(e.g., pyrrolo[1,4]benzodiazepines), such as those described in WO 00/12508, WO2005/085260, WO2007/085930, and EP 2019104 . Benzodiazepines are also known to affect cell growth and differentiation (Kamal A., et al., Bioorg Med Chem. 2008 Aug 15;16(16):7804-10 (and references cited therein); Kumar R, Mini Rev Med Chem. 2003 Jun;3(4):323-39 (and references cited therein); Bednarski J J, et al., 2004; Sutter A. P, et al., 2002; Blatt N B, et al., 2002), Kamal A. et al., Current Med. Chem., 2002; 2; 215-254, Wang J-J., J.Med. Chem., 2206; 49:1442-1449, Alley M.C. et al., Cancer Res. 2004; 64:6700-6706, Pepper C. J., Cancer Res 2004; 74:6750-6755, Thurston D.E. and Bose D.S., Chem Rev 1994; 94:433-465; and Tozuka, Z., et al., Journal of Antibiotics, (1983) 36; 1699-1708. General structure of PBDs is described in US Publication Number 20070072846. The PBDs differ in the number, type and position of substituents, in both their aromatic A rings and pyrrolo C rings, and in the degree of saturation of the C ring. Their ability to form an adduct in the minor groove enables them to interfere with DNA processing, hence their potential for use as antiproliferative agents.

[04] There still exists a need for novel benzodiazepine derivatives as effective and safe therapeutics for treating a variety of proliferative disease states, such as cancer.

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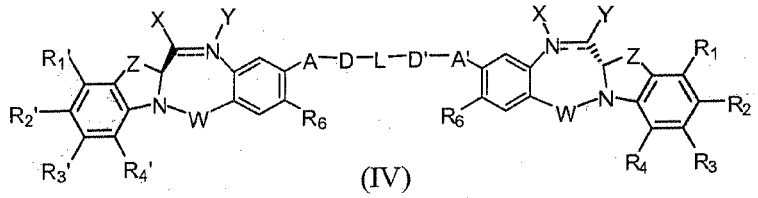
[04] There still exists a need for novel benzodiazepine derivatives as effective and safe therapeutics for treating a variety of proliferative disease states, such as cancer.

SUMMARY OF THE INVENTION

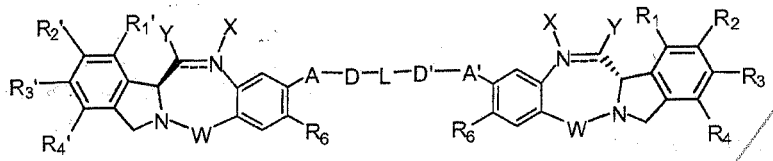
[05] One object of the invention is to provide novel benzodiazepines of formula (I) and (II), in which the diazepine ring (B) is fused with a heterocyclic ring (CD), wherein the heterocyclic ring is bicyclic,

The present invention also provides any one of the embodiments disclosed below and indicated with the numbered clauses 1 to 42.

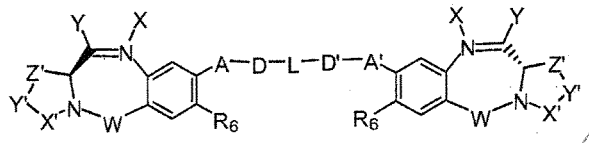
1. A compound selected from formula (IV), (V) or (VI):



(IV)



(V)



(VI)

wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond X is absent and Y is H, and when it is a single bond, X is H or an amine protecting moiety that converts the compound into a prodrug;

Y is selected from -OR, an ester represented by –OCOR', a carbonate represented by –OCOOR', a carbamate represented by –OCONR'R'', an amine or a hydroxyl amine represented by NR'R'', amide represented by –NRCOR', a peptide represented by NRCOP, wherein P is an amino acid or a polypeptide containing between 2 to 20 amino acid units, a thioether represented by SR', a

sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a halogen, cyano, an azido, or a thiol, wherein R, R' and R'' are same or different and are selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P wherein the substituent is selected from halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are each independently selected from H, linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 10-membered heterocyclic ring having 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P and R_{10} is optionally SR_{13} or COR_{13}, wherein R_{13} is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to

10 carbon atoms, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P, optionally R_{11} is OR_{14}, wherein R_{14} has the same definition as R, optionally R'' is OH;

W is C=O, C=S, CH_2, BH, SO or SO_2;

R_1, R_2, R_3, R_4, R_1', R_2', R_3' and R_4' are each independently selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)n$, wherein n is an integer from 1 to 2000, or a substituent selected from a halogen, guanidinium [$-NH(C=NH)NH_2$], OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$ wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are as defined above, optionally, any one of R_1, R_2, R_3, R_4, R_1', R_2', R_3', or R_4' is a linking group that enables linkage to a cell binding agent via a covalent bond or is selected from a polypyrrolo, poly-indolyl, poly-imidazolyl, polypyrollo-imidazolyl, poly-pyrollo-indolyl or polyimidazolo-indolyl unit optionally bearing a linking group that enables linkage to a cell binding agent,

Z is selected from $(CH_2)_n$, wherein n is 1, 2 or 3, $CR_{15}R_{16}$, NR_{17}, O or S, wherein R_{15}, R_{16} and R_{17} are each independently selected from H, linear, branched or cyclic alkyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000;

R_6 is OR, SR or NRR', wherein R and R' have the same definition as given above, optionally R_6 is a linking group;

X' is selected from CH_2, NR, CO, BH, SO or SO_2 wherein R has the same definition as given above;

Y' is O, CH_2, NR or S, wherein R has the same definition as given above;

Z' is CH_2 or $(CH_2)_n$, wherein n is 2, 3 or 4, provided that X', Y' and Z' are not all CH_2 at the same time;

A and A' are the same or different and are selected from O, -CRR'O, S, -CRR'S, $-NR_{15}$ or $CRR'NHR_{15}$, wherein R and R' have the same definition as given above and wherein R_{15} has the same definition as R .

D and D' are same or different and independently selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having 1 to 10 carbon atoms, optionally substituted with any one of halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein the definitions of R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are as defined above, or a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000;

L is an optional phenyl group or 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P that is optionally substituted, wherein the substituent is a linking group that enables linkage to a cell binding agent via a covalent bond, or is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, optionally

substituted with any one of halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are as defined above, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000; optionally, L itself is a linking group that enables linkage to a cell binding agent via a covalent bond; or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers, enantiomers or the polymorphic crystalline structures of these compounds; provided that the compound has no more than one linking group that enables linkage to a cell binding agent via a covalent bond.

2. The compounds of clause 1, wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond X is absent and Y is H, and when it is a single bond, X is H or an amine protecting group that converts the compound into a prodrug;

Y is selected from -OR, NR'R", a sulfite $-SO_3$, or a bisulfite $-OSO_3$, wherein R is selected from H, linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, aryl having from 6 to 10 carbon atoms, heterocyclic ring having from 3 to 10 carbon atoms;

W is C=O, CH_2 or SO_2;

R_1, R_2, R_3, R_4, R_1'. R_2'. R_3' and R_4' are each independently selected from H, NO_2 or a linking group that enables linkage to a cell binding agent via a covalent bond;

R_6 is OR_{18}, wherein R_{18} has the same definition as R;

Z is selected from $(CH_2)_n$, wherein n is 1, 2 or 3, $CR_{15}R_{16}$, NR_{17}, O or S, wherein R_{15}, R_{16} and R_{17} are each independently selected from H, linear, branched or cyclic alkyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000;

X' is selected from CH_2, or C=O;

Y' is O, NR, or S, wherein R is defined as above;

Z' is CH_2 or $(CH_2)_2$;

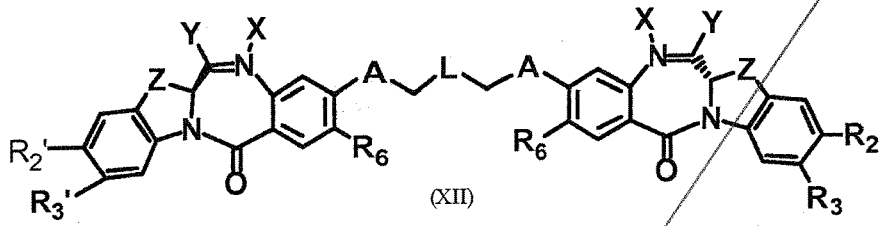
A and A' are each O;

D and D' are same or different and independently selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms;

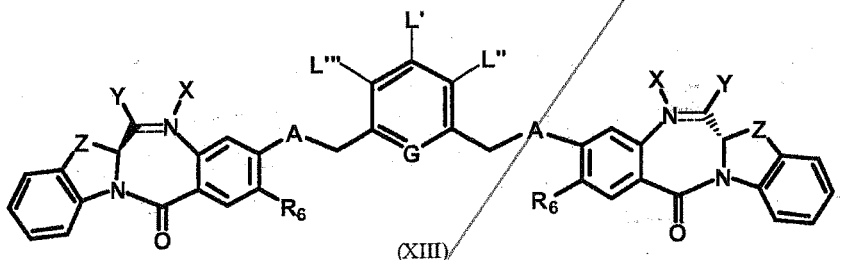
L is an optional phenyl group or a heterocycle ring having from 3 to 10 carbon atoms that is optionally substituted, wherein the substituent is a linking group that enables linkage to a cell binding agent via a covalent bond, or is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, optionally substituted with any one of halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10},a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, , -COR_{11}, $OCOR_{11}$ or $OCONR_{11}R_{12}$, a polyethylene glycol unit $(-OCH_2CH_2)$n, wherein n is an integer from 1 to 2000; optionally, L itself is a linking group that enables linkage to a cell binding agent via a covalent bond;

or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers, enantiomers or the polymorphic crystalline structures of these compounds.

