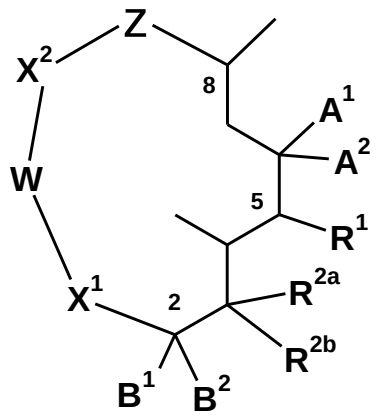
CLAIMS

WE CLAIM:

1. A macrolide based macrocycle compound of Formula **(III)**



(III)

and pharmaceutically acceptable salts, solvates and prodrugs thereof, wherein

A^1 is OH, OC_{1-6}alkyl, OC_{2-6}alkenyl, OC_{2-6}alkynyl, OR^p, or A^1 together with R^{2b} forms cyclic hemiketal or ether;

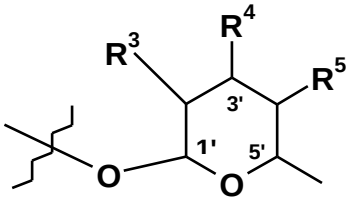
A^2 is CH_3 or H;

B^1 and B^2 are independently H, C_{1-6}alkyl or halogen, or

B^2 together with R^{2a} forms a double bond;

R^1 is S^1, OH, OC_{1-6}alkyl or OR^p;

S^1 is sugar group of formula **(b1)**:



(b1)

wherein,

R^3 is OH, H, OR^p, $–O\text{-}L^1\text{-}G$ or -OC(=O)G, provided when R^3 is $–O\text{-}L^1\text{-}G$ or -OC(=O)G group then R^4 is $–N(CH_3)_2$ and R^5 is H, wherein

L^1 $-(CH_2)_{a1}\text{-}U^1\text{-}(CH_2)_{b1}$-;

U^1 is $–N(R^6)$-, -NHC(=O)- or –C(=O)NH-;

R^6 is H or C_{1-3}alkyl;

a^1 is an integer from 2 to 6;

b^1 is an integer from 0 to 6;

G is selected from:

(i) G^1, wherein G^1 is C_{1-8}alkyl, wherein alkyl may be optionally interrupted by 1 to 3 bivalent radical groups selected from –O-, -S- and –N(R^{g1})-, where R^{g1} is H or C_{1-6}alkyl, and where alkyl may be optionally substituted by one or more groups independently selected from halogen, OH, keto, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, OC_{1-6}alkyl, haloC_{1-6}alkyl, haloC_{1-6}alkyloxy, -C(=O)OC_{1-6}alkyl, -C_{1-6}alkyl-OH, NH_2, *N*-(C_{1-6}-alkyl)amino, *N,N*-di(C_{1-6}alkyl)amino; aryl or heteroaryl wherein said aryl and heteroaryl may be mono or biyclic and independently each may be optionally substituted by one or more groups independently selected from halogen, CN, OH, NO_2, OC_{1-6}alkyl, NH_2, *N*-(C_{1-6}-alkyl)amino, *N,N*-di(C_{1-6}alkyl)amino, -C(=O)C_{1-6}alkyl, -OC(=O)C_{1-6}alkyl, -C(=O)OH, -C(=O)OC_{1-6}alkyl, -C(=O)NHC_{1-6}alkyl and -NHC(=O)C_{1-6}alkyl;

(ii) G^2, wherein G^2 is 3-7 membered cycloalkyl which may be optionally substituted by one or more groups independently selected from OH, halogen, CN, NH_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, -C_{1-6}alkyl-OH, -C(=O)C_{1-6}alkyl, -C(=O)OC_{1-6}alkyl, -C(=O)OH, -C(=O)NH_2, -C_{0-6}alkyl-aryl or C_{0-6}alkyl-heteroaryl wherein aryl and heteroaryl independently from each other may be optionally substituted by one or more groups independently selected from halogen, CN, OH, NO_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, -C_{1-6}alkyl-OH, NH_2, *N*-(C_{1-6}-alkyl)amino, *N,N*-di(C_{1-6}alkyl)amino, -C(=O)C_{1-6}alkyl, -OC(=O)C_{1-6}alkyl, -C(=O)OH, -C(=O)OC_{1-6}alkyl, -C(=O)NHC_{1-6}alkyl and -NHC(=O)C_{1-6}alkyl;

(iii) G^3, wherein G^3 is 3-7 membered heterocycloalkyl containing one or two heteroatoms independently selected from N, O and S, where heterocycloalkyl may be optionally substituted by one or more groups independently selected from OH, halogen, CN, NH_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, -C_{1-6}alkyl-OH, -C(=O)C_{1-6}alkyl, -C(=O)OC_{1-6}alkyl, -C(=O)OH and -C(=O)NH_2;

(iv) G^4, wherein G^4 is aryl wherein aryl may be optionally substituted by one or more groups independently selected from halogen, CN, OH, NO_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, -C_{1-6}alkyl-OH, NH_2, *N*-(C_{1-6}-alkyl)amino, *N,N*-di(C_{1-6}alkyl)amino, -C(=O)C_{1-6}alkyl, -O(C=O)C_{1-6}alkyl, -C(=O)OH, -C(=O)OC_{1-6}alkyl, -C(=O)NHC_{1-6}alkyl and -NHC(=O)C_{1-6}alkyl;

(v) G^5, wherein G^5 is heteroaryl wherein heteroaryl may be optionally substituted by one or more groups independently selected from halogen, CN, OH, NO_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, -C_{1-6}alkyl-OH, NH_2, *N*-(C_{1-6}-alkyl)amino, *N,N*-di(C_{1-6}alkyl)amino, -C(=O)C_{1-6}alkyl, -O(C=O)C_{1-6}alkyl, -C(=O)OH, -C(=O)OC_{1-6}alkyl, -C(=O)NHC_{1-6}alkyl and -NHC(=O)C_{1-6}alkyl;

