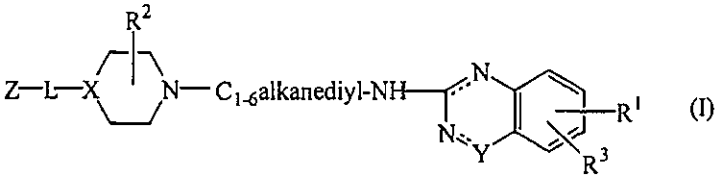
CLAIMS

1. A compound of formula (I),



(I)

the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

the dotted lines represent optional bonds;

X is >N- or >CH-;

—N⋯⋯Y— is –N-C(O)- or -N=CR^4-, wherein R^4 is hydroxy;

L is a direct bond or a bivalent radical selected from -C(O)-, -C(O)-NH-, -NH-, -C(O)-C$_{1-6}$alkanediyl-, -C(O)-O-C$_{1-6}$alkanediyl- or -C$_{1-6}$alkanediyl-;

R^1 is hydrogen, halo, C$_{1-6}$alkyloxy or C$_{1-6}$alkyl;

R^2 is hydrogen, hydroxy, C$_{1-6}$alkyloxy or aminocarbonyl;

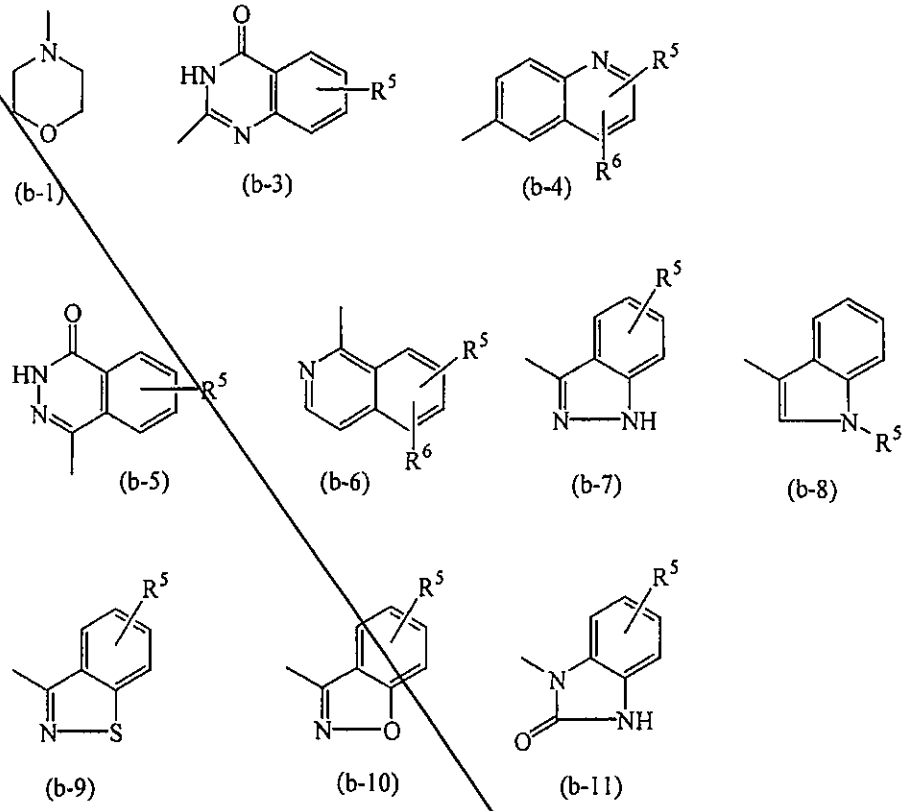
when X is substituted with R^2 than R^2 taken together with –L-Z can form a bivalent radical of formula

-C(O)-NH-CH$_2$-NR^{10}- (a-1)

wherein R^{10} is phenyl;

R^3 is hydrogen, or C$_{1-6}$alkyloxy;

Z is amino, cyano or a radical selected from

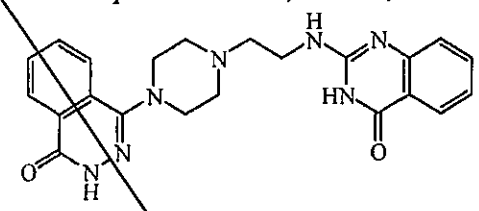


wherein each R^5, R^6, R^7 and R^8 is independently selected from hydrogen, halo, amino, C_{1-6}alkyl or C_{1-6}alkyloxy.