3. The compound of clause 1 selected from formulae (XII) and (XIII):



(XII)



(XIII)

wherein the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond X is absent and Y is H, and when it is a single bond, X is H or an amine protecting group that converts the compound into a prodrug; Y is selected from OH, an ether represented by -OR, NR'R", a sulfite $-SO_3$, or a bisulfite $-OSO_3$, wherein R, R' and R" are selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms;

One of R_2, R_3, R_2' and R_3' is a linking group that enables linkage to a cell binding agent via a covalent bond and the others are H or NO_2;

R_6 is OR, wherein R has the same definition as above;

Z is CH_2 or NR, wherein R has the same definition as above;

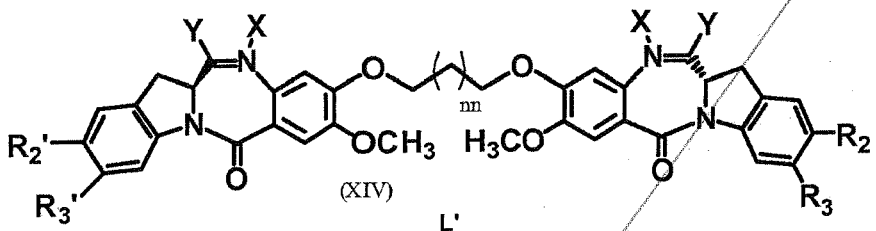
A is O or NR_1;

L is $(CH_2)_{nn}$, wherein nn is 0 or an integer between 1 and 5, or a substituted or unsubstituted alkyl or alkenyl having from 2 to 4 carbon atoms, wherein the substituent is selected from halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10},a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, , $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein R_7, R_8, R_9, R_{10}, R_{11}, R_{12} and R_{15} has the same definition as given above, optionally, L itself is a linking group that enables linkage to a cell binding agent via a covalent bond;

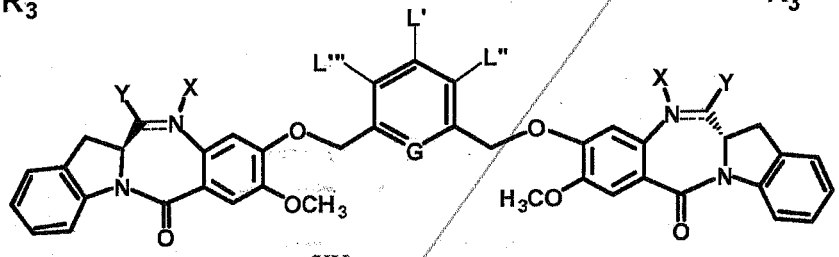
one of L', L'' or L''' is a linking group that enables linkage to a cell binding agent, while the others are H; preferably L' is the linking group; and

G is CH or N or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers, enantiomers or the polymorphic crystalline structures of these compounds.

4. The compound of clause 1 selected from formulae (XIV) and (XV):



(XIV)



(XV)

wherein the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond X is absent and Y is H, and when it is a single bond, X is H or an amine protecting group that converts the compound into a prodrug; Y is selected from OH, an ether represented by -OR, a sulfite $-SO_3$, or a bisulfite $-OSO_3$, wherein R is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms;

nn is 0 or an integer from 1 to 5;

One of R_2, R_3, R_2' and R_3' is a linking group that enables linkage to a cell binding agent via a covalent bond and the others are H or NO_2;

one of L', L'' or L''' is a linking group that enables linkage to a cell binding agent, provided that when one of L', L'' or L''' is a linking group others are H; and

G is CH or N or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers, enantiomers or the polymorphic crystalline structures of these compounds.

5. The compounds of any one of clauses 1-4, wherein one of R_1, R_2, R_3, R_4, R_1', R_2', R_3', R_4', L', L'', L''' is a linking group independently selected from:

$-O(CR_{20}R_{21})_m(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_p''Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-O(CR_{20}R_{21})_m(CR_{26}=CR_{27})_m'(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_p''Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-O(CR_{20}R_{21})_m(alkynyl)_n'(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_p''Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-O(CR_{20}R_{21})_m(piperazino)_t'(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_p''Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-O(CR_{20}R_{21})_m(pyrrolo)_t'(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_p''Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-O(CR_{20}R_{21})_mA''_m''(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_p''Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-S(CR_{20}R_{21})_m(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_p''Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-S(CR_{20}R_{21})_m(CR_{26}=CR_{27})_m'(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_p''Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-S(CR_{20}R_{21})_m(alkynyl)_n'(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_p''Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-S(CR_{20}R_{21})_m(piperazino)_t'(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_p''Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-S(CR_{20}R_{21})_m(pyrrolo)_t'(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_p''Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-S(CR_{20}R_{21})_mA''_m''(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_p''Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-NR_{33}(C=O)_p''(CR_{20}R_{21})_m(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_p''Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-NR_{33}(C=O)_p''(CR_{20}R_{21})_m(CR_{26}=CR_{27})_m'(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_p''Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-NR_{33}(C=O)_p''(CR_{20}R_{21})_m(alkynyl)_n'(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_p''Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-NR_{33}(C=O)_{p''}(CR_{20}R_{21})_m(piperazino)_{t'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-NR_{33}(C=O)_{p''}(CR_{20}R_{21})_m(pyrrolo)_{t'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-NR_{33}(C=O)_{p''}(CR_{20}R_{21})_mA''_{m''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(CR_{26}=CR_{27})_{m'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(alkynyl)_{n'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(piperazino)_{t'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_mA''_{m''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(CR_{29}=N\text{-}NR_{30})_{n''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(CR_{29}=N\text{-}NR_{30})_{n''}(CR_{26}=CR_{27})_{m'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(CR_{29}=N\text{-}NR_{30})_{n''}(alkynyl)_{n'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(CR_{29}=N\text{-}NR_{30})_{n''}A''_{m''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

wherein:

m, n, p, q, m', n', t' are integer from 1 to 10, or are optionally 0;

t, m", n" and p" are 0 or 1;

X" is selected from OR_{36}, SR_{37}, $NR_{38}R_{39}$, wherein R_{36}, R_{37}, R_{38}, R_{39} are H, or linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 20 carbon atoms and, or, a polyethylene glycol unit $-(OCH_2CH_2)_n$, R_{37}, optionally, is a thiol protecting group, or

when t = 1, COX'' forms a reactive ester selected from N-hydroxysuccinimide esters, N-hydroxyphthalimide esters, N-hydroxy sulfo-succinimide esters, para-nitrophenyl esters, dinitrophenyl esters, pentafluorophenyl esters and their derivatives, wherein said derivatives facilitate amide bond formation;

Y'' is absent or is selected from O, S, S-S or NR_{32}, wherein R_{32} has the same definition as given above for R, provided that

when Y'' is not S-S and t = 0, X'' is selected from a maleimido group, a haloacetyl group or SR_{37}, wherein R_{37} has the same definition as above;

A'' is an amino acid selected from glycine, alanine, leucine, valine, lysine, citrulline and glutamate or a polypeptide containing between 2 to 20 amino acid units;

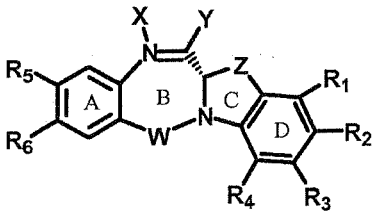
R_{20}, R_{21}, R_{22}, R_{23}, R_{24}, R_{25}, R_{26}, and R_{27} are the same or different and are H or a linear or branched alkyl having from 1 to 5 carbon atoms;

R_{29} and R_{30} are the same or different and are H or alkyl from 1 to 5 carbon atoms;

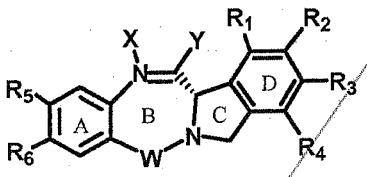
R_{33} is H or linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 12 carbon atoms, a polyethylene glycol unit $-(OCH_2CH_2)_n$, or R_{33} is $-COR_{34}$, $-CSR_{34}$, $-SOR_{34}$, or $-SO_2R_{34}$, wherein R_{34} is H or linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 20 carbon atoms or, a polyethylene glycol unit $-(OCH_2CH_2)_n$; and

one of R_{40} and R_{41} is optionally a negatively or positively charged functional group and the other is H or alkyl, alkenyl, alkynyl having 1 to 4 carbon atoms.

6. A compound selected from formula (I) or (II)



(I)



(II)

wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond X is absent and Y is H, and when it is a single bond, X is H, or an amine protecting moiety that converts the compound into a prodrug that can be transformed into the free amine in vitro or in vivo;

Y is selected from -OR, an ester represented by –OCOR', a carbonate represented by –OCOOR', a carbamate represented by –OCONR'R'', an amine or a hydroxyl amine represented by NR'R'', amide represented by –NRCOR', a peptide represented by NRCOP, wherein P is an amino acid or a polypeptide containing between 2 to 20 amino acid units, a thioether represented by SR', a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a halogen, cyano, an azido, or a thiol, wherein R, R' and R'' are same or different and are selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 20 carbon atoms a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms,

a 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P wherein the substituent is selected from halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are each independently selected from H, linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur. a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic.containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P and R_{10} optionally is SR_{13} or COR_{13}, wherein R_{13} is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P and R_{11} can also be OR_{14}, wherein R_{14} is H or has the same definition as R, optionally, R'' is an OH;

W is C=O, C=S, CH_2, BH (B=Boron), SO or SO_2;

R_1, R_2, R_3, R_4, are each independently selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, or a substituent selected from a halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_10, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, guanidinium $[-NH(C=NH)NH_2]$, $-COR_{11}$, $-OCOR_{11}$ or $-OCONR_{11}R_{12}$ wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} have the same definitions as given above , optionally, any one of R_1, R_2, R_3, R_4 is a linking group that enables linkage to a cell binding agent via a covalent bond or is selected from a polypyrrolo, poly-indolyl, poly-imidazolyl, polypyrollo-imidazolyl, poly-pyrollo-indolyl or polyimidazolo-indolyl unit optionally bearing a linking group that enables linkage to a cell binding agent;

R_5 is selected from OR_{15}, CRR'OH, SH, CRR'SH, NHR_{15} or CRR'NHR_{15}, wherein R_{15} has the same definition as R., R and R' have the same definition as given above; optionally, R_5 is a linking group that enables linkage to a cell binding agent via a covalent bond or is selected from a polypyrrolo, poly-indolyl, poly-imidazolyl, polypyrollo-imidazolyl, poly-pyrollo-indolyl or polyimidazolo-indolyl unit optionally bearing a linking group that enables linkage to a cell binding agent;;

R_6 is OR, SR, NRR', wherein R and R' have the same definition as given above, or optionally R_6 is a linking group;

Z is selected from $(CH_2)_n$, wherein n is 1, 2 or 3, $CR_{15}R_{16}$, NR_{17}, O or S, wherein R_{15}, R_{16} and R_{17} are each independently selected from H, linear, branched or cyclic alkyl having from 1 to 10

carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000; or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers, enantiomers of these compounds.

provided that the compound has no more than one linking group that enables linkage to a cell binding agent via a covalent bond.

