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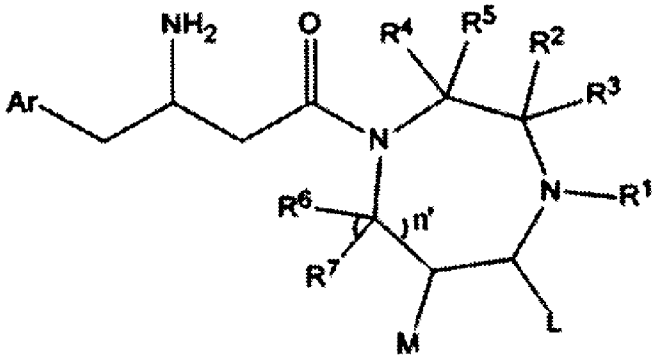
(54) **Title**: AN IMPROVED PROCESS FOR THE SYNTHESIS OF BETA AMINO ACID DERIVATIVES



Formula I

(57) **Abstract**: The present invention is related to an improved process and intermediate(s) for the synthesis of beta amino acid derivatives of formula (I). The compounds of formula I act as DPP-IV inhibitors and are useful in the treatment of Type 2 diabetes.

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AN IMPROVED PROCESS FOR THE SYNTHESIS OF BETA AMINO ACID DERIVATIVES

FIELD OF INVENTION

The present invention is related to the field of synthetic medicinal chemistry. It is related to an improved process and intermediate(s) for the synthesis of beta amino acid derivatives of formula I. The compounds of formula I act as DPP-IV inhibitors and are useful in the treatment of Type 2 diabetes.

BACKGROUND

The following discussion of the prior art is intended to present the invention in an appropriate technical context and allow its significance to be properly appreciated. Unless clearly indicated to the contrary, however, reference to any prior art in this specification should be construed as an admission that such art is widely known or forms part of common general knowledge in the field.

Type 2 diabetes is a progressive, metabolic disorder characterized by two fundamental defects: insulin resistance at peripheral target tissues and pancreatic beta-cell dysfunction. Despite good compliance to treatment, the glycaemic control of type 2 diabetes deteriorates progressively. Hence, new therapeutic agents are continuously being developed to help our diabetes population. Recent studies have shown that early intervention at prediabetes state and beta cell protection with insulin sensitizers may improve the prognosis of diabetes. DPP-IV inhibitors are a novel class of oral hypoglycemic agent with potentials in improving pancreatic beta cell function and the clinical course of type 2 diabetes. Dipeptidyl peptidase IV (DPP-IV) inhibitors, including sitagliptin, vildagliptin, alogliptin, and saxagliptin, represent a novel approach in the management of type 2 diabetes.

The first DPP-IV inhibitor in the market, Merck's Januvia (Sitagliptin), was approved by the FDA in October 2006 for use as mono therapy or with

metformins. The next drug in this class, Galvus (Vildagliptin) was approved in Europe in February 2008 by European Medicines Agency. The EMEA has also approved a new oral treatment released by Novartis, called Eucreas, a combination of vildagliptin and metformin. Onglyza (Saxagliptin) was approved by FDA in July 2009. Onglyza has been jointly developed by Bristol-Myers Squibs (BMS) and Astra Zeneca (AZ). Onglyza has been shown to reduce major adverse cardiovascular events by as much as 55%. The next in the class, namely Linagliptin developed by Boehringer Ingelheim was approved in May 2011. Other DPP-IV drugs in pipeline are Alogliptin, SYR-472, Melogliptin, Anagliptin and Teneligliptin.

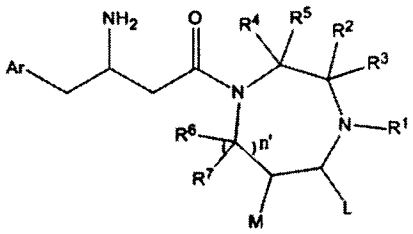
Beta-amino acid based DPP-IV inhibitors have been disclosed in PCT publications, for example, WO-2004043940, WO-2005044195, WO-2006009886, WO-2006023750, WO2006039325, WO-2003004498, WO-2005116029, WO-2005113510, WO-2006097175, WO-2005120494, WO-2005121131, WO-2005123685, WO-2005040095 WO-2007063928, WO-2007054577, WO-2007053819, WO-2006081151, WO-2004085378 and US patents such as US 7,259,160, US 7,101,871 and US 7,208,498.

Since DPP-IV inhibitors have oral route of administration and oral medication forms the largest segment of therapy among the anti-diabetics, it appears to be a promising therapy. Hence there still exists a need to provide a simple and convenient process for the preparation of DPP-IV inhibitors. The present invention provides an improved, commercially viable and industrially advantageous processes for the synthesis of beta-amino acid based DPP-IV inhibitors. The intermediates and the final end products obtained through the improved processes of this invention are obtained in a superior yield and high purity.

SUMMARY

The present invention is related to a novel process and intermediate (s) for the synthesis of beta amino acid derivatives of compounds of formula I. The compounds of the present invention are useful as DPP-IV inhibitors.