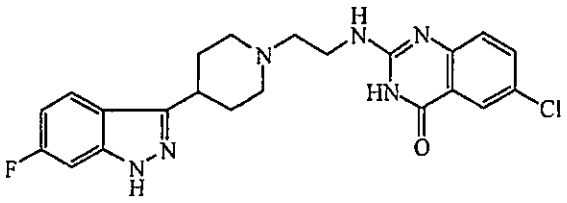
2. A compound as claimed in claim 1 wherein
L is a direct bond or a bivalent radical selected from -C(O)-, -C(O)-NH-, or -C(O)-O-C_{1-6}alkanediyl-; R^2 is hydrogen, hydroxy, or C_{1-6}alkyloxy; Z is a radical selected from (b-3), (b-4), (b-5), (b-6), (b-7), (b-8) or (b-9); each R^5, R^6, R^7 and R^8 is independently selected from hydrogen, halo, amino, C_{1-6}alkyl or C_{1-6}alkyloxy.

3. A compound as claimed in claim 1 or 2 wherein
L is a direct bond; R^1 is hydrogen, halo or C_{1-6}alkyl;
R^2 is hydrogen; R^3 is hydrogen; Z is a radical selected from (b-5) or (b-7); and each R^5 is independently selected from hydrogen or halo.

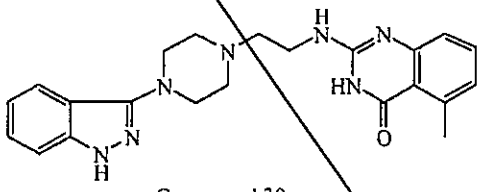
4. A compound as claimed in claim 1, 2 or 3 wherein the compound is selected from compounds No.35, No. 36, No. 39 , No. 1 and No. 43.



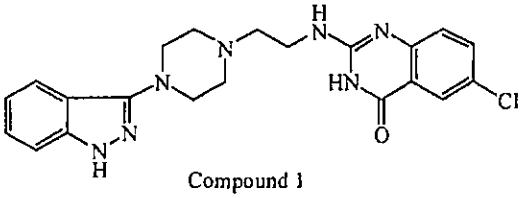
Compound 35



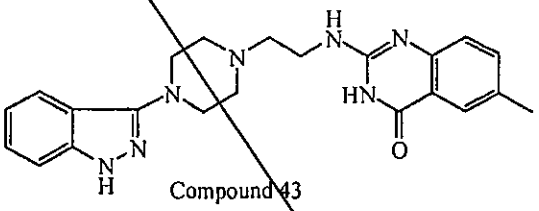
Compound 36



Compound 39



Compound 1



Compound 43

5. A compound as claimed in any of claims 1 to 4 for use as a medicine.

6. A pharmaceutical composition comprising pharmaceutically acceptable carriers and as an active ingredient a therapeutically effective amount of a compound as claimed in any one of claims 1 to 4.

7. Use of a compound as claimed in any one of claims 1 to 4 for the manufacture of a medicament for the treatment of a PARP mediated disorder.

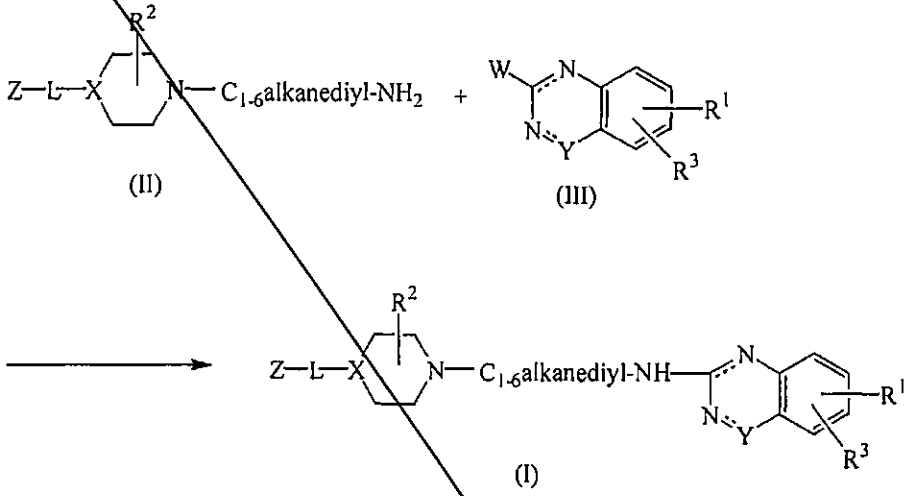
8. Use as claimed in claim 7 for the manufacture of a medicament for the treatment of a PARP-1 mediated disorder.