R^4 is –N(R^7)R^8, wherein

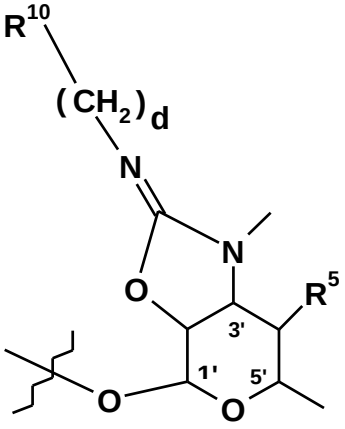
R^7 is CH_3,

R^8 is C_{1-6}alkyl, H, -C(=O)R^9 or R^p wherein R^9 is C_{1-6}alkyl or H;

R^5 is hydrogen;

or both R^4 and R^5 are hydrogen or together form a bond;

or S^1 is sugar group of formula **(b2)**:



(b2)

wherein:

R^5 is H;

d is an integer from zero to 3;

R^{10} is C_{1-4}alkyl;

R^{2a} is:

(i) S^2;

(ii) -OH;

(iii) -OC_{1-6}alkyl,

(iv) H;

(v) together with R^{2b} forms a keto group (=O);

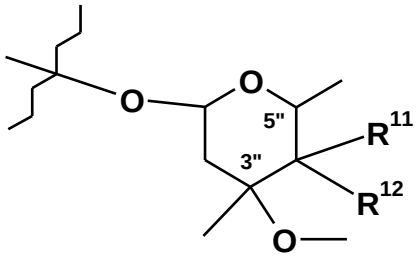
(vi) together with B^2 forms a double bond;

(vii) -OC(=O)Y^1, wherein Y^1 is G^1, G^2, G^3, G^4, G^5 or H; or

(viii) -OR^p;

R^{2b} is H, together with R^{2a} forms a keto group, together with A^1 forms cyclic hemiketal and R^{2a} is OH, or together with A^1 forms cyclic ether group and R^{2a} is H;

S^2 is sugar group of formula **(d)**



(d)

wherein,

R^{11} is:

(i) H;

(ii) together with R^{12} and carbon atom to which they are attached forms a keto or epoxy group;

(iii) one of R^{11} and R^{12} is OH and the other is $–CH_2N(R^{13})R^{14}$, wherein one of R^{13} and R^{14} is C_{1-6}alkyl and the other is H, G^1, G^2, G^3, G^4, G^5 or R^p, or wherein R^{13} and R^{14} taken together with the nitrogen atom to which they are attached form a non-aromatic heterocyclic ring containing between 2 and 6 carbon atoms which is:

a. saturated or unsaturated and contains zero or 1 additional heteroatom selected from O, S and N; and/or

b. unsubstituted or substituted by from 1 to 2 groups selected from C_{1-5}alkanoyl; C_{1-6}alkyl wherein alkyl is uninterrupted or is interrupted by 1-3 bivalent radical groups selected from-O-, -S- and and $–N(R^{18})$-, and/or wherein C_{1-6}alkyl is unsubstituted or substituted by from 1 to 2 groups selected from OH, NH_2, a non-aromatic heterocyclic ring containing between 2 and 6 carbon atoms which is unsubstituted or is substituted by a group selected from C_{1-4}alkyl, halogen, NH_2, OH, SH, C_{1-6}alkoxy and C_{1-4}hydroxyalkyl, and C_{3-7}cycloalkyl which is unsubstituted or is substituted by a group selected from C_{1-4}alkyl, halogen, NH_2, OH, SH, C_{1-6}alkoxy, C_{1-4}hydroxyalkyl; and C_{1-4}dialkylamino;

R^{12} is:

(i) OH,

(ii) together with R^{11} and carbon atom to which they are attached forms a keto or epoxy group;

(iii) -OC(=O)Y^3, wherein Y^3 is H, G^1, G^2, G^3, G^4, or G^5; or

(iv) OR^p;

R^N is hydrogen, G^1 (preferably CH^3), G^2, G^3, G^4, G^5, R^p, or R^{15} wherein R^{15} is –C_{1-4}alkyl-G, -C(=O)G, -C(=O)NH-C_{0-4}alkyl-G, wherein G is G^1, G^2, G^3, G^4 or G^5;

R^p is a protective group;

Z is –NR^NCH_2-, –NHC(=O)- or –OC(=O)- (left hand valence bond of these groups is attached to X^2 whereas right hand valence bond is attached to the C/8 carbon atom), provided when Z is –NHC(=O)- or –OC(=O)- then B^1 is OC_{1-6}alkyl;

X^1 is a bond, –C(=O)NR^X-, -NHC(=O)-, -NR^u-, -CH_2NR^u-, -CH_2O-, –C(=O)-, or -C(=O)O- (left hand valence bond of these groups is attached to the C/2 carbon atom whereas right hand valence bond is attached to W); wherein

R^u is H or C_{1-6}alkyl,

R^X is H, R^Z or –CH(R^Y)-C(=O)NHR^Z;

R^Y is H, C_{1-6}alkyl or phenyl; and

R^Z is C_{1-6}alkyl, C_{0-6}alkyl-aryl or C_{0-6}alkyl-heteroaryl wherein aryl and heteroaryl independently from each other may be optionally substituted by one or more groups independently selected from halogen, CN, OH, NO_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, -C_{1-6}alkyl-OH, NH_2, *N*-(C_{1-6}-alkyl)amino, *N,N*-di(C_{1-6}alkyl)amino, -C(=O)C_{1-6}alkyl, -OC(=O)C_{1-6}alkyl, -C(=O)OH, -C(=O)OC_{1-6}alkyl, -C(=O)NHC_{1-6}alkyl and -NHC(=O)C_{1-6}alkyl;

X^2 is a bond, –C(=O)- or -CH_2-;

W is –W^1-$(CH_2)_{m1}$-W^2-$(CH_2)_{m2}$-W^3- (left hand valence bond of W^1 is attached to X^1 whereas right hand valence bond of W^3 is attached to X^2), wherein:

m^1 is zero, 1, 2 or 3;

m^2 is zero, 1, 2 or 3;

