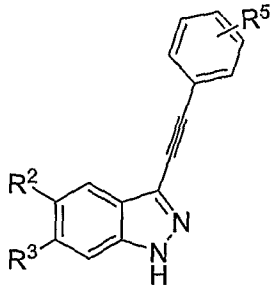
204		5-Pyridin-3-yl-6-pyrrolidin-1-yl-3-styryl-1H-indazole	367	III
205		4-Methyl-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1H-indazole-5-carbonitrile	359	VII
206		5-Chloro-6-ethanesulfonyl-3-pyridin-3-ylethynyl-1H-indazole	347	III
207		5-Chloro-6-ethanesulfonyl-3-[6-(4-methyl-piperazin-1-ylmethyl)-pyridin-2-ylethynyl]-1H-indazole	459	III
208		4-Methyl-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1H-indazole-5-carboxylic acid	378	VII
209		5-Pyridin-4-yl-6-pyrrolidin-1-yl-3-styryl-1H-indazole	367	III
210		3-(2-Pyridin-2-yl-vinyl)-6-pyrrolidin-1-yl-1H-indazole	291	III
211		3-{2-[3-(4-Methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-6-pyrrolidin-1-yl-1H-indazole	403	III

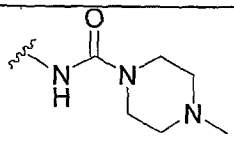
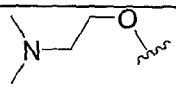
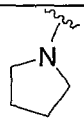
212		4-Methyl-3-styryl-5-(2H-tetrazol-5-yl)-1H-indazole	303	III
213		5-Chloro-6-ethanesulfinyl-3-pyridin-2-ylethynyl-1H-indazole	331	III
214		5-Chloro-6-ethanesulfinyl-3-(3-methyl-3H-imidazol-4-ylethynyl)-1H-indazole	334	III
215		6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazole	319	III
216		3-(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-phenylamine	438	III
217		6-Fluoro-3-[2-(3-formyl-phenyl)-vinyl]-1H-indazole-5-carbonitrile	292	VII
218		6-Fluoro-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazole-5-carbonitrile	376	VII
219		4-Methyl-piperazine-1-carboxylic acid 3-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-ylethynyl]-benzylamide	527	V

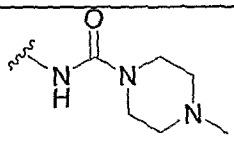
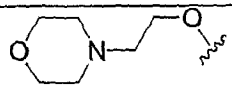
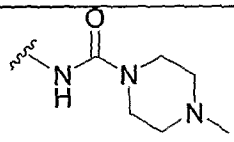
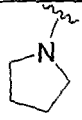
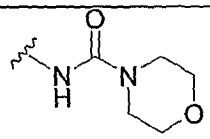
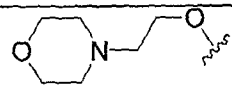
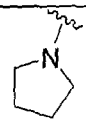
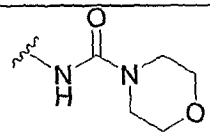
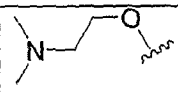
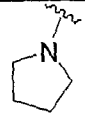
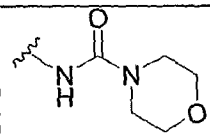
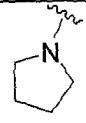
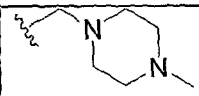
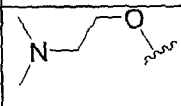
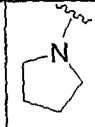
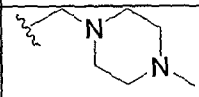
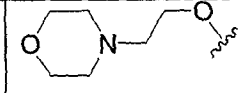
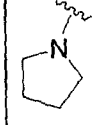
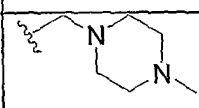
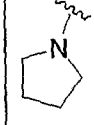
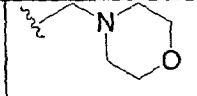
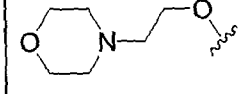
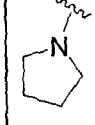
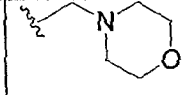
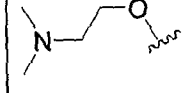
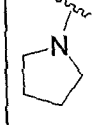
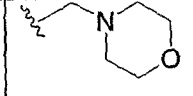
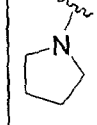
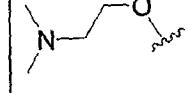
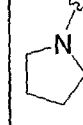
220		N-[6-Methyl-3-(3-nitro-phenylethynyl)-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide	417	III
221		3-[3-(4-Methyl-piperazin-1-ylmethyl)-phenylethynyl]-5-nitro-6-pyrrolidin-1-yl-1H-indazole	445	III
222		N-{3-[3-(4-Methyl-piperazin-1-ylmethyl)-phenylethynyl]-6-pyrrolidin-1-yl-1H-indazol-5-yl}-acetamide	457	III
223		N-{6-Methyl-3-[3-(4-methyl-piperazin-1-ylmethyl)-phenylethynyl]-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide	484	III

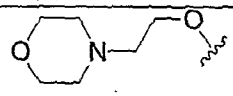
By methods analogous to those disclosed above and by varying the starting materials used in the synthesis, a wide variety of compounds of Formula I could be prepared, including, but not limited to, those in Table B:





Entry	R^5	R^2	R^3
224			

225			
226		-OH	
227			
228			
229		-OH	
230			
226			
227		-OH	
231			
232			
233		-OH	
234	H		

235	H		
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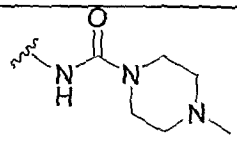
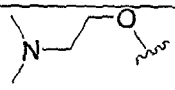
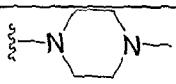
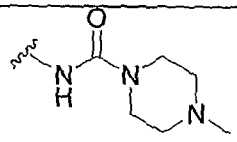
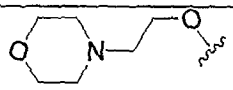
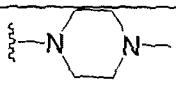
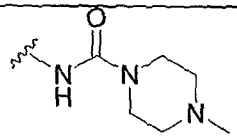
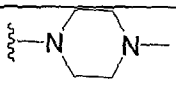
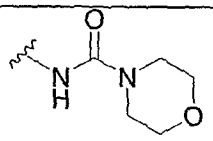
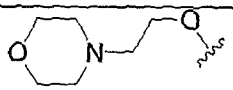
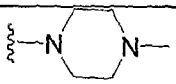
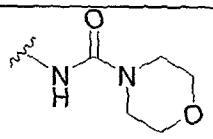
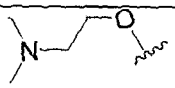
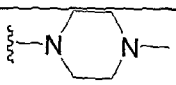
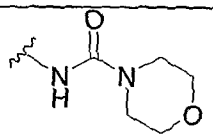
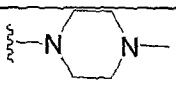
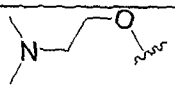
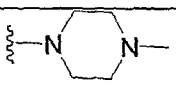
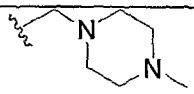
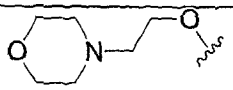
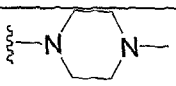
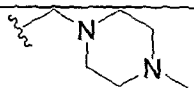
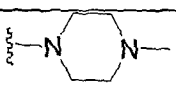
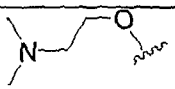
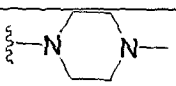
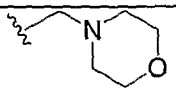
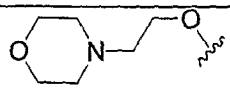
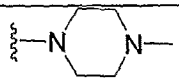
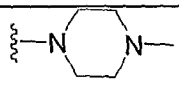
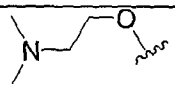
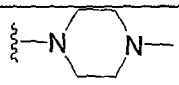
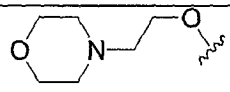
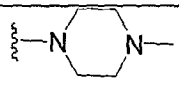
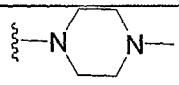
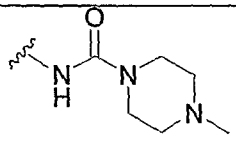
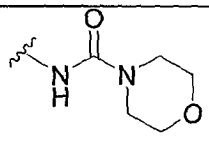
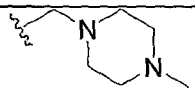
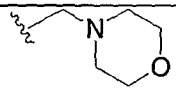
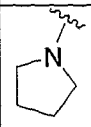
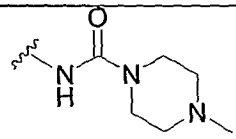
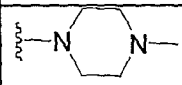
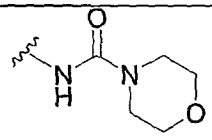
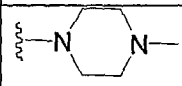
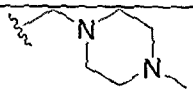
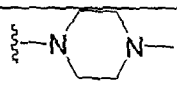
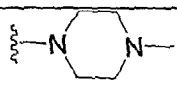
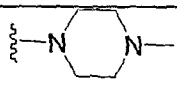
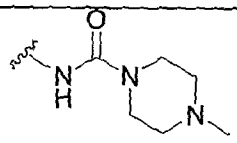
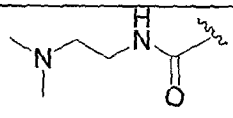
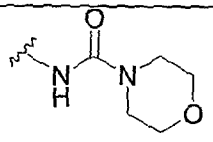
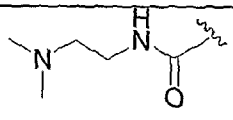
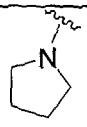
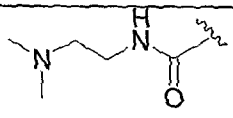
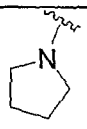
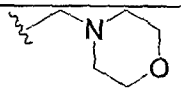
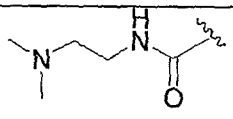
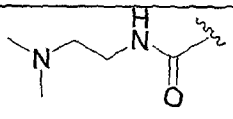
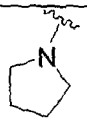
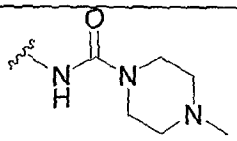
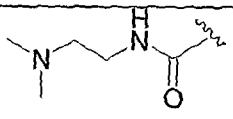
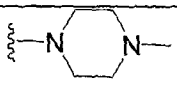
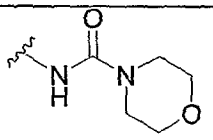
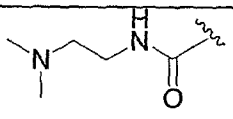
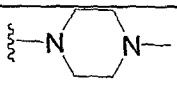
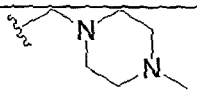
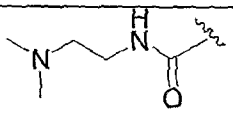
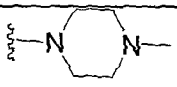
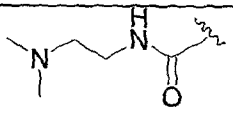
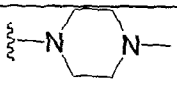
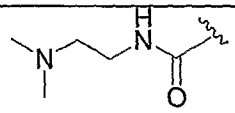
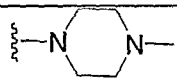
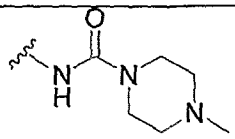
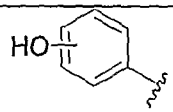
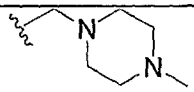
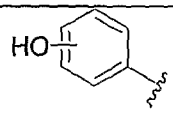
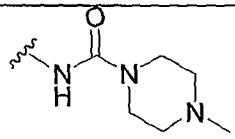
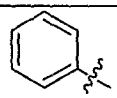
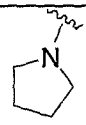
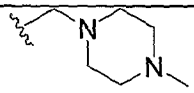
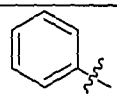
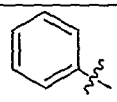
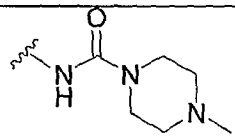
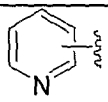
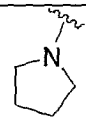
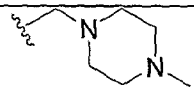
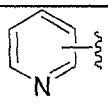
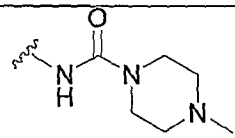
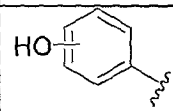
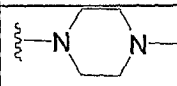
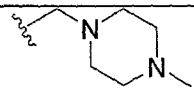
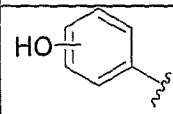
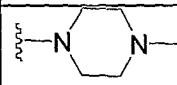
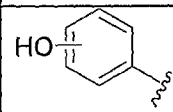
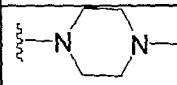
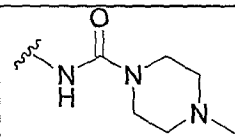
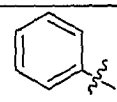
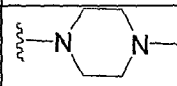
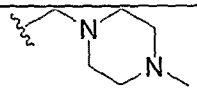
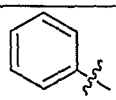
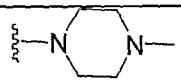
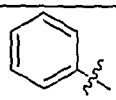
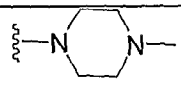
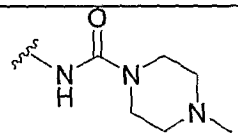
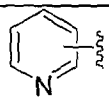
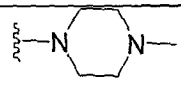
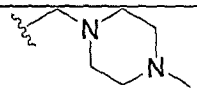
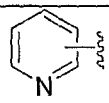
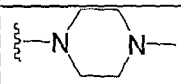
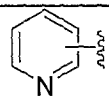
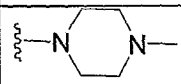
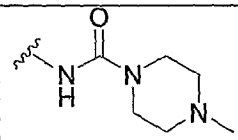
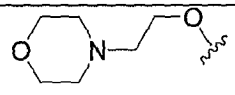
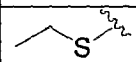
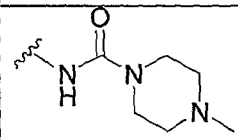
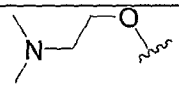
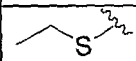
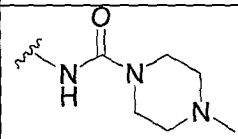
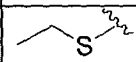
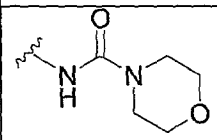
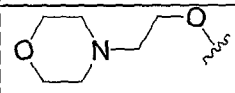
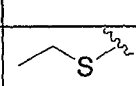
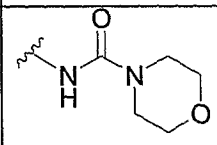
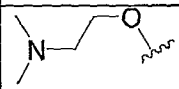
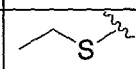
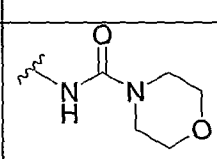
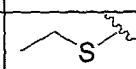
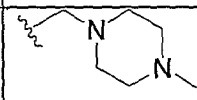
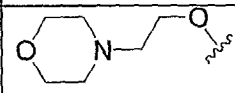
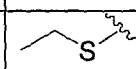
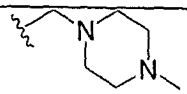
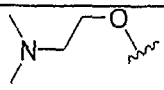
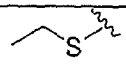
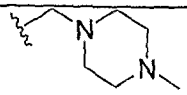
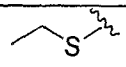
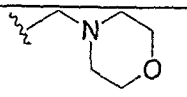
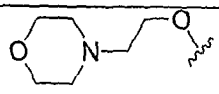
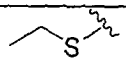
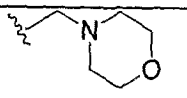
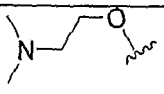
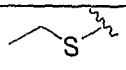
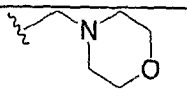
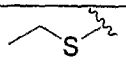
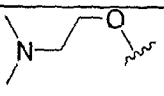
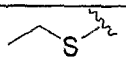
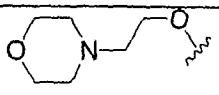
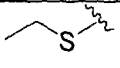
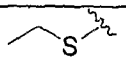
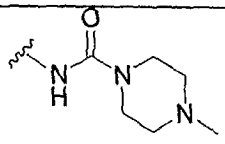
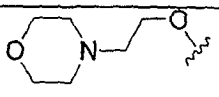
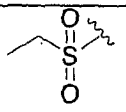
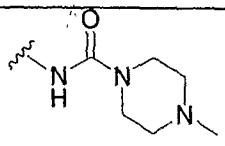
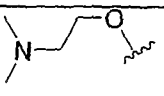
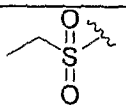
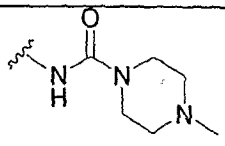
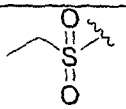
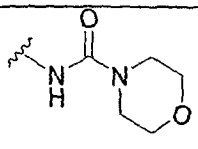
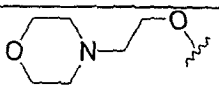
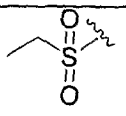
237			
238			
239		-OH	
240			
241			
242		-OH	
243			
244			
245		-OH	
246			

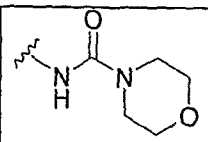
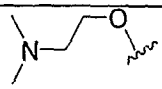
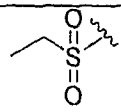
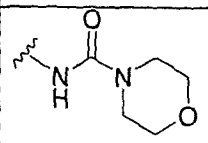
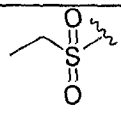
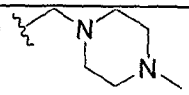
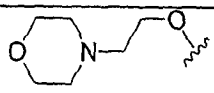
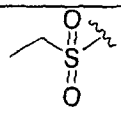
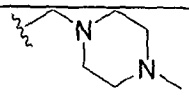
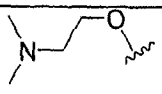
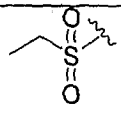
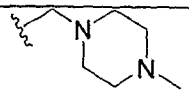
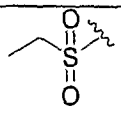
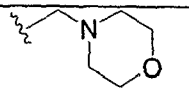
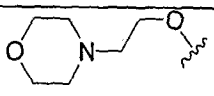
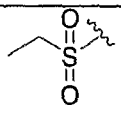
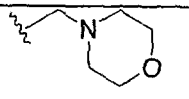
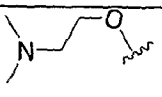
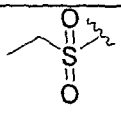
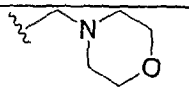
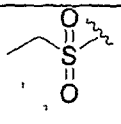
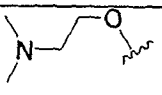
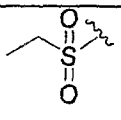
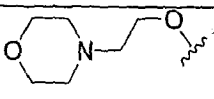
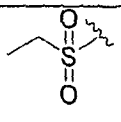
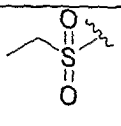
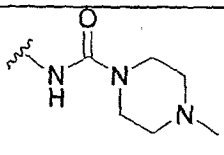
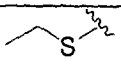
247			
248		-OH	
249	H		
250	H		
251	H	-OH	
252		-CN	
253		-CN	
254		-CN	
255		-CN	
256	H	-CN	
257		-CN	
258		-CN	

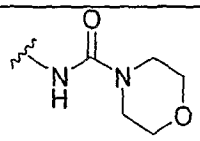
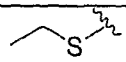
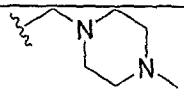
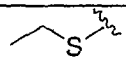
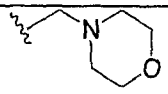
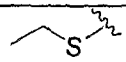
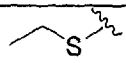
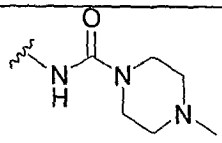
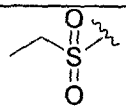
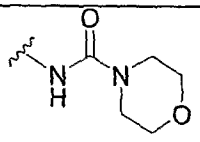
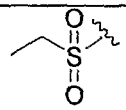
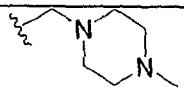
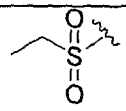
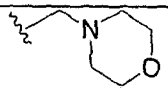
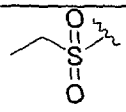
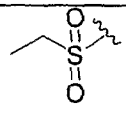
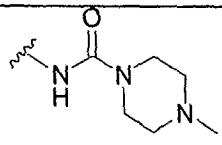
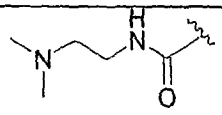
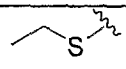
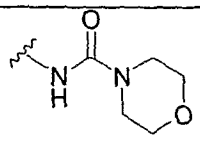
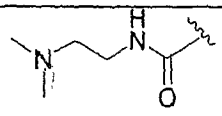
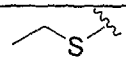
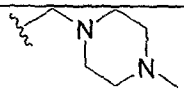
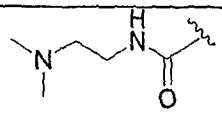
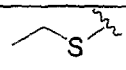
259		-CN	
260		-CN	
261	H	-CN	
262			
263			
264			
265			
266	H		
267			
268			
269			
270			