In an embodiment, the present invention relates to a process for preparing a compound of general formula I, their pharmaceutically acceptable derivatives, tautomeric forms, stereoisomers including R and S isomers, prodrugs, metabolites, salts or solvates thereof:



Formula I

wherein,

Ar represents aryl which may be phenyl, which may be unsubstituted or optionally substituted at any available position by R^8 or by one or more substituents selected from but not limited to halogen, CN, hydroxyl, NH_2, C_{1-12} alkyl or C_{1-12} alkoxy, wherein each of C_{1-12} alkoxy and C_{1-12} alkyl may be linear or branched and can be unsubstituted or optionally substituted with 1-5 halogens;

R^1 is selected from the group consisting of but not limited to $(CH_2)_nCONR^aR^b$, $(CH_2)_nCOOR^a$, $(CH_2)_nNR^aR^b$, $(CH_2)_nNR^aCOR^b$, $(CH_2)_nC(=Y)R^a$ (wherein Y is O or S), $(CH_2)_nOR^a$ (wherein each methylene group may be substituted by one or more halogen atoms), $-(CO)R^a$, $-(CO)NR^aR^b$, hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, each of which may be optionally substituted at any available position by one or more substituents selected from but not limited to hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, oxo, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one

or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^2 and R^3 together represents a single oxygen or sulphur atom which is linked to the diazepine ring by a double bond; or R^1 and R^2 together forms a double bond in the diazepine ring and R^3 represents the group $-NR^aR^b$; or R^1 and R^3 together with the nitrogen atom to which R^1 is attached forms a heterocyclic or heteroaryl ring which may additionally contain from one to three hetero atoms independently selected from O, S and N; the ring formed may optionally be substituted with one or more substituents selected from R^c or $R^{c'}$ and R^2 represent hydrogen or a double bond;

R^4 and R^5 are independently selected from the group consisting of hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^6 and R^7 are independently selected from the group consisting of hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$,

$N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^8 is independently selected from hydrogen, halogen, CN, C_{1-12} alkyl, C_{1-12} haloalkyl, C_{1-12} alkoxy, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-CF_3$, $-OCF_3$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-6} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^a and R^b are independently selected from hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl; each of which may be optionally substituted with halogen, hydroxyl, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, C_{3-8} cycloalkyl, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, aryl, heterocyclyl, heteroaryl, $(CH_2)_n$-aryl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-heteroaryl, $(CH_2)_n$-cycloalkyl, oxo, -CN, $-OR^9$, $-NO_2$, $-NR^9R^{10}$, $N(R^9)(CO)R^{10}$, $N(R^9)(CO)OR^{10}$, $N(R^9)(CO)NR^9R^{10}$, $-C(=L)R^9$ (wherein L is O or S), $-(CO)NR^9R^{10}$, $-O(CO)R^9$, $-O(CO)NR^9R^{10}$, $-COOR^9$, $-SR^9$, $S(O)_mR^9$, $SO_2NR^9R^{10}$; SO_3H, $NHSO_2R^9$, $P(O)R^9R^{10}$; or R^a and R^b may be joined together

along with the nitrogen atom to which they are attached to form a heterocyclic or heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N, the ring formed may optionally be substituted with one or more substituents selected from hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, oxo, CN, $-OR^9$, $-CF_3$, $-OCF_3$ CH_2CF_3, CF_2CF_3, $-NO_2$, $-NR^9R^{10}$, $N(R^9)(CO)R^{10}$, $N(R^9)(CO)OR^{10}$, $N(R^9)(CO)NR^9R^{10}$, $-C(=Y)R^9$ (wherein Y is O or S), $-(CO)NR^9R^{10}$, $-O(CO)C_1$-C_{12}alkyl, $-O(CO)NR^9R^{10}$, $-COOR^9$, $-SR^9$, $S(O)_mR^9$, $SO_2NR^9R^{10}$; SO_3H, $NHSO_2R^9$, $P(O)R^9R^{10}$; the ring thus formed may further be fused with 3 to 7 membered unsaturated or saturated ring, which may contain from one to three heteroatoms independently selected from O, S or N, the fused ring may optionally be substituted with one or more substituents R^c or $R^{c'}$;

R^c or $R^{c'}$ is independently selected from the group consisting of but not limited to (1) hydrogen, (2) halogen, (3) C_{1-12} alkyl which is linear or branched and which can be unsubstituted or substituted with 1-5 halogens or phenyl, which is unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl ,wherein the CO_2C_{1-6} alkyl is linear or branched ; (4) aryl which can be unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl ,wherein the CO_2C_{1-6} alkyl is linear or branched (5) a 5 or 6 membered heterocyclyl which may be saturated or unsaturated comprising 1-4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1-3 substituents independently selected from oxo, OH, halogen, C_{1-6} alkyl, and OC_{1-6} alkyl, wherein the C_{1-6} alkyl and OC_{1-6} alkyl are linear or branched and optionally substituted with 1-5 halogens; (6) $(CH_2)_n$-cycloalkyl; (7) $(CH_2)_n$-heterocyclyl, (8) $(CH_2)_n$-aryl, (9) $(CH_2)_n$-heteroaryl, (10) C_{1-12} alkylcarbonyl, (11) C_{1-12} alkoxycarbonyl, (12) CN, (13) $-OR^9$, (14) $-OCF_3$, (15) $-NO_2$, (16) $=NOR^{10}$, (17) $-NR^9R^{10}$, (18) $N(R^9)(CO)R^{10}$, (19) $N(R^9)(CO)OR^{10}$, (20) $N(R^9)(CO)NR^9R^{10}$, -(21) $C(=Y)R^9$ (wherein Y is O or S), (22) $-(CO)NR^9R^{10}$, (23)

-O(CO)R^9, (24) -O(CO)NR^9R^{10}, (25) -$COOR^9$, (26) -SR^9, (27) $S(O)_mR^9$, (28) $SO_2NR^9R^{10}$; (29) SO_3H, (30) $NHSO_2R^9$, (31) $P(O)R^9R^{10}$, (32) C_{2-12} alkenyl, (33) C_{2-12} alkynyl, (34) C_{1-12} haloalkyl, (35) C_{2-12} haloalkenyl, (36) C_{2-12} haloalkynyl, (37) C_{1-12} alkoxy, (38) C_{1-12} haloalkoxy, (39) C_{3-8} cycloalkyl, (40) heteroaryl;

with a proviso that when R^1 and R^3 together with the nitrogen atom to which R^1 is attached forms a heterocyclic or heteroaryl ring which may additionally contain from one to three hetero atoms independently selected from O, S and N , then R^c or $R^{c'}$ cannot be CO_2H.

