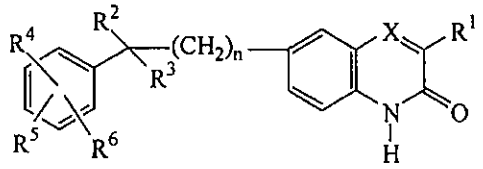
CLAIMS

1. A compound of formula (I),



(I)

the *N*-oxide forms, the addition salts and the stereo-chemically isomeric forms thereof, wherein

n is 0, 1 or 2;

X is N or CR^7, wherein R^7 is hydrogen or taken together with R^1 may form a bivalent radical of formula -CH=CH-CH=CH-;

R^1 is C_{1-6}alkyl or thiophenyl;

R^2 is hydrogen, hydroxy, C_{1-6}alkyl, C_{3-6}alkynyl or taken together with R^3 may form =O;

R^3 is a radical selected from

$-(CH_2)_s-NR^8R^9$	(a-1),
-O-H	(a-2),
$-O-R^{10}$	(a-3),
$-S-R^{11}$	(a-4), or
$-C\equiv N$	(a-5),

wherein

s is 0, 1, 2 or 3;

R^8, R^{10} and R^{11} are each independently selected from –CHO, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{1-6}alkylcarbonyl, amino, C_{1-6}alkylamino, di(C_{1-6}alkyl)aminoC_{1-6}alkyl, C_{1-6}alkyloxycarbonyl, C_{1-6}alkylcarbonylaminoC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, piperidinyl, piperidinylC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, C_{1-6}alkyloxy, thiophenylC_{1-6}alkyl, pyrrolylC_{1-6}alkyl, arylC_{1-6}alkylpiperidinyl, arylcarbonylC_{1-6}alkyl, arylcarbonylpiperidinylC_{1-6}alkyl, haloindozolylpiperidinylC_{1-6}alkyl, arylC_{1-6}alkyl(C_{1-6}alkyl)aminoC_{1-6}alkyl, and

R^9 is hydrogen or C_{1-6}alkyl;

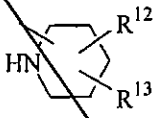
or R^3 is a group of formula

$-(CH_2)_t-Z$ (b-1),

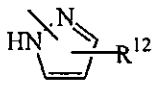
wherein

t is 0, 1, 2 or 3;

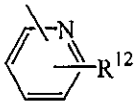
-Z is a heterocyclic ring system selected from



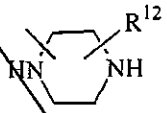
(c-1)



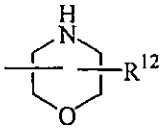
(c-3)



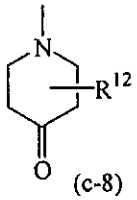
(c-5)



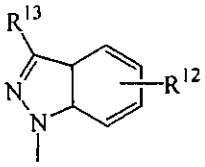
(c-6)



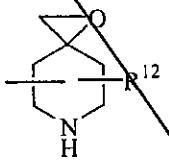
(c-7)



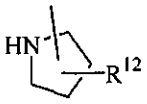
(c-8)



(c-9)

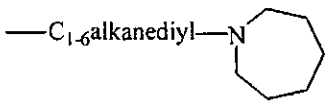


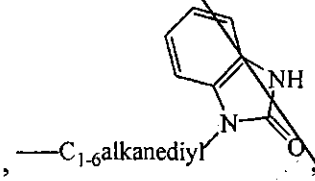
(c-10)



(c-11)

wherein R^{12} is hydrogen, halo, C_{1-6}alkyl, aminocarbonyl, amino, hydroxy, aryl,





C_{1-6}alkylaminoC_{1-6}alkyloxy, C_{1-6}alkyloxyC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkylamino, arylC_{1-6}alkyl, di(phenylC_{2-6}alkenyl), piperidinyl, piperidinylC_{1-6}alkyl, C_{3-10}cycloalkyl, C_{3-10}cycloalkylC_{1-6}alkyl, aryloxy(hydroxy)C_{1-6}alkyl, haloindazolyl, arylC_{1-6}alkyl, arylC_{2-6}alkenyl, arylC_{1-6}alkylamino, morpholino, C_{1-6}alkylimidazolyl, pyridinylC_{1-6}alkylamino; and

R^{13} is hydrogen, piperidinyl or aryl;

R^4, R^5 and R^6 are each independently selected from hydrogen, halo, trihalomethyl, trihalomethoxy, C_{1-6}alkyl, C_{1-6}alkyloxy, amino, aminoC_{1-6}alkyl, di(C_{1-6}alkyl)amino, di(C_{1-6}alkyl)aminoC_{1-6}alkyloxy or C_{1-6}alkyloxycarbonyl, or C_{1-6}alkyl substituted with 1, 2 or 3 substituents independently selected from hydroxy, C_{1-6}alkyloxy, or aminoC_{1-6}alkyloxy; or

when R^5 and R^6 are on adjacent positions they may taken together form a bivalent radical of formula

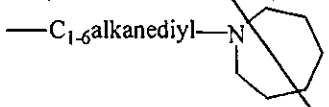
-O-CH_2-O (d-1),
-O-$(CH_2)_2$-O- (d-2),
-CH=CH-CH=CH- (d-3), or
-NH-C(O)-NR^{14}=CH- (d-4),

wherein R^{14} is C_{1-6}alkyl;

aryl is phenyl, phenyl substituted with halo, C_{1-6}alkyl or C_{1-6}alkyloxy;

with the proviso that 6-benzoyl-3-methyl-2(1H)-quinoxalinone is excluded.