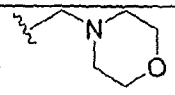
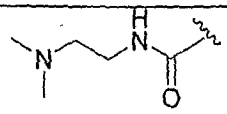
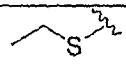
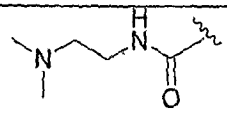
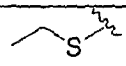
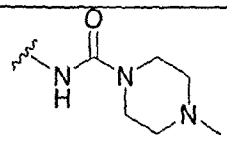
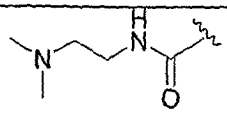
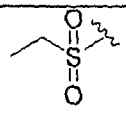
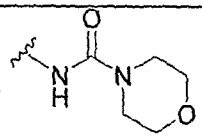
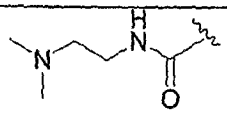
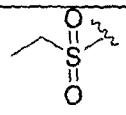
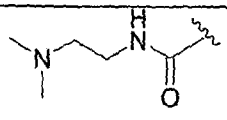
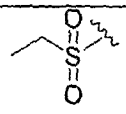
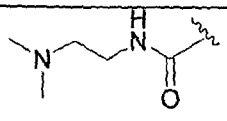
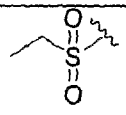
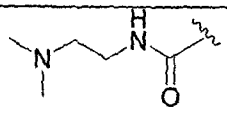
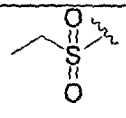
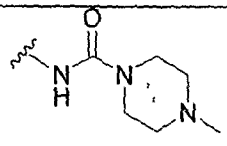
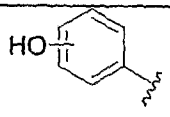
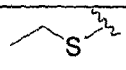
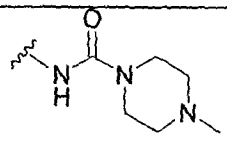
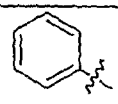
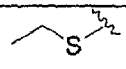
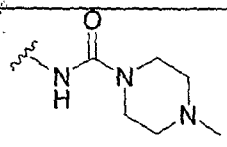
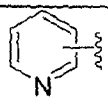
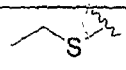
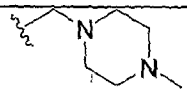
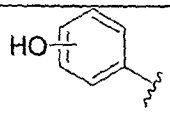
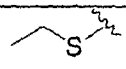
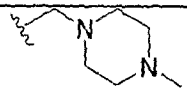
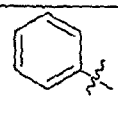
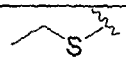
271	H		
272			
273			
274			
275			
276	H		
277			
278			
279			
280			
281	H		
282			

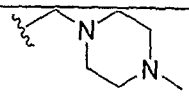
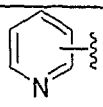
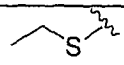
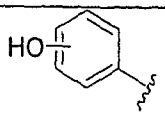
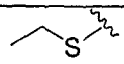
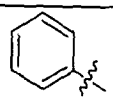
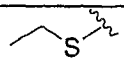
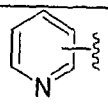
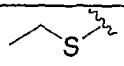
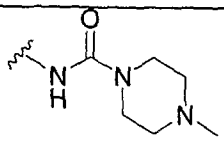
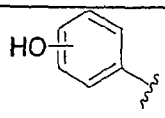
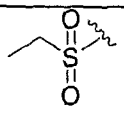
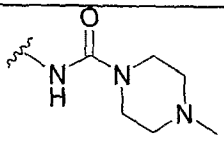
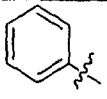
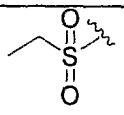
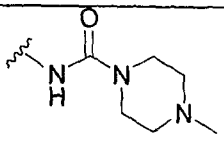
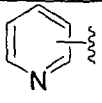
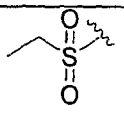
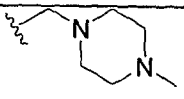
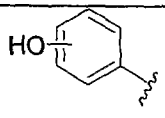
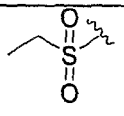
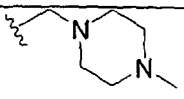
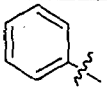
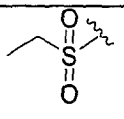
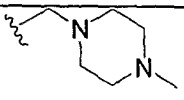
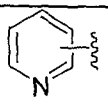
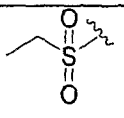
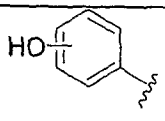
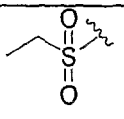
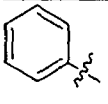
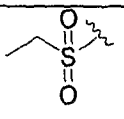
283			
284	H		
285			
286			
287	H		
288			
289			
290		-OH	
291			
292			
293		-OH	
294			

295			
296		-OH	
297			
298			
299		-OH	
300	H		
301	H		
302	H	-OH	
303			
304			
305		-OH	
306			

307			
308		-OH	
309			
310			
311		-OH	
312			
313			
314		-OH	
315	H		
316	H		
317	H	-OH	
318		-CN	

319		-CN	
320		-CN	
321		-CN	
322	H	-CN	
323		-CN	
324		-CN	
325		-CN	
326		-CN	
327	H	-CN	
328			
329			
330			

331			
332	H		
333			
334			
335			
336			
337	H		
338			
339			
340			
341			
342			

343			
344	H		
345	H		
346	H		
347			
348			
349			
350			
351			
352			
353	H		
354	H		

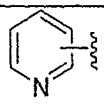
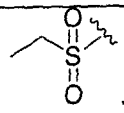
355	H		

Table B

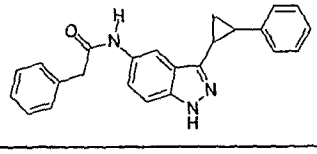
BIOLOGICAL TESTING

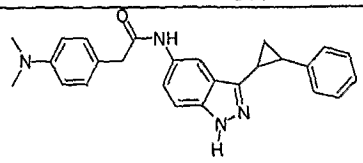
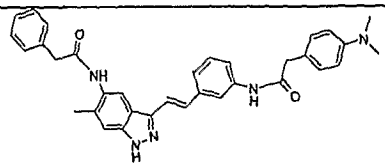
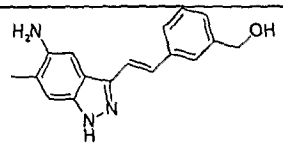
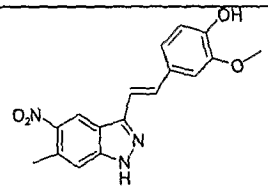
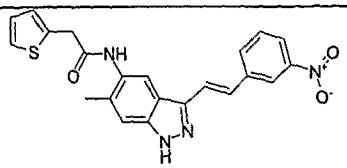
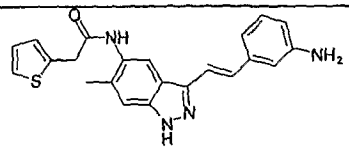
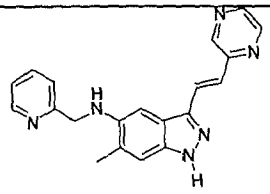
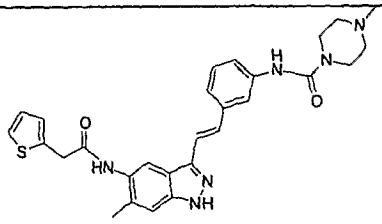
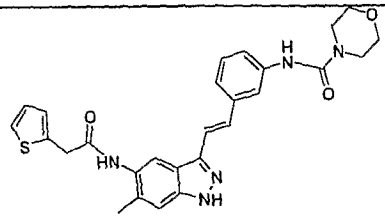
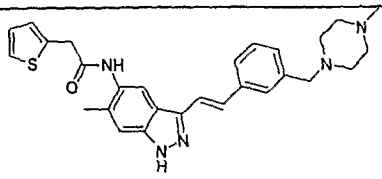
Cell-based proliferation assay for determination of GI_{50} values

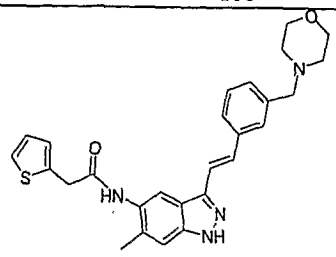
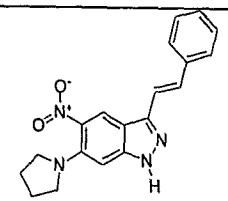
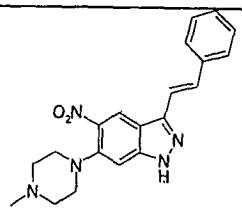
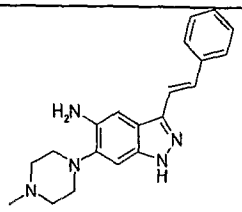
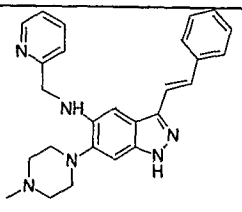
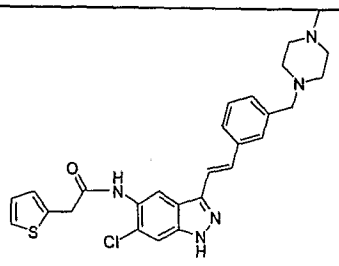
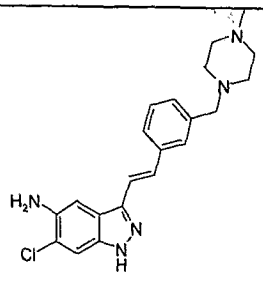
Human colon cancer cell line (Colo205) and human leukaemia cell line (HL60) were obtained from ATCC. Colo205 and HL60 cells were cultivated in RPMI 1640 containing 2 mM L-glutamine, 5% FBS, 1.0 mM sodium pyruvate. Colo205 cells were seeded in 96-wells plate at 5000 cells per well. HL60 cells were seeded in 96-wells plate at 8000 cells per well. The plates were incubated at 37°C, 5% CO_2, for 24 h. Cells were treated with compounds at various concentrations for 96 h. Cell growth for Colo205 was then measured using CyQUANT® cell proliferation assay kit (Invitrogen Pte Ltd). Cell growth for HL60 was measured using the CellTiter96 Aqueous One cell proliferation assay kit (Promega). Dose response curves were plotted to determine GI_{50} values for the compounds using the XL-fit software. GI_{50} is defined as the concentration of compound required for 50% inhibition of cell growth.

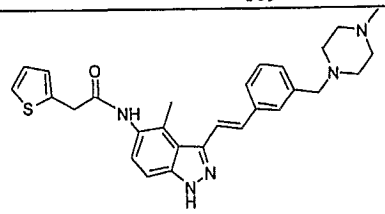
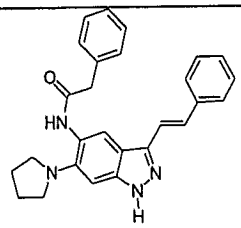
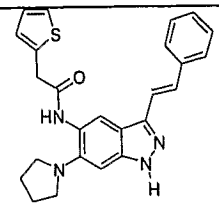
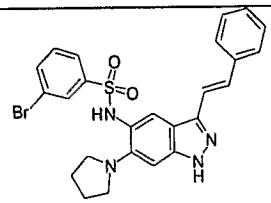
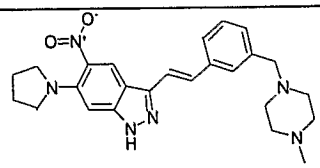
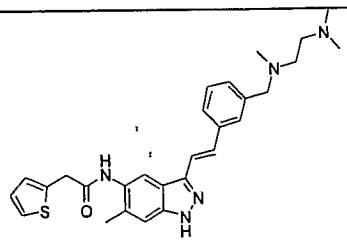
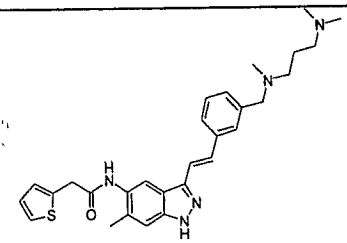
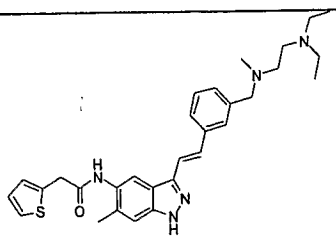
The anti-proliferative activity of representative compounds against Colo205 and HL60 cells is shown in Table C. In the table, a "+" indicates a GI_{50} of 20 μM (micromolar) or less, while a "-" indicates a GI_{50} of more than 20 μM (micromolar). These data indicate that compounds in this invention are active in the inhibition of cell proliferation.

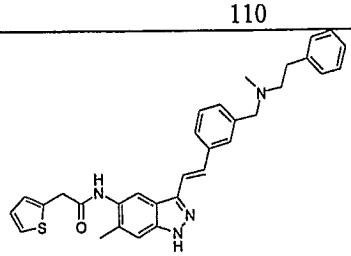
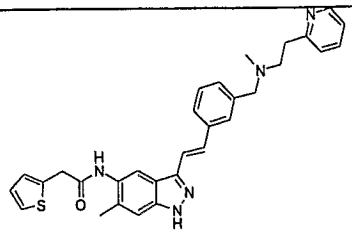
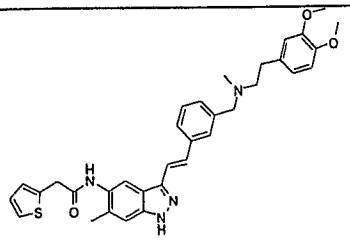
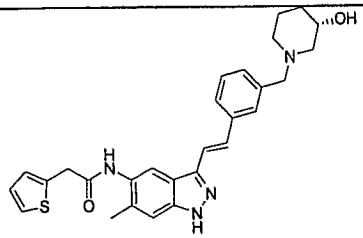
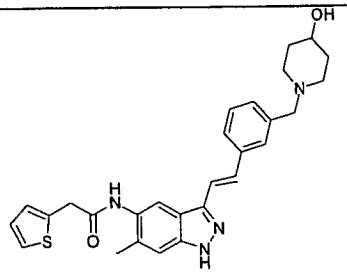
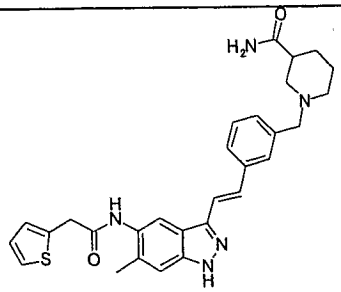
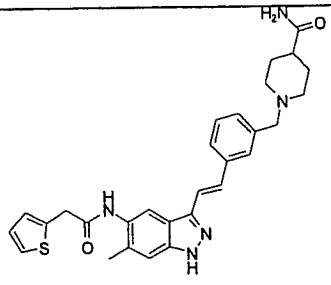
Table C. Cell-based proliferation assay GI_{50} data

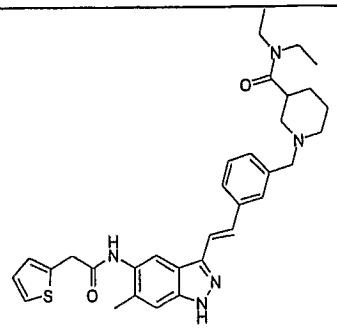
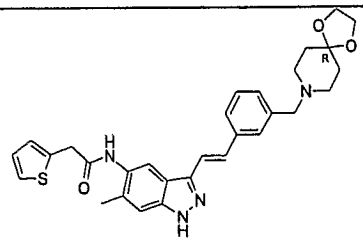
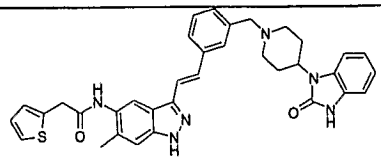
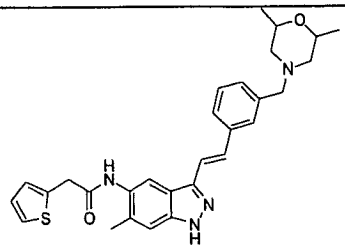
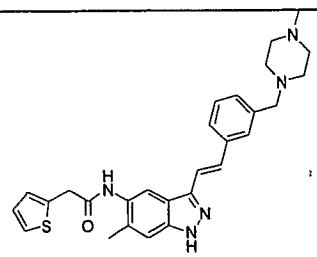
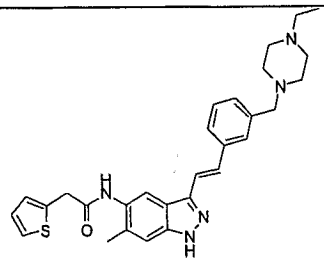
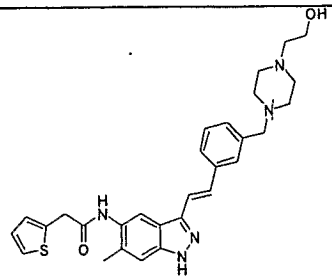
Compound	Structures	Growth inhibition of Colo205	Growth inhibition of HL60
1		+	+

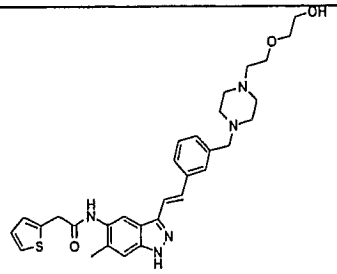
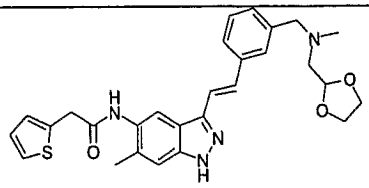
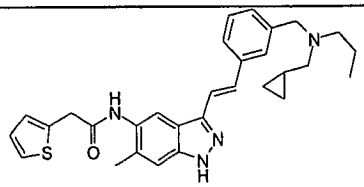
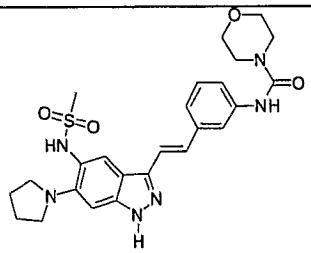
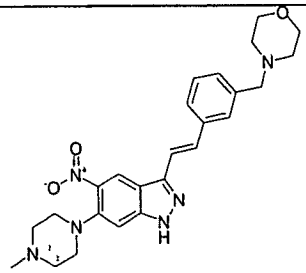
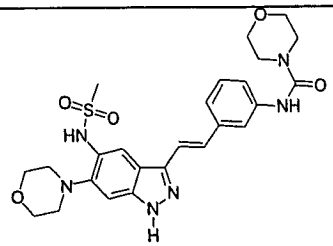
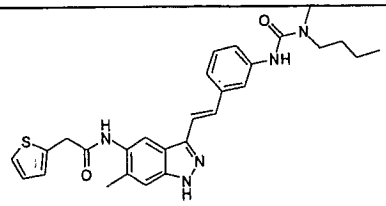
2		+	+
6		+	+
7		-	+
8		-	+
11		-	+
12		+	-
13		-	+
14		+	+
15		-	+
16		+	+

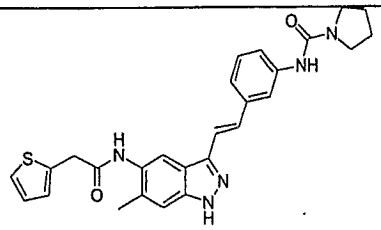
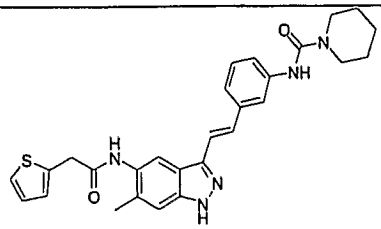
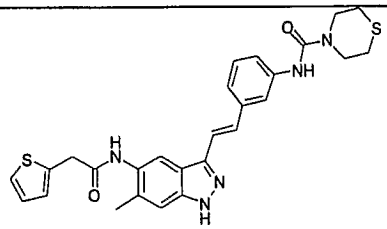
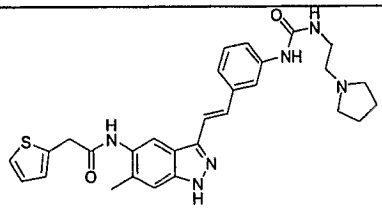
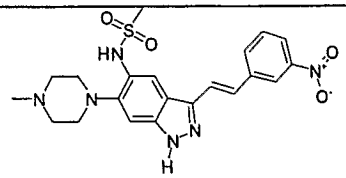
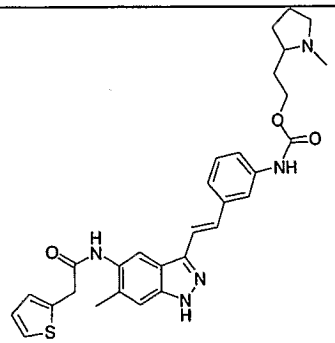
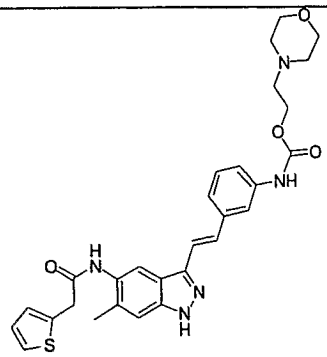
17		-	+
22		+	+
24		+	+
25		+	+
26		+	+
27		+	+
28		+	+

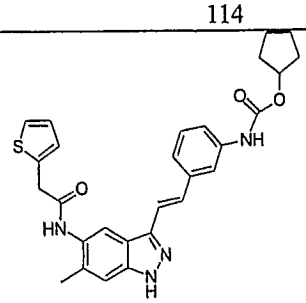
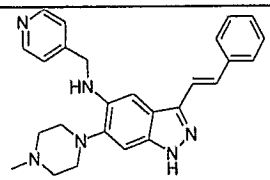
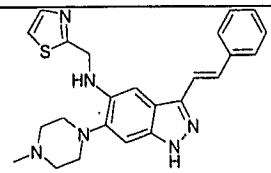
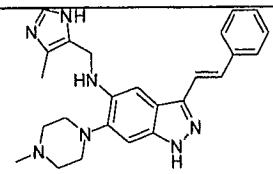
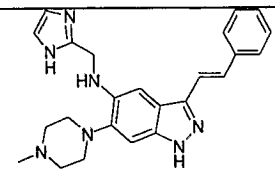
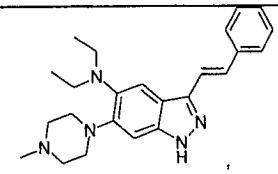
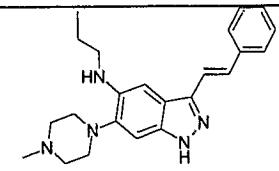
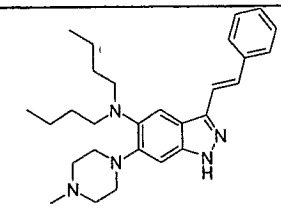
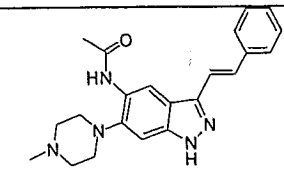
30		+	+
32		-	+
33		-	+
49		+	-
51		+	+
53		+	+
55		+	+
56		+	+