7. The compound of clause 6, wherein:

the double line == between N and C represents a double bond and X is absent and Y is H,

or the double line == between N and C represents a single bond wherein X is H and Y is selected from -OR, a sulfite $-SO_3$, or an amine protecting moiety that converts the compound into a prodrug;

W is C=O, CH_2, or SO_2;

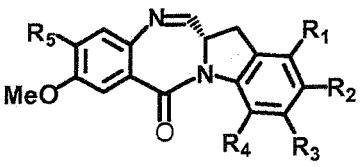
R_1, R_2, R_3, R_4, are each H; optionally, independently, any one of R_1, R_2, R_3 and R_4 can be a linking group that enables linkage to a cell binding agent via a covalent bond;

R_5 is selected from OR_{15}, CRR'OH, SH, CRR'SH, NHR_{15} or CRR'NHR_{15}, wherein R_{15} is H or has the same definition as given above for R, or is selected from a polypyrrolo, poly-indolyl, poly-imidazolyl, polypyrollo-imidazolyl, poly-pyrollo-indolyl or polyimidazolo-indolyl unit optionally bearing a linking group that enables linkage to a cell binding agent, R and R' have the same definition as given above;

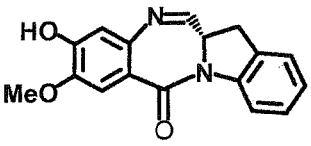
R_6 is OCH_3;

Z is selected from $(CH_2)_n$, wherein n is 1 or 2, NH, NCH_3 or S; or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers, enantiomers or the polymorphic crystalline structures of these compounds.

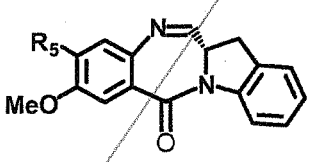
8. The compound of clause 6 selected from formulae (VII), (VIII) and (IX):



(VII)



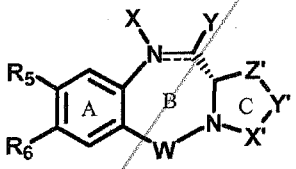
(VIII)



(IX)

wherein the substituents are described as above; or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers, enantiomers or the polymorphic crystalline structures of these compounds.

9. A compound of formula (III)



(III)

wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond X is absent and Y is H, and when it is a single bond, X is H or an amine protecting moiety that converts the compound into a prodrug;

Y is selected from -OR, an ester represented by –OCOR', a carbonate represented by –OCOOR', a carbamate represented by –OCONR'R'', an amine or a hydroxyl amine represented by NR'R'',

amide represented by –NRCOR', a peptide represented by NRCOP, wherein P is an amino acid or a polypeptide containing between 2 to 20 amino acid units, a thioether represented by SR', a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a halogen, cyano, an azido, or a thiol, wherein R, R' and R'' are same or different and selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfurheteroaryl comprising of 5- or 6-membered rings, including fused ring systems (at least one of which is aromatic) of 5-18 atoms, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P, wherein the substituent is selected from halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are each independently selected from H, linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the

rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfurheteroaryl comprising of 5- or 6-membered rings, including fused ring systems (at least one of which is aromatic) of 5-18 atoms, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P and R_{10} optionally is SR_{13} or COR_{13}, wherein R_{13} is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfurheteroaryl comprising of 5- or 6-membered rings, including fused ring systems (at least one of which is aromatic) of 5-18 atoms, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P, and R_{11} can also be OR_{14}, wherein R_{14} is H or has the same definition as R, optionally R'' is OH;

W is C=O, C=S, CH_2, BH, SO or SO_2;

R_5 is selected from OR_{15}, CRR'OH, SH, CRR'SH, NHR_{15} or CRR'NHR_{15}, wherein R_{15} is H or has the same definition as R. or is a linking group that enables linkage to a cell binding agent via a covalent bond or is selected from a polypyrrolo, poly-indolyl, poly-imidazolyl, polypyrollo-imidazolyl, poly-pyrollo-indolyl or polyimidazolo-indolyl unit optionally bearing a linking group

that enables linkage to a cell binding agent;is selected from a poly-pyrrolo, poly-indolyl, poly-imidazolyl, polypyrollo-imidazolyl, poly-pyrollo-indolyl or polyimidazolo-indolyl unit optionally bearing a linking group that enables linkage to a cell binding agent, optionally, R_5 is a linking group that enables linkage to a cell binding agent via a covalent bond;

R_6 is OR, SR or NRR', wherein R and R' have the same definition as given above, optionally R_6 is a linking group;

X' is CH_2, NR, CO, BH, SO or SO_2;

Y' is O, CH_2, NR or S;

Z' is CH_2 or $(CH_2)_n$, wherein n is 2, 3 or 4; or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers, enantiomers or the polymorphic crystalline structures of these compounds;

provided that the compound has no more than one linking group that enables linkage to a cell binding agent via a covalent bond.

10. The compound of clause 9, wherein the double line == between N and C represents a double bond and X is absent and Y = H, or the double line == between N and C represents a single bond wherein X is H and Y is selected from -OR, a sulfite -SO_3, or an amine protecting moiety that converts the compound into a prodrug;

W is C=O, CH_2, or SO_2;

R_5 is selected from OR_{15}, CRR'OH, SH, CRR'SH, NHR_15 or CRR'NHR_{15}, wherein R_{15} is H or has the same definition as given above for R, or is selected from a polypyrrolo, poly-indolyl,

poly-imidazolyl, polypyrollo-imidazolyl, poly-pyrolloindolyl or polyimidazoloindolyl unit optionally bearing a linking group that enables linkage to a cell binding agent;

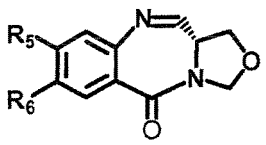
R_6 is OCH_3;

X' is selected from CH_2, or C=O;

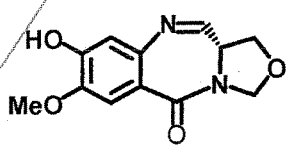
Y' is O, CH_2, NR or S;

Z' is $(CH_2)_n$, wherein n is 1 or 2, provided that X', Y' and Z' are not all CH_2 at the same time; or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers, enantiomers or the polymorphic crystalline structures of these compounds.

11. The compound of clause 9 selected from formulae (X) and (XI):



(X)



(XI)

wherein the substituents are described as above; or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers, enantiomers or the polymorphic crystalline structures of these compounds.

12. The compound of any one of clauses 6-11, wherein R_5 is selected from:

-OH,

$-O(CR_{20}R_{21})_m(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-O(CR_{20}R_{21})_m(CR_{26}=CR_{27})_{m'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-O(CR_{20}R_{21})_m(alkynyl)_{n'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-O(CR_{20}R_{21})_m(indolo)_{p'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$

$-O(CR_{20}R_{21})_m(pyrrolo)_{q'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-O(CR_{20}R_{21})_m(pyrrolo)_{q'}(imidazolo)_{q''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-O(CR_{20}R_{21})_m(imidazolo)_{q''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-O(CR_{20}R_{21})_m(pyrrolo)_{q'}(indolo)_{q''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-O(CR_{20}R_{21})_m(indolo)_{q'}(imidazolo)_{q''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-O(CR_{20}R_{21})_m(piperazino)_{t'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-O(CR_{20}R_{21})_mA''_{m''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

-SH,

$-S(CR_{20}R_{21})_m(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-S(CR_{20}R_{21})_m(CR_{26}{=}CR_{27})_{m'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-S(CR_{20}R_{21})_m(alkynyl)_{n'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-S(CR_{20}R_{21})_m(indolo)_{p'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-S(CR_{20}R_{21})_m(pyrrolo)_{q'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-S(CR_{20}R_{21})_m(imidazolo)_{q''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-S(CR_{20}R_{21})_m(pyrrolo)_{q'}(imidazolo)_{q''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-S(CR_{20}R_{21})_m(pyrrolo)_{q'}(indolo)_{q''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-S(CR_{20}R_{21})_m(indolo)_{q'}(imidazolo)_{q''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-S(CR_{20}R_{21})_m(piperazino)_{t'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-S(CR_{20}R_{21})_mA''_{m''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-NH_2$,

$-NR_{28}(CR_{20}R_{21})_m(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-NR_{28}(CR_{20}R_{21})_m(CR_{26}=CR_{27})_{m'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-NR_{28}(CR_{20}R_{21})_m(\text{alkynyl})_{n'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-NR_{28}(CR_{20}R_{21})_m(\text{indolo})_{p'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-NR_{28}(CR_{20}R_{21})_m(\text{pyrrolo})_{q'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-NR_{28}(CR_{20}R_{21})_m(\text{imidazole})_{q''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-NR_{28}(CR_{20}R_{21})_m(\text{pyrrolo})_{q'}(\text{imidazolo})_{q''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''$-

$(CR_{24}R_{25})_q(CO)_tX''$,

$-NR_{28}(CR_{20}R_{21})_m(\text{pyrrolo})_{q'}(\text{indolo})_{q''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''$-

$(CR_{24}R_{25})_q(CO)_tX''$,

$-NR_{28}(CR_{20}R_{21})_m(\text{indolo})_{q'}(\text{imidazolo})_{q''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''$-

$(CR_{24}R_{25})_q(CO)_tX''$,

$-NR_{28}(CR_{20}R_{21})_m(\text{piperazino})_{t'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-NR_{28}(CR_{20}R_{21})_mA''_{m''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(CR_{26}=CR_{27})_{m'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(\text{alkynyl})_{n'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(\text{indolo})_{p'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(\text{pyrrolo})_{q'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(\text{piperazino})_{t'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(\text{pyrrolo})_{q'}(\text{indolo})_{q''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''-(CR_{24}R_{25})_q(CO)_tX''$,

$(CR_{20}R_{21})_m(\text{imidazolo})_{q''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''-(CR_{24}R_{25})_q(CO)_tX''$,

$(CR_{20}R_{21})_m(\text{pyrrolo})_{q'}(\text{imidazolo})_{q''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''-(CR_{24}R_{25})_q(CO)_tX''$,

$(CR_{20}R_{21})_m(\text{imidazolo})_{q'}(\text{indolo})_{q''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''-(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_mA''_{m''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(CR_{29}{=}N\text{-}NR_{30})_{n''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(CR_{29}{=}N\text{-}NR_{30})_{n''}(CR_{26}{=}CR_{27})_{m'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(CR_{29}{=}N\text{-}NR_{30})_{n''}(\text{alkynyl})_{n'}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