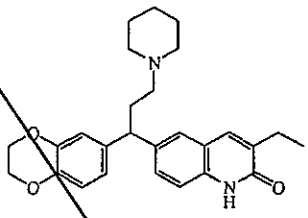
2. A compound as claimed in claim 1 wherein
R^1 is C_{1-6}alkyl; R^3 is a radical selected from (a-1), (a-2), (a-3) or (a-5) or is a group of formula (b-1); s is 0, 1 or 2; R^8 and R^{10} are each independently selected from –CHO, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, di(C_{1-6}alkyl)aminoC_{1-6}alkyl, C_{1-6}alkylcarbonylaminoC_{1-6}alkyl, piperidinylC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, C_{1-6}alkyloxy, thiophenylC_{1-6}alkyl, pyrrolylC_{1-6}alkyl, arylC_{1-6}alkylpiperidinyl, arylcarbonylC_{1-6}alkyl, arylcarbonylpiperidinylC_{1-6}alkyl, haloindozolylpiperidinylC_{1-6}alkyl, or arylC_{1-6}alkyl(C_{1-6}alkyl)aminoC_{1-6}alkyl; t is 0 or 2; -Z is a heterocyclic ring system selected from (c-1), (c-2), (c-4), (c-6), (c-8), (c-9), or (c-11); R^{12} is hydrogen,



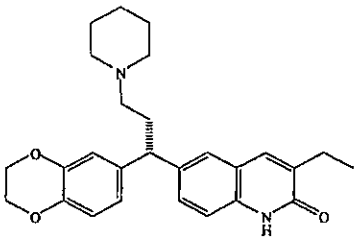
C_{1-6}alkyl, aminocarbonyl, , C_{1-6}alkyloxyC_{1-6}alkylamino, di(phenylC_{2-6}alkenyl), piperidinylC_{1-6}alkyl, C_{3-10}cycloalkyl, C_{3-10}cycloalkylC_{1-6}alkyl, haloindazolyl, or arylC_{2-6}alkenyl; R^4, R^5 and R^6 are each independently selected from hydrogen, halo, trihalomethyl, trihalomethoxy, C_{1-6}alkyl, C_{1-6}alkyloxy, di(C_{1-6}alkyl)amino, di(C_{1-6}alkyl)aminoC_{1-6}alkyloxy or C_{1-6}alkyloxycarbonyl; and when R^5 and R^6 are on adjacent positions they may taken together form a bivalent radical of formula (d-1) or (d-2).

3. A compound according to claim 1 and 2 wherein
n is 0; X is CH; R^1 is C_{1-6}alkyl; R^2 is hydrogen; R^3 is a group of formula (b-1); t is 2; -Z is a heterocyclic ring system selected from (c-1); R^{12} is hydrogen; R^{13} is hydrogen; and R^5 and R^6 are on adjacent positions and taken together form a bivalent radical of formula (d-2).

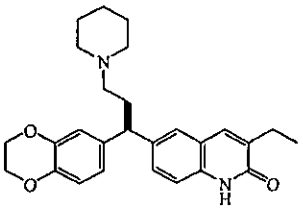
4. A compound according to claim 1, 2 and 3 wherein the compound is compounds No 16, compound No 144, and compound No. 145.



compound 16

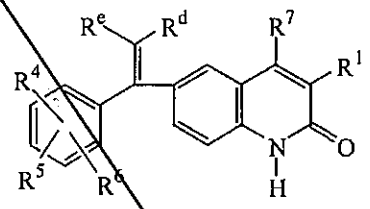


Compound 144



Compound 145

5. A compound of formula (VII-a),



(VII-a)

the *N*-oxide forms, the addition salts and the stereo-chemically isomeric forms thereof, wherein

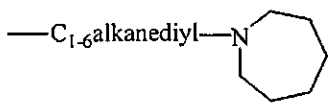
R^1, R^4, R^5, R^6, R^7 and aryl are as defined in claim 1;

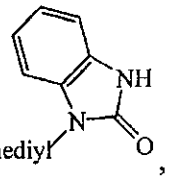
R^e is hydrogen or taken together with R^d may form a bivalent radical of formula

$-(CH_2)_2-NR^{15}-(CH_2)_2-$ (e-1), or

$-CH_2-NR^{16}-(CH_2)_3-$ (e-2),

wherein R^{15} and R^{16} are each independently selected from hydrogen, C_{1-6}alkyl,



, 

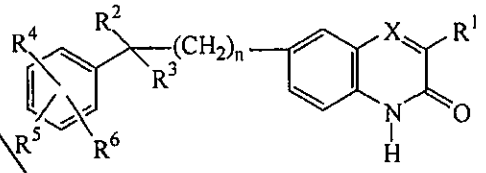
, C_{1-6}alkyloxyC_{1-6}alkyl, piperidinylC_{1-6}alkyl, C_{3-10}cycloalkylC_{1-6}alkyl, aryloxy(hydroxy)C_{1-6}alkyl, arylC_{1-6}alkyl, or arylC_{2-6}alkenyl; or

R^d is di(C_{1-6}alkyl)aminoC_{1-6}alkyl or piperidinylC_{1-6}alkyl.

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

7. 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 5.

8. Use of a compound for the manufacture of a medicament for chemosensitization or radiosensitization, 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

n is 0, 1 or 2;

X is N or CR^7, wherein R^7 is hydrogen or taken together with R^1 may form a bivalent radical of formula -CH=CH-CH=CH-;

R^1 is C_{1-6}alkyl or thiophenyl;

R^2 is hydrogen, hydroxy, C_{1-6}alkyl, C_{3-6}alkynyl or taken together with R^3 may form =O;

R^3 is a radical selected from

$-(CH_2)_s-NR^8R^9$ (a-1),
-O-H (a-2),
$-O-R^{10}$ (a-3),
$-S-R^{11}$ (a-4), or
$-C\equiv N$ (a-5),

wherein

s is 0, 1, 2 or 3;