R^9 and R^{10} are independently selected from hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, each of which may be optionally substituted with halogen, hydroxyl or C_{1-6} alkoxy, or $R^9$and R^{10} may be joined together to form a heterocyclic or heteroaryl ring which may contain from one to three heteroatoms independently selected from O, S and N, which may optionally be substituted with one or more substituents independently selected from R^c or $R^{c'}$;

R^{12} is C_{1-6} alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 groups independently selected from halogen, CO_2H, and CO_2C_{1-6} alkyl, wherein the CO_2C_{1-6} alkyl is linear or branched;

M and L independently represent a hydrogen atom or they may join together to form a ring,

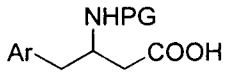
n' is 0 or 1

m can be 1 or 2;

n can be 1, 2, 3 or 4;

comprising:

a) coupling a compound of Formula II,



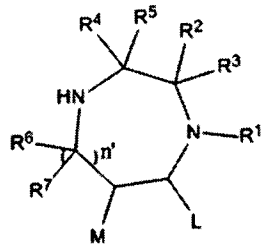
Formula II

wherein

Ar is as defined above; and

PG is an amino protecting groups selected from acetyl, trifluoroacetyl, benzyloxycarbonyl (CBz), t-butoxycarbonyl (Boc), 9-fluorenylmethyloxycarbonyl (Fmoc), 2,2,2-trichloroethyloxycarbonyl, allyloxycarbonyl and the like;

with a compound of Formula III or its salt



Formula III

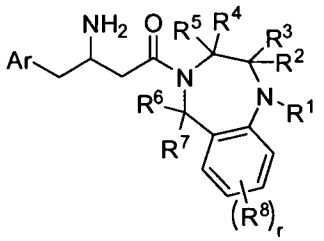
wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, M, L and n' are as defined above;

using 1,1- carbonyl diimidazole, in a solvent and optionally in the presence of a base;

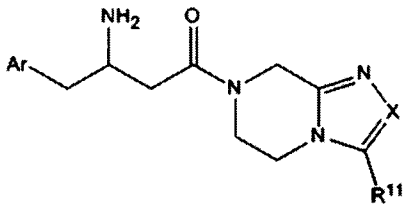
b) removing the protecting group (PG) from the compound obtained in step (a) using deprotecting agent; and

c) optionally converting the product obtained in step (b) to a salt.

In another embodiment the present invention relates to a process for preparing compounds of formula VI or VII, their pharmaceutically acceptable derivatives, tautomeric forms, stereoisomers including R and S isomers, prodrugs, metabolites, salts or solvates thereof:



OR



Formula VI **Formula VII**

wherein,

Ar represents aryl which may be phenyl, which may be unsubstituted or optionally substituted at any available position by one or more substituents selected from but not limited to halogen, CN, hydroxyl, NH_2, C_{1-12} alkyl or C_{1-12} alkoxy, wherein each of C_{1-12} alkoxy and C_{1-12} alkyl may be linear or branched and can be unsubstituted or optionally substituted with 1-5 halogens;

R^1 is selected from the group consisting of but not limited to $(CH_2)_nCONR^aR^b$, $(CH_2)_nCOOR^a$, $(CH_2)_nNR^aR^b$, $(CH_2)_nNR^aCOR^b$, $(CH_2)_nC(=Y)R^a$ (wherein Y is O or S), $(CH_2)_nOR^a$ (wherein each methylene group may be substituted by one or more halogen atoms), $-(CO)R^a$, $-(CO)NR^aR^b$, hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, each of which may be optionally substituted at any available position by one or more substituents selected from but not limited to hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, oxo, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be

optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^2 and R^3 together represents a single oxygen or sulphur atom which is linked to the diazepine ring by a double bond; or R^1 and R^2 together forms a double bond in the diazepine ring and R^3 represents the group $-NR^aR^b$; or R^1 and R^3 together with the nitrogen atom to which R^1 is attached forms a heterocyclic or heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N; the ring formed may optionally be substituted with one or more substituents selected from R^c or $R^{c'}$ and R^2 represent hydrogen or a double bond;

R^4 and R^5 are independently selected from the group consisting of hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^6 and R^7 are independently selected from the group consisting of hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-}

$_8$ cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^8 is independently selected from hydrogen, halogen, CN, C_{1-12} alkyl, C_{1-12} haloalkyl, C_{1-12} alkoxy, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-CF_3$, $-OCF_3$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-6} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^a and R^b are independently selected from hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl; each of which may be optionally substituted with halogen, hydroxyl, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, C_{3-8} cycloalkyl, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, aryl, heterocyclyl, heteroaryl, $(CH_2)_n$-aryl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-heteroaryl, $(CH_2)_n$-cycloalkyl, oxo, -CN, $-OR^9$, $-NO_2$, $-NR^9R^{10}$, $N(R^9)(CO)R^{10}$, $N(R^9)(CO)OR^{10}$, $N(R^9)(CO)NR^9R^{10}$, $-C(=Y)R^9$ (wherein Y is O or S), $-(CO)NR^9R^{10}$, $-O(CO)R^9$, $-O(CO)NR^9R^{10}$, $-COOR^9$, $-SR^9$, $S(O)_mR^9$, $SO_2NR^9R^{10}$; SO_3H, $NHSO_2R^9$, $P(O)R^9R^{10}$; or R^a and R^b may be joined together along with the nitrogen atom to which they are attached to form a heterocyclic or

heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N, the ring formed may optionally be substituted with one or more substituents selected from hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, oxo, CN, $-OR^9$, $-CF_3$, $-OCF_3$ CH_2CF_3, CF_2CF_3, $-NO_2$, $-NR^9R^{10}$, $N(R^9)(CO)R^{10}$, $N(R^9)(CO)OR^{10}$, $N(R^9)(CO)NR^9R^{10}$, $-C(=Y)R^9$ (wherein Y is O or S), $-(CO)NR^9R^{10}$, $-O(CO)C_1$-C_{12}alkyl, $-O(CO)NR^9R^{10}$, $-COOR^9$, $-SR^9$, $S(O)_mR^9$, $SO_2NR^9R^{10}$; SO_3H, $NHSO_2R^9$, $P(O)R^9R^{10}$; the ring thus formed may further be fused with 3 to 7 membered unsaturated or saturated ring, which may contain from one to three heteroatoms independently selected from O, S or N, the fused ring may optionally be substituted with one or more substituents R^c or $R^{c'}$;