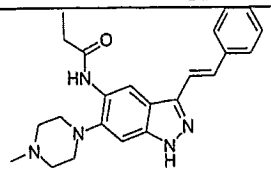
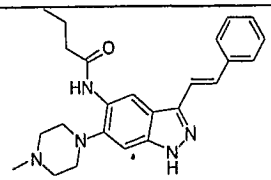
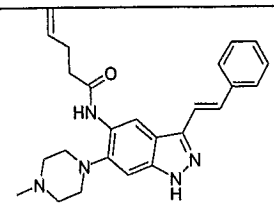
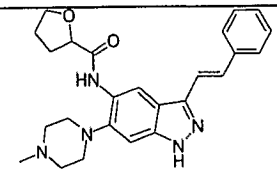
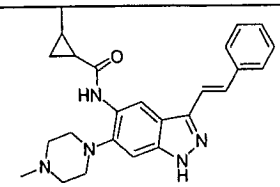
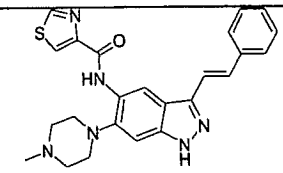
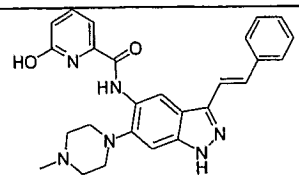
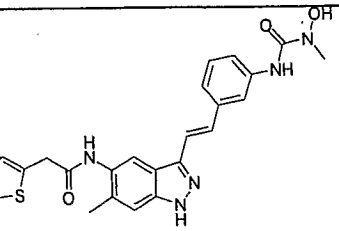
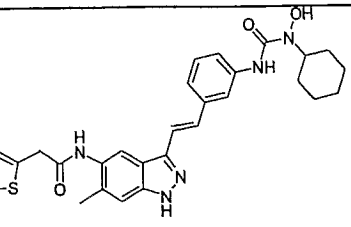
57		+	+
59		+	+
60		+	+
61		+	-
62		-	+
63		+	+
64		+	+

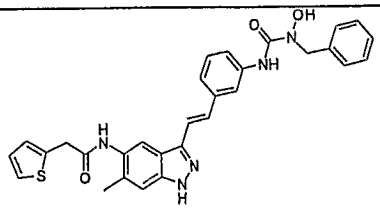
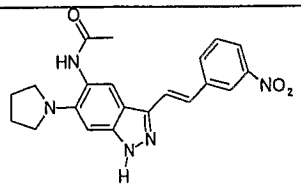
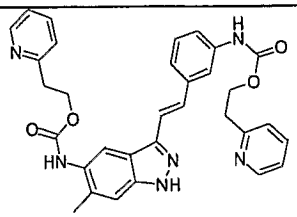
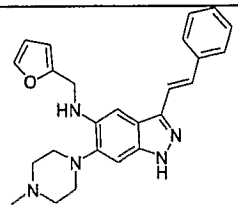
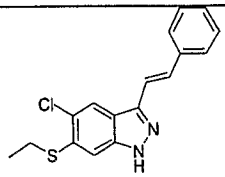
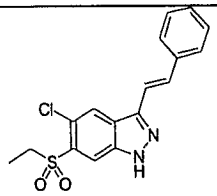
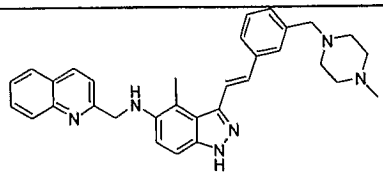
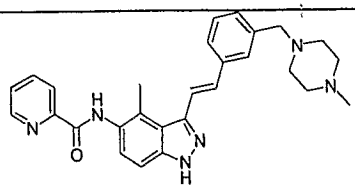
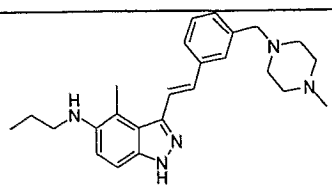
65		+	+
66		-	+
68		+	+
69		+	+
70		+	+
71		+	+
73		+	-

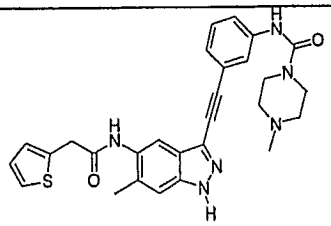
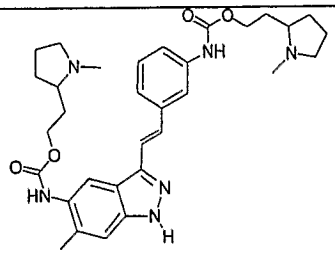
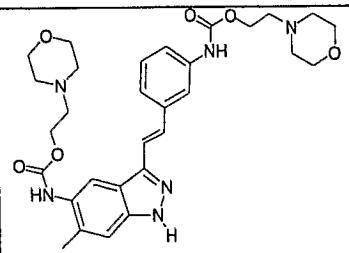
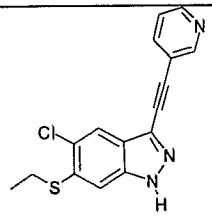
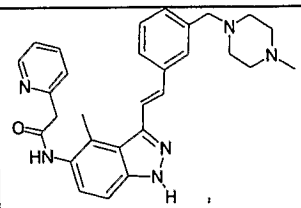
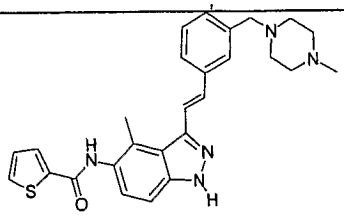
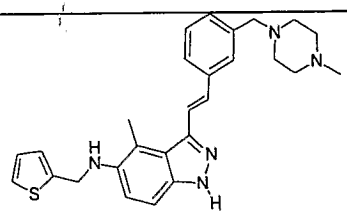
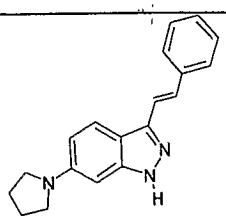
76		+	-
83		+	-
84		+	+
92		+	+
100		+	+
105		-	+
110		+	-

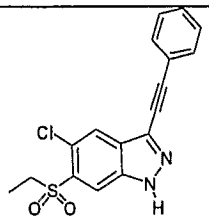
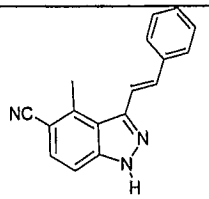
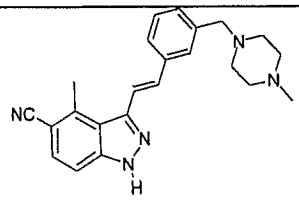
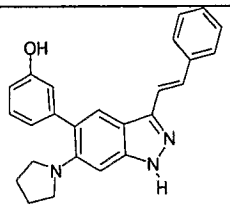
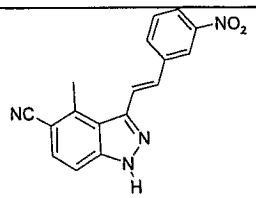
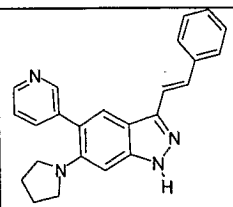
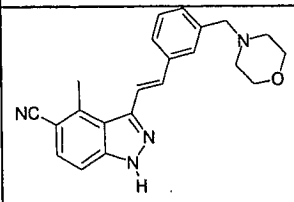
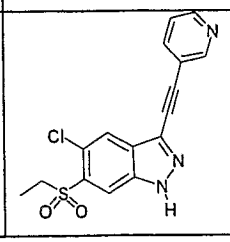
113		+	-
114		+	+
115		+	-
118		+	-
127		+	+
130		+	+
131		+	-

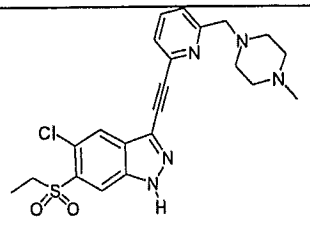
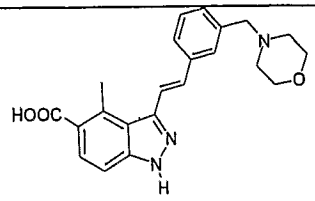
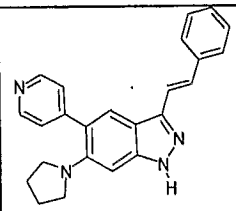
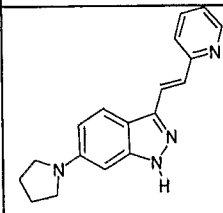
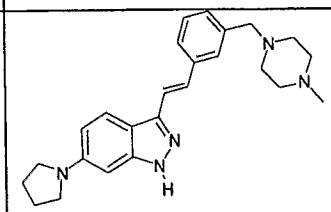
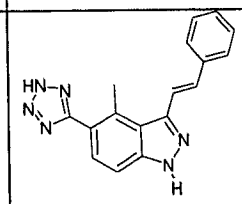
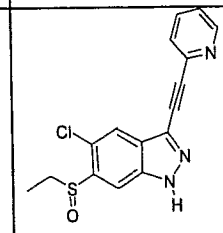
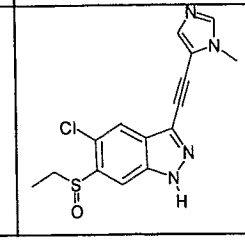
134		+	-
140		+	+
141		+	+
142		+	+
143		+	+
144		+	+
145		+	+
146		+	+
147		-	+

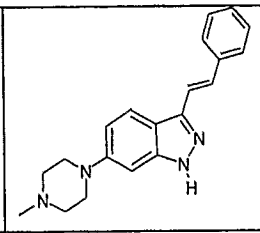
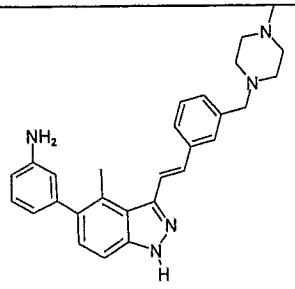
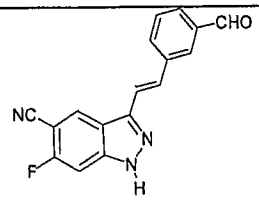
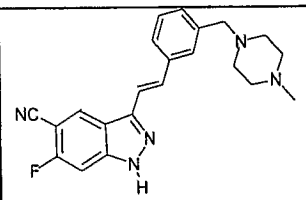
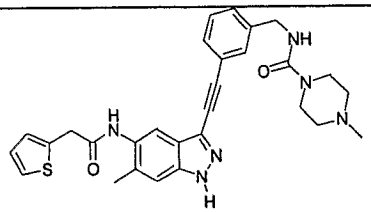
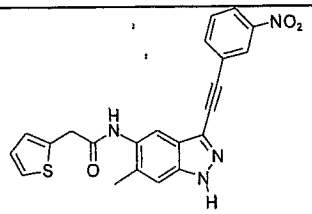
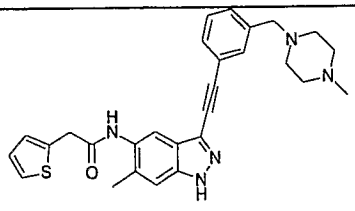
148		-	+
149		+	+
150		+	+
151		+	+
152		+	-
154		+	+
155		+	+
172		+	-
174		+	+

175		+	+
176		+	+
177		-	+
178		+	+
180		-	+
181		+	+
183		+	+
187		+	+
189		+	+

191		-	+
192		-	+
193		+	+
194		-	-
195		-	-
196		+	+
197		+	+
198		+	+

199		+	+
200		-	+
201		+	+
202		+	+
203		-	-
204		+	+
205		+	+
206		-	+

207		-	+
208		-	-
209		-	+
210		+	+
211		+	+
212		-	-
213		-	+
214		-	+

215		+	+
216		+	+
217		-	-
218		+	+
219		-	-
220		-	-
223		-	+

***In vivo* antineoplastic (or anti-tumor) effect:**

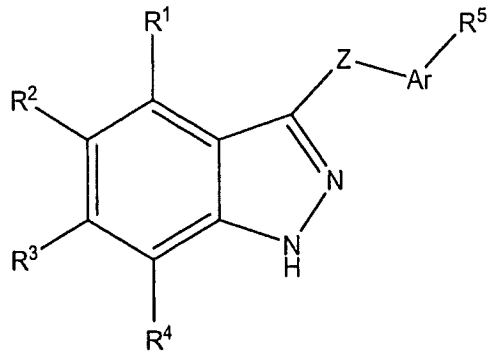
The efficacy of the compounds of the invention can then be determined using in vivo animal xenograft studies. The animal xenograft model is one of the most commonly used in vivo cancer models.

In these studies Female atymic nude mice (Harlan), 12-14 weeks of age would be implanted subcutaneously in the flank with 5×10^6 cells of HCT116 or with 1×10^6 cells of Colo205 human colon carcinoma suspended in 50% Matrigel. When the tumor reaches the size 100 mm^3, the xenograft nude mice would be paired-match into various treatment groups. Selected compounds of this invention would be dissolved in appropriate vehicles, such as 10%DMA/10% Cremophore/80%water and administered to xenograft nude mice intraperitonelly daily for 21 days. The dosing volume will be 0.2-ml/20g mouse. Tumor volume will be calculated every second day of post injection using the formula: Tumor volume (mm^3) = ($w^2 \times l$)/2, where w = width and l = length in mm of an HCT116 or Colo205 carcinoma. Compounds in this invention that are tested would show significant reduction in tumor volume relative to controls treated with vehicle only. The result will therefore indicate that compounds in this invention are efficacious in treating proliferative diseases such as cancer.

The details of specific embodiments described in this invention are not to be construed as limitations. Various equivalents and modifications may be made without departing from the essence and scope of this invention, and it is understood that such equivalent embodiments are part of this invention.

What is claimed is:

1. A compound of the formula (I):



Formula I

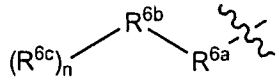
wherein

R^1, R^2, R^3 and R^4 are each independently selected from the group consisting of: H, halogen, nitro, cyano, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, aminoalkyl, acylamino, arylamino, sulfonylamino, sulfinylamino, -COOH, -COR^6, -$COOR^6$, -$CONHR^6$, -$NHCOR^6$, -NHR^6, -NR^6R^8, -$NHCOOR^6$, -$NHCONHR^6$, -$NHCON(OH)R^6$, -$NHCSN(OH)R^6$ -$NHSO_2NR^6$, -$NHSO_2R^6$, alkoxycarbonyl, alkylaminocarbonyl, sulfonyl, alkylsulfonyl, alkylsulfinyl, arylsulfonyl, arylsulfinyl, aminosulfonyl, -SR^6, -$R^7S(O)R^9$, -$R^7S(O)_2R^9$, -$R^7C(O)N(R^8)R^9$, -$R^7SO_2N(R^8)R^9$, -$R^7N(R^8)C(O)R^9$, -$R^7N(R^8)SO_2R^9$, -$R^7N(R^8)C(O)N(R^8)R^9$, -$R^7N(R^8)SO_2N(R^8)R^9$, and acyl, each of which may be optionally substituted;

R^5 is selected from the group consisting of: H, halogen, nitro, cyano, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl,

alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, aminoalkyl, acylamino, arylamino, sulfonylamino, sulfinylamino, -COOH, -COR^6, -$COOR^6$, -$CONHR^6$, -$NHCOR^6$, -$NHCOOR^6$, -$NHCONHR^6$, -$NHCSN(OH)R^6$ alkoxycarbonyl, alkylaminocarbonyl, sulfonyl, alkylsulfonyl, alkylsulfinyl, arylsulfonyl, arylsulfinyl, aminosulfonyl, -SR^6, -R^7R^9, -$R^7S(O)R^9$, -$R^7S(O)_2R^9$, -$R^7C(O)N(R^8)R^9$, -$R^7SO_2N(R^8)R^9$, -$R^7N(R^8)C(O)R^9$, -$R^7N(R^8)SO_2R^9$, -$R^7N(R^8)C(O)N(R^8)R^9$, -$R^7N(R^8)SO_2N(R^8)R^9$, and acyl, each of which may be optionally substituted;

each R^6 is independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, and acyl, each of which may be optionally substituted; or R^6 is a group of the formula:



R^{6a} is selected from the group consisting of a bond, alkyl, heteroalkyl and aryl, each of which may be optionally substituted;

R^{6b} is selected from the group consisting of a bond, alkyl, -CO-, cycloalkyl, aryl and heteroaryl, each of which may be optionally substituted;

R^{6c} is selected from the group consisting of H, alkyl, chloro, bromo, iodo hydroxy, alkoxy, CH_3CONH- and heteroaryl;

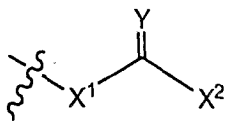
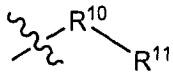
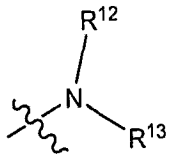
n is an integer from 0 to 5;

each R^7 is a bond or is selected from the group consisting of alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl and acyl, each of which may be optionally substituted;

each R^8 is selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, and acyl, each of which may be optionally substituted;

each R^9 is independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted, or

R^9 is selected from the group consisting of

wherein X^1 is selected from the group consisting of $-N(R^6)$, -O- and -S-;

wherein Y is selected from the group consisting of O and S;

wherein X^2 is selected from the group consisting of $-OR^{14}$, $-SR^{14}$ and $-NR^{15}R^{16}$;

R^{10} is selected from the group consisting of alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted;

R^{11} is selected from the group consisting of H, halogen, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy,

cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, NH_2CO-, $(R^6)_2NCO$-, aminoalkyl and acyl, each of which may be optionally substituted;

R^{12} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted;

R^{13} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted; or

R^{12} and R^{13} together with the nitrogen to which they are attached form an optionally substituted heterocycloalkyl group;

R^{14} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted;

R^{15} and R^{16} are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl,

heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted, or

R^{15} and R^{16} together with the nitrogen to which they are attached form a heterocycloalkyl group;

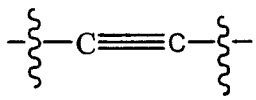
Z is a single bond or is selected from the group consisting of $-CH_2-$, $-CH_2CH_2-$, -CH=CH-, C_3-C_6 alkylene, C_3-C_6 alkenylene, C_2-C_6 alkynylene and C_3-C_6 cycloalkyl, each of which may be optionally substituted;

Ar is selected from the group consisting of aryl and heteroaryl, each of which may be optionally substituted;

or a pharmaceutically acceptable salt, N-oxide or prodrug thereof.

2. A compound of claim 1 wherein Z is -CH=CH- and is in the E configuration.

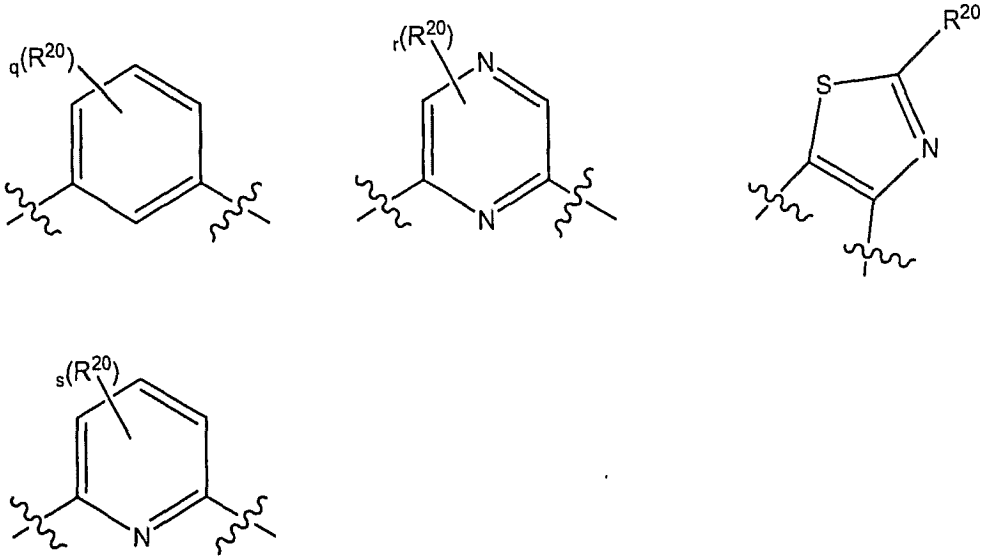
3. A compound according to claim 1 wherein Z is a group of formula:



4. A compound according to any one of claims 1 to 3 wherein Ar is selected from the group consisting of monocyclic aryl, monocyclic heteroaryl, bicyclic aryl and bicyclic heteroaryl, each of which may be optionally substituted.

5. A compound according to any one of the preceding claims wherein Ar is selected from the group consisting of phenyl, pyrazine, thiazole, and pyridyl, each of which may be optionally substituted.

6. A compound according to any one of claims 1 to 5 wherein Ar is selected from the group consisting of:



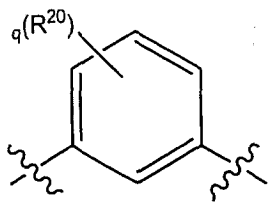
wherein R^{20} is selected from the group consisting of H, halogen, nitro, cyano, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, aminoalkyl, acylamino, arylamino, sulfonylamino, sulfinylamino, -COOH, alkoxycarbonyl, alkylaminocarbonyl, sulfonyl, alkylsulfonyl, alkylsulfinyl, arylsulfonyl, arylsulfinyl, aminosulfonyl and acyl, each of which may be optionally substituted;

q is an integer selected from the group consisting of 0, 1, 2, 3, and 4;

r is an integer selected from the group consisting of 0, 1, and 2;

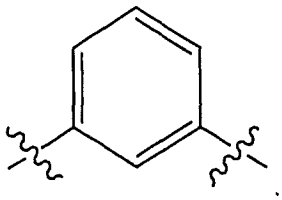
s is an integer selected from eth group consisting of 0, 1, 2, and 3.