R^8, R^{10} and R^{11} are each independently selected from –CHO, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{1-6}alkylcarbonyl, amino, C_{1-6}alkylamino, di(C_{1-6}alkyl)aminoC_{1-6}alkyl, C_{1-6}alkyloxycarbonyl, C_{1-6}alkylcarbonylaminoC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, piperidinyl, piperidinylC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, C_{1-6}alkyloxy, thiophenylC_{1-6}alkyl,

pyrrolylC_{1-6}alkyl, arylC_{1-6}alkylpiperidinyl, arylcarbonylC_{1-6}alkyl, arylcarbonylpiperidinylC_{1-6}alkyl, haloindozolylpiperidinylC_{1-6}alkyl, arylC_{1-6}alkyl(C_{1-6}alkyl)aminoC_{1-6}alkyl, and

R^9 is hydrogen or C_{1-6}alkyl;

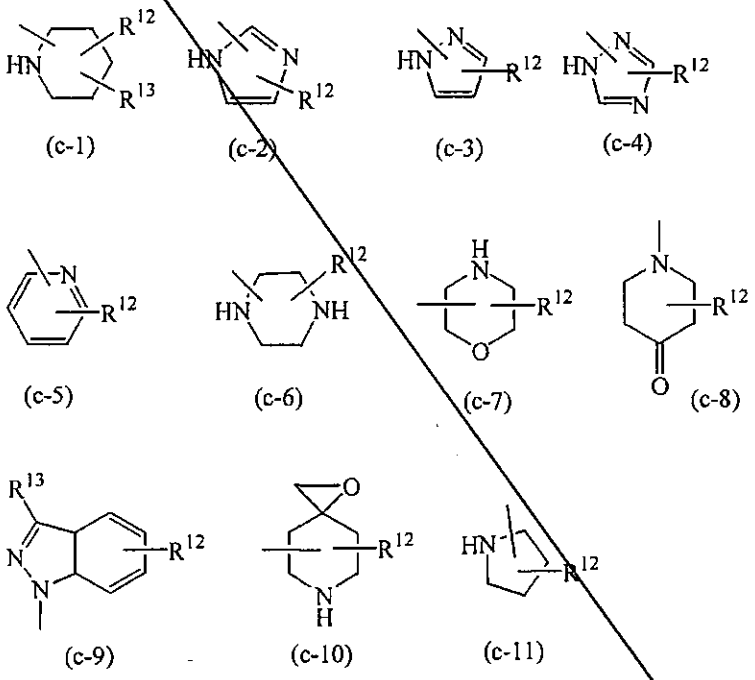
or R^3 is a group of formula

$$-(CH_2)_t-Z \qquad (b\text{-}1),$$

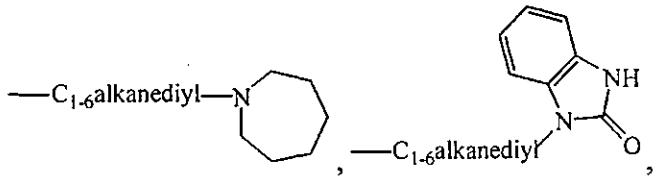
wherein

t is 0, 1, 2 or 3;

-Z is a heterocyclic ring system selected from



wherein R^{12} is hydrogen, halo, C_{1-6}alkyl, aminocarbonyl, amino, hydroxy, aryl,



C_{1-6}alkylaminoC_{1-6}alkyloxy, C_{1-6}alkyloxyC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkylamino, arylC_{1-6}alkyl, di(phenylC_{2-6}alkenyl), piperidinyl, piperidinylC_{1-6}alkyl, C_{3-10}cycloalkyl, C_{3-10}cycloalkylC_{1-6}alkyl, aryloxy(hydroxy)C_{1-6}alkyl, haloindazolyl, arylC_{1-6}alkyl, arylC_{2-6}alkenyl, arylC_{1-6}alkylamino, morpholino, C_{1-6}alkylimidazolyl, pyridinylC_{1-6}alkylamino; and

R^{13} is hydrogen, piperidinyl or aryl;

R^4, R^5 and R^6 are each independently selected from hydrogen, halo, trihalomethyl, trihalomethoxy, C_{1-6}alkyl, C_{1-6}alkyloxy, amino, aminoC_{1-6}alkyl, di(C_{1-6}alkyl)amino, di(C_{1-6}alkyl)aminoC_{1-6}alkyloxy or C_{1-6}alkyloxycarbonyl, or C_{1-6}alkyl substituted with 1, 2 or 3 substituents independently selected from hydroxy, C_{1-6}alkyloxy, or aminoC_{1-6}alkyloxy; or

when R^5 and R^6 are on adjacent positions they may taken together form a bivalent radical of formula

-O-CH_2-O (d-1),

-O-$(CH_2)_2$-O- (d-2),

-CH=CH-CH=CH- (d-3), or

-NH-C(O)-NR^{14}=CH- (d-4),

wherein R^{14} is C_{1-6}alkyl;

aryl is phenyl, phenyl substituted with halo, C_{1-6}alkyl or C_{1-6}alkyloxy.

9. Use of a compound according to claim 5 for the manufacture of a medicament for the treatment of a PARP mediated disorder.

10. Use according to claim 8 or 9 wherein the medicament is for chemosensitization.

11. Use according to claims 8 or 9 wherein the medicament is for radiosensitization.

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

13. A combination of a compound according to claim 5 with a chemotherapeutic agent.

14. A process for preparing a compound as claimed in claim 1 or claim 5, characterized by

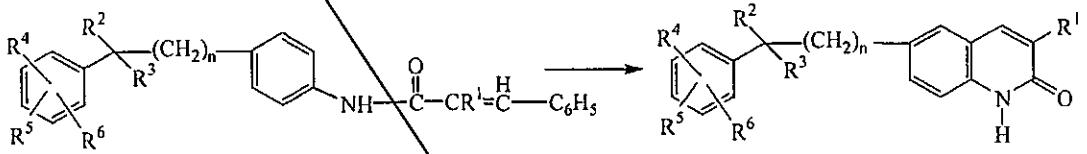
a) the hydrolysis of intermediates of formula (VIII), according to art-known methods, by submitting the intermediates of formula (VIII) to appropriate reagents, such as, tinchloride, acetic acid and hydrochloric acid, in the presence of a reaction inert solvent, e.g. tetrahydrofuran,