W^1, W^2 and W^3 are:

(i) one of, two of or non of W^1, W^2 and W^3 are absent and the remaining of W^1, W^2 and $W^3$are independently selected from:

a. 3-7 membered cycloalkyl which may be optionally substituted by one or more groups independently selected from OH, halogen, CN, NH_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, -C_{1-6}alkyl-OH, -C(=O)C_{1-6}alkyl, -C(=O)OC_{1-6}alkyl, -C(=O)OH, -C(=O)NH_2, -C_{0-6}alkyl-aryl or C_{0-6}alkyl-heteroaryl wherein aryl and heteroaryl independently from each other may be optionally

substituted by one or more groups independently selected from halogen, CN, OH, NO_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, -C_{1-6}alkyl-OH, NH_2, *N*-(C_{1-6}-alkyl)amino, *N,N*-di(C_{1-6}alkyl)amino, -C(=O)C_{1-6}alkyl, -OC(=O)C_{1-6}alkyl, -C(=O)OH, -C(=O)OC_{1-6}alkyl, -C(=O)NHC_{1-6}alkyl and -NHC(=O)C_{1-6}alkyl;

b. 4-7 membered cycloalkenyl containing one or two double bonds which may be optionally substituted by one or more groups independently selected from OH, halogen, CN, NH_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, -C_{1-6}alkyl-OH, -C(=O)C_{1-6}alkyl, -C(=O)OC_{1-6}alkyl, -C(=O)OH and -C(=O)NH_2;

c. 3-7 membered heterocycloalkyl containing one or two heteroatoms independently selected from N, O and S, where heterocycloalkyl may be optionally substituted by one or more groups independently selected from OH, halogen, CN, NH_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, -C_{1-6}alkyl-OH, -C(=O)C_{1-6}alkyl, -C(=O)OC_{1-6}alkyl, -C(=O)OH, -C(=O)NH_2, -C_{0-6}alkyl-aryl, -O-C_{0-6}alkyl-aryl, -C_{0-6}alkyl-heteroaryl, -C_{0-6}alkyl-cycloalkyl or -C_{0-6}alkyl-heterocycloalkyl, wherein aryl, heteroaryl, cycloalkyl, and heterocycloalkyl independently from each other may be optionally substituted by one or more groups independently selected from halogen, CN, OH, NO_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, C_{1-6}alkyl-OH, NH_2, *N*-(C_{1-6}-alkyl)amino, *N,N*-di(C_{1-6}alkyl)amino, -C(=O)C_{1-6}alkyl, -OC(=O)C_{1-6}alkyl, -C(=O)OH, -C(=O)OC_{1-6}alkyl, -C(=O)NHC_{1-6}alkyl and -NHC(=O)C_{1-6}alkyl;

d. 4-7 membered heterocycloalkenyl containing one or two heteroatoms independently selected from N, O and S and one or two double bonds where heterocycloalkenyl may be optionally substituted by one or more groups independently selected from OH, halogen, CN, NH_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, -C_{1-6}alkyl-OH, -C(=O)C_{1-6}alkyl, -C(=O)OC_{1-6}alkyl, -C(=O)OH and -C(=O)NH_2;

e. 6 membered aryl which may be optionally substituted by one or more groups independently selected from halogen, CN, OH, NO_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, -C_{1-6}alkyl-OH, NH_2, *N*-(C_{1-6}-alkyl)amino, *N,N*-di(C_{1-6}alkyl)amino,

-C(=O)C_{1-6}alkyl, -O(C=O)C_{1-6}alkyl, -C(=O)OH, -C(=O)OC_{1-6}alkyl, -C(=O)NHC_{1-6}alkyl and -NHC(=O)C_{1-6}alkyl;

f. 5-6 membered heteroaryl containing two or three heteroatoms independently selected from N, O and S, wherein heteroaryl may be optionally substituted by one or more groups independently selected from halogen, CN, OH, NO_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, -C_{1-6}alkyl-OH, NH_2, *N*-(C_{1-6}-alkyl)amino, *N,N*-di(C_{1-6}alkyl)amino, -C(=O)C_{1-6}alkyl, -O(C=O)C_{1-6}alkyl, -C(=O)OH, -C(=O)OC_{1-6}alkyl, -C(=O)NHC_{1-6}alkyl and -NHC(=O)C_{1-6}alkyl;

g. –C(R^{W1a})(R^{W2a})-, wherein R^{W1a} is hydrogen, and R^{W2a} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, halogen, OH, CN, -C(=O)OH, -C(=O)NH_2, haloC_{1-6}alkyl, OC_{1-6}alkyl, C_{1-6}alkyl-OH, -C_{1-6}alkylOC_{1-6}alkyl, -C_{1-6}alkylSC_{1-6}alkyl, -C_{1-6}alkyl-C(=O)OH, C_{1-6}alkyl-C(=O)OC_{1-6}alkyl, -C_{1-6}alkylOC(=O)C_{1-6}alkyl, -C_{1-6}alkylC(=O)NH_2, -C_{1-6}alkyl-NH_2, -C_{1-6}alkyl-NH(C_{1-6}alkyl), -C_{1-6}alkyl-N(C_{1-6}alkyl)$_2$, -C_{1-6}alkylNHC(=O)OC_{1-6}alkyl, -C_{1-6}alkyl-NHC(=O)C_{2-6}alkenyl, -C_{1-6}alkyl-NHC(=O)-C_{0-4}alkyl-heteroaryl, -C_{1-6}alkylNHS$O_2$$C_{1-6}$alkyl, -$C_{1-6}$alkylNHS$O_2$$C_{2-6}$alkenyl, -$C_{1-6}$alkylNHS$O_2$cycloalkyl, -$C_{0-6}$alkyl-aryl, -$C_{2-6}$alkenyl-aryl, -$C_{0-6}$alkyl-heteroaryl, -$C_{2-6}$alkenyl-heteroaryl, -$C_{0-6}$alkyl-cycloalkyl, or -$C_{0-6}$alkyl-heterocycloalkyl, wherein alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, and heterocycloalkyl independently from each other may be optionally substituted by one or more groups independently selected from halogen, CN, OH, NO_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, C_{1-6}alkyl-OH, NH_2, *N*-(C_{1-6}-alkyl)amino, *N,N*-di(C_{1-6}alkyl)amino, -C(=O)C_{1-6}alkyl, -OC(=O)C_{1-6}alkyl, -C(=O)OH, -C(=O)OC_{1-6}alkyl, -C(=O)NHC_{1-6}alkyl, -NHC(=O)C_{1-6}alkyl, -C_{1-6}alkylNHS$O_2$$C_{1-6}$alkyl, and -$C_{1-6}$alkyl-NH(C=NH)$NHR^g$ wherein R^g is H, amino protecting group, -C_{0-6}alkyl-aryl, -OC_{0-6}alkylaryl, -C_{0-6}alkyl-heteroaryl, -C_{0-6}alkyl-cycloalkyl or -C_{0-6}alkyl-heterocycloalkyl, wherein aryl, heteroaryl, cycloalkyl, and heterocycloalkyl independently from each other may be optionally substituted by one or more groups independently selected from halogen, CN, OH, NO_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, C_{1-6}alkyl-OH, NH_2, *N*-(C_{1-6}-alkyl)amino, *N,N*-di(C_{1-6}alkyl)amino,