7. A compound of according to claim 6 wherein Ar is a group of formula:



8. A compound according to claim 6 or 7 wherein q is 1 and R^{20} is selected from the group consisting of chloro, bromo, iodo, methyl, ethyl, propyl, hydroxy, alkoxy and nitro.

9. A compound according to any one of claims 1 to 8 wherein Ar is a group of formula:



10. A compound according to any one of claims 1 to 9 wherein R^1 is selected from the group consisting of H, methyl, ethyl, propyl and butyl.

11. A compound according to any one of claims 1 to 10 wherein R^1 is H.

12. A compound according to any one of claims 1 to 10 wherein R^1 is methyl.

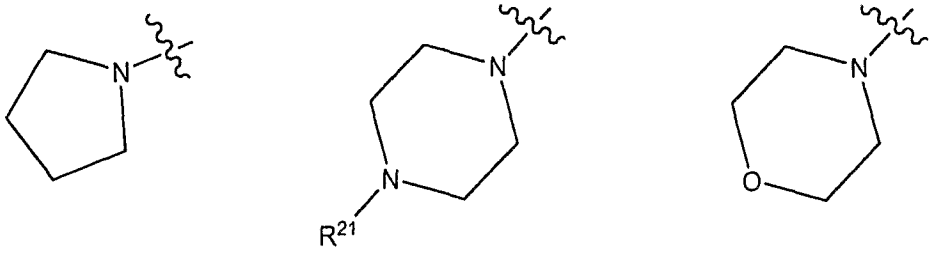
13. A compound according to any one of claims 1 to 12 wherein R^4 is selected from the group consisting of H, methyl, ethyl, propyl and butyl.

14. A compound according to any one of claims 1 to 13 wherein R^4 is H.

15. A compound according to any one of claims 1 to 14 wherein R^3 is selected from the group consisting of H, alkyl, heterocycloalkyl, chloro, bromo, iodo, alkylsulfanyl, alkylsulfinyl and alkylsulfonyl, each of which may be optionally substituted.

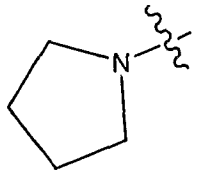
16. A compound according to any one of claims 1 to 15 wherein R^3 is optionally substituted heterocycloalkyl.

17. A compound according to any one of claims 1 to 16 wherein R^3 is selected from the group consisting of:

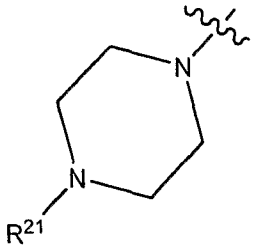


wherein R^{21} is selected from the group consisting of H, methyl, ethyl, propyl, butyl, pentyl and hexyl.

18. A compound according to any one of claims 1 to 17 wherein R^3 is a group of formula:

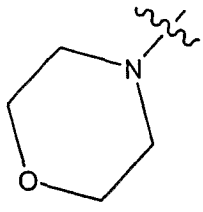


19. A compound according to any one of claims 1 to 17 wherein R^3 is a group of formula:



wherein R^{21} is selected from the group consisting of H, methyl, ethyl, propyl, butyl, pentyl and hexyl.

20. A compound according to any one of claims 1 to 17 wherein R^3 is a group of formula:



21. A compound according to any one of claims 1 to 20 wherein R^2 is selected from the group consisting of: halogen, nitro, amino, -NHCOR^6, -NHR^6, -NR^{6}R^8, -NHCOOR^6, -NHCONHR^6, -NHCON(OH)R^6, -NHSO$_2$NR^6,and -NHSO$_2$R^6, each of which may be optionally substituted.

22. A compound according to any one of claims 1 to 21 wherein R^2 is -NHCOR^6.

23. A compound according to any one of claims 1 to 21 wherein R^2 is -NHR^6.

24. A compound according to any one of claims 1 to 21 wherein R^2 is -NHSO$_2$R^6.

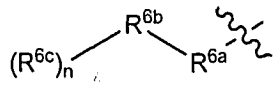
25. A compound according to any one of claims 1 to 21 wherein R^2 is -NHCON(OH)R^6.

26. A compound according to any one of claims 1 to 21 wherein R^2 is nitro.

27. A compound according to any one of claims 1 to 21 wherein R^2 is amino.

28. A compound according to any one of claims 1 to 21 wherein R^2 is chloro.

29. A compound according to any one of claims 21 to 25 wherein R^6 is selected from the group consisting of alkyl, alkenyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, and heteroarylalkyl, each of which may be optionally substituted; or R^6 is a group of the formula:



wherein:

R^{6a} is selected from the group consisting of a bond, alkyl, heteroalkyl and aryl, each of which may be optionally substituted;

R^{6b} is selected from the group consisting of a bond, alkyl, -CO-, cycloalkyl, aryl and heteroaryl, each of which may be optionally substituted;

R^{6c} is selected from the group consisting of H, alkyl, chloro, bromo, iodo hydroxy, alkoxy, CH_3CONH- and heteroaryl;

n is an integer from 0 to 5.

30. A compound according to claim 29 wherein R^6 is selected from the group consisting of cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl and heteroarylalkyl, each of which may be optionally substituted.

31. A compound according to claim 30 wherein R^6 is a group of the formula:

$$A(CH_2)_t\text{-}$$

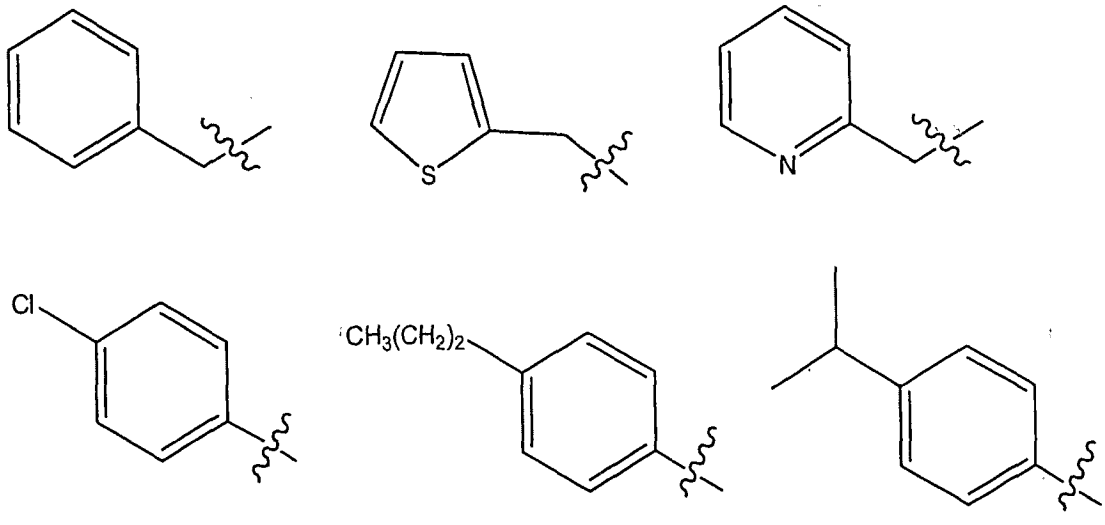
wherein A is selected from the group consisting of aryl, heteroaryl, cycloalkyl and heterocycloalkyl, each of which may be optionally substituted; and

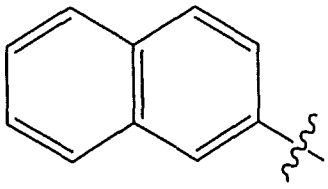
t is an integer selected from the group consisting of O, 1, 2, and 3.

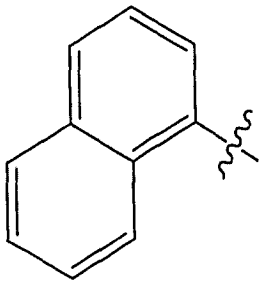
32. A compound according to claim 31 wherein t is 0 or 1.

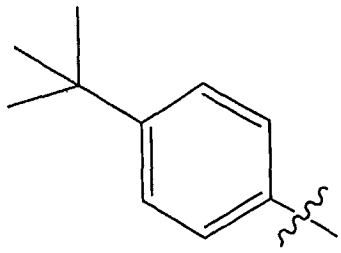
33. A compound according to claim 32 wherein t = 1.

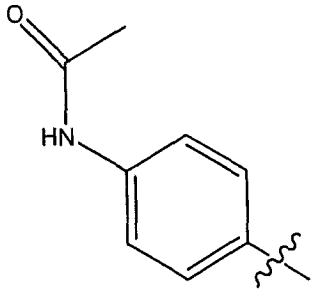
34. A compound according claim 31 wherein R^6 is a group of formula:

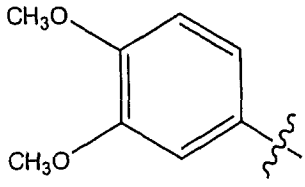


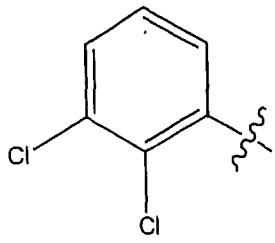


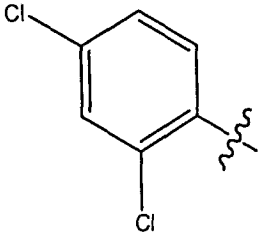


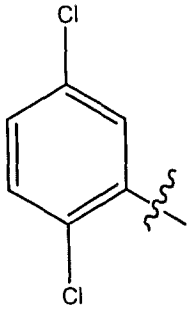


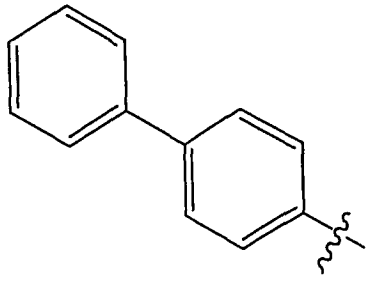

O
HN

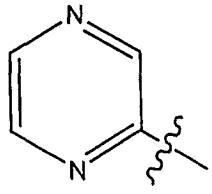

CH3O
CH3O

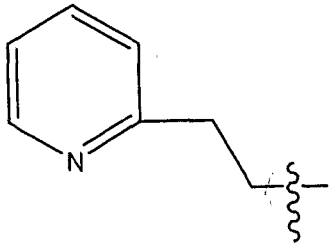

Cl
Cl

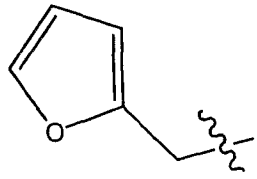

Cl
Cl

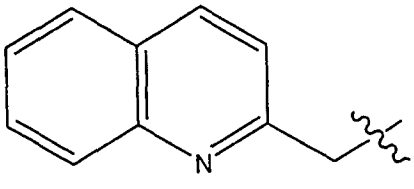

Cl
Cl

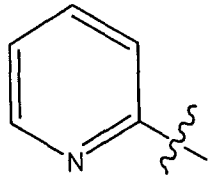


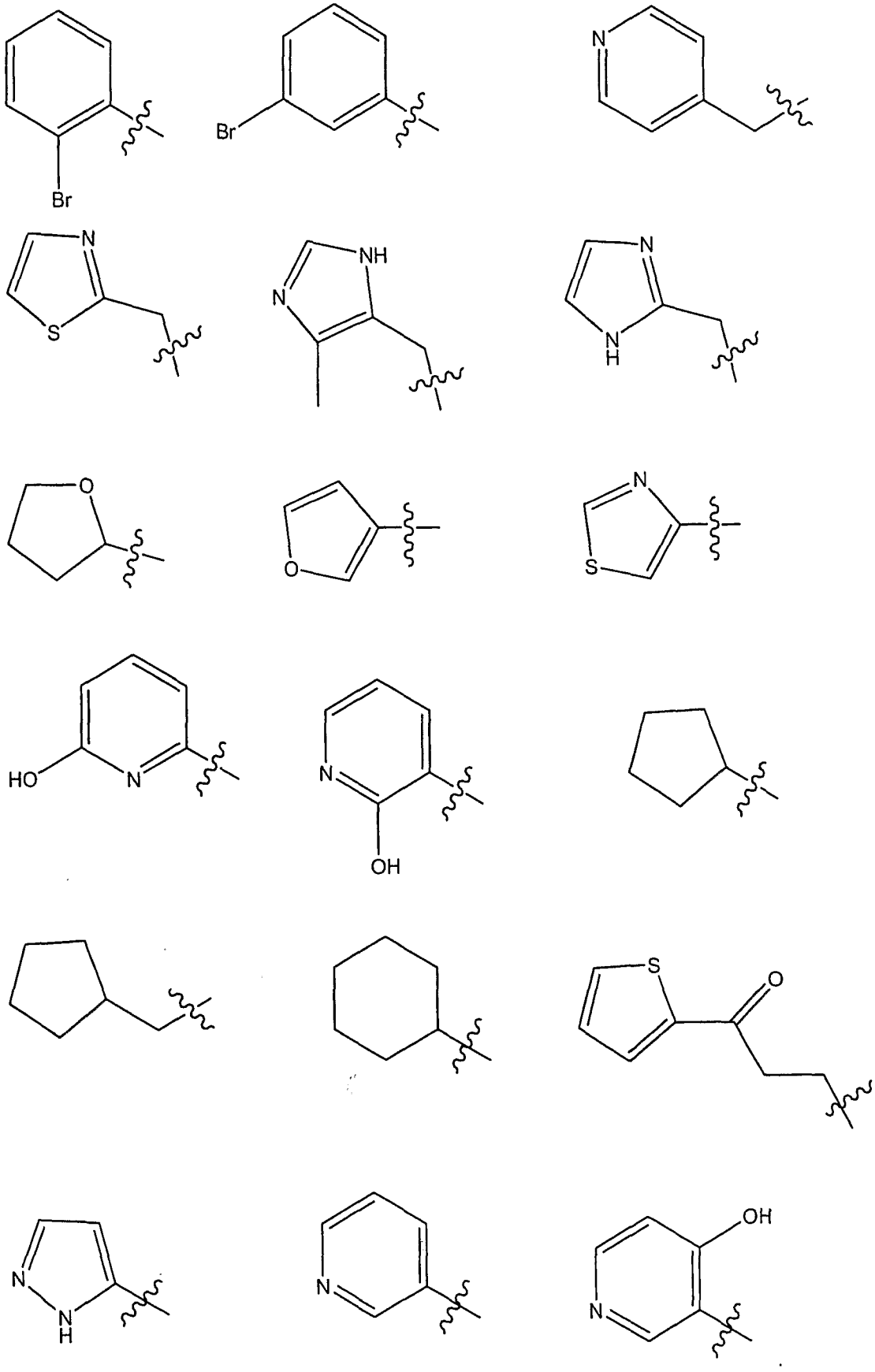

N
N


N

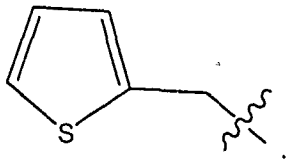

O


N


N



35. A compound according to claim 29 wherein R^6 is a group of the formula:



36. A compound according to any one of claims 1 to 35 wherein R^5 is selected from the group consisting of: H, nitro, alkyl, heteroalkyl, heterocycloalkylalkyl, hydroxyalkyl, alkoxy, amino, $-R^7R^9$, $-R^7N(R^8)C(O)R^9$, each of which may be optionally substituted.

37. A compound according to claim 35 wherein R^5 is $-R^7R^9$.

38. A compound according to claim 35 wherein R^5 is $-R^7N(R^8)C(O)R^9$.

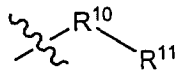
39. A compound according to any one of claims 36 to 38 wherein R^7 is a bond or alkyl.

40. A compound according to any one of claims 36 to 39 wherein R^7 is a bond.

41. A compound according to any one of claims 36 to 39 wherein R^7 is methyl.

42. A compound according to any one of claims 36 to 41 wherein R^8 is H.

43. A compound according to any one of claims 36 to 42 wherein R^9 is a group of formula



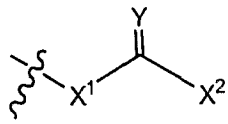
wherein R^{10} is selected from the group consisting of alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted;

R^{11} is selected from the group consisting of H, halogen, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, NH_2CO-, $(R^6)_2NCO$-, aminoalkyl and acyl, each of which may be optionally substituted.

44. A compound according to claim 43 wherein R^{10} is selected from the group consisting of heterocycloalkyl, and arylalkyl.

45. A compound according to claim 43 or 44 wherein R^{11} is selected from the group consisting of H, halogen, alkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, arylalkyl, hydroxyalkyl, alkoxyaryl, NH_2CO-, $(R^6)_2NCO$-, and acyl, each of which may be optionally substituted.

46. A compound according to any one of claims 36 to 42 wherein R^9 is a group of formula



wherein X^1 is selecetd from the group consisting of $-N(R^6)$, -O- and –S-;

wherein Y is selected from the group consisting of O and S;

wherein X^2 is selected from the group consisting of $-OR^{14}$, $-SR^{14}$ and $-NR^{15}R^{16}$;

R^{14} is selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy,

heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted;

R^{15} and R^{16} are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, arylalkyloxy, phenoxy, benzyloxy, heteroaryloxy, amino, alkylamino, and aminoalkyl, each of which may be optionally substituted, or

R^{15} and R^{16} together with the nitrogen to which they are attached form a heterocycloalkyl group.

47. A compound according to claim 46 wherein X^1 is NH.

48. A compound according to claim 46 or 47 wherein Y is O.

49. A compound according to claim 46 or 47 wherein Y is S.

50. A compound according to any one of claims 46 to 49 wherein X^2 is $-OR^{14}$.

51. A compound according to claim 50 wherein R^{14} is selected from the group consisting of alkyl, alkenyl, cycloalkyl, heteroalkyl, heteroarylalkyl and heterocycloalkylalkyl, each of which may be optionally substituted.

52. A compound according to any one of claims 46 to 49 wherein X^2 is $NR^{15}R^{16}$.

53. A compound according to any one of claims 46 to 49 wherein X^2 is NHR^{16}.

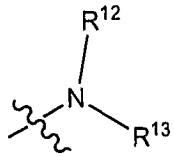
54. A compound according to claim 52 wherein R^{15} is selected from the group consisting of H, alkyl and hydroxy.

55. A compound according to claim 52 wherein R^{15} is selected from the group consisting of H, methyl and hydroxy.

56. A compound according to any one of claims 52 to 55 wherein R^{16} is selected from the group consisting of alkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, heteroarylalkyl, arylalkyl, cycloalkyl, heterocycloalkylalkyl and heteroarylalkyl, each of which may be optionally substituted.

57. A compound according to claim 52 wherein R^{15} and R^{16}, together with the nitrogen atom to which they are attached form an optionally substituted heterocycloalkyl group.

58. A compound according to any one of claims 36 to 42 wherein R^9 is:



wherein R^{12} and R^{13} are as defined above.

59. A compound according to claim 58 wherein R^{12} is selected from the group consisting of H, alkyl, heteroalkyl, arylalkyl, and heteroarylalkyl.

60. A compound according to claim 58 or 59 wherein R^{12} is selected from the group consisting of H, methyl, ethyl, 2-hydroxy-ethyl, propyl, and isopropyl.

61. A compound according to any one of claims 58 to 60 wherein R^{13} is selected from the group consisting of H, alkyl, heteroalkyl, arylalkyl, and heteroarylalkyl.

62. A compound according to claim 61 wherein R^{13} is selected from the group consisting of H, methyl, ethyl, 2-dimethyl-amino-ethyl, 2-di-ethyl-amino-ethyl, 2-phenyl-ethyl, propyl, 3-dimethyl-amino-propyl, benzyl, and 3-pyridin-3-yl-methyl.

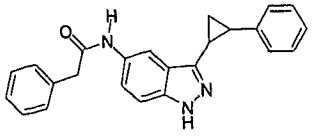
63. A compound according to claim 58 wherein R^{12} and R^{13} along with the nitrogen atom to which they are attached form an optionally substituted heterocycloalkyl group.

64. A compound according to claim 63 wherein the optionally substituted heterocycloalkyl group is selected from optionally substituted piperazine, optionally

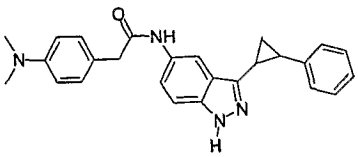
substituted, morpholine, optionally substituted piperidine, and optionally substituted thiomorpholine.

65. A compound according to any one of claims 1 to 64 wherein the optional substituent is selected from the group consisting of: halogen, =O, =S, -CN, $-NO_2$, $-CF_3$, $-OCF_3$, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkoxyheteroaryl, alkenyloxy, alkynyloxy, cycloalkyloxy, cycloalkenyloxy, heterocycloalkyloxy, heterocycloalkenyloxy, aryloxy, heteroaryloxy, arylalkyl, heteroarylalkyl, arylalkyloxy, -amino, alkylamino, acylamino, aminoalkyl, arylamino, sulfonyl, alkylsulfonyl, arylsulfonyl, aminosulfonyl, aminoalkyl, alkoxyalky, -COOH, $-COR^6$, $-C(O)OR^6$, -SH, $-SR^6$, $-OR^6$ and acyl.