R^c or $R^{c'}$ is independently selected from the group consisting of but not limited to (1) hydrogen, (2) halogen, (3) C_{1-12} alkyl which is linear or branched and which can be unsubstituted or substituted with 1-5 halogens or phenyl, which is unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl ,wherein the CO_2C_{1-6} alkyl is linear or branched (4) aryl which can be unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl, wherein the CO_2C_{1-6} alkyl is linear or branched (5) a 5 or 6 membered heterocyclyl which may be saturated or unsaturated comprising 1-4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1-3 substituents independently selected from oxo, OH, halogen, C_{1-6} alkyl, and OC_{1-6} alkyl, wherein the C_{1-6} alkyl and OC_{1-6} alkyl are linear or branched and optionally substituted with 1-5 halogens; (6) $(CH_2)_n$-cycloalkyl, (7) $(CH_2)_n$-heterocyclyl, (8) $(CH_2)_n$-aryl, (9) $(CH_2)_n$-heteroaryl, (10) C_{1-12} alkylcarbonyl, (11) C_{1-12} alkoxycarbonyl, (12) CN, (13) $-OR^9$, (14) $-OCF_3$, (15) $-NO_2$, (16) $=NOR^{10}$, (17) $-NR^9R^{10}$, (18) $N(R^9)(CO)R^{10}$, (19) $N(R^9)(CO)OR^{10}$, (20) $N(R^9)(CO)NR^9R^{10}$, (21) $C(=Y)R^9$ (wherein Y is O or S), (22) $-(CO)NR^9R^{10}$, (23) $-O(CO)R^9$, (24) $-O(CO)NR^9R^{10}$,(25) $-COOR^9$, (26) $-SR^9$, (27) $S(O)_mR^9$, (28)

$SO_2NR^9R^{10}$; (29) SO_3H, (30) $NHSO_2R^9$, (31) $P(O)R^9R^{10}$, (32) C_{2-12} alkenyl, (33) C_{2-12} alkynyl, (34) C_{1-12} haloalkyl, (35) C_{2-12} haloalkenyl, (36) C_{2-12} haloalkynyl, (37) C_{1-12} alkoxy, (38) C_{1-12} haloalkoxy, (39) C_{3-8} cycloalkyl, (40) heteroaryl;

with a proviso that when R^1 and R^3 together with the nitrogen atom to which R^1 is attached form an imidazole ring, R^c or $R^{c'}$ cannot be CO_2H.

or

with a proviso that when R^1 and R^3 together with the nitrogen atom to which R^1 is attached forms a heterocyclic or heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N, R^c or $R^{c'}$ cannot be CO_2H.

R^9 and R^{10} are independently selected from hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, each of which may be optionally substituted with halogen, hydroxyl or C_{1-6} alkoxy, or $R^9$and R^{10} may be joined together to form a heterocyclic or heteroaryl ring which may contain from one to three heteroatoms independently selected from O, S and N, which may optionally be substituted with one or more substituents independently selected from R^c or $R^{c'}$;

R^{12} is C_{1-6} alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 groups independently selected from halogen, CO_2H, and CO_2C_{1-6} alkyl, wherein the CO_2C_{1-6} alkyl is linear or branched;

X is selected from the group consisting of N and CR^{11};

R^{11} is selected from the group consisting of R^c or $R^{c'}$;

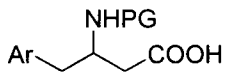
m can be 1 or 2;

n can be 1, 2, 3 or 4;

r can be 1, 2, 3 or 4.

comprising,

a) coupling a compound of Formula II,



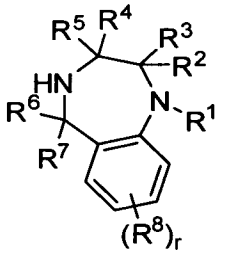
Formula II

wherein

Ar is as defined above; and

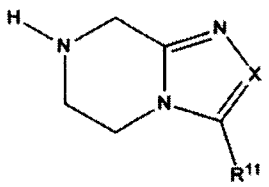
PG is an amino protecting groups selected from acetyl, trifluoroacetyl, benzyloxycarbonyl (CBz), t-butoxycarbonyl (Boc), 9-fluorenylmethyloxycarbonyl (Fmoc), 2,2,2-trichloroethyloxycarbonyl, allyloxycarbonyl and the like;

with a compound of Formula VIII or IX or their salts respectively,



Formula VIII

OR



Formula IX

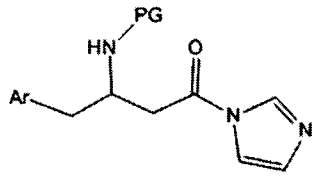
wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^{11}, X and r are as defined above;

using 1,1- carbonyl diimidazole, in a solvent and optionally in the presence of a base;

b) removing the protecting group (PG) from the compound obtained in step (a) using deprotecting agents, and

c) optionally converting the product obtained in step (b) to a salt.

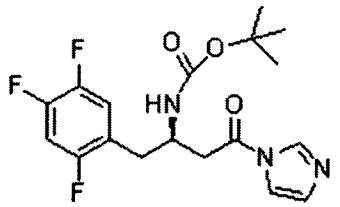
In yet another embodiment, the present invention relates to a compound of formula IV, their pharmaceutically acceptable derivatives, tautomeric forms, stereoisomers including R and S isomers, prodrugs, metabolites, salts or solvates thereof:



Formula IV

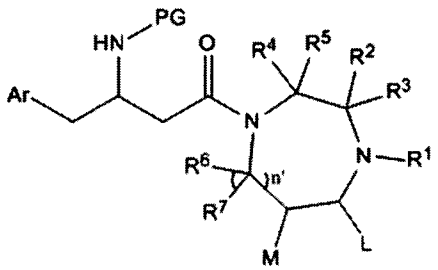
wherein Ar and PG are as defined above.