-C(=O)C_{1-6}alkyl, -OC(=O)C_{1-6}alkyl, -C(=O)OH, -C(=O)OC_{1-6}alkyl, -C(=O)NHC_{1-6}alkyl and -NHC(=O)C_{1-6}alkyl;

h. –C(R^{W1b})(R^{W2b})- group wherein R^{W1b} and R^{W2b} together with carbon atom to which they are attached form:

i. 3-7 membered spiro cycloalkyl group which may be optionally substituted by one or more groups independently selected from halogen, CN, keto (=O), OH, NO_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, C_{1-6}alkyl-OH, NH_2, *N*-(C_{1-6}-alkyl)amino, *N,N*-di(C_{1-6}alkyl)amino, -C(=O)C_{1-6}alkyl, -OC(=O)C_{1-6}alkyl, -C(=O)OH, -C(=O)OC_{1-6}alkyl, -C(=O)NHC_{1-6}alkyl and -NHC(=O)C_{1-6}alkyl; or

ii. 3-7 membered spiro heterocycloalkyl group where heterocycloalkyl group may contain one or two heteroatoms selected form O, S and N;

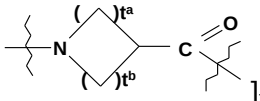
i. –N(R^{Wn})-, wherein R^{Wn} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, -C_{1-6}alkylOC_{1-6}alkyl, -C_{1-6}alkyl-C(=O)OH, -C_{1-6}alkyl-C(=O)OC_{1-6}alkyl, -C_{1-6}alkylOC(=O)C_{1-6}alkyl, -C_{1-6}alkyl-NH_2, -C_{1-6}alkylNHC(=O)OC_{1-6}alkyl, -C_{1-6}alkyl-aryl wherein aryl may be optionally substituted by one or more groups independently selected from halogen, CN, OH, NO_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, OC_{1-6}alkyl, haloC_{1-6}alkyloxy, C_{1-6}alkyl-OH, NH_2, *N*-(C_{1-6}-alkyl)amino, *N,N*-di(C_{1-6}alkyl)amino, -(C=O)C_{1-6}alkyl, -O(C=O)C_{1-6}alkyl, -C(=O)OH, -C(=O)OC_{1-6}alkyl, -C(=O)NHC_{1-6}alkyl and -NHC(=O)C_{1-6}alkyl;

j. –C(R^{W1c})(R^{W2c})- group wherein R^{W1c} and R^{W2c} together with carbon atom to which they are attached form:

i. >C=C-aryl, or

ii. >C=C-heteroaryl,

wherein aryl and heteroaryl independently from each other may be optionally substituted by one or more groups independently selected from halogen, CN, OH, NO_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, OC_{1-6}alkyl, haloC_{1-6}alkyloxy, C_{1-6}alkyl-OH, NH_2, *N*-(C_{1-6}-alkyl)amino, *N,N*-di(C_{1-6}alkyl)amino, -(C=O)C_{1-6}alkyl, -O(C=O)C_{1-6}alkyl, -C(=O)OH, -C(=O)OC_{1-6}alkyl, -C(=O)NHC_{1-6}alkyl and -NHC(=O)C_{1-6}alkyl;

k. [–NHCH(R^t)C(=O)-]$_{t1}$ or []$_{t2}$ group,
wherein:
t^1 and t^2 independently are 1 to 5,
t_a and t_b independently are 0 to 3, provided the sum of t^a and t^b is 2 to 6,
R^t is residue of natural amino acid selected from H, C_{1-6}alkyl, -C(=O)C_{1-6}alkyl, -C(=O)OC_{1-6}alkyl, -OC_{1-6}alkyl, -C_{1-6}alkyl-OH, -C_{1-6}alkyl-OC_{1-6}alkyl, -C_{1-6}alkyl-SC_{1-6}alkyl, CN, -C(=O)OH, -C(=O)NH_2, -C_{0-6}alkyl-aryl or -C_{0-6}alkyl-heteroaryl wherein aryl and heteroaryl may be mono or biyclic and each may be optionally substituted by one or more groups independently selected from halogen, CN, OH, NO_2, OC_{1-6}alkyl, NH_2, *N*-(C_{1-6}-alkyl)amino, *N,N*-di(C_{1-6}alkyl)amino, -(C=O)C_{1-6}alkyl, -O(C=O)C_{1-6}alkyl, -C(=O)OH, -C(=O)OC_{1-6}alkyl, -C(=O)NHC_{1-6}alkyl and -NHC(=O)C_{1-6}alkyl;

l. -NHC(R^{W1d})(R^{W2d})C(R^{W1e})(R^{W2e})-NHC(=O)- group wherein R^{W1d} and R^{W1e} are hydrogen, and R^{W2d} and R^{W2e} are independently from each other C_{0-4}alkylaryl wherein aryl may be optionally substituted by one or more groups independently selected from halogen, CN, OH, NO_2, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, -OC_{1-6}alkyl, haloC_{1-6}alkyloxy, -C_{1-6}alkyl-OH, NH_2, *N*-(C_{1-6}-alkyl)amino, *N,N*-di(C_{1-6}alkyl)amino, -C(=O)C_{1-6}alkyl, -O(C=O)C_{1-6}alkyl, -C(=O)OH, -C(=O)OC_{1-6}alkyl, -C(=O)NHC_{1-6}alkyl and -NHC(=O)C_{1-6}alkyl;