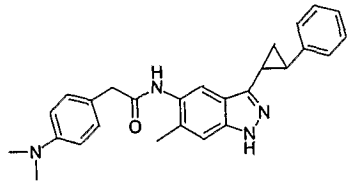
66. The compound of claim 1 wherein the compound is selected from compounds, and their pharmaceutically acceptable salts, selected from the group consisting of



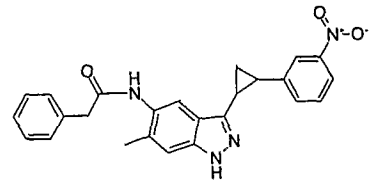
2-Phenyl-N-[3-(2-phenyl-cyclopropyl)-1H-indazol-5-yl]-acetamide



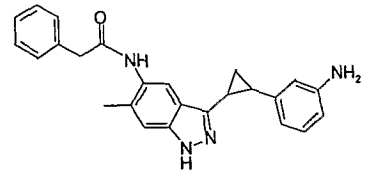
2-(4-Dimethylamino-phenyl)-N-[3-(2-phenyl-cyclopropyl)-1H-indazol-5-yl]-acetamide



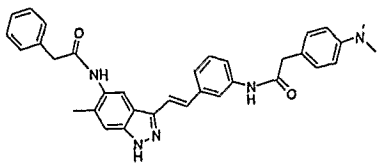
2-(4-Dimethylamino-phenyl)-N-[6-methyl-3-(2-phenyl-cyclopropyl)-1H-indazol-5-yl]-acetamide



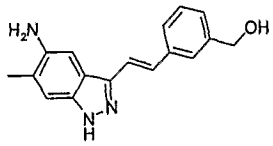
N-{6-Methyl-3-[2-(3-nitro-phenyl)-cyclopropyl]-1H-indazol-5-yl}-2-phenyl-acetamide



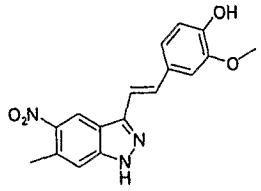
N-{3-[2-(3-Amino-phenyl)-cyclopropyl]-6-methyl-1H-indazol-5-yl}-2-phenyl-acetamide



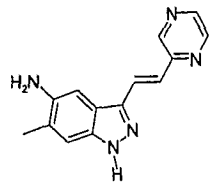
2-(4-Dimethylamino-phenyl)-N-{3-[2-(6-methyl-5-phenylacetylamino-1H-indazol-3-yl)-vinyl]-phenyl}-acetamide



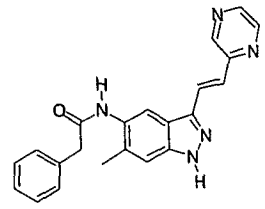
{3-[2-(5-Amino-6-methyl-1H-indazol-3-yl)-vinyl]-phenyl}-methanol



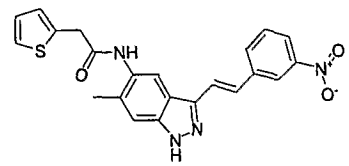
2-Methoxy-4-[2-(6-methyl-5-nitro-1H-indazol-3-yl)-vinyl]-phenol



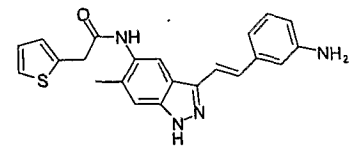
6-Methyl-3-(2-pyrazin-2-yl-vinyl)-1H-indazol-5-ylamine



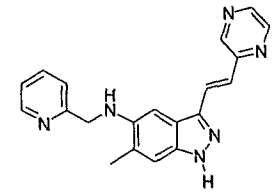
N-[6-Methyl-3-(2-pyrazin-2-yl-vinyl)-1H-indazol-5-yl]-2-phenyl-acetamide



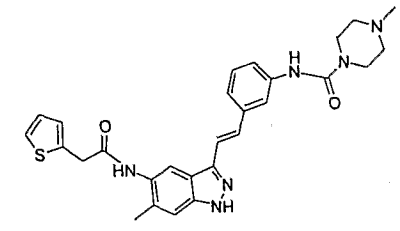
N-{6-Methyl-3-[2-(3-nitro-phenyl)-vinyl]-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide



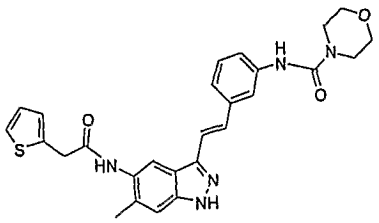
N-{3-[2-(3-Amino-phenyl)-vinyl]-6-methyl-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide



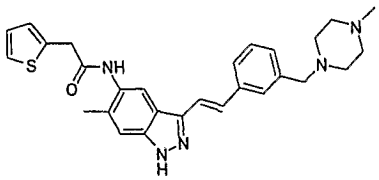
[6-Methyl-3-(2-pyrazin-2-yl-vinyl)-1H-indazol-5-yl]-pyridin-2-ylmethyl-amine



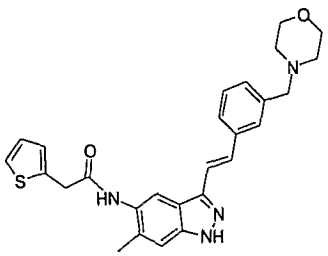
4-Methyl-piperazine-1-carboxylic acid (3-{2-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-amide



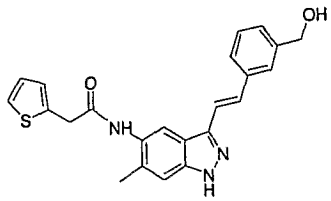
Morpholine-4-carboxylic acid (3-{2-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-amide



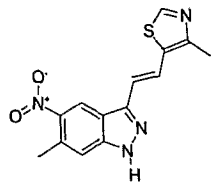
N-(6-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



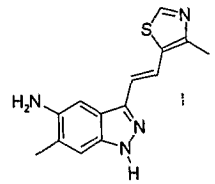
N-{6-Methyl-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide



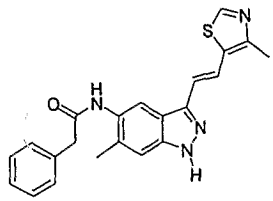
N-{3-[2-(3-Hydroxymethyl-phenyl)-vinyl]-6-methyl-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide



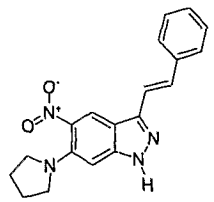
6-Methyl-3-[2-(4-methyl-thiazol-5-yl)-vinyl]-5-nitro-1H-indazole



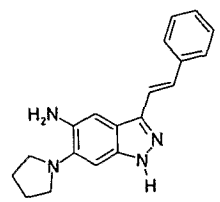
6-Methyl-3-[2-(4-methyl-thiazol-5-yl)-vinyl]-1H-indazol-5-ylamine



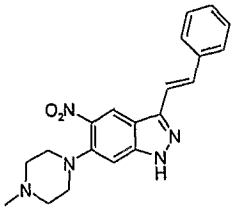
N-{6-Methyl-3-[2-(4-methyl-thiazol-5-yl)-vinyl]-1H-indazol-5-yl}-2-phenyl-acetamide



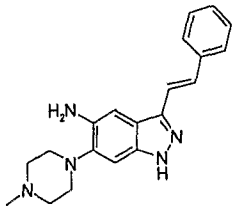
5-Nitro-6-pyrrolidin-1-yl-3-styryl-1H-indazole



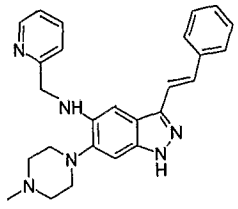
6-Pyrrolidin-1-yl-3-styryl-1H-indazol-5-ylamine



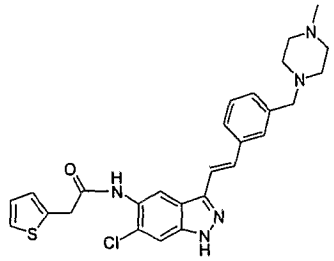
6-(4-Methyl-piperazin-1-yl)-5-nitro-3-styryl-1H-indazole



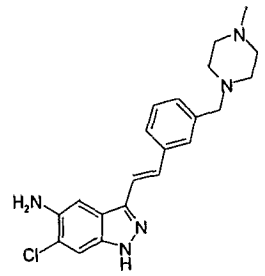
6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-ylamine



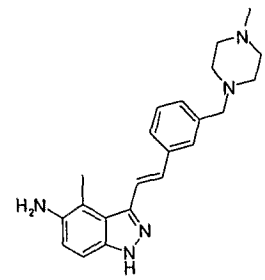
[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-pyridin-2-ylmethyl-amine



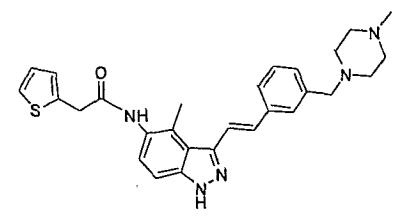
N-(6-Chloro-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



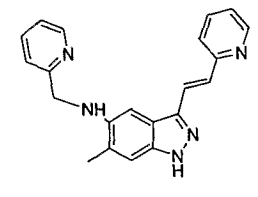
6-Chloro-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-ylamine



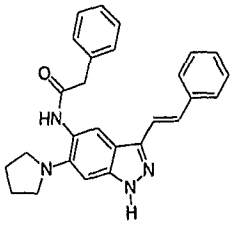
4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-ylamine



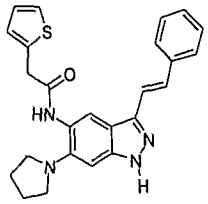
N-(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



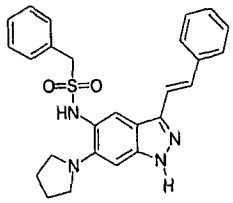
[6-Methyl-3-(2-pyridin-2-yl-vinyl)-1H-indazol-5-yl]-pyridin-2-ylmethyl-amine



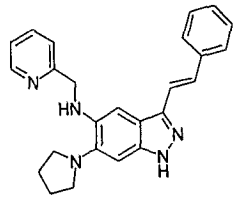
2-Phenyl-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-acetamide



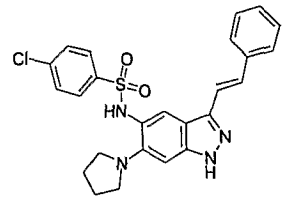
N-(6-Pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



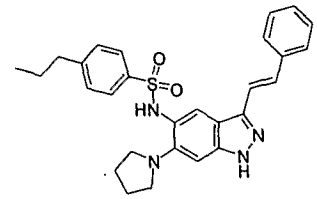
C-Phenyl-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-methanesulfonamide



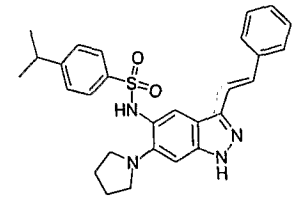
Pyridin-2-ylmethyl-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-amine



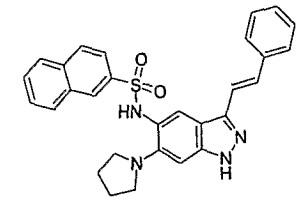
4-Chloro-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide



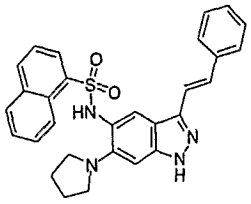
4-Propyl-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide



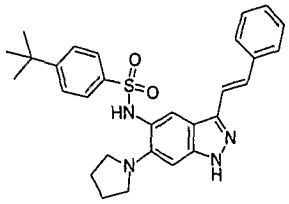
4-Isopropyl-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide



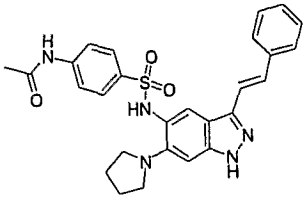
Naphthalene-2-sulfonic acid (6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-amide



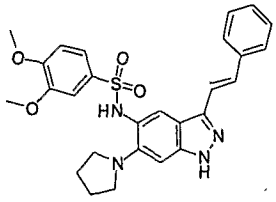
Naphthalene-1-sulfonic acid (6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-amide



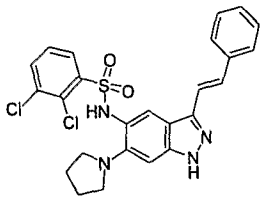
4-tert-Butyl-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide



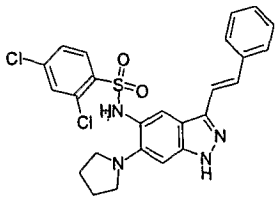
N-[4-(6-Pyrrolidin-1-yl-3-styryl-1H-indazol-5-ylsulfamoyl)-phenyl]-acetamide



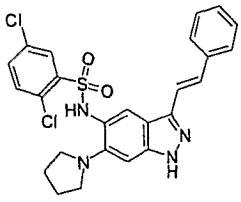
3,4-Dimethoxy-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide



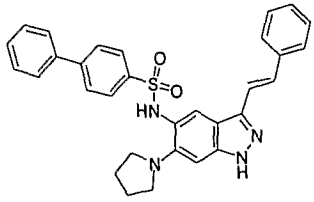
2,3-Dichloro-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide



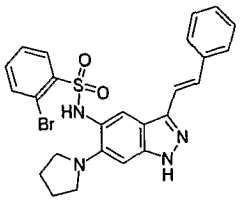
2,4-Dichloro-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide



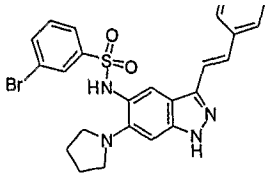
2,5-Dichloro-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide



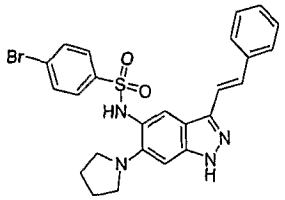
Biphenyl-4-sulfonic acid (6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-amide



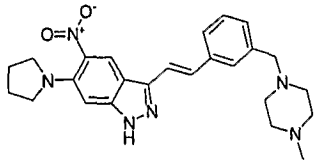
2-Bromo-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide



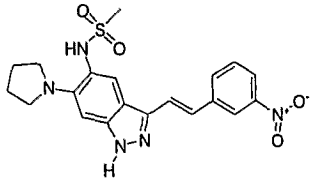
3-Bromo-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide



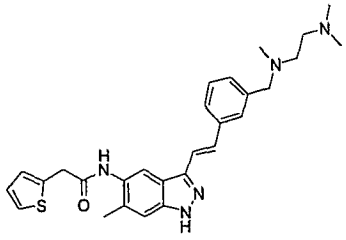
4-Bromo-N-(6-pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-benzenesulfonamide



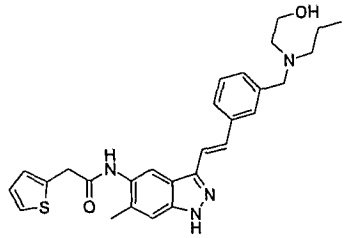
3-{2-[3-(4-Methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-5-nitro-6-pyrrolidin-1-yl-1H-indazole



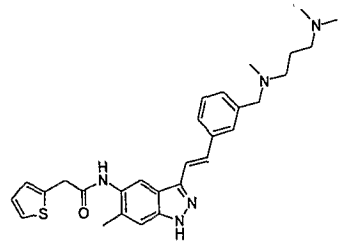
N-{3-[2-(3-Nitro-phenyl)-vinyl]-6-pyrrolidin-1-yl-1H-indazol-5-yl}-methanesulfonamide



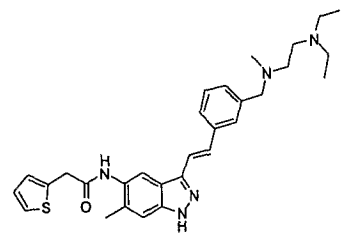
N-{3-[2-(3-{[(2-Dimethylamino-ethyl)-methyl-amino]-methyl}-phenyl)-vinyl]-6-methyl-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide



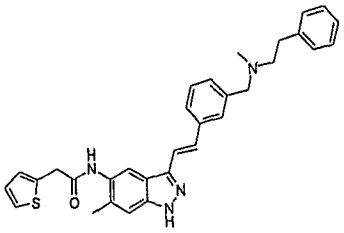
N-{3-[2-(3-{[(2-Hydroxy-ethyl)-propyl-amino]-methyl}-phenyl)-vinyl]-6-methyl-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide



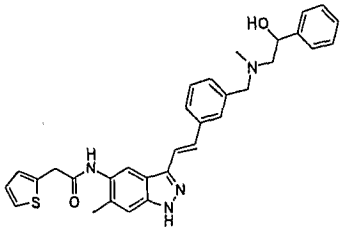
N-{3-[2-(3-{[(3-Dimethylamino-propyl)-methyl-amino]-methyl}-phenyl)-vinyl]-6-methyl-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide



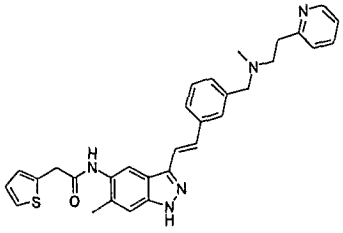
N-{3-[2-(3-{[(2-Diethylamino-ethyl)-methyl-amino]-methyl}-phenyl)-vinyl]-6-methyl-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide



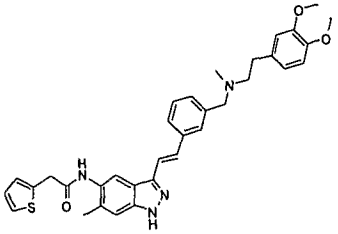
N-[6-Methyl-3-(2-{3-[(methyl-phenethyl-amino)-methyl]-phenyl}-vinyl)-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide



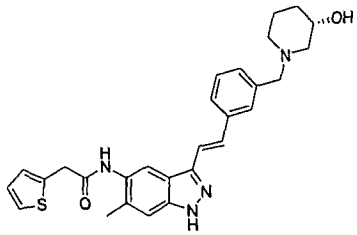
N-{3-[2-(3-{[(2-Hydroxy-2-phenyl-ethyl)-methyl-amino]-methyl}-phenyl)-vinyl]-6-methyl-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide



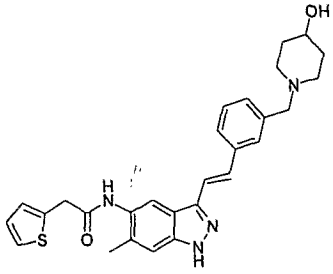
N-{6-Methyl-3-[2-(3-{[methyl-(2-pyridin-2-yl-ethyl)-amino]-methyl}-phenyl)-vinyl]-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide



N-(3-{2-[3-({[2-(3,4-Dimethoxy-phenyl)-ethyl]-methyl-amino}-methyl)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



N-(3-{2-[3-(3-Hydroxy-piperidin-1-ylmethyl)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



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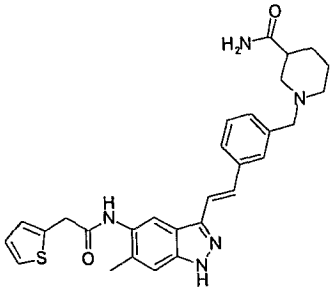

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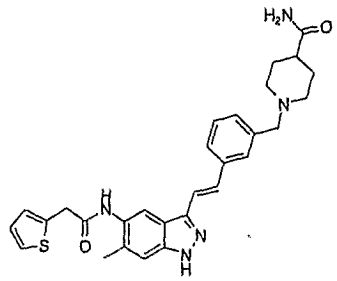

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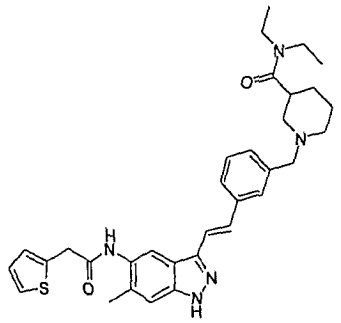

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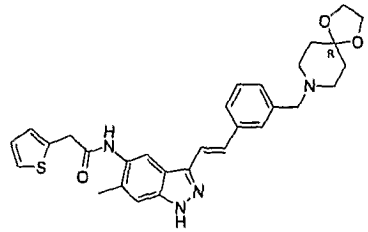
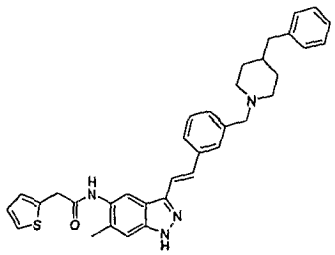
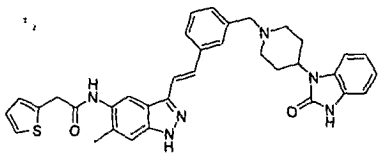


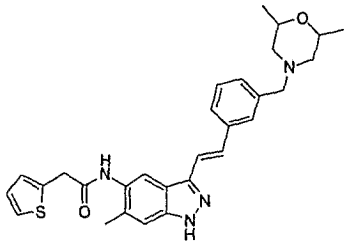
N-(3-{2-[3-(1,4-Dioxa-8-aza-spiro[4.5]dec-8-ylmethyl)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



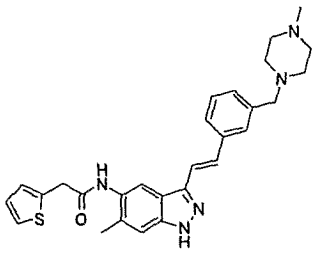
N-(3-{2-[3-(4-Benzyl-piperidin-1-ylmethyl)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



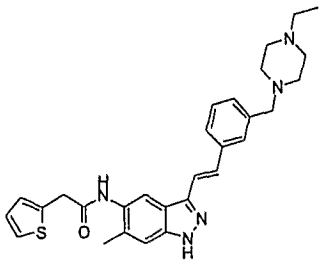
N-[6-Methyl-3-(2-{3-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-ylmethyl]-phenyl}-vinyl)-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide



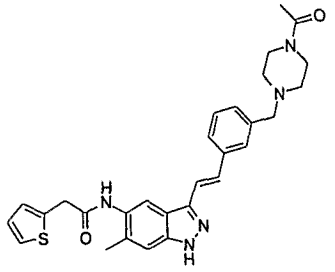
N-(3-{2-[3-(2,6-Dimethyl-morpholin-4-ylmethyl)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



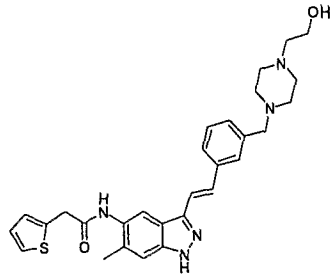
N-(6-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



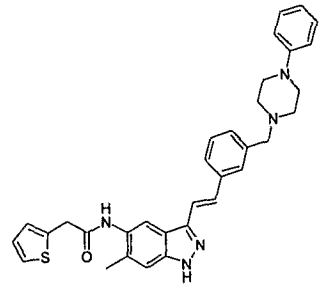
N-(3-{2-[3-(4-Ethyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



N-(3-{2-[3-(4-Acetyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



N-[3-(2-{3-[4-(2-Hydroxy-ethyl)-piperazin-1-ylmethyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide



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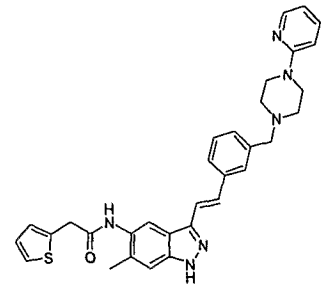
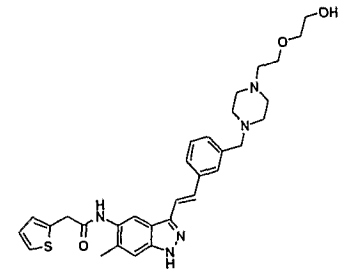
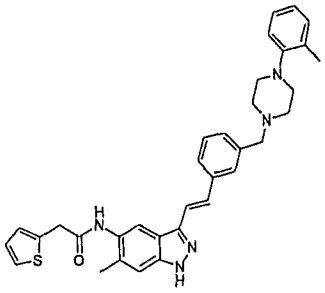