In a preferred embodiment the present invention relates to a compound of formula V, its pharmaceutically acceptable derivatives, tautomeric forms, stereoisomers including R and S isomers, prodrugs, metabolites, salts or solvates thereof:

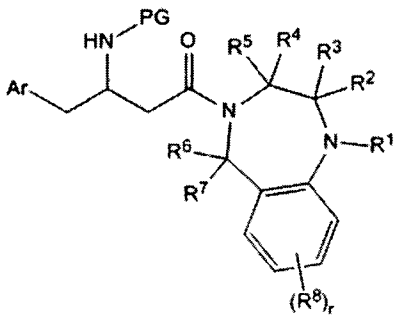


Formula V

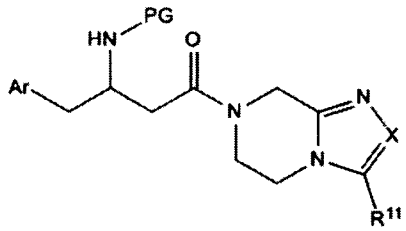
In a further embodiment, the present invention relates to compounds of formula X, XI and XII and their pharmaceutically acceptable derivatives, tautomeric forms, stereoisomers including R and S isomers, prodrugs, metabolites, salts or solvates thereof:



Formula X



Formula XI



Formula XII

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^{11}, M, L, X, n', r, Ar and PG are as defined above.

These and other features, aspects, and advantages of the present subject matter will become better understood with reference to the following description and appended claims. This summary is provided to introduce a selection of concepts in a simplified form. This summary is not intended to limit the scope of the claimed subject matter.

DETAILED DESCRIPTION OF THE INVENTION

DEFINITIONS:

The terms "alkyl", "alkenyl", and "alkynyl" refers to straight or branched 1 to 12 carbon atoms. These groups may further be substituted with one or more substituents selected from but not limited to, halogen, hydroxyl, oxo, carboxyl, carboxyalkyl, azido, alkenyl, alkynyl, alkoxy, cycloalkyl, cycloalkynyl, acyl acyloxy, aryl, heterocyclyl and heteroaryl.

The term "cycloalkyl" refers to cyclic alkyl groups constituting 3 to 20 carbon atoms having a single cyclic ring or multiple condensed rings, for example, fused or spiro systems which may optionally contain one or more olefinic bonds, unless otherwise constrained by the definition. Such cycloalkyl groups include, by way of example, single ring structures, for example, cyclopropyl, cyclobutyl, cyclopentenyl, cyclohexyl, cyclooctyl, and the like, or multiple ring structures, for example, adamantyl, and bicyclo[2.2.1] heptane, or cyclic alkyl groups to which is fused an aryl group, for example, indane and the like. Cycloalkyl groups may

further be substituted with one or more substituents selected from but not limited to, halogen, hydroxyl, oxo, carboxy, carboxyalkyl, azido, alkenyl, alkynyl, alkoxy, cycloalkyl, cycloalkynyl, acyl acyloxy, aryl, heterocyclyl, heteroaryl.

The term "alkoxy" denotes the group O-alkyl wherein alkyl is the same as defined above.

The term "aralkyl" refers to alkyl-aryl linked through alkyl (wherein alkyl is the same as defined above) portion and the said alkyl portion contains carbon atoms from 1-6 and the aryl is as defined herein, after. The examples of aralkyl groups include benzyl and the like.

The term "aryl" refers to a carbocyclic aromatic group, for example phenyl or naphthyl ring and the like optionally substituted with one or more substituents selected from but not limited to, halogen, hydroxyl, alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy, acyl, aryloxy, CF_3, $COOR^d$ (wherein R^d can be hydrogen, alkyl, alkenyl, cycloalkyl, aralkyl, heterocyclylalkyl or heteroarylalkyl), cyano, nitro, carboxy, heterocyclyl, heteroaryl, heterocyclylalkyl or heteroarylalkyl. The aryl group may optionally be fused with cycloalkyl group, wherein the said cycloalkyl group may optionally contain heteroatoms selected from O, N and S.

The term "aryloxy" refers to the group O- aryl wherein aryl is as defined above.

The term "heteroaryl" refers to an aromatic ring structure or a bicyclic aromatic group with one or more heteroatom(s) independently selected from N, O and S and optionally substituted at any available position by substituent(s) selected from but not limited to halogen, hydroxyl, alkyl, alkenyl, alkynyl, cycloalkyl, acyl, carboxy, aryl, alkoxy, aralkyl, cyano, nitro, heterocyclyl, or heteroaryl. Examples of heteroaryl groups include oxazolyl, imidazolyl, pyrrolyl, 1,2,3,-triazolyl, 1,2,4-triazolyl, tetrazolyl, thiazolyl, oxadiazolyl, benzoimidazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, thienyl, isoxazolyl, triazinyl, furanyl, benzofuranyl, indolyl, benzothiazolyl, benzoxazolyl, and the like.

The term "heterocyclyl" refers to a cyclic, bicyclic or tricyclic cycloalkyl group, fully or partially unsaturated having 5 to 10 carbon atoms; with one or more heteroatom(s) independently selected from N, O and S, and are optionally benzo-fused or fused with heteroaryl of 5-6 ring members; the rings may be optionally substituted wherein the substituents are selected from but not limited to halogen,

hydroxyl, alkyl, alkenyl, alkynyl, cycloalkyl, acyl, carboxy, aryl, alkoxy, aralkyl, cyano, nitro, heterocyclyl, or heteroaryl. Examples of heterocyclyl groups include but are not limited to oxazolidinyl, tetrahydrofuranyl, dihydrofuranyl, dihydropyridinyl, dihydroisooxazolyl, dihydrobenzofuryl, azabicyclohexyl, dihydroindonyl, piperidinyl or piperazinyl.