(VIII) (I)

wherein R^1 to R^6, X and n are as defined in claim 1;

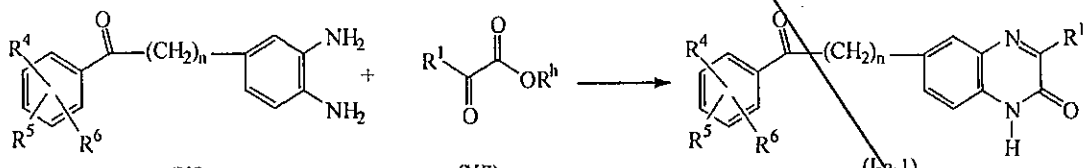
b) the cyclization of intermediates of formula (X), according to art-known cyclizing procedures into compounds of formula (I) wherein X is CH herein referred to as compounds of formula (I-j), preferably in the presence of a suitable Lewis Acid, e.g. aluminum chloride either neat or in a suitable solvent such as, for example, an aromatic hydrocarbon, e.g. benzene, chlorobenzene, methylbenzene and the like; halogenated hydrocarbons, e.g. trichloromethane, tetrachloromethane and the like; an ether, e.g. tetrahydrofuran, 1,4-dioxane and the like or mixtures of such solvents,



(X) (I-j)

wherein R^1 to R^6 and X are as defined in claim 1;

c) the condensation of an appropriate ortho-benzenediamine of formula (XI) with an ester of formula (XII) into compounds of formula (I), wherein X is N and R^2 taken together with R^3 forms =O, herein referred to as compounds of formula (I-a-1), in the presence of a carboxylic acid, e.g. acetic acid and the like, a mineral acid such as, for example hydrochloric acid, sulfuric acid, or a sulfonic acid such as, for example, methanesulfonic acid, benzenesulfonic acid, 4-methylbenzenesulfonic acid and the like,

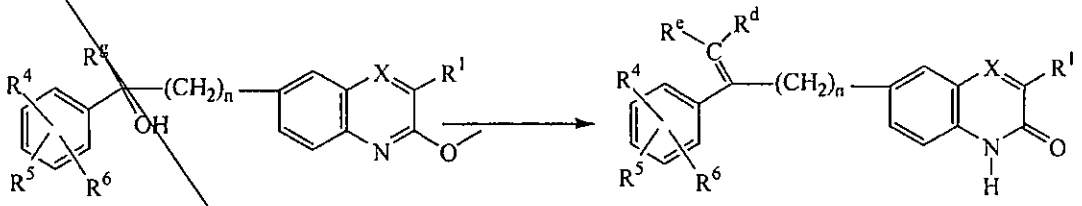


(XI) (XII) (I-a-1)

wherein R^1, R^4 to R^6, and n are as defined in claim 1 and wherein R^h is C_{1-6}alkyl;

d) hydrolysing intermediates of formula (VI), wherein R^3 is a group of formula (b-1) or a radical of formula (a-1) wherein s is other than 0, herein referred to as R^g,

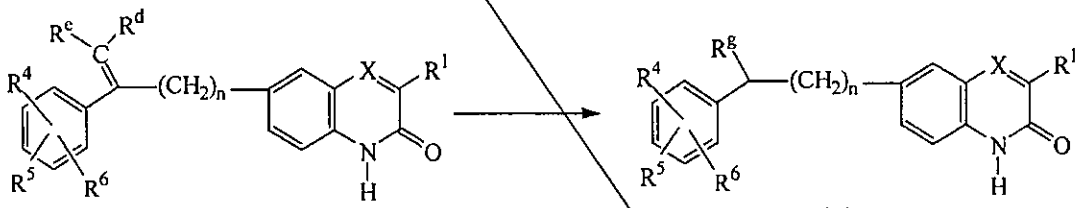
according to art-known methods, such as stirring the intermediate (VI) in an aqueous acid solution in the presence of a reaction inert solvent with the formation of intermediates and compounds of formula (VII), wherein R^d and R^e are appropriate radicals or taken together with the carbon to which they are attached, form an appropriate heterocyclic ring system as defined in –Z,



(VI) (VII)

wherein R^1, $R^4$to R^6, X, n and R^e and R^d are as defined in claim 1 or claim 5;

e) converting intermediates of formula (VII), by a selective hydrogenation of said intermediate with an appropriate reducing agent and an appropriate reductant in a suitable solvent with the formation of compounds of formula (I) wherein R^2 is hydrogen and R^g is as defined above, herein referred to as compounds of formula (I-i).

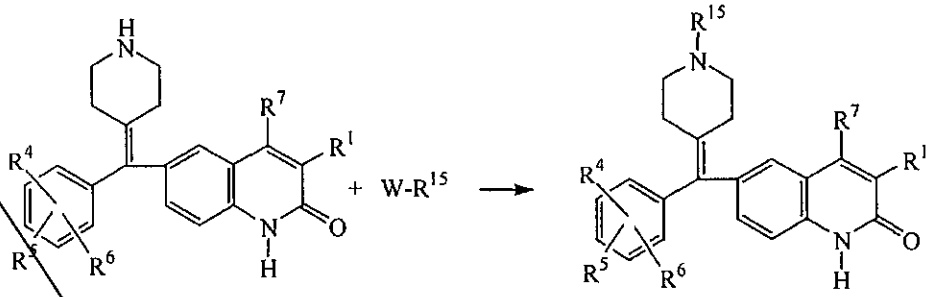


(VII) (I-i)

wherein R^1, $R^4$to R^6, X, n and R^e and R^d are as defined in claim 1 or claim 5;