9. Use as claimed in claim 7 or 8 wherein the treatment involves chemosensitization.

10. Use as claimed in claim 7 or 8 wherein the treatment involves radiosensitization.

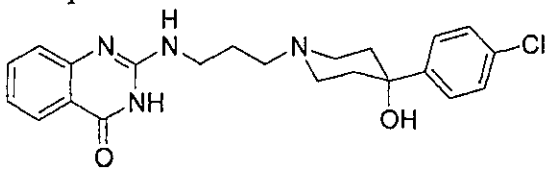
11. A combination of a compound as claimed in any one of claims 1 to 4 with a chemotherapeutic agent.

12. A process for preparing a compound as claimed in claim 1, characterized by reacting an intermediate of formula (II) with an intermediate of formula (III), wherein W is an appropriate leaving group, with the formation of a compound of formula (I-a), wherein L^1 is -C_{1-6}alkanediyl-NH- and both dotted lines can be a bond, in a reaction-inert solvent and with the addition of an appropriate base,



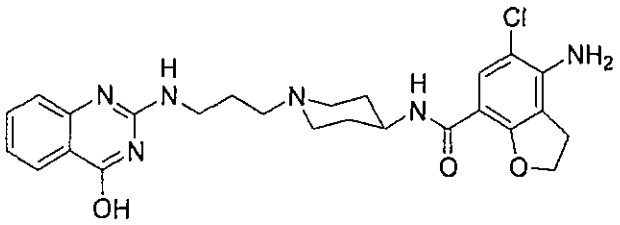
with the variables as defined in claim 1.

13. A compound of formula



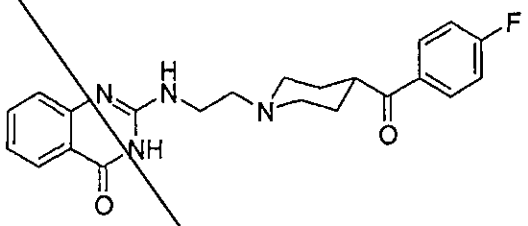
the *N*-oxide, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof.

14. A compound of formula



the *N*-oxide, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof.

15. A compound of formula

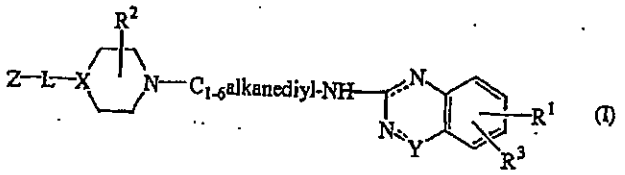


the *N*-oxide, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof.

16. Use of a compound as claimed in any one of claims 1 to 4 and 13 to 15 for the manufacture of a medicament for the treatment of cancer.

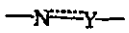
CLAIMS

1. A compound of formula (I),



(I)

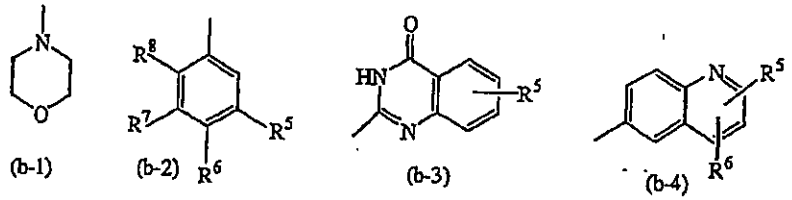
the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein
the dotted lines represent optional bonds;
X is >N- or >CH-;*



is -N-C(O)- or -N=CR^4-, wherein R^4 is hydroxy;
L is a direct bond or a bivalent radical selected from -C(O)-, -C(O)-NH-, -NH-, -C(O)-C_{1-6}alkanediyl-, -C(O)-O-C_{1-6}alkanediyl- or -C_{1-6}alkanediyl-;
R^1 is hydrogen, halo, C_{1-6}alkyloxy or C_{1-6}alkyl;
R^2 is hydrogen, hydroxy, C_{1-6}alkyloxy or aminocarbonyl;
when X is substituted with R^2 than R^2 taken together with -L-Z can form a bivalent radical of formula

-C(O)-NH-CH_2-NR^{10}- (a-1)

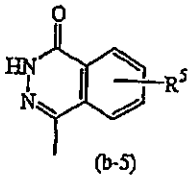
wherein R^{10} is phenyl;
R^3 is hydrogen, or C_{1-6}alkyloxy;
Z is amino, cyano or a radical selected from

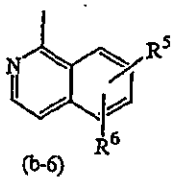

(b-1)

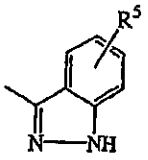
(b-2)