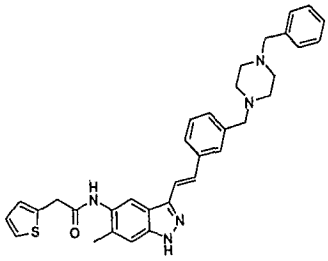
N-(6-Methyl-3-{2-[3-(4-pyridin-2-yl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



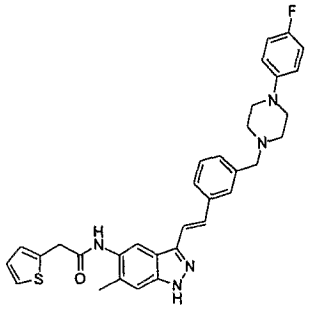
N-{3-[2-(3-{4-[2-(2-Hydroxy-ethoxy)-ethyl]-piperazin-1-ylmethyl}-phenyl)-vinyl]-6-methyl-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide



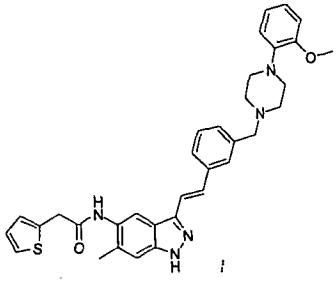
N-(6-Methyl-3-{2-[3-(4-o-tolyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



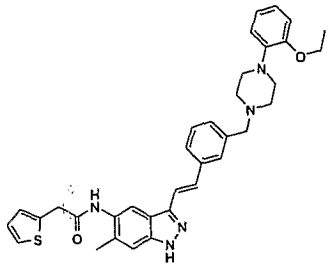
N-(3-{2-[3-(4-Benzyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



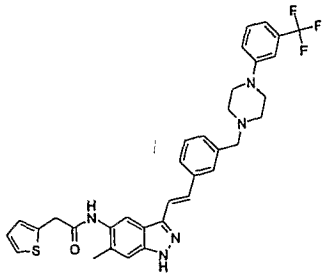
N-[3-(2-{3-[4-(4-Fluoro-phenyl)-piperazin-1-ylmethyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide



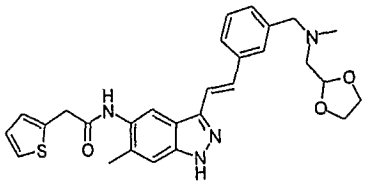
N-[3-(2-{3-[4-(2-Methoxy-phenyl)-piperazin-1-ylmethyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide



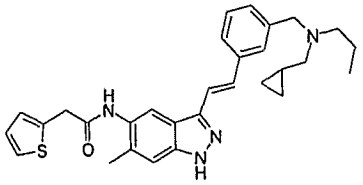
N-[3-(2-{3-[4-(2-Ethoxy-phenyl)-piperazin-1-ylmethyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide



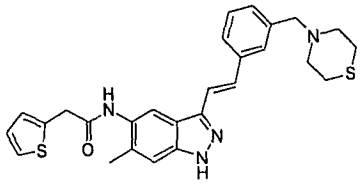
N-[6-Methyl-3-(2-{3-[4-(3-trifluoromethyl-phenyl)-piperazin-1-ylmethyl]-phenyl}-vinyl)-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide



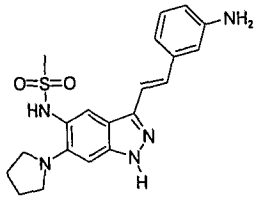
N-[3-(2-{3-[([1,3]Dioxolan-2-ylmethyl-methyl-amino)-methyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide



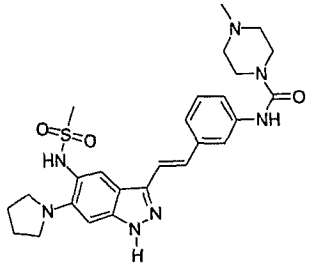
N-[3-(2-{3-[(Cyclopropylmethyl-propyl-amino)-methyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide



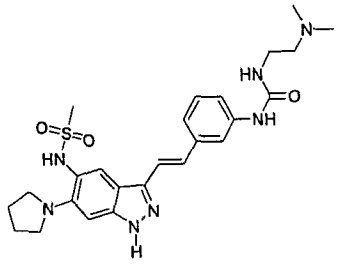
N-{6-Methyl-3-[2-(3-thiomorpholin-4-ylmethyl-phenyl)-vinyl]-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide



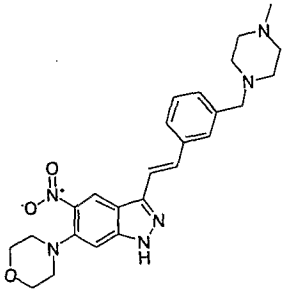
N-{3-[2-(3-Amino-phenyl)-vinyl]-6-pyrrolidin-1-yl-1H-indazol-5-yl}-methanesulfonamide



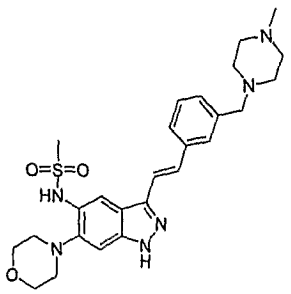
4-Methyl-piperazine-1-carboxylic acid {3-[2-(5-methanesulfonylamino-6-pyrrolidin-1-yl-1H-indazol-3-yl)-vinyl]-phenyl}-amide



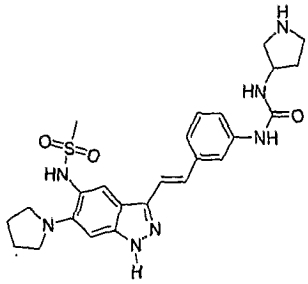
N-[3-(2-{3-[3-(2-Dimethylamino-ethyl)-ureido]-phenyl}-vinyl)-6-pyrrolidin-1-yl-1H-indazol-5-yl]-methanesulfonamide



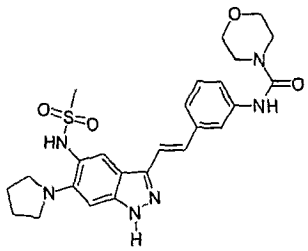
3-{2-[3-(4-Methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-6-morpholin-4-yl-5-nitro-1H-indazole



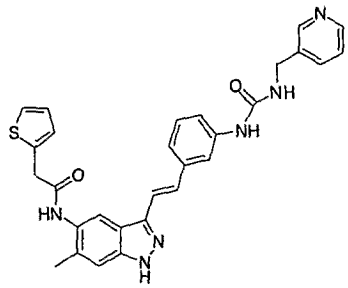
N-(3-{2-[3-(4-Methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-6-morpholin-4-yl-1H-indazol-5-yl)-methanesulfonamide



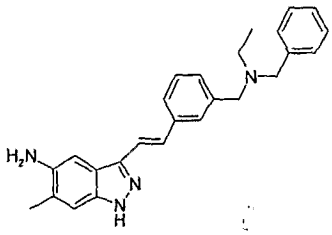
N-(6-Pyrrolidin-1-yl-3-{2-[3-(3-pyrrolidin-3-yl-ureido)-phenyl]-vinyl}-1H-indazol-5-yl)-methanesulfonamide



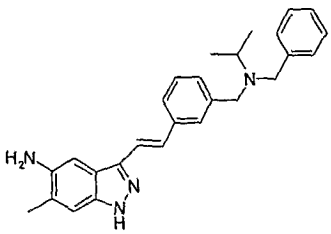
Morpholine-4-carboxylic acid {3-[2-(5-methanesulfonylamino-6-pyrrolidin-1-yl-1H-indazol-3-yl)-vinyl]-phenyl}-amide



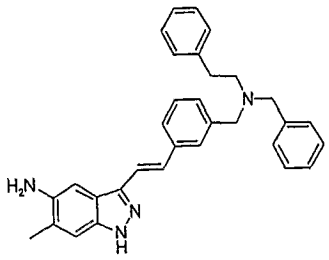
N-(6-Methyl-3-{2-[3-(3-pyridin-3-ylmethyl-ureido)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



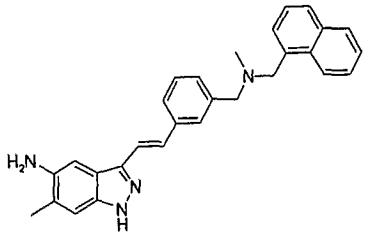
3-(2-{3-[(Benzyl-ethyl-amino)-methyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-ylamine



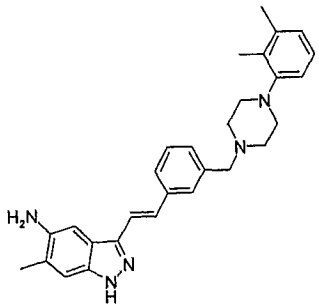
3-(2-{3-[(Benzyl-isopropyl-amino)-methyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-ylamine



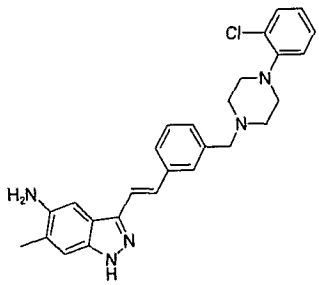
3-(2-{3-[(Benzyl-phenethyl-amino)-methyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-ylamine



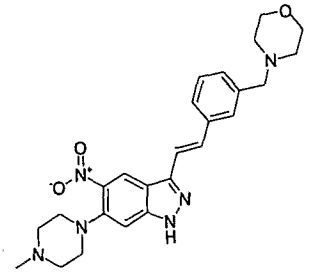
6-Methyl-3-(2-{3-[(methyl-naphthalen-1-ylmethyl-amino)-methyl]-phenyl}-vinyl)-1H-indazol-5-ylamine



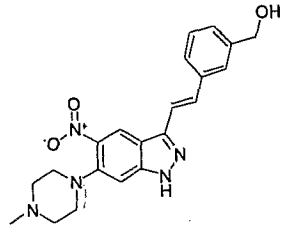
3-(2-{3-[4-(2,3-Dimethyl-phenyl)-piperazin-1-ylmethyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-ylamine



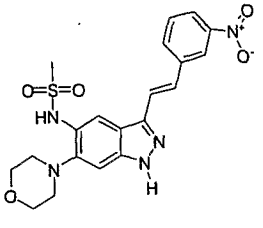
3-(2-{3-[4-(2-Chloro-phenyl)-piperazin-1-ylmethyl]-phenyl}-vinyl)-6-methyl-1H-indazol-5-ylamine



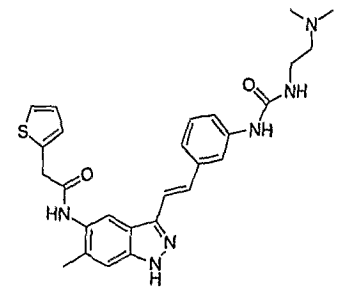
6-(4-Methyl-piperazin-1-yl)-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-5-nitro-1H-indazole



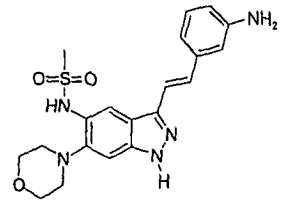
(3-{2-[6-(4-Methyl-piperazin-1-yl)-5-nitro-1H-indazol-3-yl]-vinyl}-phenyl)-methanol



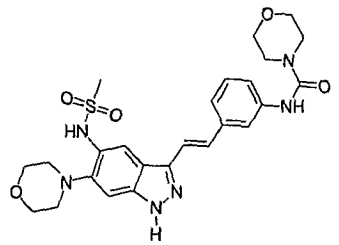
N-{6-Morpholin-4-yl-3-[2-(3-nitro-phenyl)-vinyl]-1H-indazol-5-yl}-methanesulfonamide



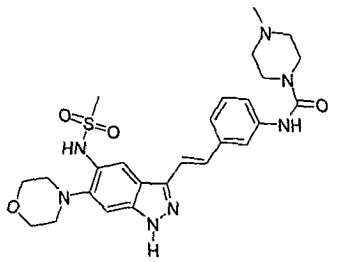
N-[3-(2-{3-[3-(2-Dimethylamino-ethyl)-ureido]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide



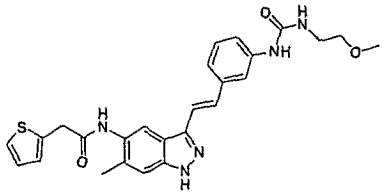
N-{3-[2-(3-Amino-phenyl)-vinyl]-6-morpholin-4-yl-1H-indazol-5-yl}-methanesulfonamide



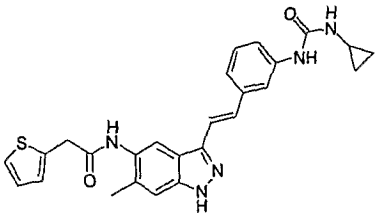
Morpholine-4-carboxylic acid {3-[2-(5-methanesulfonylamino-6-morpholin-4-yl-1H-indazol-3-yl)-vinyl]-phenyl}-amide



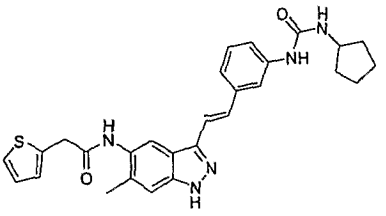
4-Methyl-piperazine-1-carboxylic acid {3-[2-(5-methanesulfonylamino-6-morpholin-4-yl-1H-indazol-3-yl)-vinyl]-phenyl}-amide



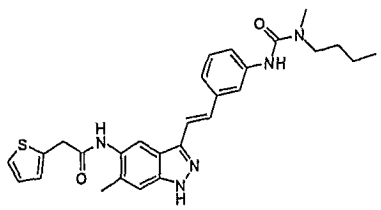
N-[3-(2-{3-[3-(2-Methoxy-ethyl)-ureido]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide



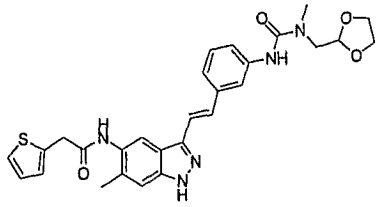
N-(3-{2-[3-(3-Cyclopropyl-ureido)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



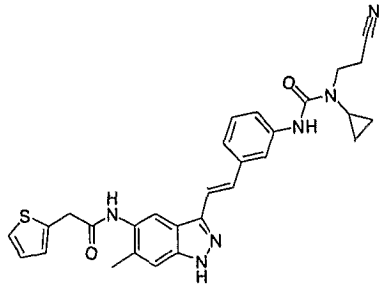
N-(3-{2-[3-(3-Cyclopentyl-ureido)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



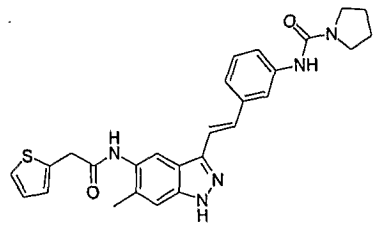
N-(3-{2-[3-(3-Butyl-3-methyl-ureido)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



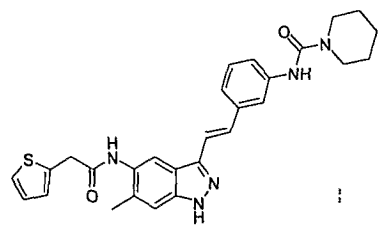
N-(3-{2-[3-(3-[1,3]Dioxolan-2-ylmethyl-3-methyl-ureido)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



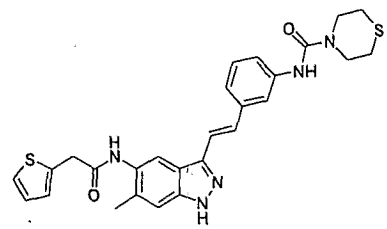
N-[3-(2-{3-[3-(2-Cyano-ethyl)-3-cyclopropyl-ureido]-phenyl}-vinyl)-6-methyl-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide



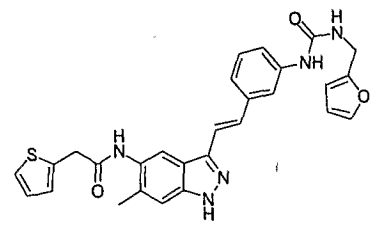
Pyrrolidine-1-carboxylic acid (3-{2-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-amide



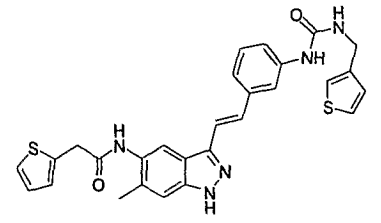
Piperidine-1-carboxylic acid (3-{2-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-amide



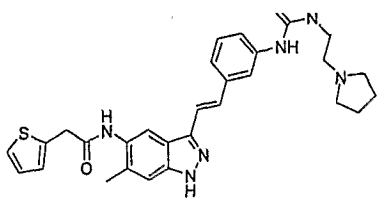
Thiomorpholine-4-carboxylic acid (3-{2-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-amide



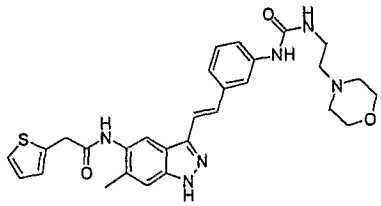
N-(3-{2-[3-(3-Furan-2-ylmethyl-ureido)-phenyl]-vinyl}-6-methyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



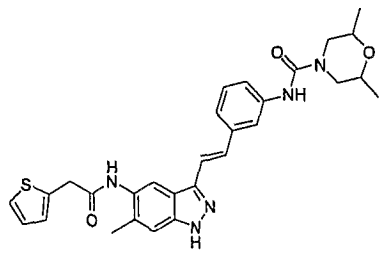
N-(6-Methyl-3-{2-[3-(3-thiophen-3-ylmethyl-ureido)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



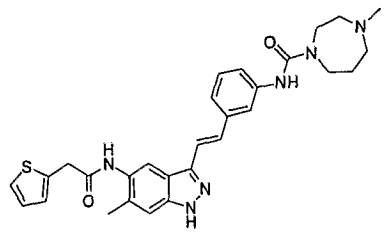
N-[6-Methyl-3-(2-{3-[3-(2-pyrrolidin-1-yl-ethyl)-ureido]-phenyl}-vinyl)-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide



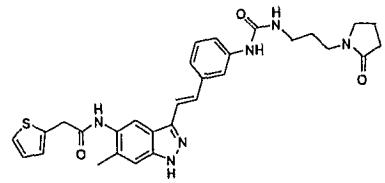
N-[6-Methyl-3-(2-{3-[3-(2-morpholin-4-yl-ethyl)-ureido]-phenyl}-vinyl)-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide



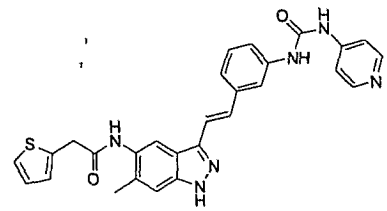
2,6-Dimethyl-morpholine-4-carboxylic acid (3-{2-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-amide



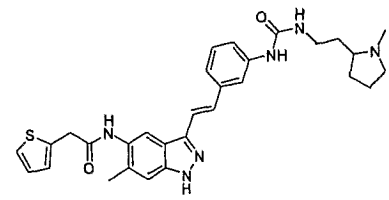
4-Methyl-[1,4]diazepane-1-carboxylic acid (3-{2-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-amide



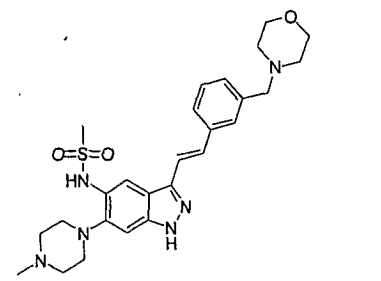
N-{6-Methyl-3-[2-(3-{3-[3-(2-oxo-pyrrolidin-1-yl)-propyl]-ureido}-phenyl)-vinyl]-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide



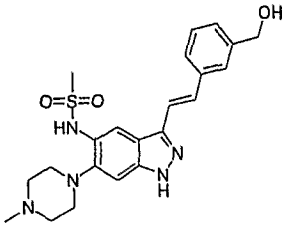
N-(6-Methyl-3-{2-[3-(3-pyridin-4-yl-ureido)-phenyl]-vinyl}-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



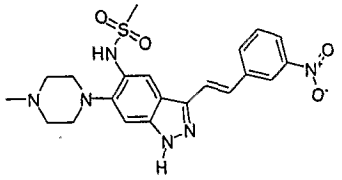
N-{6-Methyl-3-[2-(3-{3-[2-(1-methyl-pyrrolidin-2-yl)-ethyl]-ureido}-phenyl)-vinyl]-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide



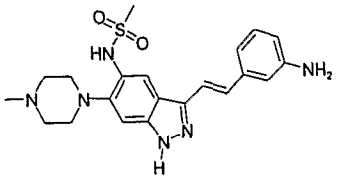
N-{6-(4-Methyl-piperazin-1-yl)-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1H-indazol-5-yl}-methanesulfonamide



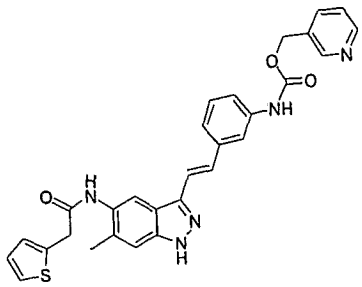
N-[3-[2-(3-Hydroxymethyl-phenyl)-vinyl]-6-(4-methyl-piperazin-1-yl)-1H-indazol-5-yl]-methanesulfonamide



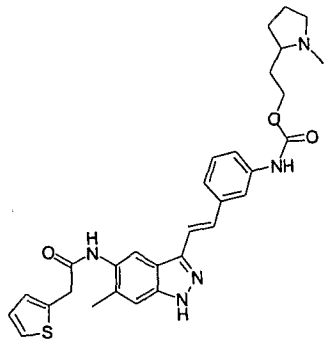
N-{6-(4-Methyl-piperazin-1-yl)-3-[2-(3-nitro-phenyl)-vinyl]-1H-indazol-5-yl}-methanesulfonamide