(ii) W^1 and W^3 are selected from (i-a) to (i-l), W^2 is -CH=CH-, -CH(OH)CH(OH)-, -CH=CH-CH(OH)-, or –CH=CH-CH=CH-, X^2 is –C(=O)- or –CH_2-, X^1 is –C(=O)NH- or –C(=O)O- ;

(iii) W^1 is –CH=CH-, X^1 is a bond and W^2 and W^3 are independently selected from (i-a) to (i-l);

(iv) W^2 is >C(=O) or –C(=O)NH- and W^1 and W^3 are independently selected from (i-a) to (i-l), provided when W^1 is absent, m^1 cannot be zero; or

(v) all absent.

2. The compound according to claim 1, wherein R^N is C_{1-6}alkyl (preferably CH_3) or hydrogen.

3. The compound according to claim 1, wherein A^1 is OH or -OC_{1-6}alkyl (preferably OCH_3).

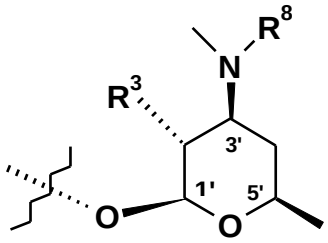
4. The compound according to claim 1, wherein R^1 is S^1 or OH.

5. The compound according to claim 1, wherein R^{2a} is S^2, OH or $-OC(=O)Y^1$, wherein S^2 and Y^1 are as defined in claim 1 above.

6. The compound according to claim 1, wherein R^{2b} is H.

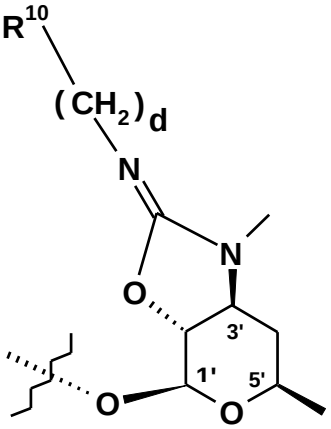
7. The compound according to claim 1, wherein B^1 and B^2 independently are H or C_{1-6}alkyl (suitably H or CH_3).

8. The compound according to claim 1, wherein S^1 is sugar group of formula



(b1-ii)

or

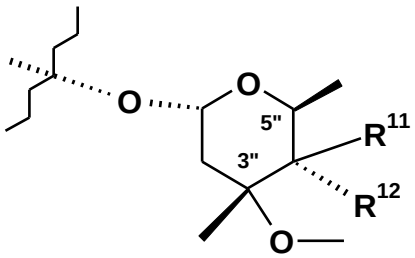


(b2-ii)

wherein R^3, R^8, d, and R^{10} are as defined in claim 1 above.

9. The compound according to claim 8, wherein R^3 is OH, H or $-O-L^1$-G group, R^{10} is C_{1-6}alkyl, and L^1, G and d are as defined in claim 1 above.

10. The compound according to claim 1, wherein S^2 is sugar group of formula



(d-i)

, and wherein R^{11} and R^{12} are as defined in claim 1 above.

11. The compound according to claim 10, wherein

(i) R^{11} is H and R^{12} is OH; or

(ii) one of R^{11} and R^{12} is OH and the other is $–CH_2N(R^{13})R^{14}$, wherein R^{13} and R^{14} are as defined in claim 1 above.

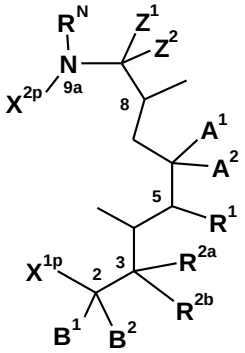
12. The compound according to claim 11, wherein

(i) one of R^{13} and R^{14} is C_{1-6}alkyl (suitably methyl or ethyl) and the other is H or C_{1-6}alkyl (suitably methyl or ethyl); or

(ii) R^{13} and R^{14} together with nitrogen to which they are attached form a heterocyclic ring (suitably morpholinyl).

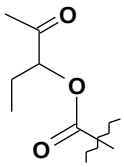
13. A process for preparation of compound of formula (III), or pharmaceutically acceptable salt, solvate or prodrug thereof as defined in claim 1, wherein the process comprises following steps:

(a-1) providing a seco (opened ring) macrolide compound of Formula (I) or a salt or solvate thereof



(I)

wherein,

X^{1p} is , -C(=O)OH, $–C(=O)NH_2$, $-C(=S)NH_2$, $-C(=O)NHNH_2$, $-CH_2NH_2$, $-CH_2OH$,

-C(=O)H, -CN or $–NH_2$;

X^{2p} is hydrogen,$–CH(CH_3)C(=O)H$, $-C(=S)NH_2$ or $-C(=O)NH_2$;

Z^1 and Z^2

(i) are both hydrogen, or

(ii) together with carbon atom to which they are attached form a keto group provided R^N is hydrogen and A^1 is OC_{1-6}alkyl;

and A^1, A^2, B^1, B^2, R^1, R^{2a}, R^{2b}, R^N, and R^p are as defined in claim 1;

(b-1) reacting the compound of formula (I) obtained in step (a-1) with a compound of formula X^{1m}-W^m-X^{2m}, wherein X^{1m} and X^{2m} are the appropriate reactive or leaving groups or groups convertable to X^1 and X^2 as defined above for formula (III), and W^m is W or the appropriate precursor convertable to W wherein W is as defined for formula (III) above;