The term "Heteroarylalkyl" refers to alkyl-heteroaryl group linked through alkyl portion, wherein the alkyl and heteroalkyl are the same as defined previously.

The term "Heterocyclylalkyl" refers to alkyl-heterocyclyl group linked through alkyl portion, wherein the alkyl and heterocyclyl are the same as defined previously.

The term "Halogen" refers to fluoro, chloro, bromo or iodo.

The term "Protecting Group" or "PG" refers to a group which is in a modified form to preclude undesired side reactions at the protected site. The term protecting group, unless otherwise specified, may be used with groups, for example, hydroxyl, amino, carboxyl and examples of such groups are found in T.W. Greene. et al. "*Protecting Groups in Organic Synthesis*," 3rd Ed, Wiley, New York, which is incorporated herein by reference. The species of the carboxylic protecting groups, amino protecting groups or hydroxyl protecting groups employed are not critical, as long as the derivatised moieties/moiety is/are stable to conditions of subsequent reactions and can be removed without disrupting the remainder of the molecule. Examples of suitable hydroxyl and amino protecting groups include but are not limited to trimethylsilyl, triethylsilyl, *o*-nitrobenzyloxycarbonyl, *p*-nitrobenzyloxycarbonyl, *t*-butyldiphenylsilyl, *t*-butyldimethylsilyl, acetyl, trifluoroacetyl, benzyloxycarbonyl (CBz), *t*-butoxycarbonyl (Boc), 9-fluorenylmethyloxycarbonyl (Fmoc), 2,2,2-trichloroethyloxycarbonyl, allyloxycarbonyl and the like. Examples of suitable carboxyl protecting groups are benzhydryl, *o*-nitrobenzyl, *p*-nitrobenzyl, 2-naphthylmethyl, allyl, 2-chloroallyl, benzyl, 2,2,2- trichloroethyl, trimethylsilyl, *t*-butyldimethylsilyl, *t*-butyldiphenylsilyl, 2-(trimethylsilyl)ethyl, phenacyl, *p*-methoxybenzyl, acetonyl, *p*-methoxyphenyl, 4-pyridylmethyl, *t*-butyl and the like.

The term "therapeutically effective amount" means the amount of a compound that, when administered to a subject for treating a disease, is sufficient to effect such treatment for the disease. The "therapeutically effective amount" will vary

depending on the compound, the disease and its severity, weight, physical condition and responsiveness of the subject to be treated, among other factors.

A "pharmaceutically acceptable salt" refers to salts prepared from pharmaceutically acceptable non-toxic bases or acids including inorganic or organic bases and inorganic or organic acids.

The term "coupling agent" refers to CDI (1,1' carbonyl diimidazole), EDC [1-ethyl-3-(3-dimethylaminopropyl) carbodiimide] /HOBT (1-hydroxybenzotriazole); DCC (dicyclohexyl carbodiimide), DMAP (4-dimethylaminopyridine); HATU [O-(7-azabenzotriazole-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate; HOAT (1-hydroxy-7-azabenzotriazole); BOP [(benzotriazolyl-1-yloxy)-tris(dimethylamine) phosphonium hexafluorophosphate]; mixed anhydride method using ethyl chloroformate or methyl chloroformate in a suitable solvent such as DMF, DCM, acetonitrile, toluene, THF and the like or mixtures thereof and in the presence of a suitable base such as NMM (N-methylmorpholine), DIPEA (N,N-diisopropylethylamine), triethylamine and the like.

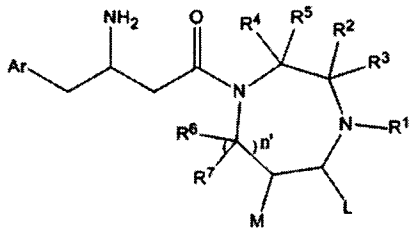
The term "amino protecting groups" include but are not limited to acetyl, trifluoroacetyl, benzyloxycarbonyl (CBz), t-butoxycarbonyl (Boc), 9-fluorenylmethyloxycarbonyl (Fmoc), 2,2,2-trichloroethyloxycarbonyl, allyloxycarbonyl and the like. The appropriate conditions for the removal of the amine protecting groups can be readily selected by those having well known skill in the art. Examples of reagents used for deprotecting the amine protecting moiety include but are not limited to use of acidic conditions (trifluoroacetic acid, hydrochloric acid, phosphoric acid, p-toluenesulphonic acid and the like), basic conditions (piperidine and the like) or hydrogenation conditions (palladium on charcoal or platinum and the like).

The present invention is related to a novel process and intermediates useful for the synthesis of compounds of formula I.

Chemically, compounds of formula I are derivatives of beta-amino acid. They can be synthesized by many routes. An essential step that would be common in many feasible routes employed for the synthesis of these compounds is the amide bond formation. There could be alternate approaches for the amide bond formation.

One of these approaches is by coupling of two fragments, one fragment containing carboxylic acid group and the other containing the secondary nitrogen atom, which can be free or present as a part of a heterocyclic ring, in the presence of suitable coupling agent.