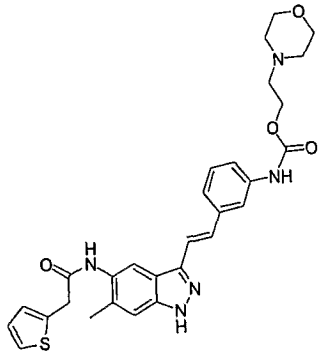
N-[3-[2-(3-Amino-phenyl)-vinyl]-6-(4-methyl-piperazin-1-yl)-1H-indazol-5-yl]-methanesulfonamide



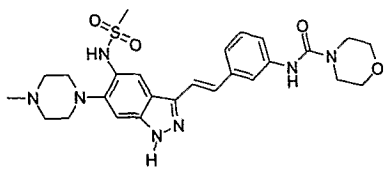
(3-{2-[6-Methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-carbamic acid pyridin-3-ylmethyl ester



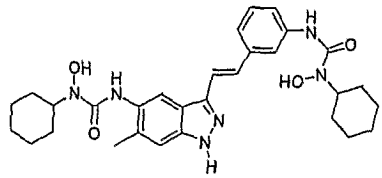
(3-{2-[6-Methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-carbamic acid 2-(1-methyl-pyrrolidin-2-yl)-ethyl ester

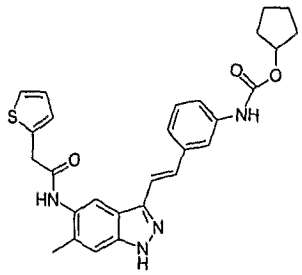


(3-{2-[6-Methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-carbamic acid 2-morpholin-4-yl-ethyl ester

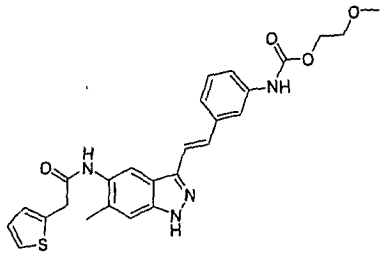


Morpholine-4-carboxylic acid (3-{2-[5-methanesulfonylamino-6-(4-methyl-piperazin-1-yl)-1H-indazol-3-yl]-vinyl}-phenyl)-amide

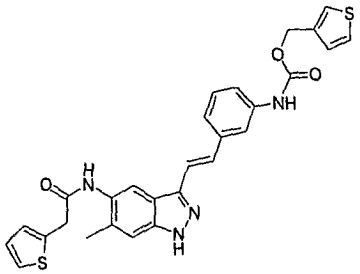




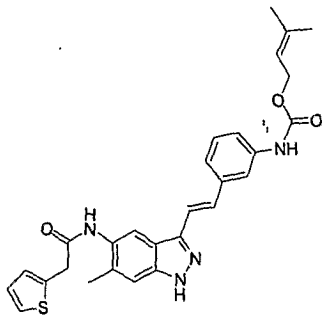
(3-{2-[6-Methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-carbamic acid cyclopentyl ester



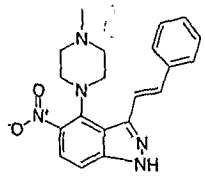
(3-{2-[6-Methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-carbamic acid 2-methoxy-ethyl ester



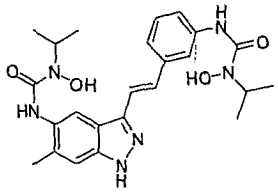
(3-{2-[6-Methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-carbamic acid thiophen-3-ylmethyl ester

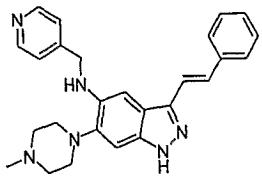


(3-{2-[6-Methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-yl]-vinyl}-phenyl)-carbamic acid 3-methyl-but-2-enyl ester

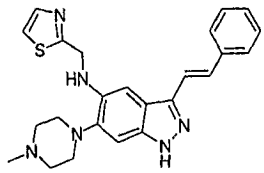


4-(4-Methyl-piperazin-1-yl)-5-nitro-3-styryl-1H-indazole

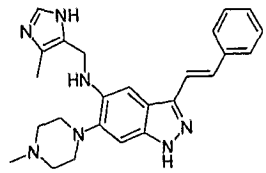




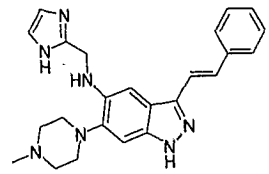
[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-pyridin-4-ylmethyl-amine



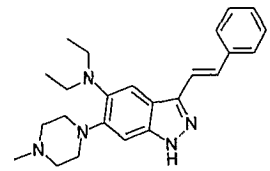
[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-thiazol-2-ylmethyl-amine



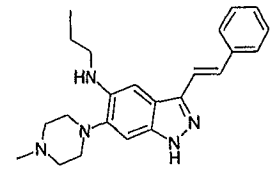
(5-Methyl-3H-imidazol-4-ylmethyl)-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amine



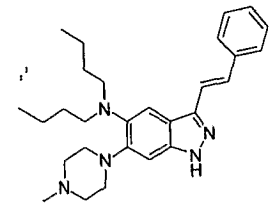
(1H-Imidazol-2-ylmethyl)-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amine



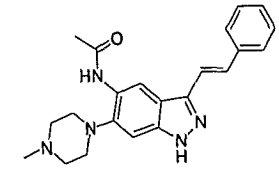
Diethyl-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amine



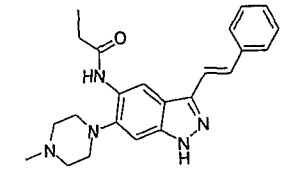
[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-propyl-amine



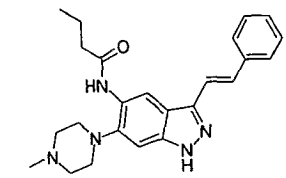
Dibutyl-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amine



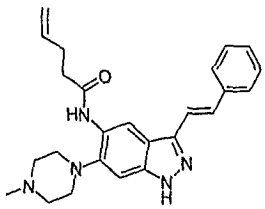
N-[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-acetamide



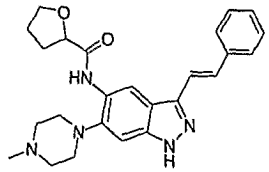
N-[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-propionamide



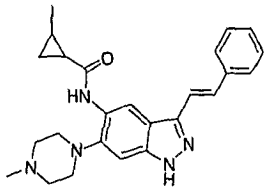
N-[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-butyramide



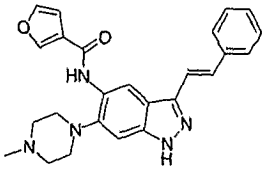
Pent-4-enoic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide



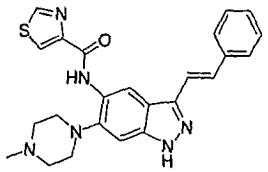
Tetrahydro-furan-2-carboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide



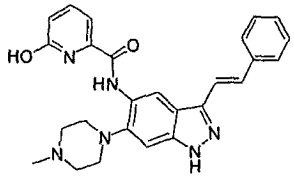
2-Methyl-cyclopropanecarboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide



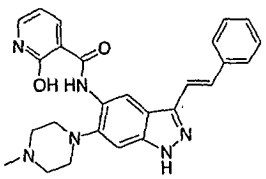
Furan-3-carboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide



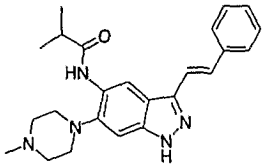
Thiazole-4-carboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide



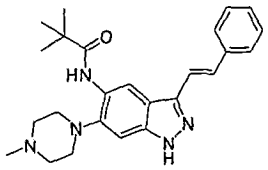
6-Hydroxy-pyridine-2-carboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide



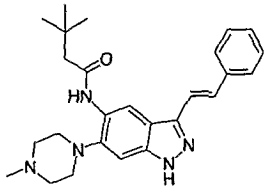
2-Hydroxy-N-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-nicotinamide



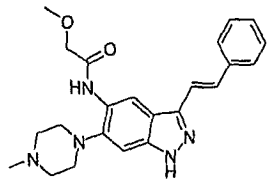
N-[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-isobutyramide



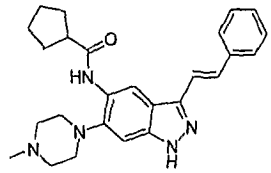
2,2-Dimethyl-N-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-propionamide



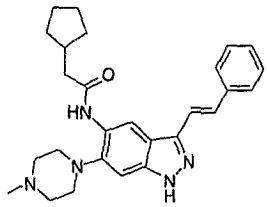
3,3-Dimethyl-N-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-butyramide



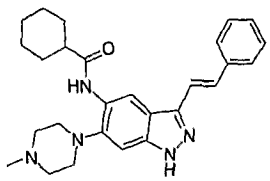
2-Methoxy-N-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-acetamide



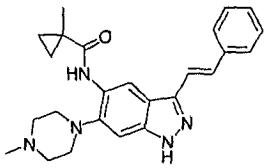
Cyclopentanecarboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide



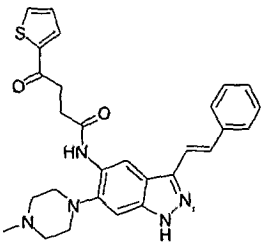
2-Cyclopentyl-N-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-acetamide



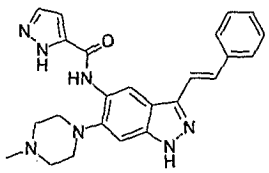
Cyclohexanecarboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide



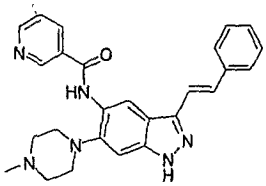
1-Methyl-cyclopropanecarboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide



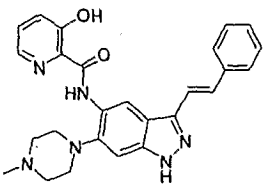
N-[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-4-oxo-4-thiophen-2-yl-butyramide



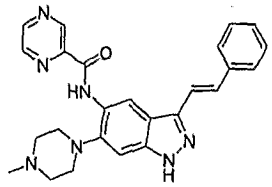
2H-Pyrazole-3-carboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide



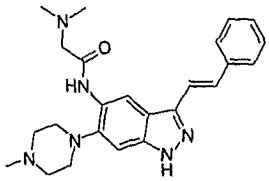
N-[6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-nicotinamide



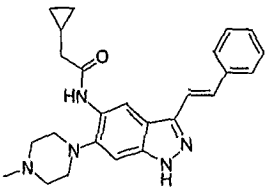
3-Hydroxy-pyridine-2-carboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide



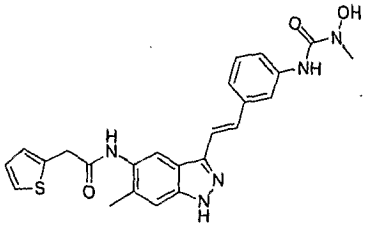
Pyrazine-2-carboxylic acid [6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amide

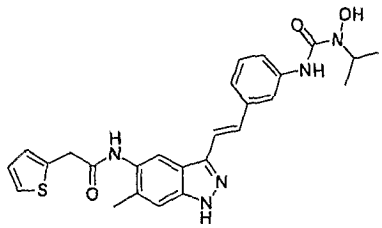


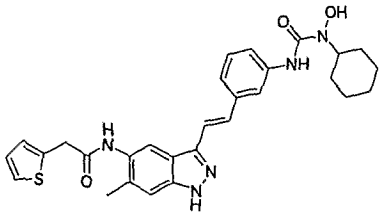
2-Dimethylamino-N-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-acetamide

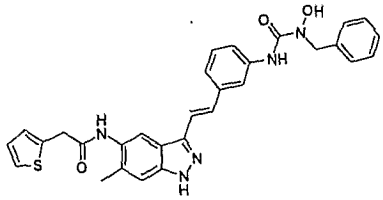


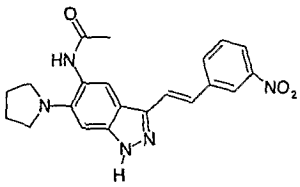
2-Cyclopropyl-N-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-acetamide



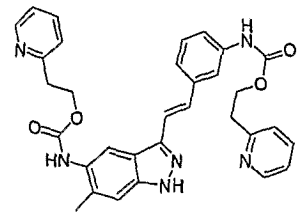




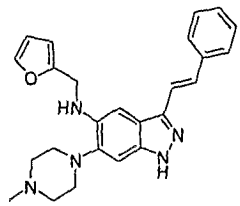




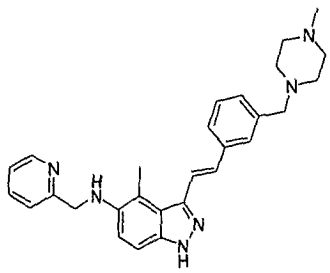
N-{3-[2-(3-Nitro-phenyl)-vinyl]-6-pyrrolidin-1-yl-1H-indazol-5-yl}-acetamide



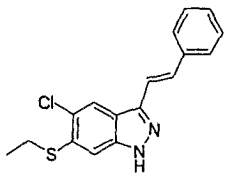
(6-Methyl-3-{2-[3-(2-pyridin-2-yl-ethoxycarbonylamino)-phenyl]-vinyl}-1H-indazol-5-yl)-carbamic acid 2-pyridin-2-yl-ethyl ester



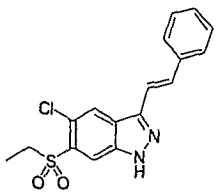
Furan-2-ylmethyl-[6-(4-methyl-piperazin-1-yl)-3-styryl-1H-indazol-5-yl]-amine



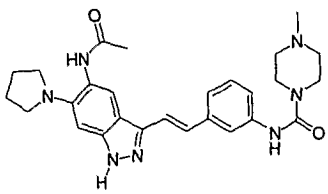
(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-pyridin-2-ylmethyl-amine



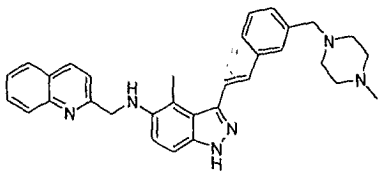
5-Chloro-6-ethylsulfanyl-3-styryl-1H-indazole



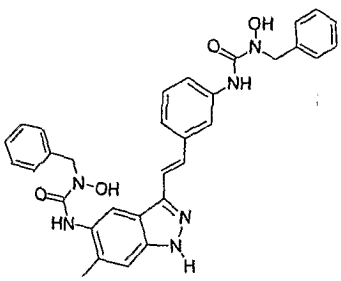
5-Chloro-6-ethanesulfonyl-3-styryl-1H-indazole

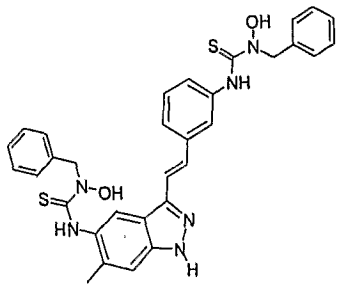


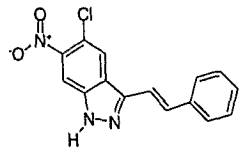
4-Methyl-piperazine-1-carboxylic acid {3-[2-(5-acetylamino-6-pyrrolidin-1-yl-1H-indazol-3-yl)-vinyl]-phenyl}-amide



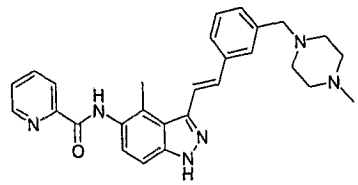
(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-quinolin-2-ylmethyl-amine



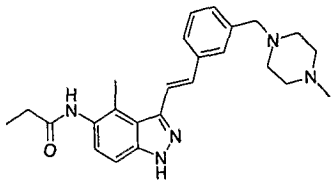




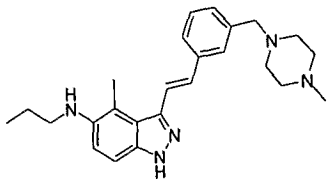
5-Chloro-6-nitro-3-styryl-1H-indazole



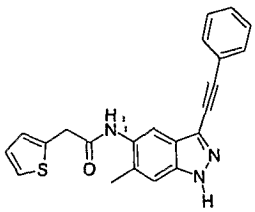
Pyridine-2-carboxylic acid (4-methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-amide



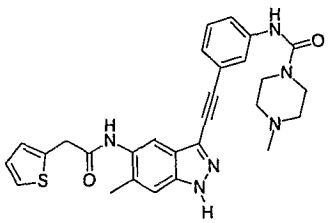
N-(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-propionamide



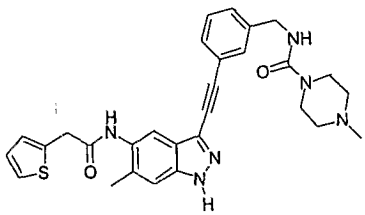
(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-propyl-amine



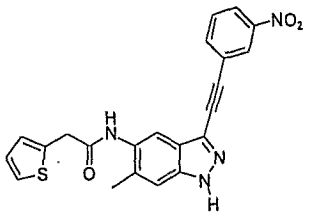
N-(6-Methyl-3-phenylethynyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



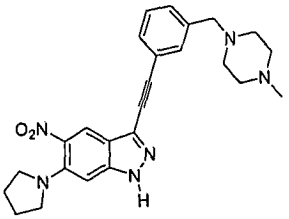
4-Methyl-piperazine-1-carboxylic acid {3-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-ylethynyl]-phenyl}-amide



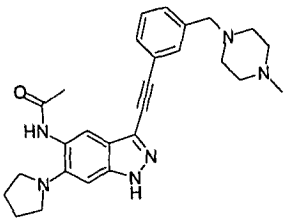
4-Methyl-piperazine-1-carboxylic acid 3-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-ylethynyl]-benzylamide



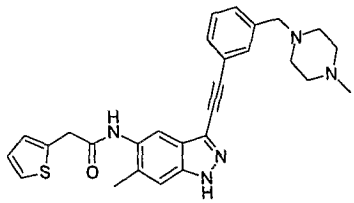
N-[6-Methyl-3-(3-nitro-phenylethynyl)-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide



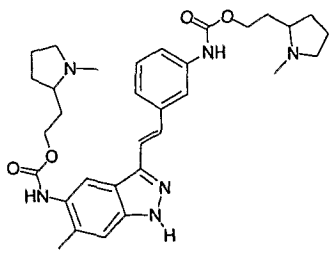
3-[3-(4-Methyl-piperazin-1-ylmethyl)-phenylethynyl]-5-nitro-6-pyrrolidin-1-yl-1H-indazole



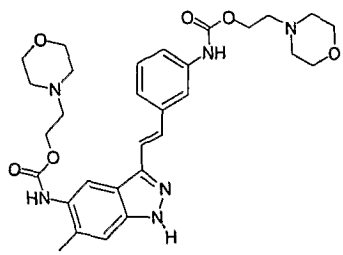
N-{3-[3-(4-Methyl-piperazin-1-ylmethyl)-phenylethynyl]-6-pyrrolidin-1-yl-1H-indazol-5-yl}-acetamide



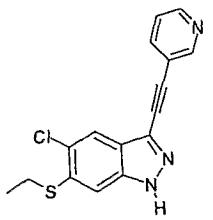
N-{6-Methyl-3-[3-(4-methyl-piperazin-1-ylmethyl)-phenylethynyl]-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide



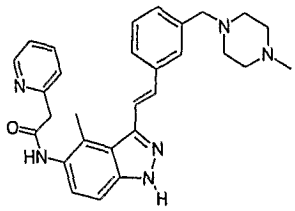
[6-Methyl-3-(2-{3-[2-(1-methyl-pyrrolidin-2-yl)-ethoxycarbonylamino]-phenyl}-vinyl)-1H-indazol-5-yl]-carbamic acid 2-(1-methyl-pyrrolidin-2-yl)-ethyl ester



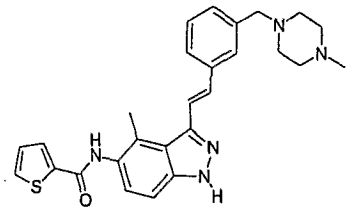
(6-Methyl-3-{2-[3-(2-morpholin-4-yl-ethoxycarbonylamino)-phenyl]-vinyl}-1H-indazol-5-yl)-carbamic acid 2-morpholin-4-yl-ethyl ester



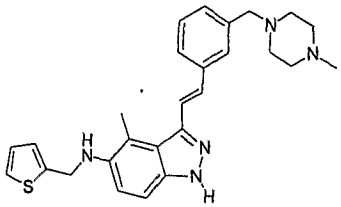
5-Chloro-6-ethylsulfanyl-3-pyridin-3-ylethynyl-1H-indazole



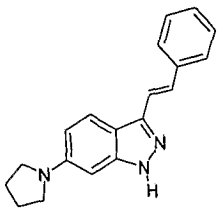
N-(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-2-pyridin-2-yl-acetamide



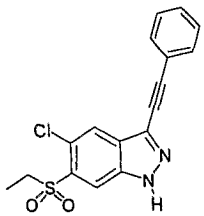
Thiophene-2-carboxylic acid (4-methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-amide



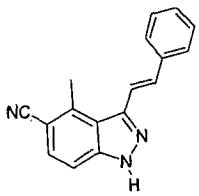
(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-thiophen-2-ylmethyl-amine



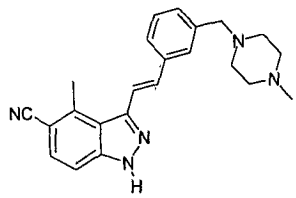
6-Pyrrolidin-1-yl-3-styryl-1H-indazole



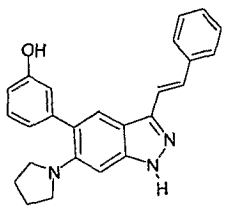
5-Chloro-6-ethanesulfonyl-3-phenylethynyl-1H-indazole



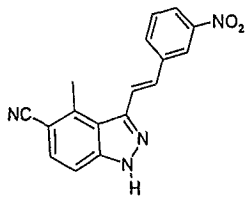
4-Methyl-3-styryl-1H-indazole-5-carbonitrile



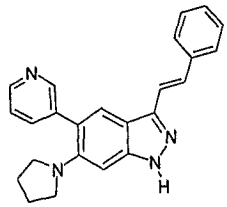
4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazole-5-carbonitrile



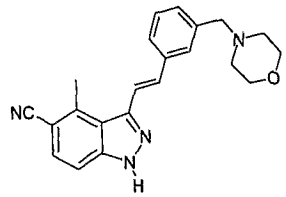
3-(6-Pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-phenol