(c-1) cyclizing compound obtained in step (b-1) and thereafter, if required after any of steps (a-1) to (c-1), subjecting the resulting compound to one or more of the following operations:

(i) removal of the protecting group R^p,

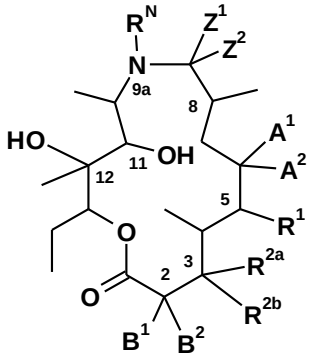
(ii) conversion of X^{1m}, X^{2m} and W^m to X^1, X^2 and W,

(iii) removal of S^2 sugar group and/or S^1 sugar group,

(iv) conversion of the resulting compound of formula (III) into a pharmaceutically acceptable salt, solvate, or prodrug thereof.

14. The process according to claim 13, wherein step (a-1) comprises process steps (a) to (m) for preparation of the compound of formula (I) as follows:

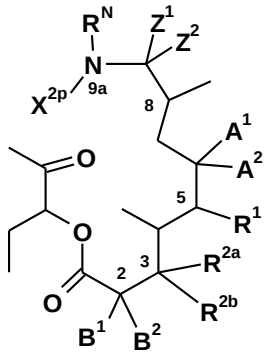
(a) reacting a 9a-aza-9a-homoerythromycin compound of formula **(II)**



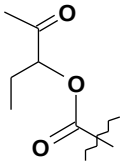
(II)

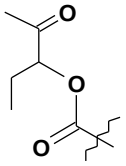
wherein,

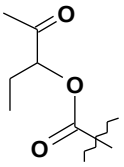
Z^1, Z^2, A^1, A^2, R^1, R^{2a}, R^{2b}, B^1, B^2 and R^N are as defined for formula (I) in claim 13, with a suitable oxidative cleavage reactant (suitably lead tetracaetate or periodic acid salts such as sodium periodate) in a suitable solvent or mixture of solvents to give:



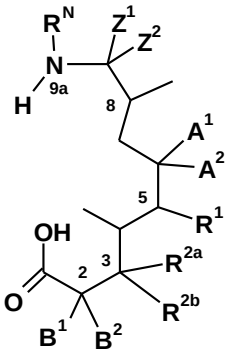
(I-A)

(i) a seco macrolide compound of formula (**I-A**), which is subset of formula (I), wherein X^{1p} is , X^{2p} is hydrogen, Z^1 and Z^2 are both hydrogen, A^1, A^2, R^1, R^{2a}, R^{2b}, B^1, B^2 and R^N are as defined for formula (I) when starting from compound of formula (II), wherein Z^1 and Z^2 are both hydrogen, or

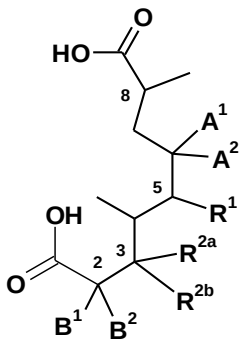
(ii) a seco macrolide compound of formula (**I-A**), which is subset of formula (I) wherein X^{1p} is , X^{2p} is $–CH(CH_3)C(=O)H$, Z^1 and Z^2 together with carbon atom to which they are attached form a keto group, R^N is hydrogen, A^1 is $-OC_{1\text{-}6}$alkyl, A^2, R^1, R^{2a}, R^{2b}, B^1 and B^2, are as defined for formula (I) when starting from compound of formula (II) wherein Z^1 and Z^2 together with carbon atom to which they are attached form a keto group;

(b) hydrolyzing a compound of formula (I-A) wherein X^{1p} is  obtained in step (a) to give compound of formula (**I-B**), which is subset of formula (I) wherein X^{1p} is $–C(=O)OH$, X^{2p} is hydrogen, Z^1, Z^2, A^1, A^2, R^1, R^{2a}, R^{2b}, B^1, B^2 and R^N are as defined for formula (I) above; and optionally subjecting a compound of formula (I-B) wherein X^{1p} is $–C(=O)OH$, X^{2p} is hydrogen, R^N is hydrogen and Z^1 and Z^2 together with carbon atom to which they are attached form a keto group to a

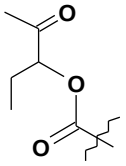
further hydrolyzing conditions to give di-carboxylic acid of formula (XC), wherein A^1, A^2, B^1, B^2, R^1, R^{2a} and R^{2b} are as defined for formula (I); or

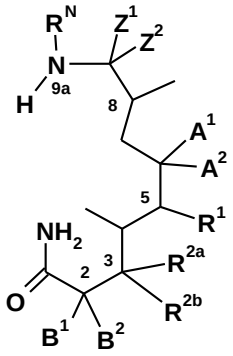


(I-B)



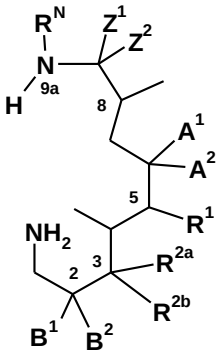
(XC)

(c) reacting a compound of formula (IA) wherein X^{1p} is , X^{2p} is hydrogen obtained in step (a) or compound of formula (I-B) wherein X^{1p} is –C(=O)OH and X^{2p} is hydrogen obtained in step (b) with ammonium salt in the presence of base and coupling agent or with ammonia in organic solvents, or with ammonia hydroxide to give a compound of formula (**I-C**), which is subset of formula (I) wherein X^{1p} is $–C(=O)NH_2$, X^{2p} is hydrogen, Z^1, Z^2, A^1, A^2, R^1, R^{2a}, R^{2b}, B^1, B^2 and R^N are as defined for formula (I) above; or