$-(CR_{20}R_{21})_m(CR_{29}{=}N\text{-}NR_{30})_{n''}A''_{m''}(CR_{22}R_{23})_n(OCH_2CH_2)_p(CR_{40}R_{41})_{p''}Y''(CR_{24}R_{25})_q(CO)_tX''$,

wherein:

m, n, p, q, m', n', p', q', q'', are integer from 1 to 10 and can be 0;

t, m", n" and p" are 0 or 1;

X" is selected from OR_{36}, SR_{37}, $NR_{38}R_{39}$, wherein R_{36}, R_{37}, R_{38}, R_{39} are H, or linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 20 carbon atoms and, or, a polyethylene glycol unit $-(OCH_2CH_2)_n$, optionally R_{37} is a thiol protecting group, or

when t = 1, COX'' forms a reactive ester selected from N-hydroxysuccinimide esters, N-hydroxyphthalimide esters, N-hydroxy sulfo-succinimide esters, para-nitrophenyl esters, dinitrophenyl esters, pentafluorophenyl esters and their derivatives, wherein said derivatives facilitate amide formation;

Y'' is absent or is selected from O, S, S-S or NR_{32}, wherein R_{32} has the same definition as given above for R, or

when Y" is not S-S and t = 0, X" is selected from a maleimido group, a haloacetyl group or SR_{37}, wherein R_{37} has the same definition as above;

A" is an amino acid selected from glycine, alanine, leucine, valine, lysine, citrulline and glutamate or a polypeptide containing between 2 to 20 amino acid units;

R_{20}, R_{21}, R_{22}, R_{23}, R_{24}, R_{25}, R_{26}, R_{27} are the same or different and are H or a linear or branched alkyl having from 1 to 5 carbon atoms;

R_{28} is H or alkyl;

R_{29} and R_{30} are the same or different and are H or alkyl from 1 to 5 carbon atoms;

optionally, one of R_{40} and R_{41} is a negatively or positively charged functional group and the other is H or alkyl, alkenyl, alkynyl having 1 to 4 carbon atoms.

13. A compound selected from the title compounds in Examples 1~10 and in Table 7~9.

14. A pharmaceutical composition comprising a compound of any one of clauses 1-13, and a pharmaceutically acceptable carrier.

15. The pharmaceutical composition of clause 14, further comprising a second compound, which is a chemotherapeutic agent.

16. A method of inhibiting abnormal cell growth or treating a proliferative disorder, an autoimmune disorder, destructive bone disorder, infectious disease, viral disease, fibrotic disease, neurodegenerative disorder, pancreatitis or kidney disease in a mammal comprising

administering to said mammal a therapeutically effective amount of the compound of any one of clauses 1-13 and, optionally, a second compound, which is a chemotherapeutic agent. .

17. The method of clause 16, wherein said chemotherapeutic agent is administered to said mammal sequentially or consecutively.

18. A conjugate comprising the compound of any one of clauses 1-13 linked to a cell binding agent.

19. The conjugate of clause 18, wherein the cell-binding agent binds to target cells selected from tumor cells, virus infected cells, microorganism infected cells, parasite infected cells, autoimmune cells, activated cells, myeloid cells, activated T-cells, B cells, or melanocytes; cells expressing the CD4, CD6, CD19, CD20, CD22, CD30, CD33, CD37, CD38, CD40, CD44, CD56, EpCAM, CanAg, CALLA, or Her-2 antigens, Her-3 antigens or cells expressing insulin growth factor receptor, epidermal growth factor receptor, and folate receptor.

20. The conjugate of clause 18, wherein the cell-binding agent is an antibody, a single chain antibody, an antibody fragment that specifically binds to the target cell, a monoclonal antibody, a single chain monoclonal antibody, or a monoclonal antibody fragment that specifically binds the a target cell, a chimeric antibody, a chimeric antibody fragment that specifically binds to the target cell, a domain antibody, a domain antibody fragment that specifically binds to the target cell, a lymphokine, a hormone, a vitamin, a growth factor, a colony stimulating factor, or a nutrient-transport molecule.

21. The conjugate of clause 20, wherein the antibody is a resurfaced antibody, a resurfaced single chain antibody, or a resurfaced antibody fragment.

22. The conjugate of clause 20, wherein the antibody is a monoclonal antibody, a single chain monoclonal antibody, or a monoclonal antibody fragment thereof.

23. The conjugate of clause 20, wherein the antibody is a humanized antibody, a humanized single chain antibody, or a humanized antibody fragment.

24. The conjugate of clause 20, wherein the antibody is a chimeric antibody, a chimeric antibody fragment, a domain antibody, or a domain antibody fragment.

25. The conjugate of clause 23, wherein the antibody is MY9, anti-B4 or C242.

26. The conjugate of clause 23, wherein the antibody is humanized or resurfaced MY9, humanized or resurfaced anti-B4, or humanized or resurfaced C242.

27. The conjugate of clause 19, wherein the tumor cells are selected from breast cancer cells, prostate cancer cells, ovarian cancer cells, colorectal cancer cells, gastric cancer cells, squamous cancer cells, small-cell lung cancer cells, and testicular cancer cells.

28. A pharmaceutical composition comprising the conjugate of clause 18 and a pharmaceutically acceptable carrier.

29. The pharmaceutical composition of clause 28, further comprising a second compound, which is a chemotherapeutic agent.

30. A method of inhibiting abnormal cell growth or treating a proliferative disorder, an autoimmune disorder, destructive bone disorder, infectious disease, viral disease, fibrotic disease, neurodegenerative disorder, pancreatitis or kidney disease in a mammal comprising administering to said mammal a therapeutically effective amount of the conjugate of clause 18 and, optionally, a chemotherapeutic agent.

31. The method of clause 30, wherein said second chemotherapeutic agent is administered to said mammal sequentially or consecutively.

32. The method of clause 30, wherein the proliferative disorder is a tumor.

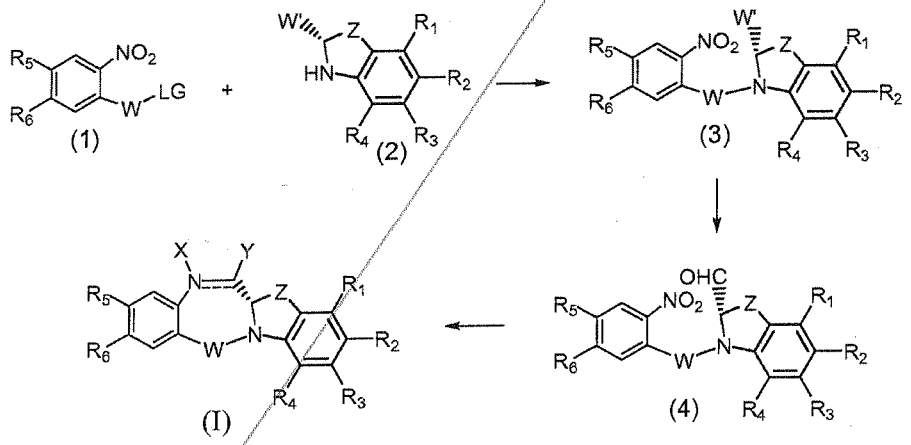
33. The method of clause 32, wherein tumor cells are selected from breast cancer cells, prostate cancer cells, ovarian cancer cells, colorectal cancer cells, gastric cancer cells, squamous cancer cells, small-cell lung cancer cells, and testicular cancer cells.

34. A process for the preparation of a compound of formula (I) comprising the steps of:

a) coupling compound of formula (1) and compound of formula (2) to give compound of formula (3);

b) converting compound of formula (3) into aldehyde of formula (4); and

c) converting compound of formula (4) into compound of formula (I),



wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond X is absent and Y is H, and when it is a single bond, X is H, or an

amine protecting moiety that converts the compound into a prodrug that can be transformed into the free amine in vitro or in vivo;

Y is selected from -OR, an ester represented by –OCOR', a carbonate represented by –OCOOR', a carbamate represented by –OCONR'R'', an amine or a hydroxyl amine represented by NR'R'', amide represented by –NRCOR', a peptide represented by NRCOP, wherein P is an amino acid or a polypeptide containing between 2 to 20 amino acid units, a thioether represented by SR', a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a halogen, cyano, an azido, or a thiol, wherein R, R' and R'' are same or different and are selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 20 carbon atoms a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, a 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P wherein the substituent is selected from halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are each independently selected from H, linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring

containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur. a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic.containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P and R_{10} optionally is SR_{13} or COR_{13}, wherein R_{13} is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, , a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P and R_{11} can also be OR_{14}, wherein R_{14} is H or has the same definition as R, optionally, R'' is an OH;

W is C=O, C=S, CH_2, BH (B=Boron), SO or SO_2;

R_1, R_2, R_3, R_4, are each independently selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, or a substituent selected from a halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_10, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, guanidinium $[-NH(C=NH)NH_2]$, $-COR_{11}$, $-OCOR_{11}$ or $-OCONR_{11}R_{12}$ wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} have the same definitions as given above ,

optionally, any one of R_1, R_2, R_3, R_4 is a linking group that enables linkage to a cell binding agent via a covalent bond or is selected from a polypyrrolo, poly-indolyl, poly-imidazolyl, polypyrollo-imidazolyl, poly-pyrollo-indolyl or polyimidazolo-indolyl unit optionally bearing a linking group that enables linkage to a cell binding agent;

R_5 is selected from OR_{15}, CRR'OH, SH, CRR'SH, NHR_{15} or CRR'NHR_{15}, wherein R_{15} has the same definition as R., R and R' have the same definition as given above; optionally, R_5 is a linking group that enables linkage to a cell binding agent via a covalent bond or is selected from a polypyrrolo, poly-indolyl, poly-imidazolyl, polypyrollo-imidazolyl, poly-pyrollo-indolyl or polyimidazolo-indolyl unit optionally bearing a linking group that enables linkage to a cell binding agent;;

R_6 is OR, SR, NRR', wherein R and R' have the same definition as given above, or optionally R_6 is a linking group;

Z is selected from $(CH_2)_n$, wherein n is 1, 2 or 3, $CR_{15}R_{16}$, NR_{17}, O or S, wherein R_{15}, R_{16} and R_{17} are each independently selected from H, linear, branched or cyclic alkyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000; or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers, enantiomers of these compounds.

provided that the compound has no more than one linking group that enables linkage to a cell binding agent via a covalent bond.