In an embodiment, the present invention relates to a process for preparing a compound of general formula I or its pharmaceutically acceptable salts,



Formula I

wherein,

Ar represents aryl which may be phenyl, which may be unsubstituted or optionally substituted at any available position by R^8 or by one or more substituents selected from but not limited to halogen, CN, hydroxyl, NH_2, C_{1-12} alkyl or C_{1-12} alkoxy, wherein each of C_{1-12} alkoxy and C_{1-12} alkyl may be linear or branched and can be unsubstituted or optionally substituted with 1-5 halogens;

R^1 is selected from the group consisting of but not limited to $(CH_2)_nCONR^aR^b$, $(CH_2)_nCOOR^a$, $(CH_2)_nNR^aR^b$, $(CH_2)_nNR^aCOR^b$, $(CH_2)_nC(=Y)R^a$ (wherein Y is O or S), $(CH_2)_nOR^a$ (wherein each methylene group may be substituted by one or more halogen atoms), $-(CO)R^a$, $-(CO)NR^aR^b$, hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, each of which may be optionally substituted at any available position by one or more substituents selected from but not limited to hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, oxo, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, -

$O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^2 and R^3 together represents a single oxygen or sulphur atom which is linked to the diazepine ring by a double bond; or R^1 and R^2 together forms a double bond in the diazepine ring and R^3 represents the group $-NR^aR^b$; or R^1 and R^3 together with the nitrogen atom to which R^1 is attached forms a heterocyclic or heteroaryl ring which may additionally contain from one to three hetero atoms independently selected from O, S and N; the ring formed may optionally be substituted with one or more substituents selected from R^c or $R^{c'}$ and R^2 represent hydrogen or a double bond;

R^4 and R^5 are independently selected from the group consisting of hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^6 and R^7 are independently selected from the group consisting of hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl,

C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^8 is independently selected from hydrogen, halogen, CN, C_{1-12} alkyl, C_{1-12} haloalkyl, C_{1-12} alkoxy, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-CF_3$, $-OCF_3$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-6} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^a and R^b are independently selected from hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl; each of which may be optionally substituted with halogen, hydroxyl, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, C_{3-8} cycloalkyl, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, aryl, heterocyclyl, heteroaryl, $(CH_2)_n$-aryl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-heteroaryl, $(CH_2)_n$-cycloalkyl, oxo, -CN, $-OR^9$, $-NO_2$, $-NR^9R^{10}$, $N(R^9)(CO)R^{10}$, $N(R^9)(CO)OR^{10}$, $N(R^9)(CO)NR^9R^{10}$, $-C(=L)R^9$ (wherein L

is O or S), -(CO)NR^9R^{10}, -O(CO)R^9, -O(CO)NR^9R^{10}, -COOR^9, -SR^9, S(O)$_m R^9$, $SO_2NR^9R^{10}$; SO_3H, $NHSO_2R^9$, P(O)R^9R^{10}; or R^a and R^b may be joined together along with the nitrogen atom to which they are attached to form a heterocyclic or heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N, the ring formed may optionally be substituted with one or more substituents selected from hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, oxo, CN, –OR^9, -CF_3, -OCF_3 CH_2CF_3, CF_2CF_3, -NO_2, -NR^9R^{10}, N(R^9)(CO)R^{10}, N(R^9)(CO)OR^{10}, N(R^9)(CO)NR^9R^{10}, -C(=Y)R^9 (wherein Y is O or S), -(CO)NR^9R^{10}, -O(CO)C_1-C_{12}alkyl, -O(CO)NR^9R^{10}, -COOR^9, -SR^9, S(O)$_m R^9$, $SO_2NR^9R^{10}$; SO_3H, $NHSO_2R^9$, P(O)R^9R^{10}; the ring thus formed may further be fused with 3 to 7 membered unsaturated or saturated ring, which may contain from one to three heteroatoms independently selected from O, S or N, the fused ring may optionally be substituted with one or more substituents R^c or $R^{c'}$;

R^c or $R^{c'}$ is independently selected from the group consisting of but not limited to (1) hydrogen, (2) halogen, (3) C_{1-12} alkyl which is linear or branched and which can be unsubstituted or substituted with 1-5 halogens or phenyl, which is unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl ,wherein the CO_2C_{1-6} alkyl is linear or branched; (4) aryl which can be unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl ,wherein the CO_2C_{1-6} alkyl is linear or branched (5) a 5 or 6 membered heterocyclyl which may be saturated or unsaturated comprising 1-4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1-3 substituents independently selected from oxo, OH, halogen, C_{1-6} alkyl, and OC_{1-6} alkyl, wherein the C_{1-6} alkyl and OC_{1-6} alkyl are linear or branched and optionally substituted with 1-5 halogens; (6) $(CH_2)_n$-cycloalkyl; (7) $(CH_2)_n$-heterocyclyl, (8) $(CH_2)_n$-aryl, (9) $(CH_2)_n$-heteroaryl, (10) C_{1-12} alkylcarbonyl, (11) C_{1-12} alkoxycarbonyl, (12) CN, (13) –OR^9, (14) -OCF_3, (15) -

NO_2, (16) =NOR^{10}, (17) -NR^9R^{10}, (18) $N(R^9)(CO)R^{10}$, (19) $N(R^9)(CO)OR^{10}$, (20) $N(R^9)(CO)NR^9R^{10}$, -(21) $C(=Y)R^9$ (wherein Y is O or S), (22) -$(CO)NR^9R^{10}$, (23) -$O(CO)R^9$, (24) -$O(CO)NR^9R^{10}$,(25) -$COOR^9$, (26) -SR^9, (27) $S(O)_mR^9$, (28) $SO_2NR^9R^{10}$; (29) SO_3H, (30) $NHSO_2R^9$, (31) $P(O)R^9R^{10}$, (32) C_{2-12} alkenyl, (33) C_{2-12} alkynyl, (34) C_{1-12} haloalkyl, (35) C_{2-12} haloalkenyl, (36) C_{2-12} haloalkynyl, (37) C_{1-12} alkoxy, (38) C_{1-12} haloalkoxy, (39) C_{3-8} cycloalkyl, (40) heteroaryl;

with a proviso that when R^1 and R^3 together with the nitrogen atom to which R^1 is attached forms a heterocyclic or heteroaryl ring which may additionally contain from one to three hetero atoms independently selected from O, S and N, then R^c or $R^{c'}$ cannot be CO_2H.