15. A process for preparing a compound as claimed in claim 5, characterized by

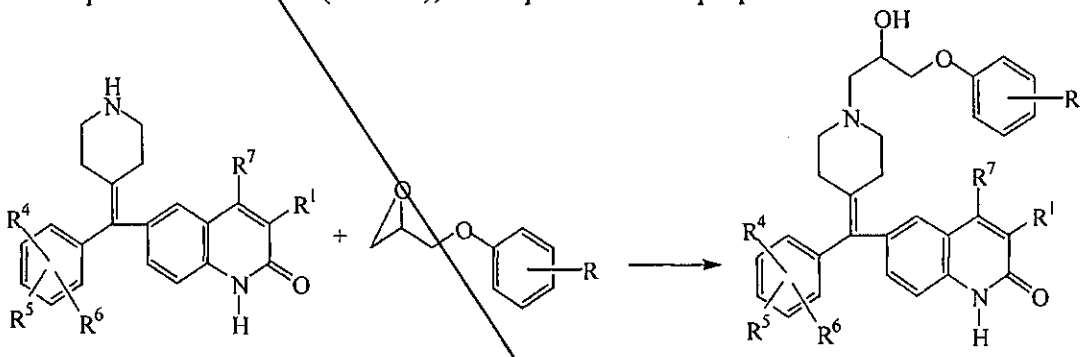
a) reacting a compound of formula (VII-a), wherein R^e taken together with R^d forms a bivalent radical of formula (e-1) or (e-2) (e.g. a bivalent radical of formula (e-1)) and R^{15} or R^{16} (e.g. R^{15}) are hydrogen, herein referred to as compounds of formula (VII-a-2), with an intermediate of formula (XIX) wherein W is an appropriate leaving group such as, for example, chloro, bromo, methanesulfonyloxy or benzenesulfonyloxy and R^{15} or R^{16} (e.g. R^{15}) are other than hydrogen, with the formation of compounds of formula (VII-a-1), defined as compounds of formula (VII-a), wherein R^e taken together with R^d forms a bivalent radical of formula (e-1) or (e-2) (e.g. a bivalent radical of formula (e-1)) and R^{15} or R^{16} (e.g. R^{15}) are other than hydrogen, in a reaction-inert solvent; or



(VII-a-2) (XIX) (VII-a-1)

wherein R^1, $R^4$to R^7 and R^{15} are as defined in claim 5;

b) reacting a compound of formula (VII-a-2) with an intermediate of formula (XX) wherein R is an appropriate substituent whit the formation of compounds of formula (VII-a) wherein R^{15} or R^{16} (e.g. R^{15}) are aryloxy(hydroxy)C_{1-6}alkyl, herein referred to as compounds of formula (VII-a-3), in the presence of 2-propanol.



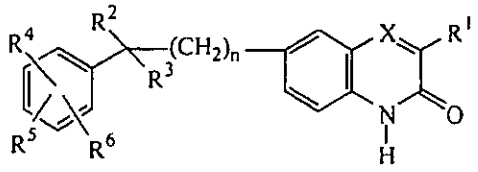
(VII-a-2) (XX) (VII-a-3)

wherein R^1 and $R^4$to R^7 are as defined in claim 5;

16. Use of a compound according to any one of claims 1 to 5 for the manufacture of a medicament for the treatment of cancer.

CLAIMS

1. A compound of formula (I),



(I)

an *N*-oxide form thereof, an addition salt thereof or a stereo-chemically isomeric form thereof, wherein

n is 0, 1 or 2;

X is N or CR^7, wherein R^7 is hydrogen or taken together with R^1 may form a bivalent radical of formula -CH=CH-CH=CH-;

R^1 is C_{1-6}alkyl or thiophenyl;

R^2 is hydrogen, hydroxy, C_{1-6}alkyl, C_{3-6}alkynyl or taken together with R^3 may form =O;

R^3 is a radical selected from

$-(CH_2)_s-NR^8R^9$	(a-1),
-O-H	(a-2),
$-O-R^{10}$	(a-3),
$-S-R^{11}$	(a-4), or
—C≡N	(a-5),

wherein

s is 0, 1, 2 or 3;

R^8, R^{10} and R^{11} are each independently selected from –CHO, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{1-6}alkylcarbonyl, amino, C_{1-6}alkylamino, di(C_{1-6}alkyl)aminoC_{1-6}alkyl, C_{1-6}alkyloxycarbonyl, C_{1-6}alkylcarbonylaminoC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, piperidinyl, piperidinylC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, C_{1-6}alkyloxy, thiophenylC_{1-6}alkyl, pyrrolylC_{1-6}alkyl, arylC_{1-6}alkylpiperidinyl, arylcarbonylC_{1-6}alkyl, arylcarbonylpiperidinylC_{1-6}alkyl, haloindozolylpiperidinylC_{1-6}alkyl, arylC_{1-6}alkyl(C_{1-6}alkyl)aminoC_{1-6}alkyl, and

R^9 is hydrogen or C_{1-6}alkyl;

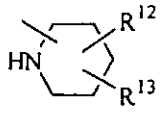
or R^3 is a group of formula

$-(CH_2)_t-Z$ (b-1),

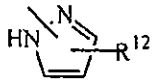
wherein

t is 0, 1, 2 or 3;

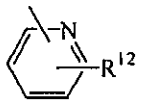
-Z is a heterocyclic ring system selected from



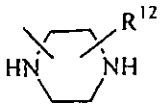
(c-1)



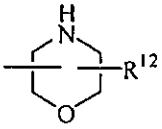
(c-3)



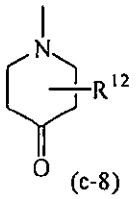
(c-5)



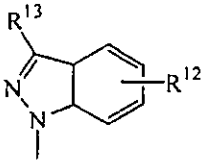
(c-6)



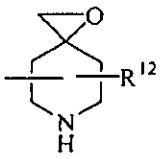
(c-7)