LG is a leaving group;

W' is COOR or CH_2OW", wherein R has the same definition as above, and

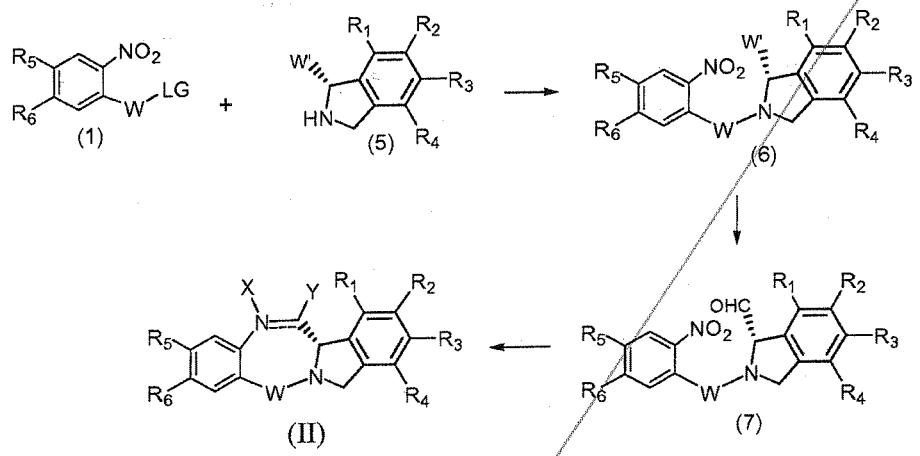
W" is a protecting group.

35. A process for the preparation of compound of formula (II) comprising the steps of:

a) coupling compound of formula (1) and compound of formula (5) to give compound of formula (6);

b) converting compound of formula (6) into aldehyde of formula (7); and

c) converting compound of formula (7) into compound of formula (II),



wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond X is absent and Y is H, and when it is a single bond, X is H, or an amine protecting moiety that converts the compound into a prodrug that can be transformed into the free amine in vitro or in vivo;

Y is selected from -OR, an ester represented by –OCOR', a carbonate represented by –OCOOR', a carbamate represented by –OCONR'R'', an amine or a hydroxyl amine represented by NR'R'', amide represented by –NRCOR', a peptide represented by NRCOP, wherein P is an amino acid

or a polypeptide containing between 2 to 20 amino acid units, a thioether represented by SR', a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a halogen, cyano, an azido, or a thiol, wherein R, R' and R'' are same or different and are selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 20 carbon atoms a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, a 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P wherein the substituent is selected from halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are each independently selected from H, linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur. a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic.containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P and R_{10} optionally is SR_{13} or COR_{13}, wherein R_{13} is selected from linear,

branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, , a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P and R_{11} can also be OR_{14}, wherein R_{14} is H or has the same definition as R, optionally, R'' is an OH;

W is C=O, C=S, CH_2, BH (B=Boron), SO or SO_2;

R_1, R_2, R_3, R_4, are each independently selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, or a substituent selected from a halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_10, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R$', a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, guanidinium $[-NH(C=NH)NH_2]$, $-COR_{11}$, $-OCOR_{11}$ or $-OCONR_{11}R_{12}$ wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} have the same definitions as given above , optionally, any one of R_1, R_2, R_3, R_4 is a linking group that enables linkage to a cell binding agent via a covalent bond or is selected from a polypyrrolo, poly-indolyl, poly-imidazolyl, polypyrollo-imidazolyl, poly-pyrollo-indolyl or polyimidazolo-indolyl unit optionally bearing a linking group that enables linkage to a cell binding agent;

R_5 is selected from OR_{15}, CRR'OH, SH, CRR'SH, NHR_{15} or CRR'NHR_{15}, wherein R_{15} has the same definition as R., R and R' have the same definition as given above; optionally, R_5 is a linking group that enables linkage to a cell binding agent via a covalent bond or is selected from a polypyrrolo, poly-indolyl, poly-imidazolyl, polypyrollo-imidazolyl, poly-pyrollo-indolyl or polyimidazolo-indolyl unit optionally bearing a linking group that enables linkage to a cell binding agent;;

R_6 is OR, SR, NRR', wherein R and R' have the same definition as given above, or optionally R_6 is a linking group;

Z is selected from $(CH_2)_n$, wherein n is 1, 2 or 3, $CR_{15}R_{16}$, NR_{17}, O or S, wherein R_{15}, R_{16} and R_{17} are each independently selected from H, linear, branched or cyclic alkyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000; or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers, enantiomers of these compounds.

provided that the compound has no more than one linking group that enables linkage to a cell binding agent via a covalent bond.

LG is a leaving group;

W' is COOR or CH_2OW", wherein R has the same definition as above, and

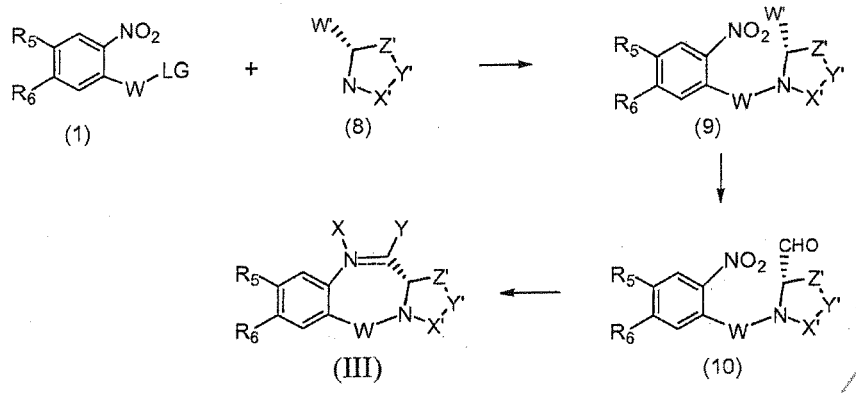
W" is a protecting group.

36. A process for the preparation of compound of formula (III) comprising steps of:

a) coupling compound of formula (1) and compound of formula (8) to give compound of formula (9);

b) converting compound of formula (9) into aldehyde of formula (10); and

c) converting compound of formula (10) into compound of formula (II),



wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond X is absent and Y is H, and when it is a single bond, X is H or an amine protecting moiety that converts the compound into a prodrug;

Y is selected from -OR, an ester represented by –OCOR', a carbonate represented by –OCOOR', a carbamate represented by –OCONR'R'', an amine or a hydroxyl amine represented by NR'R'', amide represented by –NRCOR', a peptide represented by NRCOP, wherein P is an amino acid or a polypeptide containing between 2 to 20 amino acid units, a thioether represented by SR', a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a halogen, cyano, an azido, or a thiol, wherein R, R' and R'' are same or different and selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system,

wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfurheteroaryl comprising of 5- or 6-membered rings, including fused ring systems (at least one of which is aromatic) of 5-18 atoms, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P, wherein the substituent is selected from halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are each independently selected from H, linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfurheteroaryl comprising of 5- or 6-membered rings, including fused ring systems (at least one of which is aromatic) of 5-18 atoms, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P and R_{10} optionally is SR_{13} or COR_{13}, wherein R_{13} is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or

more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfurheteroaryl comprising of 5- or 6-membered rings, including fused ring systems (at least one of which is aromatic) of 5-18 atoms, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P and R_{11} can also be OR_{14}, wherein R_{14} is H or has the same definition as R, optionally R'' is OH;

W is C=O, C=S, CH_2, BH, SO or SO_2;

R_5 is selected from OR_{15}, CRR'OH, SH, CRR'SH, NHR_{15} or CRR'NHR_{15}, wherein R_{15} is H or has the same definition as R. or is a linking group that enables linkage to a cell binding agent via a covalent bond or is selected from a polypyrrolo, poly-indolyl, poly-imidazolyl, polypyrollo-imidazolyl, poly-pyrollo-indolyl or polyimidazolo-indolyl unit optionally bearing a linking group that enables linkage to a cell binding agent;is selected from a poly-pyrrolo, poly-indolyl, poly-imidazolyl, polypyrollo-imidazolyl, poly-pyrollo-indolyl or polyimidazolo-indolyl unit optionally bearing a linking group that enables linkage to a cell binding agent, optionally, R_5 is a linking group that enables linkage to a cell binding agent via a covalent bond;

R_6 is OR, SR or NRR', wherein R and R' have the same definition as given above, optionally R_6 is a linking group;

X' is CH_2, NR, CO, BH, SO or SO_2;

Y' is O, CH_2, NR or S;

Z' is CH_2 or $(CH_2)_n$, wherein n is 2, 3 or 4; or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers, enantiomers or the polymorphic crystalline structures of these compounds;

provided that the compound has no more than one linking group that enables linkage to a cell binding agent via a covalent bond;

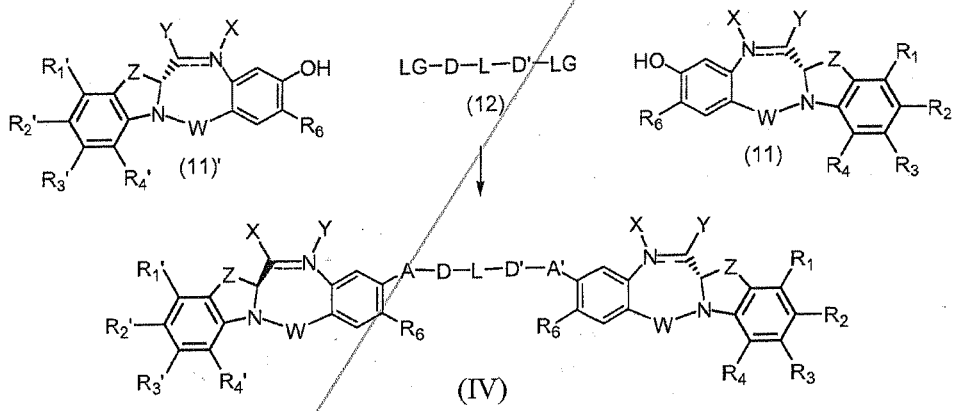
LG is a leaving group;

W' is COOR or CH_2OW", wherein R has the same definition as above, and

W" is a protecting group.