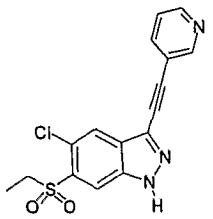
4-Methyl-3-[2-(3-nitro-phenyl)-vinyl]-1H-indazole-5-carbonitrile



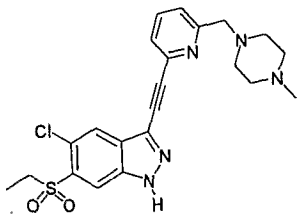
5-Pyridin-3-yl-6-pyrrolidin-1-yl-3-styryl-1H-indazole



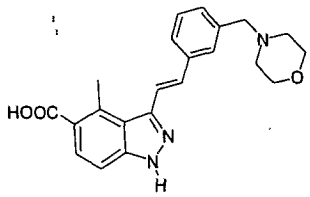
4-Methyl-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1H-indazole-5-carbonitrile



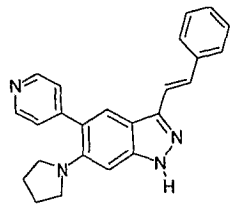
5-Chloro-6-ethanesulfonyl-3-pyridin-3-ylethynyl-1H-indazole



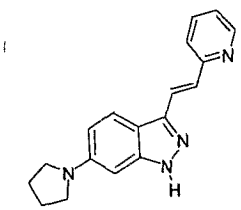
5-Chloro-6-ethanesulfonyl-3-[6-(4-methyl-piperazin-1-ylmethyl)-pyridin-2-ylethynyl]-1H-indazole



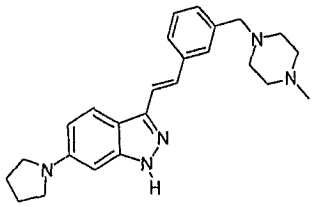
4-Methyl-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1H-indazole-5-carboxylic acid



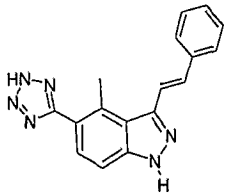
5-Pyridin-4-yl-6-pyrrolidin-1-yl-3-styryl-1H-indazole



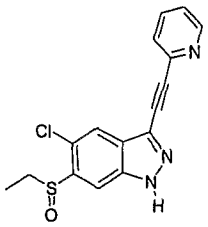
3-(2-Pyridin-2-yl-vinyl)-6-pyrrolidin-1-yl-1H-indazole



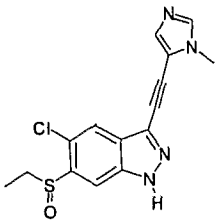
3-{2-[3-(4-Methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-6-pyrrolidin-1-yl-1H-indazole



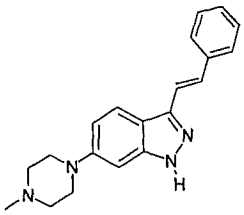
4-Methyl-3-styryl-5-(2H-tetrazol-5-yl)-1H-indazole



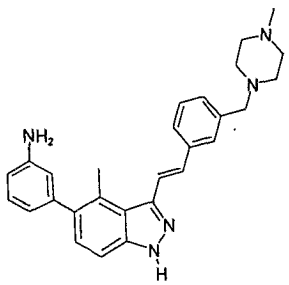
5-Chloro-6-ethanesulfinyl-3-pyridin-2-ylethynyl-1H-indazole



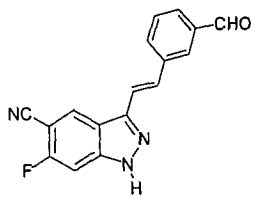
5-Chloro-6-ethanesulfinyl-3-(3-methyl-3H-imidazol-4-ylethynyl)-1H-indazole



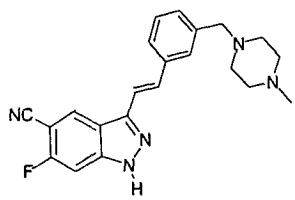
6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazole



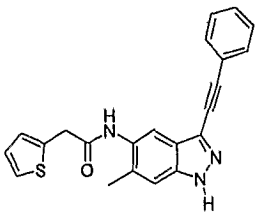
3-(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-phenylamine



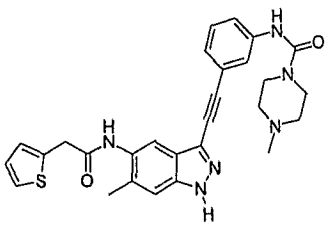
6-Fluoro-3-[2-(3-formyl-phenyl)-vinyl]-1H-indazole-5-carbonitrile



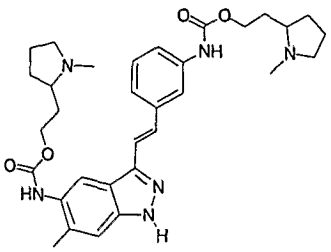
6-Fluoro-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazole-5-carbonitrile



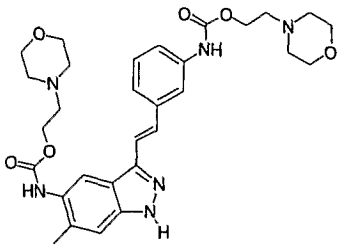
N-(6-Methyl-3-phenylethynyl-1H-indazol-5-yl)-2-thiophen-2-yl-acetamide



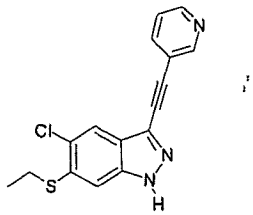
4-Methyl-piperazine-1-carboxylic acid {3-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-ylethynyl]-phenyl}-amide



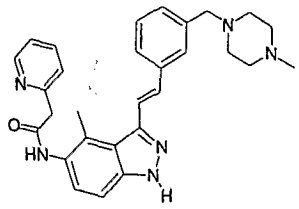
[6-Methyl-3-(2-{3-[2-(1-methyl-pyrrolidin-2-yl)-ethoxycarbonylamino]-phenyl}-vinyl)-1H-indazol-5-yl]-carbamic acid 2-(1-methyl-pyrrolidin-2-yl)-ethyl ester



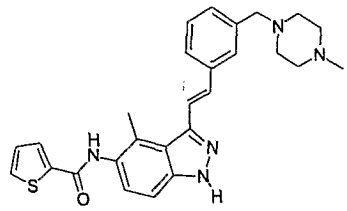
(6-Methyl-3-{2-[3-(2-morpholin-4-yl-ethoxycarbonylamino)-phenyl]-vinyl}-1H-indazol-5-yl)-carbamic acid 2-morpholin-4-yl-ethyl ester



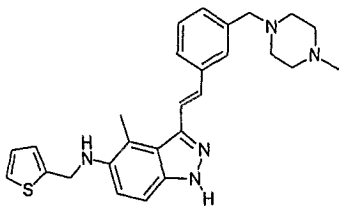
5-Chloro-6-ethylsulfanyl-3-pyridin-3-ylethynyl-1H-indazole



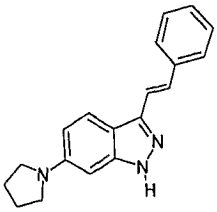
N-(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-2-pyridin-2-yl-acetamide



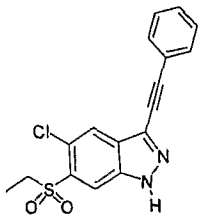
Thiophene-2-carboxylic acid (4-methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-amide



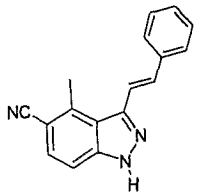
(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-thiophen-2-ylmethyl-amine



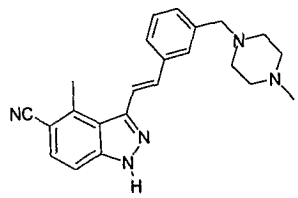
6-Pyrrolidin-1-yl-3-styryl-1H-indazole



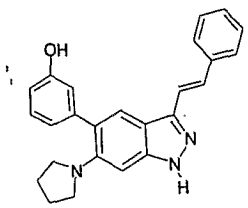
5-Chloro-6-ethanesulfonyl-3-phenylethynyl-1H-indazole



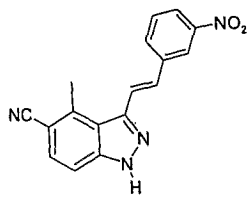
4-Methyl-3-styryl-1H-indazole-5-carbonitrile



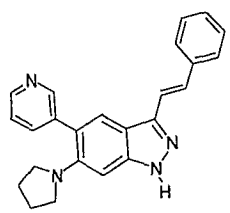
4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazole-5-carbonitrile



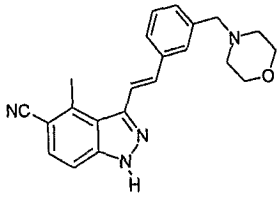
3-(6-Pyrrolidin-1-yl-3-styryl-1H-indazol-5-yl)-phenol



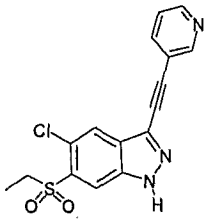
4-Methyl-3-[2-(3-nitro-phenyl)-vinyl]-1H-indazole-5-carbonitrile



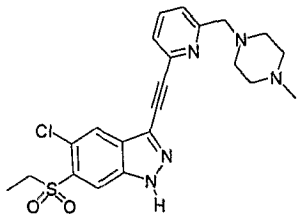
5-Pyridin-3-yl-6-pyrrolidin-1-yl-3-styryl-1H-indazole



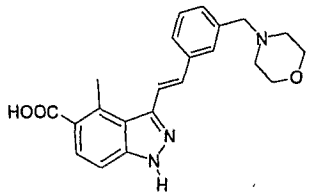
4-Methyl-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1H-indazole-5-carbonitrile



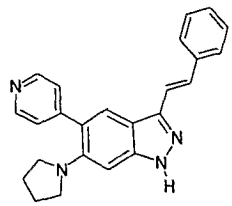
5-Chloro-6-ethanesulfonyl-3-pyridin-3-ylethynyl-1H-indazole



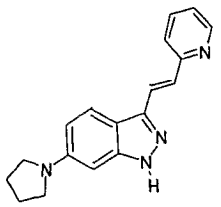
5-Chloro-6-ethanesulfonyl-3-[6-(4-methyl-piperazin-1-ylmethyl)-pyridin-2-ylethynyl]-1H-indazole



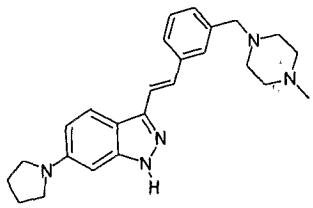
4-Methyl-3-[2-(3-morpholin-4-ylmethyl-phenyl)-vinyl]-1H-indazole-5-carboxylic acid



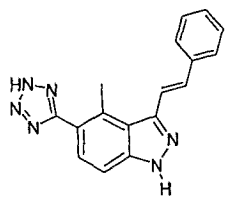
5-Pyridin-4-yl-6-pyrrolidin-1-yl-3-styryl-1H-indazole



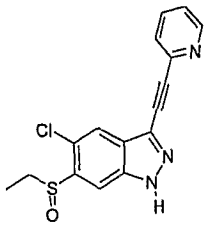
3-(2-Pyridin-2-yl-vinyl)-6-pyrrolidin-1-yl-1H-indazole



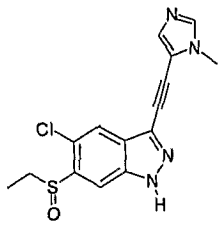
3-{2-[3-(4-Methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-6-pyrrolidin-1-yl-1H-indazole



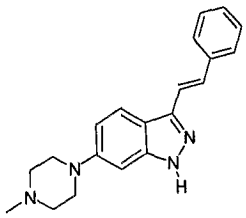
4-Methyl-3-styryl-5-(2H-tetrazol-5-yl)-1H-indazole



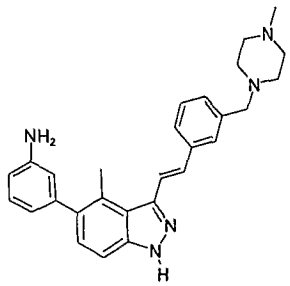
5-Chloro-6-ethanesulfinyl-3-pyridin-2-ylethynyl-1H-indazole



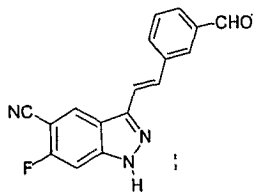
5-Chloro-6-ethanesulfinyl-3-(3-methyl-3H-imidazol-4-ylethynyl)-1H-indazole



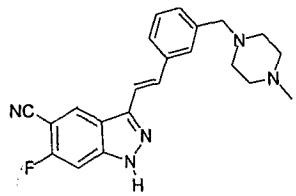
6-(4-Methyl-piperazin-1-yl)-3-styryl-1H-indazole



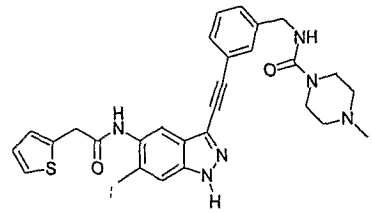
3-(4-Methyl-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazol-5-yl)-phenylamine



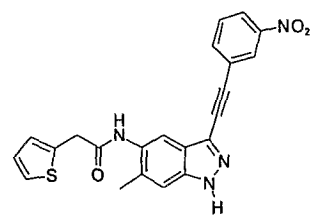
6-Fluoro-3-[2-(3-formyl-phenyl)-vinyl]-1H-indazole-5-carbonitrile



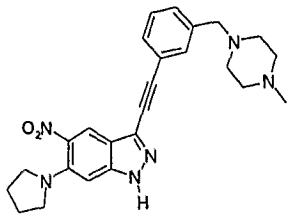
6-Fluoro-3-{2-[3-(4-methyl-piperazin-1-ylmethyl)-phenyl]-vinyl}-1H-indazole-5-carbonitrile



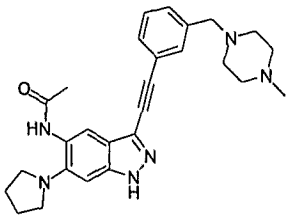
4-Methyl-piperazine-1-carboxylic acid 3-[6-methyl-5-(2-thiophen-2-yl-acetylamino)-1H-indazol-3-ylethynyl]-benzylamide



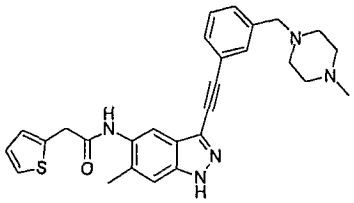
N-[6-Methyl-3-(3-nitro-phenylethynyl)-1H-indazol-5-yl]-2-thiophen-2-yl-acetamide



3-[3-(4-Methyl-piperazin-1-ylmethyl)-phenylethynyl]-5-nitro-6-pyrrolidin-1-yl-1H-indazole



N-{3-[3-(4-Methyl-piperazin-1-ylmethyl)-phenylethynyl]-6-pyrrolidin-1-yl-1H-indazol-5-yl}-acetamide



N-{6-Methyl-3-[3-(4-methyl-piperazin-1-ylmethyl)-phenylethynyl]-1H-indazol-5-yl}-2-thiophen-2-yl-acetamide.

67. A pharmaceutical composition including a compound according to any one of claims 1 to 66 and a pharmaceutically acceptable diluent, excipient or carrier.

68. Use of a compound according to any one of claims 1 to 66 in the preparation of a medicament for the treatment of a disorder caused by, associated with or accompanied by disruptions of cell proliferation.

69. A use according to claim 68 wherein the disorder is a proliferative disorder.

70. A use according to claim 69 wherein the proliferative disorder is cancer.

71. A method of treatment of a disorder caused by, associated with or accompanied by disruptions of cell proliferation in a patient the method including administration of a therapeutically effective amount of a compound according to any one of claims 1 to 66 to the patient.

72. A method according to claim 71 wherein the disorder is a proliferative disorder.

73. A method according to claim 71 wherein the disorder is cancer.

74. A method according to claim 73 wherein the cancer is a bone cancer including Ewing's sarcoma, osteosarcoma, chondrosarcoma and the like, brain and CNS tumours including acoustic neuroma, neuroblastomas, glioma and other brain tumours, spinal cord

tumours, breast cancers, colorectal cancers, advanced colorectal adenocarcinomas, endocrine cancers including adenocortical carcinoma, pancreatic cancer, pituitary cancer, thyroid cancer, parathyroid cancer, thymus cancer, multiple endocrine neoplasma, gastrointestinal cancers including stomach cancer, oesophageal cancer, small intestine cancer, Liver cancer, extra hepatic bile duct cancer, gastrointestinal carcinoid tumour, gall bladder cancer, genitourinary cancers including testicular cancer, penile cancer, prostrate cancer, gynaecological cancers including cervical cancer, ovarian cancer, vaginal cancer, uterus/endometrium cancer, vulva cancer, gestational trophoblastic cancer, fallopian tube cancer, uterine sarcoma, head and neck cancers including oral cavity cancer, lip cancer, salivary gland cancer, larynx cancer, hypopharynx cancer, orthopharynx cancer, nasal cancer, paranasal cancer, nasopharynx cancer, leukaemia's including childhood leukaemia, acute lymphocytic leukaemia, acute myeloid leukaemia, chronic lymphocytic leukaemia, chronic myeloid leukaemia, hairy cell leukaemia, acute promyelocytic leukaemia, plasma cell leukaemia, myelomas, haematological disorders including myelodysplastic syndromes, myeloproliferative disorders, aplastic anaemia, Fanconi anaemia, Waldenstroms Macroglobulinemia, lung cancers including small cell lung cancer, non-small cell lung cancer, lymphomas including Hodgkin's disease, non-Hodgkin's lymphoma, cutaneous T-cell lymphoma, peripheral T-cell lymphoma, B-cell lymphoma, Burkitt's lymphoma, AIDS related Lymphoma, eye cancers including retinoblastoma, intraocular melanoma, skin cancers including melanoma, non-melanoma skin cancer, merkel cell cancer, soft tissue sarcomas such as childhood soft tissue sarcoma, adult soft tissue sarcoma, Kaposi's sarcoma, urinary system cancers including kidney cancer, Wilms tumour, bladder cancer, urethral cancer, and transitional cell cancer.

75. A method according to claim 74 wherein the cancer is breast cancer, lung cancer, ovarian cancer, prostate cancer, head and neck cancer, renal (e.g. renal cell carcinoma), gastric and brain cancer.

76. A method according to claim 74 wherein the cancer is B-cell lymphoma (e.g. Burkitt's lymphoma), leukaemia's (e.g. acute promyelocytic leukaemia), cutaneous T-cell lymphoma (CTCL) and peripheral T-cell lymphoma.

77. A method according to claim 74 wherein the cancer is a solid tumor or a hematologic malignancy.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SG2006/000351

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: **1-65 (in part)**
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

Claims 1-65 are directed to a vast number of compounds based on an indazole with numerous substitutions. The claims are not all adequately supported in the description within the meaning of PCT Article 6 and have been searched based on representative examples set forth in claim 66.

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SG2006/000351

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl.

C07D 231/56 (2006.01) ***A61K 31/416*** (2006.01) ***A61P 43/00*** (2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
STN CA (substructure search based upon claim 66)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US6,897,231 B2 (BHAGWAT *et al*) 24th of May 2005 See example compounds 159, 162, 179, 184, 197, 198, 201 and 210 starting on page 71	1-7, 9-11, 13-15, 36, 65, 67-75
X	WO 2001/053268 B1 (AGOURON PHARMACEUTICALS, INC. USA) 26th of July 2001 See example compounds 1-2, 15-17, 22, 24, 27-28, and 41-46 starting on page 35	1-7, 9-11, 13-15, 36, 65, 67-75
X	WO 2003/064397 A1 (VERTEX PHARMACEUTICALS, INC. USA) 7th of August 2003 See example compounds I-1058, I-1060 and I-1061 starting on page 43	1, 3-7, 9-11, 13-15, 21-22, 29, 36, 67-75
X	WO 2003/101968 A1 (EISAI COMPANY, LTD. JAPAN) 11th of December 2003 See example compounds 100-1363 starting on page 467	1-2, 4-11, 13-15, 21-23, 27, 29-34, 36, 65 67-75

[X] Further documents are listed in the continuation of Box C [X] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
15 January 2007	06 FEB 2007
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized officer **KATHERINE MOERMAN** Telephone No : (02) 6283 2714

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	WO 2004/050088 A1 (KYOWA HAKKO KOGYO, CO. LTD. JAPAN) 17th of June 2004	
X	See example compounds 2-26 starting on page 19	1-2, 4-7, 9-11, 13-15, 21-23, 29-34, 36, 65, 67-75
	WO 2005/094823 A1 (KYOWA HAKKO KOGYO, CO. LTD. JAPAN) 13th of October 2005	
X	See example compounds 1-11 starting on page 21	1-2, 4-7, 9-11, 13-15, 21-22, 29-32, 36, 65
	WO 1997/023480 A1 (DU PONT MERCK PHARMACEUTICAL CO. USA) 3rd of July 1997	
X	See example compounds 3001-3068l and 4001-4068l starting on page 429	1, 4-11, 13-15, 36, 65

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/SG2006/000351

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member					
US	6,897,231	AU	79089/01	AU	2004232981	BR	PI0409417
		CA	2417650	CA	2522682	EP	1313711
		EP	1618093	MX	PA05010958	NZ	524045
		US	2002103229	US	2004077877	US	2004127536
		US	2005009876	US	2005107457	WO	0210137
		WO	2004094388	ZA	200300886		
WO	01/53268	AR	032438	AU	29539/01	BG	107011
		BR	0107783	CA	2388885	CN	1394205
		EE	200200398	EP	1250326	HR	20020675
		HU	0203965	IS	6474	MA	27589
		MX	PA02007058	NO	20022117	NZ	518531
		OA	12160	PL	357590	SK	10052002
		US	6555539	US	6919461	US	2002161022
		US	2003139463	US	2005239855	US	2006111322
		ZA	200203040				
WO	03/064397	CA	2473986	CN	1812973	EP	1467972
		JP	2006176530	MX	PA04007126	NO	20043531
		PL	371512	RU	2004125852	US	7041687
		US	2004009968				
WO	03/101968	AU	2003241925	CA	2482838	CN	1656079
		EP	1510516	US	2005208582	US	2005261339
WO	2004050088	AU	2003289287	CA	2508319	EP	1582211
		US	2006058366				
WO	2005094823						
WO	97/23480	AU	13456/97	CA	2240439	EP	0939757
		HR	960611	US	5756028	US	5760028
		ZA	9610873				

Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.

END OF ANNEX