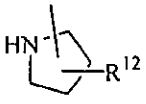
(c-8)



(c-9)

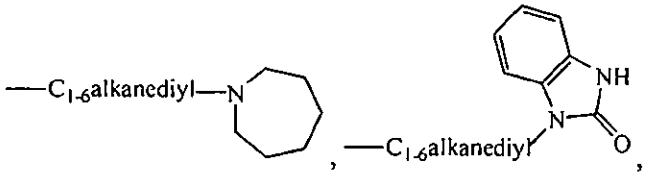


(c-10)



(c-11)

wherein R^{12} is hydrogen, halo, C_{1-6}alkyl, aminocarbonyl, amino, hydroxy, aryl,



C_{1-6}alkylaminoC_{1-6}alkyloxy, C_{1-6}alkyloxyC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkylamino, arylC_{1-6}alkyl, di(phenylC_{2-6}alkenyl), piperidinyl, piperidinylC_{1-6}alkyl, C_{3-10}cycloalkyl, C_{3-10}cycloalkylC_{1-6}alkyl, aryloxy(hydroxy)C_{1-6}alkyl, haloindazolyl, arylC_{1-6}alkyl, arylC_{2-6}alkenyl, arylC_{1-6}alkylamino, morpholino, C_{1-6}alkylimidazolyl, pyridinylC_{1-6}alkylamino; and

R^{13} is hydrogen, piperidinyl or aryl;

R^4, R^5 and R^6 are each independently selected from hydrogen, halo, trihalomethyl, trihalomethoxy, C_{1-6}alkyl, C_{1-6}alkyloxy, amino, aminoC_{1-6}alkyl, di(C_{1-6}alkyl)amino, di(C_{1-6}alkyl)aminoC_{1-6}alkyloxy or C_{1-6}alkyloxycarbonyl, or C_{1-6}alkyl substituted with 1, 2 or 3 substituents independently selected from hydroxy, C_{1-6}alkyloxy, or aminoC_{1-6}alkyloxy; or

when R^5 and R^6 are on adjacent positions they may taken together form a bivalent radical of formula

$-O-CH_2-O$ (d-1),

$-O-(CH_2)_2-O-$ (d-2),

$-CH=CH-CH=CH-$ (d-3), or

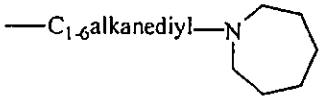
$-NH-C(O)-NR^{14}=CH-$ (d-4),

wherein R^{14} is C_{1-6}alkyl;

aryl is phenyl, phenyl substituted with halo, C_{1-6}alkyl or C_{1-6}alkyloxy;

with the proviso that 6-benzoyl-3-methyl-2(1H)-quinoxalinone is excluded.

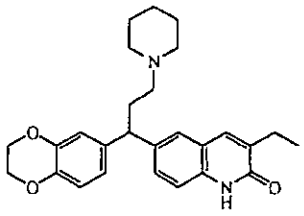
2. A compound as claimed in claim 1 wherein
R^1 is C_{1-6}alkyl; R^3 is a radical selected from (a-1), (a-2), (a-3) or (a-5) or is a group of formula (b-1); s is 0, 1 or 2; R^8 and R^{10} are each independently selected from –CHO, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, di(C_{1-6}alkyl)aminoC_{1-6}alkyl, C_{1-6}alkylcarbonylaminoC_{1-6}alkyl, piperidinylC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, C_{1-6}alkyloxy, thiophenylC_{1-6}alkyl, pyrrolylC_{1-6}alkyl, arylC_{1-6}alkylpiperidinyl, arylcarbonylC_{1-6}alkyl, arylcarbonylpiperidinylC_{1-6}alkyl, haloindozolylpiperidinylC_{1-6}alkyl, or arylC_{1-6}alkyl(C_{1-6}alkyl)aminoC_{1-6}alkyl; t is 0 or 2; -Z is a heterocyclic ring system selected from (c-1), (c-6), (c-8), (c-9), or (c-11); R^{12} is hydrogen,



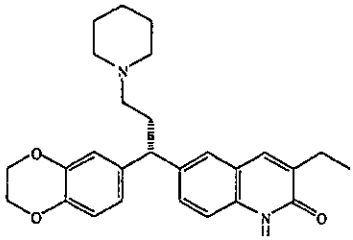
C_{1-6}alkyl, aminocarbonyl, , C_{1-6}alkyloxyC_{1-6}alkylamino, di(phenylC_{2-6}alkenyl), piperidinylC_{1-6}alkyl, C_{3-10}cycloalkyl, C_{3-10}cycloalkylC_{1-6}alkyl, haloindazolyl, or arylC_{2-6}alkenyl; R^4, R^5 and R^6 are each independently selected from hydrogen, halo, trihalomethyl, trihalomethoxy, C_{1-6}alkyl, C_{1-6}alkyloxy, di(C_{1-6}alkyl)amino, di(C_{1-6}alkyl)aminoC_{1-6}alkyloxy or C_{1-6}alkyloxycarbonyl; and when R^5 and R^6 are on adjacent positions they may taken together form a bivalent radical of formula (d-1) or (d-2).

3. A compound according to claim 1 or claim 2 wherein
n is 0; X is CH; R^1 is C_{1-6}alkyl; R^2 is hydrogen; R^3 is a group of formula (b-1); t is 2; -Z is a heterocyclic ring system selected from (c-1); R^{12} is hydrogen; R^{13} is hydrogen; and R^5 and R^6 are on adjacent positions and taken together form a bivalent radical of formula (d-2).