37. A process for the preparation of compound of formula (IV) comprising the steps of:

coupling compound of formula (11), compound of formula (11)' and compound of formula (12) to give compound of formula (IV),



wherein wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond X is absent and Y is H, and when it is a single bond, X is H or an amine protecting moiety that converts the compound into a prodrug;

Y is selected from -OR, an ester represented by –OCOR', a carbonate represented by –OCOOR', a carbamate represented by –OCONR'R'', an amine or a hydroxyl amine represented by NR'R'', amide represented by –NRCOR', a peptide represented by NRCOP, wherein P is an amino acid or a polypeptide containing between 2 to 20 amino acid units, a thioether represented by SR', a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a halogen, cyano, an azido, or a thiol, wherein R, R' and R'' are same or different and are selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P wherein the substituent is selected from halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are each independently selected from H, linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more

heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 10-membered heterocyclic ring having 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P and R_{10} is optionally SR_{13} or COR_{13}, wherein R_{13} is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P, optionally R_{11} is OR_{14}, wherein R_{14} has the same definition as R,, optionally R'' is OH;

W is C=O, C=S, CH_2, BH, SO or SO_2;

R_1, R_2, R_3, R_4, R_1', R_2', R_3' and R_4' are each independently selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)n$, wherein n is an integer from 1 to 2000, or a substituent selected from a halogen, guanidinium [$-NH(C=NH)NH_2$], OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R$', a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$ wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} have the same definitions as given above, optionally, any one of R_1, R_2, R_3, R_4, R_1', R_2', R_3', or R_4' is a linking group that enables linkage to a cell binding agent via a covalent bond or is selected from a polypyrrolo, poly-

indolyl, poly-imidazolyl, polypyrollo-imidazolyl, poly-pyrollo-indolyl or polyimidazolo-indolyl unit optionally bearing a linking group that enables linkage to a cell binding agent,

Z is selected from $(CH_2)_n$, wherein n is 1, 2 or 3, $CR_{15}R_{16}$, NR_{17}, O or S, wherein R_{15}, R_{16} and R_{17} are each independently selected from H, linear, branched or cyclic alkyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000;

R_6 is OR, SR or NRR', wherein R and R' have the same definition as given above, optionally R_6 is a linking group;

A and A' are the same or different and are selected from O, -CRR'O, S, -CRR'S, $-NR_{15}$ or $CRR'NHR_{15}$, wherein R and R' have the same definition as given above and wherein R_{15} has the same definition as R .

D and D' are same or different and independently selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having 1 to 10 carbon atoms, optionally substituted with any one of halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein the definitions of R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are as defined above, or a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000;

L is an optional phenyl group or 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P that is optionally substituted, wherein the substituent is a linking group that enables linkage to a cell binding agent via a covalent bond, or is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, optionally

substituted with any one of halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein the definitions of R_7, R_8, R_9, R_{10}, R_{11} and R_{12} have the same definitions as given above, a polyethylene glycol unit $(-OCH_2CH_2)n$, wherein n is an integer from 1 to 2000; optionally, L itself is a linking group that enables linkage to a cell binding agent via a covalent bond; or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers, enantiomers or the polymorphic crystalline structures of these compounds; provided that the compound has no more than one linking group that enables linkage to a cell binding agent via a covalent bond; and

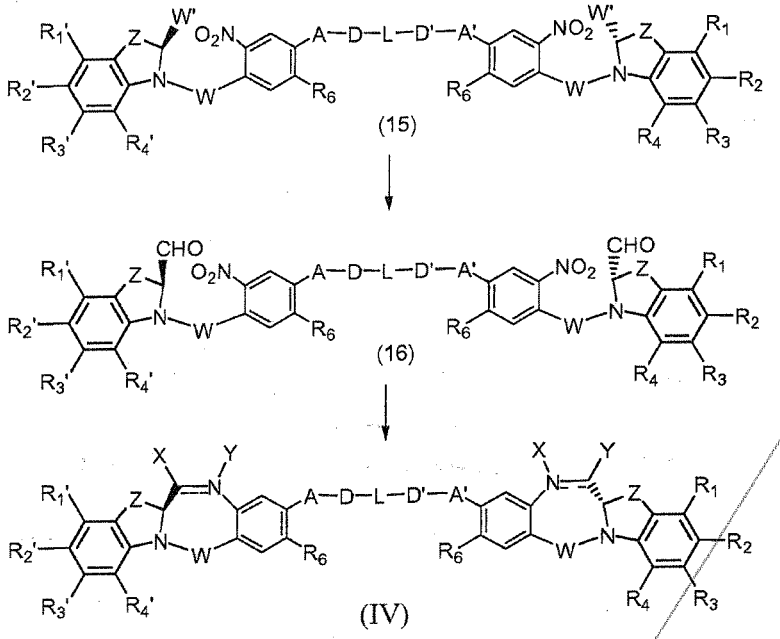
LG is a leaving group;

.

38. A process for the preparation of compound of formula (IV) comprising steps of:

a) converting compound of formula (15) into aldehyde of formula (16); and

b) converting compound of formula (16) into compound of formula (IV),



wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond X is absent and Y is H, and when it is a single bond, X is H or an amine protecting moiety that converts the compound into a prodrug;

Y is selected from -OR, an ester represented by –OCOR', a carbonate represented by –OCOOR', a carbamate represented by –OCONR'R'', an amine or a hydroxyl amine represented by NR'R'', amide represented by –NRCOR', a peptide represented by NRCOP, wherein P is an amino acid or a polypeptide containing between 2 to 20 amino acid units, a thioether represented by SR', a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a halogen, cyano, an azido, or a thiol, wherein R, R' and R'' are same or different and are selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)n$, wherein n is an

integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P wherein the substituent is selected from halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein the definitions of R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are each independently selected from H, linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 10-membered heterocyclic ring having 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P, and R_{10} is optionally SR_{13} or COR_{13} , wherein R_{13} is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6

to 18 carbon atoms, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P, optionally R_{11} is OR_{14}, wherein R_{14} has the same definition as R, optionally R'' is OH;

W is C=O, C=S, CH_2, BH, SO or SO_2;

R_1, R_2, R_3, R_4, R_1', R_2', R_3' and R_4' are each independently selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)n$, wherein n is an integer from 1 to 2000, or a substituent selected from a halogen, guanidinium $[-NH(C=NH)NH_2]$, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$ wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} have the same definitions as given above, optionally, any one of R_1, R_2, R_3, R_4, R_1', R_2', R_3', or R_4' is a linking group that enables linkage to a cell binding agent via a covalent bond or is selected from a polypyrrolo, poly-indolyl, poly-imidazolyl, polypyrollo-imidazolyl, poly-pyrollo-indolyl or polyimidazolo-indolyl unit optionally bearing a linking group that enables linkage to a cell binding agent,

Z is selected from $(CH_2)_n$, wherein n is 1, 2 or 3, $CR_{15}R_{16}$, NR_{17}, O or S, wherein R_{15}, R_{16} and R_{17} are each independently selected from H, linear, branched or cyclic alkyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000;

R_6 is OR, SR or NRR', wherein R and R' have the same definition as given above, optionally R_6 is a linking group;

A and A' are the same or different and are selected from O, -CRR'O, S, -CRR'S, -NR_{15} or CRR'NHR_{15}, wherein R and R' have the same definition as given above and wherein R_{15} has the same definition as R .

D and D' are same or different and independently selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having 1 to 10 carbon atoms, optionally substituted with any one of halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by -SO_2R', a sulfite -SO_3, a bisulfite -OSO_3, a sulfonamide represented by SO_2NRR', cyano, an azido, -COR_{11}, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein the definitions of R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are as defined above, or a polyethylene glycol unit (-OCH_2CH_2)$_n$, wherein n is an integer from 1 to 2000;

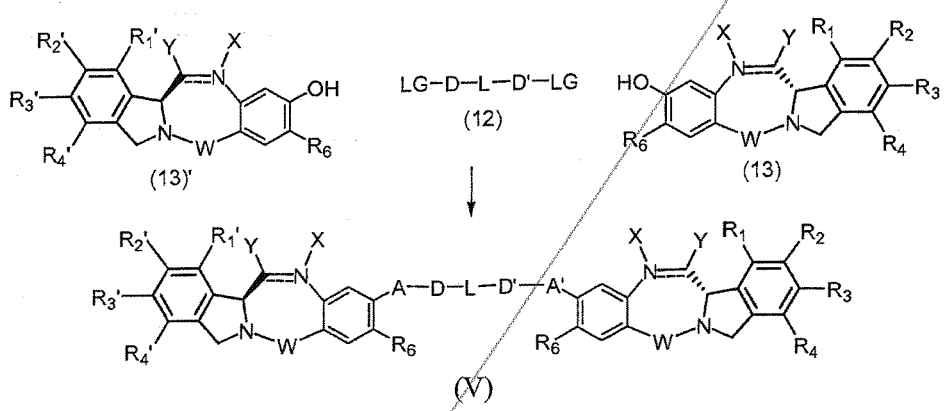
L is an optional phenyl group or 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P that is optionally substituted, wherein the substituent is a linking group that enables linkage to a cell binding agent via a covalent bond, or is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, optionally substituted with any one of halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by -SO_2R', a sulfite -SO_3, a bisulfite -OSO_3, a sulfonamide represented by SO_2NRR', cyano, an azido, -COR_{11}, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein the definitions of R_7, R_8, R_9, R_{10}, R_{11} and R_{12} have the same definitions as given above, a polyethylene glycol unit (-OCH_2CH_2)n, wherein n is an integer from 1 to 2000; optionally, L itself is a linking group that enables linkage to a cell binding agent via a covalent bond; or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers,

racemates, diastereomers, enantiomers or the polymorphic crystalline structures of these compounds; provided that the compound has no more than one linking group that enables linkage to a cell binding agent via a covalent bond;

W' is COOR or CH_2OW'', wherein R has the same definition as above, and

W'' is a protecting group.

39. A process for the preparation of compound of formula (V) comprising the step of coupling compound of formula (13), compound of formula (13)' and compound of formula (12) to give compound of formula (V),



wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond X is absent and Y is H, and when it is a single bond, X is H or an amine protecting moiety that converts the compound into a prodrug;

Y is selected from -OR, an ester represented by –OCOR', a carbonate represented by –OCOOR', a carbamate represented by –OCONR'R'', an amine or a hydroxyl amine represented by NR'R'', amide represented by –NRCOR', a peptide represented by NRCOP, wherein P is an amino acid or a polypeptide containing between 2 to 20 amino acid units, a thioether represented by SR', a

sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a halogen, cyano, an azido, or a thiol, wherein R, R' and R'' are same or different and are selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P wherein the substituent is selected from halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein the definitions of R_7, R_8, R_9, R_{10}, R_{11} and R_{12}, are each independently selected from H, linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 10-membered heterocyclic ring having 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P, and R_{10} is optionally SR_{13} or COR_{13}, wherein R_{13} is selected from linear, branched or cyclic alkyl, alkenyl

or alkynyl having from 1 to 10 carbon atoms, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P, optionally R_{11} is OR_{14}, wherein R_{14} has the same definition as R, optionally R'' is OH;

W is C=O, C=S, CH_2, BH, SO or SO_2;

R_1, R_2, R_3, R_4, R_1', R_2', R_3' and R_4' are each independently selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)n$, wherein n is an integer from 1 to 2000, or a substituent selected from a halogen, guanidinium [$-NH(C=NH)NH_2$], OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R$', a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$ wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} have the same definitions as given above, optionally, any one of R_1, R_2, R_3, R_4, R_1', R_2', R_3', or R_4' is a linking group that enables linkage to a cell binding agent via a covalent bond or is selected from a polypyrrolo, poly-indolyl, poly-imidazolyl, polypyrollo-imidazolyl, poly-pyrollo-indolyl or polyimidazolo-indolyl unit optionally bearing a linking group that enables linkage to a cell binding agent,

Z is selected from $(CH_2)_n$, wherein n is 1, 2 or 3, $CR_{15}R_{16}$, NR_{17}, O or S, wherein R_{15}, R_{16} and R_{17} are each independently selected from H, linear, branched or cyclic alkyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000; R_6 is OR, SR or NRR', wherein R and R' have the same definition as given above, optionally R_6 is a linking group;

A and A' are the same or different and are selected from O, -CRR'O, S, -CRR'S, $-NR_{15}$ or CRR'NHR_{15}, wherein R and R' have the same definition as given above and wherein R_{15} has the same definition as R .