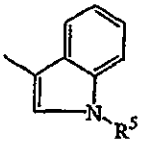
(b-3)

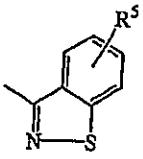
(b-4)

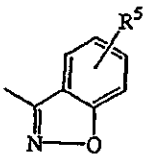

(b-5)

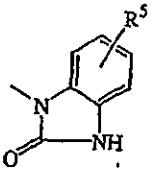

(b-6)


(b-7)


(b-8)


(b-9)


(b-10)


(b-11)

wherein each R^5, R^6, R^7 and R^8 is independently selected from hydrogen, halo, amino, C_{1-6}alkyl or C_{1-6}alkyloxy; or R^7 and R^8 taken together may form a bivalent radical of formula

$-CH_2-CR^9_2-O-$ (c-1),

$-(CH_2)_3-O-$ (c-2),

$-O-(CH_2)_2-O-$ (c-3)

or

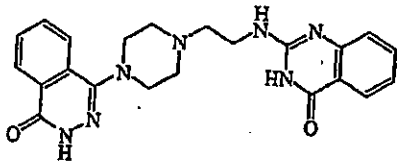
$-CH=CH-CH=CH-$ (c-4)

wherein each R^9 is independently selected from hydrogen or C_{1-6}alkyl;
with the proviso that
when X is >N-, then Z is other than the radical (b-2) and
when X is >CH- and L is -C(O)-NH- or -C(O)-O-C_{1-6}alkanediyl- and Z is the radical (b-2) and R^7 and R^8 taken together form a bivalent radical of formula (c-1), (c-2) or (c-3) then R^5 is other than chloro.

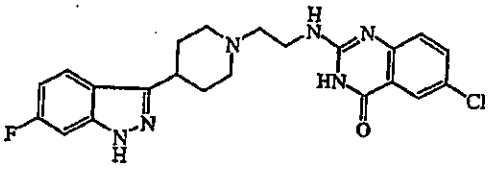
2. A compound as claimed in claim 1 wherein
L is a direct bond or a bivalent radical selected from -C(O)-, -C(O)-NH-, or- C(O)-O-C_{1-6}alkanediyl-; R^2 is hydrogen, hydroxy, or C_{1-6}alkyloxy; Z is a radical selected from (b-2), (b-3), (b-4), (b-5), (b-6), (b-7), (b-8) or (b-9); each R^5, R^6, R^7 and R^8 is independently selected from hydrogen, halo, amino, C_{1-6}alkyl or C_{1-6}alkyloxy; or R^7 and R^8 taken together may form a bivalent radical of formula (c-1), (c-2), (c-3) or (c-4).

3. A compound according to claim 1 and 2 wherein
L is a direct bond; R^1 is hydrogen, halo or C_{1-6}alkyl;
R^2 is hydrogen; R^3 is hydrogen; Z is a radical selected from (b-5) or (b-7); and each
R^5 is independently selected from hydrogen or halo.

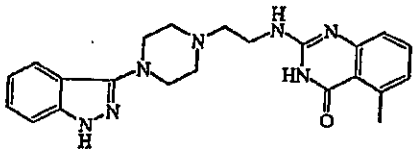
4. A compound according to claim 1,2 and 3 wherein the compound is selected from compounds No.35, No. 36, No. 39 , No. 1 and No. 43.



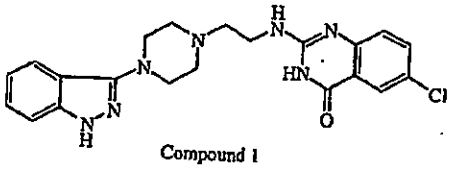
Compound 35



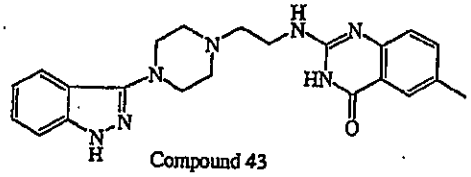
Compound 36



Compound 39



Compound 1



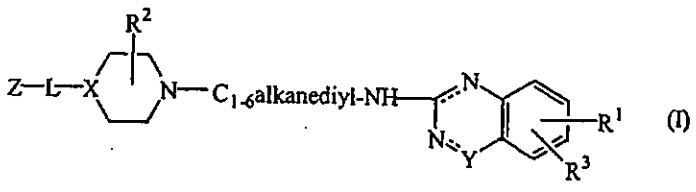
Compound 43

5. A compound as claimed in any of claims 1 to 4 for use as a medicine.

6. A pharmaceutical composition comprising pharmaceutically acceptable carriers and as an active ingredient a therapeutically effective amount of a compound as claimed in claim 1 to 4.