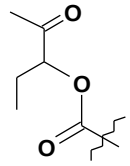


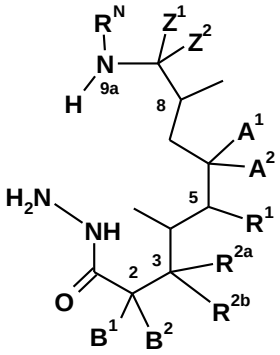
(I-C)

(d) reducing amide compound of formula (I-B) wherein X^{1p} is $–C(=O)NH_2$, and X^{2p} is hydrogen obtained in step (c) using sutable reducing agent (for example $LiAlH_4$, $NaBH_4$, $LiEt_3BH$, or borane-THF) to compound of formula (**I-D**), which is subset of formula (I) wherein X^{1p} is $–CH_2NH_2$, X^{2p} is hydrogen, Z^1, Z^2, A^1, A^2, R^1, R^{2a}, R^{2b}, B^1, B^2 and R^N are as defined for formula (I) above; or

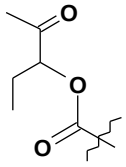


(I-D)

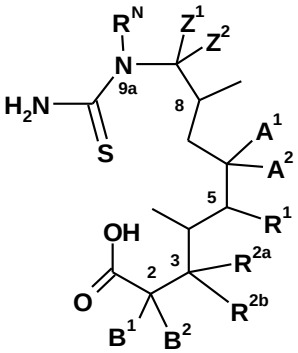
(e) reacting a compound of formula (I-A) obtained in step (a) wherein X^{1p} is  with hydrazine hydrate in a suitable solvent to give compound of formula (**I-E**), which is subset of formula (I) wherein X^{1p} is –C(=O)-NH-NH_2 group, X^{2p} is hydrogen, Z^1, Z^2, A^1, A^2, R^1, R^{2a}, R^{2b}, B^1, B^2 and R^N are as defined for formula (I) above; or



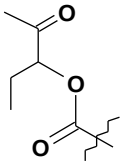
(I-E)

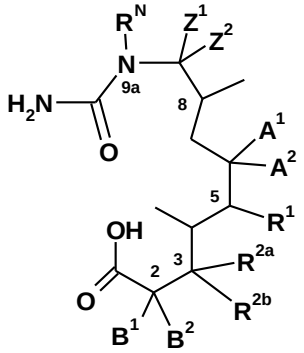
(f) reacting a compound of formula (I-A) obtained in step (a) wherein X^{1p} is  or a compound of formula (I-B) obtained in step (b) wherein X^{1p} is –C(=O)OH with thiocarbonyldiimidazole followed by the amonolysis reaction conditions (provided when starting from compound of formula (I-A) then C/1-keto ester hydrolysis step (b) is usually performed prior amonolysis), or in alternative with thiocyanates or isothiocyanates to give compound of formula (**I-FA**), which is subset of formula (I) wherein X^{1p} is –C(=O)OH group, X^{2p} is –

$C(=S)NH_2$ group, Z^1, Z^2, A^1, A^2, R^1, R^{2a}, R^{2b}, B^1, B^2 and R^N are as defined for formula (I) above; or

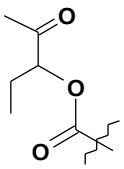


(I-FA)

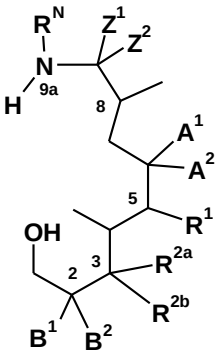
(g) reacting a compound of formula (I-A) obtained in step (a) wherein X^{1p} is  or a compound of formula (I-B) obtained in step (b) wherein X^{1p} is –C(=O)OH with carbonyldiimidazole followed by the amonolysis reaction conditions (provided when starting from compound of formula (I-A) then C/1-keto ester hydrolysis step (b) is usually performed prior amonolysis), or in alternative with alkali metal cyanates or isocyanates to give compound of formula (**I-FB**), which is subset of formula (I) wherein X^{1p} is –C(=O)OH group, X^{2p} is $–C(=O)NH_2$ group, Z^1, Z^2, A^1, A^2, R^1, R^{2a}, R^{2b}, B^1, B^2 and R^N are as defined for formula (I) above; or



(I-FB)

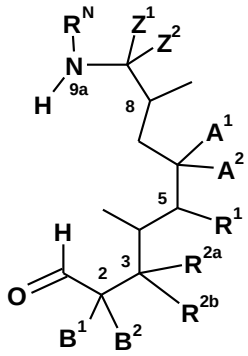
(h) subjecting a compound of formula (I-A) obtained in step (a) wherein X^{1p} is  or a compound of formula (I-B) obtained in step (b) wherein X^{1p} is –C(=O)OH to the standard carboxylic acid reduction conditions to give

compound of formula (**I-KA-a**), which is subset of formula (I) wherein X^{1p} is –CH_2OH group, X^{2p} is hydrogen, Z^1, Z^2, A^1, A^2, R^1, R^{2a}, R^{2b}, B^1, B^2 and R^N are as defined for formula (I) above; or



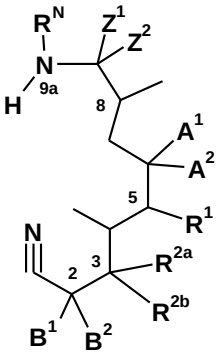
(I-KA-a)

(i) reacting a compound of formula (I-KA-a) obtained in step (h) wherein X^{1p} is –CH_2OH group and X^{2p} is hydrogen with the standard oxidizing reagents to give compound of formula (**I-KA**), which is subset of formula (I) wherein X^{1p} is –C(=O)H group, X^{2p} is hydrogen, Z^1, Z^2, A^1, A^2, R^1, R^{2a}, R^{2b}, B^1, B^2 and R^N are as defined for formula (I) above; or



(I-KA)