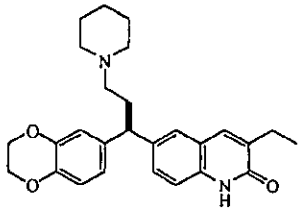
4. A compound according to any one of claims 1, 2 or 3 wherein the compound is compounds No 16, compound No 144, and compound No. 145.



compound 16



Compound 144



Compound 145

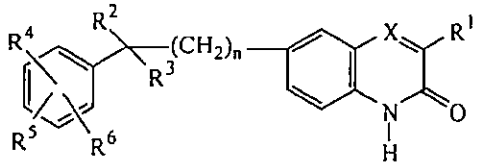
5. A compound according to claim 1 wherein R^3 is a radical selected from (a-1), (a-2), (a-3), (a-4) or (a-5).

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

7. 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 5.

8. A process of preparing a pharmaceutical composition as claimed in claim 7 wherein the pharmaceutically acceptable carriers and a compound as claimed in any one of claims 1 to 5 are intimately mixed.

9. Use of a compound for the manufacture of a medicament for chemosensitization or radiosensitization, wherein said compound is a compound of formula (I)



(I)

an *N*-oxide form, a pharmaceutically acceptable addition salt thereof or a stereochemically isomeric form thereof, wherein

n is 0, 1 or 2;

X is N or CR^7, wherein R^7 is hydrogen or taken together with R^1 may form a bivalent radical of formula -CH=CH-CH=CH-;

R^1 is C_{1-6}alkyl or thiophenyl;

R^2 is hydrogen, hydroxy, C_{1-6}alkyl, C_{3-6}alkynyl or taken together with R^3 may form =O;

R^3 is a radical selected from

$-(CH_2)_s-NR^8R^9$ (a-1),

-O-H (a-2),

$-O-R^{10}$ (a-3),

$-S-R^{11}$ (a-4), or

—C≡N (a-5),

wherein

s is 0, 1, 2 or 3;

R^8, R^{10} and R^{11} are each independently selected from –CHO, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{1-6}alkylcarbonyl, amino, C_{1-6}alkylamino, di(C_{1-6}alkyl)aminoC_{1-6}alkyl, C_{1-6}alkyloxycarbonyl, C_{1-6}alkylcarbonylaminoC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, piperidinyl, piperidinylC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, C_{1-6}alkyloxy, thiophenylC_{1-6}alkyl, pyrrolylC_{1-6}alkyl, arylC_{1-6}alkylpiperidinyl, arylcarbonylC_{1-6}alkyl, arylcarbonylpiperidinylC_{1-6}alkyl, haloindozolylpiperidinylC_{1-6}alkyl, arylC_{1-6}alkyl(C_{1-6}alkyl)aminoC_{1-6}alkyl, and

R^9 is hydrogen or C_{1-6}alkyl;

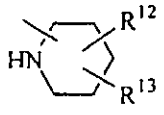
or R^3 is a group of formula

$-(CH_2)_t-Z$ (b-1),

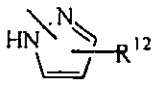
wherein

t is 0, 1, 2 or 3;

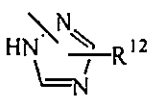
-Z is a heterocyclic ring system selected from



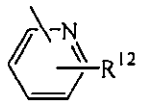
(c-1)



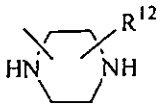
(c-3)



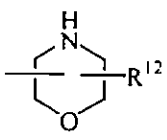
(c-4)



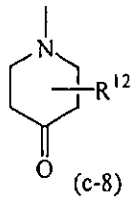
(c-5)



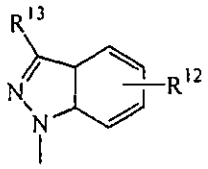
(c-6)

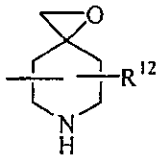


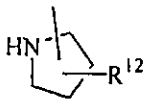
(c-7)



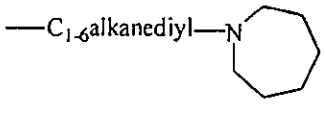
(c-8)

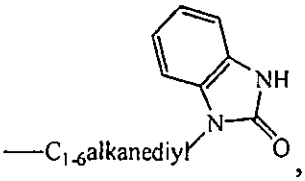

(c-9)


(c-10)


(c-11)

wherein R^{12} is hydrogen, halo, C_{1-6}alkyl, aminocarbonyl, amino, hydroxy, aryl,


,


,

C_{1-6}alkylaminoC_{1-6}alkyloxy, C_{1-6}alkyloxyC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkylamino, arylC_{1-6}alkyl, di(phenylC_{2-6}alkenyl), piperidinyl, piperidinylC_{1-6}alkyl, C_{3-10}cycloalkyl, C_{3-10}cycloalkylC_{1-6}alkyl, aryloxy(hydroxy)C_{1-6}alkyl, haloindazolyl, arylC_{1-6}alkyl, arylC_{2-6}alkenyl, arylC_{1-6}alkylamino, morpholino, C_{1-6}alkylimidazolyl, pyridinylC_{1-6}alkylamino; and

R^{13} is hydrogen, piperidinyl or aryl;

R^4, R^5 and R^6 are each independently selected from hydrogen, halo, trihalomethyl, trihalomethoxy, C_{1-6}alkyl, C_{1-6}alkyloxy, amino, aminoC_{1-6}alkyl, di(C_{1-6}alkyl)amino, di(C_{1-6}alkyl)aminoC_{1-6}alkyloxy or C_{1-6}alkyloxycarbonyl, or C_{1-6}alkyl substituted with 1, 2 or 3 substituents independently selected from hydroxy, C_{1-6}alkyloxy, or aminoC_{1-6}alkyloxy; or

when R^5 and R^6 are on adjacent positions they may taken together form a bivalent radical of formula

-O-CH_2-O	(d-1),
-O-$(CH_2)_2$-O-	(d-2),
-CH=CH-CH=CH-	(d-3), or
-NH-C(O)-NR^{14}=CH-	(d-4),

wherein R^{14} is C_{1-6}alkyl;

aryl is phenyl, phenyl substituted with halo, C_{1-6}alkyl or C_{1-6}alkyloxy.