7. A process of preparing a pharmaceutical composition as claimed in claim 6 wherein the pharmaceutically acceptable carriers and a compound as claimed in claim 1 to 4 are intimately mixed.

8. Use of a compound for the manufacture of a medicament for the treatment of a TANK and PARP mediated disorder, wherein said compound is a compound of formula (I)



(I)

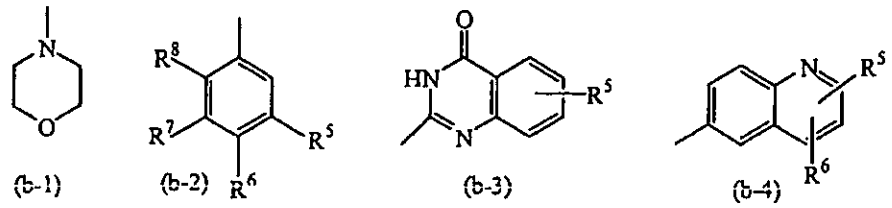
the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein
the dotted lines represent optional bonds;
X is >N- or >CH-;

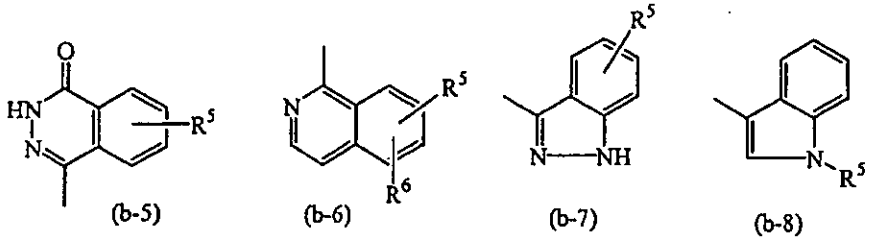


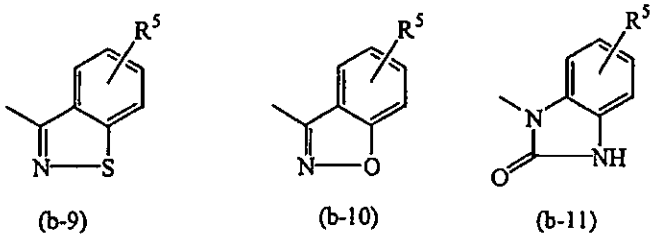
is -N-C(O)- or -N=CR^4-, wherein R^4 is hydroxy;
L is a direct bond or a bivalent radical selected from -C(O)-, -C(O)-NH-, -NH-, -C(O)-C_{1-6}alkanediyl-, -C(O)-O-C_{1-6}alkanediyl- or -C_{1-6}alkanediyl-;
R^1 is hydrogen, halo, C_{1-6}alkyloxy or C_{1-6}alkyl;
R^2 is hydrogen, hydroxy, C_{1-6}alkyloxy or aminocarbonyl;
when X is substituted with R^2 than R^2 taken together with -L-Z can form a bivalent radical of formula

-C(O)-NH-CH_2-NR^{10}- (a-1)

wherein R^{10} is phenyl;
R^3 is hydrogen, or C_{1-6}alkyloxy;
Z is amino, cyano or a radical selected from







wherein each R^5, R^6, R^7 and R^8 is independently selected from hydrogen, halo, amino, C_{1-6}alkyl or C_{1-6}alkyloxy; or R^7 and R^8 taken together may form a bivalent radical of formula

- CH_2-CR^9_2-O- (c-1),

-$(CH_2)_3$-O- (c-2),

-O-$(CH_2)_2$-O- (c-3)

or

-CH=CH-CH=CH- (c-4)

wherein each R^9 is independently selected from hydrogen or C_{1-6}alkyl.

9. Use according to claim 8 of a compound of formula (I) for the manufacture of a medicament for inhibiting growth in cancer cells.

10. Use according to claim 8 and 9 wherein the treatment involves chemosensitization.

11. Use according to claims 7 and 8 wherein the treatment involves radiosensitization.

12. A combination of a compound of formula (I) as claimed in any of claims 1 to 4 with a chemotherapeutic agent.

13. A process for preparing a compound as claimed in claim 1, **characterized by** reacting an intermediate of formula (II) with an intermediate of formula (III), wherein W is an appropriate leaving group, with the formation of a compound of formula (I-a), wherein L^i is -C_{1-6}alkanediyl-NH- and both dotted lines can be a bond, in a reaction-inert solvent

and with the addition of an appropriate base,