D and D' are same or different and independently selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having 1 to 10 carbon atoms, optionally substituted with any one of halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein the definitions of R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are as defined above, or a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000;

L is an optional phenyl group or 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P that is optionally substituted, wherein the substituent is a linking group that enables linkage to a cell binding agent via a covalent bond, or is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, optionally substituted with any one of halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide

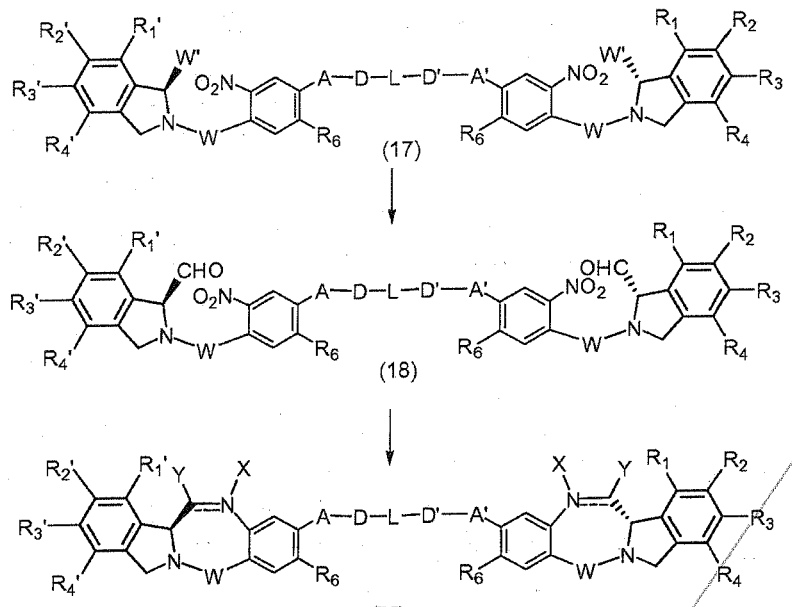
represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} have the same definitions as given above, a polyethylene glycol unit $(-OCH_2CH_2)n$, wherein n is an integer from 1 to 2000; optionally, L itself is a linking group that enables linkage to a cell binding agent via a covalent bond; or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers, enantiomers or the polymorphic crystalline structures of these compounds; provided that the compound has no more than one linking group that enables linkage to a cell binding agent via a covalent bond; and

LG is a leaving group.

40. A process for the preparation of compound of formula (V) comprising the steps of:

a) converting compound of formula (17) into aldehyde of formula (18); and

b) converting compound of formula (18) into compound of formula (V),



(V)

wherein the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond X is absent and Y is H, and when it is a single bond, X is H or an amine protecting moiety that converts the compound into a prodrug;

Y is selected from -OR, an ester represented by –OCOR', a carbonate represented by –OCOOR', a carbamate represented by –OCONR'R'', an amine or a hydroxyl amine represented by NR'R'', amide represented by –NRCOR', a peptide represented by NRCOP, wherein P is an amino acid or a polypeptide containing between 2 to 20 amino acid units, a thioether represented by SR', a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a halogen, cyano, an azido, or a thiol, wherein R, R' and R'' are same or different and are selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms

independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P wherein the substituent is selected from halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein the definitions of R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are each independently selected from H, linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 10-membered heterocyclic ring having 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P, and R_{10} is optionally SR_{13} or COR_{13} , wherein R_{13} is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from

O, S, N and P, optionally R_{11} is OR_{14}, wherein R_{14} has the same definition as R, optionally R'' is OH;

W is C=O, C=S, CH_2, BH, SO or SO_2;

R_1, R_2, R_3, R_4, R_1', R_2', R_3' and R_4' are each independently selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)n$, wherein n is an integer from 1 to 2000, or a substituent selected from a halogen, guanidinium [$-NH(C=NH)NH_2$], OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R$', a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$ wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} have the same definitions as given above, optionally, any one of R_1, R_2, R_3, R_4, R_1', R_2', R_3', or R_4' is a linking group that enables linkage to a cell binding agent via a covalent bond or is selected from a polypyrrolo, poly-indolyl, poly-imidazolyl, polypyrollo-imidazolyl, poly-pyrollo-indolyl or polyimidazolo-indolyl unit optionally bearing a linking group that enables linkage to a cell binding agent,

Z is selected from $(CH_2)_n$, wherein n is 1, 2 or 3, $CR_{15}R_{16}$, NR_{17}, O or S, wherein R_{15}, R_{16} and R_{17} are each independently selected from H, linear, branched or cyclic alkyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000;

R_6 is OR, SR or NRR', wherein R and R' have the same definition as given above, optionally R_6 is a linking group;

A and A' are the same or different and are selected from O, -CRR'O, S, -CRR'S, -NR_{15} or CRR'NHR_{15}, wherein R and R' have the same definition as given above and wherein R_{15} has the same definition as R .

D and D' are same or different and independently selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having 1 to 10 carbon atoms, optionally substituted with any one of halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by -SO_2R', a sulfite -SO_3, a bisulfite -OSO_3, a sulfonamide represented by SO_2NRR', cyano, an azido, -COR_{11}, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein the definitions of R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are as defined above, or a polyethylene glycol unit (-$OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000;

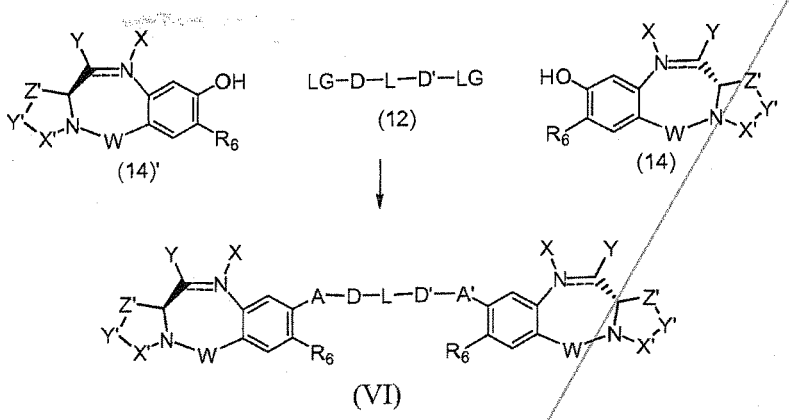
L is an optional phenyl group or 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P that is optionally substituted, wherein the substituent is a linking group that enables linkage to a cell binding agent via a covalent bond, or is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, optionally substituted with any one of halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by -SO_2R', a sulfite -SO_3, a bisulfite -OSO_3, a sulfonamide represented by SO_2NRR', cyano, an azido, -COR_{11}, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} have the same definitions as given above, a polyethylene glycol unit (-OCH_2CH_2)n, wherein n is an integer from 1 to 2000; optionally, L itself is a linking group that enables linkage to a cell binding agent via a covalent bond; or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers,

enantiomers or the polymorphic crystalline structures of these compounds; provided that the compound has no more than one linking group that enables linkage to a cell binding agent via a covalent bond;

W' is COOR or CH_2OW", wherein R has the same definition as above; and

W" is a protecting group.

41. A process for the preparation of compound of formula (VI) comprising the step of coupling compound of formula (14), compound of formula (14)' and compound of formula (12) to give compound of formula (VI),



wherein

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond X is absent and Y is H, and when it is a single bond, X is H or an amine protecting moiety that converts the compound into a prodrug;

Y is selected from -OR, an ester represented by –OCOR', a carbonate represented by –OCOOR', a carbamate represented by –OCONR'R'', an amine or a hydroxyl amine represented by NR'R'', amide represented by –NRCOR', a peptide represented by NRCOP, wherein P is an amino acid or a polypeptide containing between 2 to 20 amino acid units, a thioether represented by SR', a

sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a halogen, cyano, an azido, or a thiol, wherein R, R' and R'' are same or different and are selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P wherein the substituent is selected from halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are each independently selected from H, linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 10-membered heterocyclic ring having 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P and R_{10} is optionally SR_{13} or COR_{13}, wherein R_{13} is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to

10 carbon atoms, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P, optionally R_{11} is OR_{14}, wherein R_{14} has the same definition as R, optionally R'' is OH;

W is C=O, C=S, CH_2, BH, SO or SO_2;

Z is selected from $(CH_2)_n$, wherein n is 1, 2 or 3, $CR_{15}R_{16}$, NR_{17}, O or S, wherein R_{15}, R_{16} and R_{17} are each independently selected from H, linear, branched or cyclic alkyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000;

R_6 is OR, SR or NRR', wherein R and R' have the same definition as given above, optionally R_6 is a linking group;

X' is selected from CH_2, NR, CO, BH, SO or SO_2 wherein R has the same definition as given above;

Y' is O, CH_2, NR or S, wherein R has the same definition as given above;

Z' is CH_2 or $(CH_2)_n$, wherein n is 2, 3 or 4, provided that X', Y' and Z' are not all CH_2 at the same time;

A and A' are the same or different and are selected from O, -CRR'O, S, -CRR'S, $-NR_{15}$ or $CRR'NHR_{15}$, wherein R and R' have the same definition as given above and wherein R_{15} has the same definition as R .