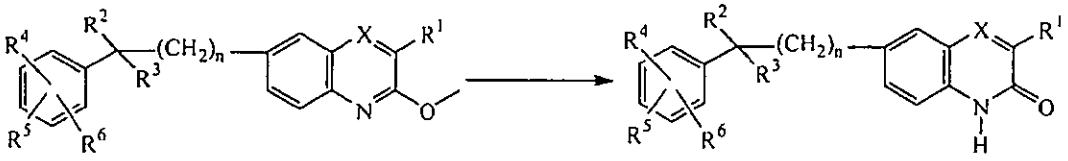
10. Use according to claim 9 wherein the medicament is for chemosensitization.

11. Use according to claim 9 wherein the medicament is for radiosensitization.

12. A combination of a compound as claimed in any one of claims 1 to 5 with a chemotherapeutic agent.

13. A process for preparing a compound as claimed in claim 1, comprising the steps of:

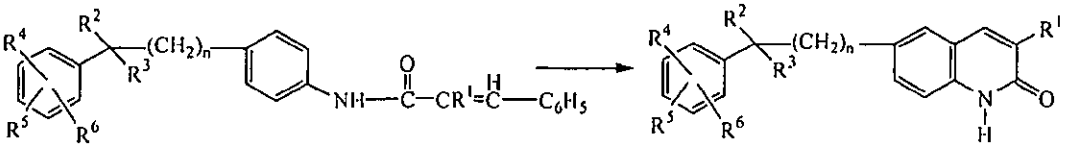
a) the hydrolysis of intermediates of formula (VIII), according to art-known methods, by submitting the intermediates of formula (VIII) to appropriate reagents,



(VIII) (I)

wherein R^1 to R^6, X and n are as defined in claim 1;

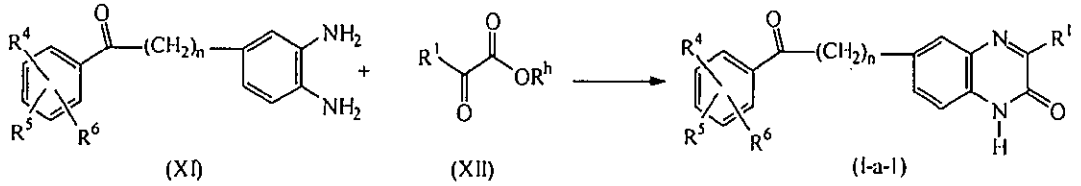
b) the cyclization of intermediates of formula (X), according to art-known cyclizing procedures into compounds of formula (I) wherein X is CH herein referred to as compounds of formula (I-j), either neat or in a suitable solvent or solvent mixtures;



(X) (I-j)

wherein R^1 to R^6 and n are as defined in claim 1;

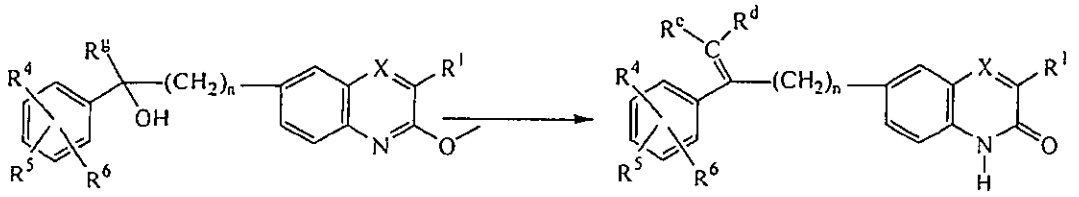
c) the condensation of an appropriate ortho-benzenediamine of formula (XI) with an ester of formula (XII) into compounds of formula (I), wherein X is N and R^2 taken together with R^3 forms =O, herein referred to as compounds of formula (I-a-1), in the presence of a carboxylic acid, a mineral acid or a sulfonic acid,



(XI) (XII) (I-a-1)

wherein R^1, R^4 to R^6 and n are as defined in claim 1 and wherein R^h is C_{1-6}alkyl;

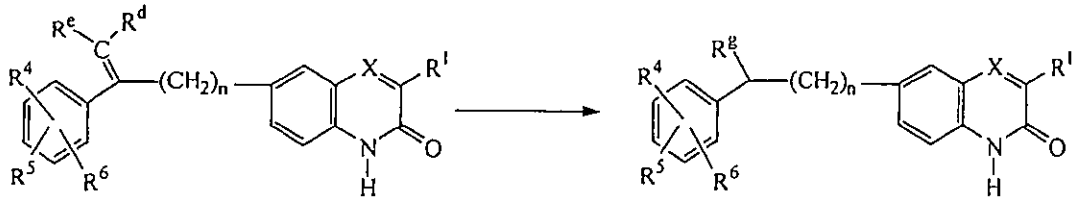
d) hydrolysing intermediates of formula (VI), wherein R^3 is a group of formula (b-1) or a radical of formula (a-1) wherein s is other than 0, herein referred to as R^g, according to art-known methods, with the formation of intermediates and compounds of formula (VII), wherein R^d and R^e are appropriate radicals or taken together with the carbon to which they are attached, form an appropriate heterocyclic ring system as defined in –Z, or



(VI) (VII)

wherein R^1, R^4 to R^6, X and n are as defined in claim 1;

e) converting intermediates of formula (VII), by a selective hydrogenation of said intermediate with an appropriate reducing agent and an appropriate reductant in a suitable solvent with the formation of compounds of formula (I) wherein R^2 is hydrogen and R^g is as defined above, herein referred to as compounds of formula (I-i).



(VII) (I-i)

wherein R^1, R^4 to R^6, X and n are as defined in claim 1.

14. Use of a compound according to any one of claims 1 to 5 for the manufacture of a medicament for the treatment of cancer.

15. A compound as claimed in claim 1 when produced by the process of claim 13.