(j) subjecting compound of formula (I-C) obtained in step (c) where X^{1p} is –$C(=O)NH_2$ group and X^{2p} is hydrogen to dehydration reaction (for example thionyl chloride, phosphorus pentoxide, thionyl chloride, phosphorus pentoxide, phosphorus oxychloride, titanium tetrachloride, pivaloyl chloride, ethyl dichlorophosphate, trichloroacetyl chloride, silanes/TBAF) to give compound of formula (**I-MN**), which is subset of formula (I) wherein X^{1p} is –CN, X^{2p} is hydrogen, Z^1, Z^2, A^1, A^2, R^1, R^{2a}, R^{2b}, B^1, B^2 and R^N are as defined for formula (I) above; or



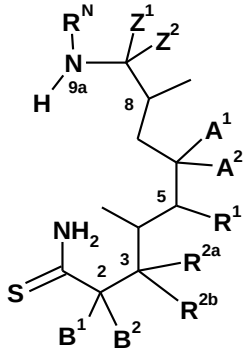
(I-MN)

(k) reacting

a. a compound of formula (I-C) obtained in step (c) where X^{1p} –C(=O)NH_2, and X^{2p} is hydrogen with Lawesson's or Bellau's reagents or with P_4S_{10} alone or in combination with hexamethyldisiloxane, or in alternative

b. a compound of formula (I-MN) obtained in step (j) where X^{1p} –CN, and X^{2p} is hydrogen using alkali metal hydrogen sulfide or ammonium sulfide under high pressure, phosphorus decasulfide, thioacids, thioacetic acid in combination with Lewis acid or benzylamine or calcium hydride, thioacetamide, DowexSH, *O*-dialkyldithiophosphates,12 diphenylphosphinodithioacids, sodium trimethylsilanethiolate, sodium hydrosulfide hydrate and diethyl amine hydrochloride, sodium hydrosulfide hydrate and magnesium chloride hexahydrate, and $(P_4S_{11})Na_2$

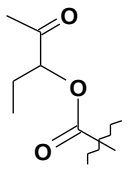
to give compound of formula (**I-M**), which is subset of formula (I) wherein X^{1p} is –C(=S)NH_2, X^{2p} is hydrogen, Z^1, Z^2, A^1, A^2, R^1, R^{2a}, R^{2b}, B^1, B^2 and R^N are as defined for formula (I) above; or



(I-M)

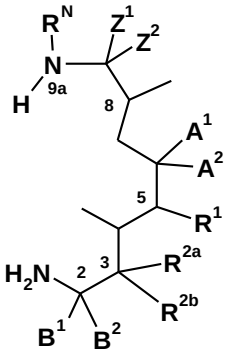
(l) subjecting

a. a compound of formula (I-B) obtained in step (b) where X^{1p} –C(=O)OH, and X^{2p} is hydrogento the modified Curtius rearrangement followed by mild acidic hydrolysis or hydrogenation of the carbamate group, or



b. a compound of formula (I-A) obtained in step (a) where X^{1p} is and X^{2p} is hydrogen to the modified Lossen rearrangement followed by mild acidic hydrolysis or hydrogenation of the carbamate group,

to give compound of formula (**I-RE**), which is subset of formula (I) wherein X^{1p} is $-NH_2$, X^{2p} is hydrogen, Z^1, Z^2, A^1, A^2, R^1, R^{2a}, R^{2b}, B^1, B^2 and R^N are as defined for formula (I) above; and



(I-RE)

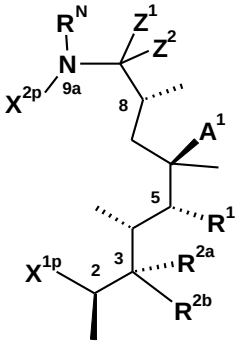
(m) if required after any of previous steps (a) – (l), subjecting the resulting compound to one or more of the following operations:

(i) removal of the protecting group R^p,

(ii) removal of S^2 sugar group and/or S^1 sugar group,

(iii) conversion of the resulting compound of formula (I) into a salt or solvate thereof.

15. The process according to claim 13, wherein the compound of formula (I) is represented by formula (I-ii)

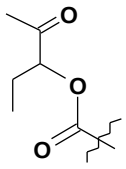


(I-ii)

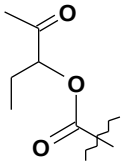
wherein

X^{1p}, X^{2p}, R^N, Z^1, Z^2, A^1, R^1, R^{2a} and R^{2b} are as defined above in claim 13.

16. The process according to claim 13, wherein

(a) X^{2p} is hydrogen, X^{1p} is , -C(=O)OH, –C(=O)NH_2, -C(=S)NH_2, -C(=O)$NHNH_2$, -CH_2NH_2, -CH_2OH, -C(=O)H, -CN or –NH_2;

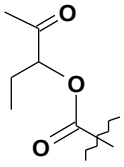
(b) X^{2p} is -C(=S)NH_2 or -C(=O)NH_2, X^{1p} is -C(=O)OH; or

(c) X^{2p} is –$CH(CH_3)$C(=O)H and X^{1p} is .

17. The process according to claim 13, wherein

(a) X^{2p} is hydrogen, X^{1p} is –C(=O)NH_2, -C(=S)NH_2, -C(=O)$NHNH_2$, -CH_2NH_2, -CH_2OH, -C(=O)H, -CN or –NH_2; or

(b) X^{2p} is -C(=S)NH_2 or -C(=O)NH_2, X^{1p} is -C(=O)OH; or

(c) X^{2p} is –$CH(CH_3)$C(=O)H and X^{1p} is .

18. A pharmaceutical composition, comprising a pharmaceutically acceptable carrier and a pharmaceutically effective amount of a compound according to claim 1, optionally comprising a further therapeutic agent.

19. Use of a compound according to claim 1 or a pharmaceutical composition according to claim 18 in the manufacture of a medicament for the treatment of diseases or conditions selected from conditions involving inflammation or immune responses, and/or autoimmune diseases, wherein the diseases or conditions are associated with IL-6 and/or TNF-alpha production.

20. The use according to claim 19, wherein the compound or the pharmaceutical composition is to be administered in combination with a further therapeutic agent.

21. A compound according to claim 1 or a pharmaceutical composition according to claim 18 for use in therapy.