D and D' are same or different and independently selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having 1 to 10 carbon atoms, optionally substituted with any one of halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by -SO_2R', a sulfite -SO_3, a bisulfite -OSO_3, a sulfonamide represented by SO_2NRR', cyano, an azido, -COR_{11}, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein the definitions of R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are as defined above, or a polyethylene glycol unit (-$OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000;

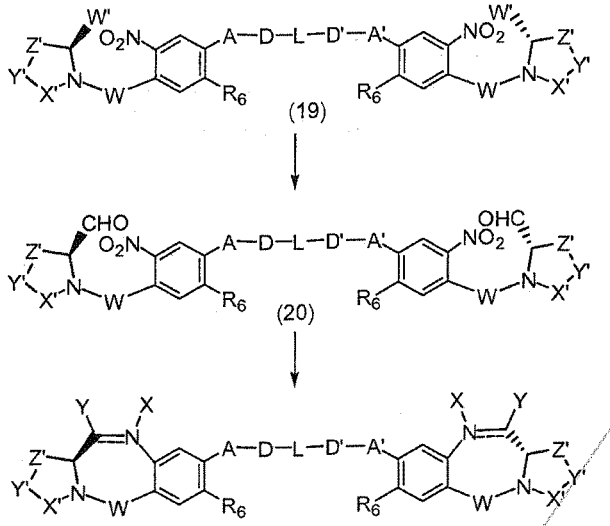
L is an optional phenyl group or 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P that is optionally substituted, wherein the substituent is a linking group that enables linkage to a cell binding agent via a covalent bond, or is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, optionally substituted with any one of halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by -SO_2R', a sulfite -SO_3, a bisulfite -OSO_3, a sulfonamide represented by SO_2NRR', cyano, an azido, -COR_{11}, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} have the same definitions as given above, a polyethylene glycol unit (-$OCH_2CH_2)n$, wherein n is an integer from 1 to 2000; optionally, L itself is a linking group that enables linkage to a cell binding agent via a covalent bond; or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers, enantiomers or the polymorphic crystalline structures of these compounds; provided that the compound has no more than one linking group that enables linkage to a cell binding agent via a covalent bond; and

LG is a leaving group.

42. A process for the preparation of compound of formula (VI) comprising the steps of:

a) converting compound of formula (19) into aldehyde of formula (20); and

b) converting compound of formula (20) into compound of formula (VI),



wherein

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond X is absent and Y is H, and when it is a single bond, X is H or an amine protecting moiety that converts the compound into a prodrug;

Y is selected from -OR, an ester represented by –OCOR', a carbonate represented by –OCOOR', a carbamate represented by –OCONR'R'', an amine or a hydroxyl amine represented by NR'R'', amide represented by –NRCOR', a peptide represented by NRCOP, wherein P is an amino acid or a polypeptide containing between 2 to 20 amino acid units, a thioether represented by SR', a

sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite - OSO_3, a halogen, cyano, an azido, or a thiol, wherein R, R' and R'' are same or different and are selected from H, substituted or unsubstituted linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P wherein the substituent is selected from halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by $-SO_2R'$, a sulfite $-SO_3$, a bisulfite $-OSO_3$, a sulfonamide represented by SO_2NRR', cyano, an azido, $-COR_{11}$, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are each independently selected from H, linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 10-membered heterocyclic ring having 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P and R_{10} is optionally SR_{13} or COR_{13}, wherein R_{13} is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to

10 carbon atoms, a 5- or 6-membered heteroaryl ring containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5 to 18 membered fused ring system, wherein at least one of the rings is aromatic, containing one or more heteroatoms independently selected from nitrogen, oxygen, and sulfur, aryl having from 6 to 18 carbon atoms, 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P, optionally R_{11} is OR_{14}, wherein R_{14} has the same definition as R, optionally R'' is OH;

W is C=O, C=S, CH_2, BH, SO or SO_2;

Z is selected from $(CH_2)_n$, wherein n is 1, 2 or 3, $CR_{15}R_{16}$, NR_{17}, O or S, wherein R_{15}, R_{16} and R_{17} are each independently selected from H, linear, branched or cyclic alkyl having from 1 to 10 carbon atoms, a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000;

R_6 is OR, SR or NRR', wherein R and R' have the same definition as given above, optionally R_6 is a linking group;

X' is selected from CH_2, NR, CO, BH, SO or SO_2 wherein R has the same definition as given above;

Y' is O, CH_2, NR or S, wherein R has the same definition as given above;

Z' is CH_2 or $(CH_2)_n$, wherein n is 2, 3 or 4, provided that X', Y' and Z' are not all CH_2 at the same time;

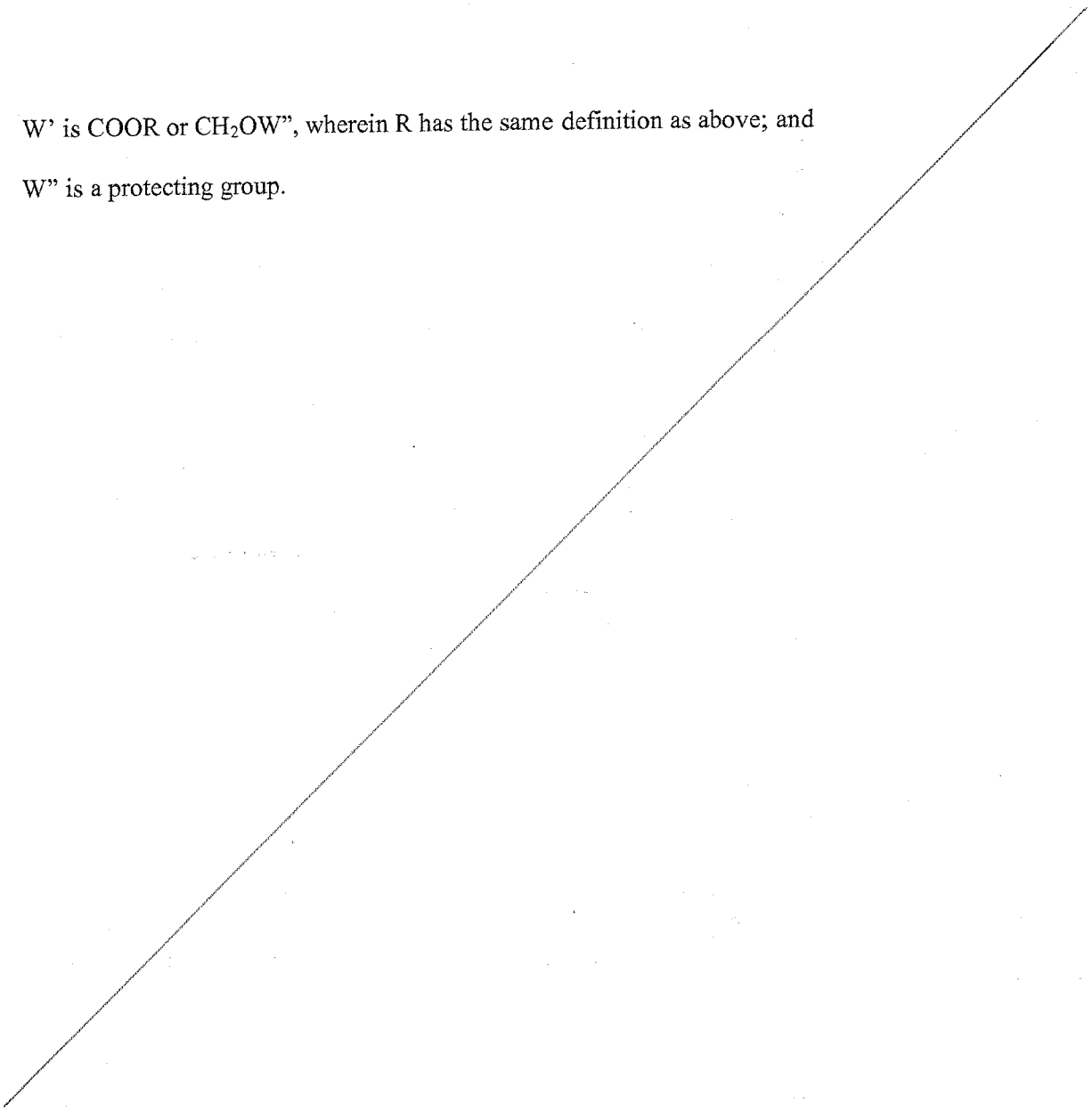
A and A' are the same or different and are selected from O, -CRR'O, S, -CRR'S, $-NR_{15}$ or $CRR'NHR_{15}$, wherein R and R' have the same definition as given above and wherein R_{15} has the same definition as R .

D and D' are same or different and independently selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having 1 to 10 carbon atoms, optionally substituted with any one of halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by -SO_2R', a sulfite -SO_3, a bisulfite -OSO_3, a sulfonamide represented by SO_2NRR', cyano, an azido, -COR_{11}, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein the definitions of R_7, R_8, R_9, R_{10}, R_{11} and R_{12} are as defined above, or a polyethylene glycol unit $(-OCH_2CH_2)_n$, wherein n is an integer from 1 to 2000;

L is an optional phenyl group or 3 to 18-membered heterocyclic ring having 1 to 6 heteroatoms selected from O, S, N and P that is optionally substituted, wherein the substituent is a linking group that enables linkage to a cell binding agent via a covalent bond, or is selected from linear, branched or cyclic alkyl, alkenyl or alkynyl having from 1 to 10 carbon atoms, optionally substituted with any one of halogen, OR_7, NR_8R_9, NO_2, NRCOR', SR_{10}, a sulfoxide represented by SOR', a sulfone represented by -SO_2R', a sulfite -SO_3, a bisulfite -OSO_3, a sulfonamide represented by SO_2NRR', cyano, an azido, -COR_{11}, $OCOR_{11}$ or $OCONR_{11}R_{12}$, wherein R_7, R_8, R_9, R_{10}, R_{11} and R_{12} have the same definitions as given above, a polyethylene glycol unit (-OCH_2CH_2)n, wherein n is an integer from 1 to 2000; optionally, L itself is a linking group that enables linkage to a cell binding agent via a covalent bond; or their pharmaceutically acceptable solvates, salts, hydrates or hydrated salts, their optical isomers, racemates, diastereomers, enantiomers or the polymorphic crystalline structures of these compounds; provided that the compound has no more than one linking group that enables linkage to a cell binding agent via a covalent bond;

W' is COOR or CH_2OW", wherein R has the same definition as above; and

W" is a protecting group.



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SUMMARY OF THE INVENTION

[05] One object of the invention is to provide novel benzodiazepines of formula (I) and (II), in which the diazepine ring (B) is fused with a heterocyclic ring (CD), wherein the heterocyclic ring is bicyclic,