R^9 and R^{10} are independently selected from hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, each of which may be optionally substituted with halogen, hydroxyl or C_{1-6} alkoxy, or $R^9$and R^{10} may be joined together to form a heterocyclic or heteroaryl ring which may contain from one to three heteroatoms independently selected from O, S and N, which may optionally be substituted with one or more substituents independently selected from R^c or $R^{c'}$;

R^{12} is C_{1-6} alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 groups independently selected from halogen, CO_2H, and CO_2C_{1-6} alkyl, wherein the CO_2C_{1-6} alkyl is linear or branched;

M and L independently represent a hydrogen atom or they may join together to form a ring;

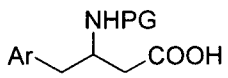
n' is 0 or 1

m can be 1 or 2;

n can be 1, 2, 3 or 4;

comprising:

a) coupling a compound of Formula II,



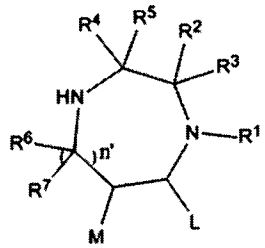
Formula II

wherein

Ar is as defined above; and

PG is an amino protecting groups selected from acetyl, trifluoroacetyl, benzyloxycarbonyl (CBz), t-butoxycarbonyl (Boc), 9-fluorenylmethyloxy carbonyl (Fmoc), 2,2,2-trichloroethyloxycarbonyl, allyloxycarbonyl and the like;

with a compound of Formula III or its salt



Formula III

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, M, L and n' are as defined above;

using 1,1- carbonyl diimidazole, in a solvent and optionally in the presence of a base;

b) removing the protecting group (PG) from the compound obtained in step (a) using a deprotecting agent; and

c) optionally converting the product obtained in step (b) to a salt.

Examples of solvent (s) that can be used in the present invention can be selected form the group comprising Dimethylfomamide (DMF), Dimethyl acetamide (DMAc), Dichloromethane (DCM), acetonitrile (ACN) , toluene, tetrahydrofuran (THF) or mixtures thereof.

In a preferred embodiment, the solvent is acetonitrile and / or Dimethylformamide.

Examples of base (s) that can be used in the present invention can be selected form the group comprising *N*-methylmorpholine (NMM), *N,N*-diisopropylethylamine (DIPEA) and triethylamine (TEA) or mixtures thereof.

In a preferred embodiment, the base is *N,N*-diisopropylethylamine.

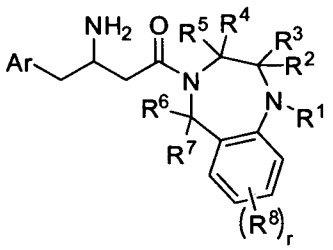
Examples of deprotecting agent that can be used in the present invention can be selected form the group comprising trifluoroacetic acid, hydrochloric acid,

phosphoric acid, p-toluenesulphonic acid, piperidine, palladium on charcoal and platinum.

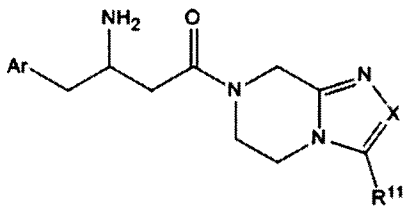
In a preferred embodiment, the deprotecting agent is hydrochloric acid.

The process steps of the present invention can be carried out without the need for isolating the intermediates.

In another embodiment the present invention relates to a process for preparing compounds of formula VI or VII, their pharmaceutically acceptable derivatives, tautomeric forms, stereoisomers including R and S isomers, prodrugs, metabolites, salts or solvates thereof:



OR



Formula VI **Formula VII**

wherein,

Ar represents aryl which may be phenyl, which may be unsubstituted or optionally substituted at any available position by one or more substituents selected from but not limited to halogen, CN, hydroxyl, NH_2, C_{1-12} alkyl or C_{1-12} alkoxy, wherein each of C_{1-12} alkoxy and C_{1-12} alkyl may be linear or branched and can be unsubstituted or optionally substituted with 1-5 halogens;

R^1 is selected from the group consisting of but not limited to $(CH_2)_nCONR^aR^b$, $(CH_2)_nCOOR^a$, $(CH_2)_nNR^aR^b$, $(CH_2)_nNR^aCOR^b$, $(CH_2)_nC(=Y)R^a$ (wherein Y is O or S), $(CH_2)_nOR^a$ (wherein each methylene group may be substituted by one or

more halogen atoms), -(CO)R^a, -(CO)NR^aR^b, hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, each of which may be optionally substituted at any available position by one or more substituents selected from but not limited to hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, oxo, -OR^a, -SR^a, -NO_2, -NR^aR^b, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, -(CO)R^a, -(CO)NR^aR^b, -$O(CO)R^a$, -$O(CO)NR^aR^b$, -$COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^2 and R^3 together represents a single oxygen or sulphur atom which is linked to the diazepine ring by a double bond; or R^1 and R^2 together forms a double bond in the diazepine ring and R^3 represents the group -NR^aR^b; or R^1 and R^3 together with the nitrogen atom to which R^1 is attached forms a heterocyclic or heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N; the ring formed may optionally be substituted with one or more substituents selected from R^c or $R^{c'}$ and R^2 represent hydrogen or a double bond;

R^4 and R^5 are independently selected from the group consisting of hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, -OR^a, -SR^a, -NO_2, -NR^aR^b, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, -(CO)R^a, -(CO)NR^aR^b, -$O(CO)R^a$, -$O(CO)NR^aR^b$, -$COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted

at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^6 and R^7 are independently selected from the group consisting of hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^8 is independently selected from hydrogen, halogen, CN, C_{1-12} alkyl, C_{1-12} haloalkyl, C_{1-12} alkoxy, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-CF_3$, $-OCF_3$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-6} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^a and R^b are independently selected from hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl; each of which may be optionally substituted with halogen, hydroxyl, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, C_{3-8} cycloalkyl, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, aryl, heterocyclyl, heteroaryl, $(CH_2)_n$-aryl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-heteroaryl, $(CH_2)_n$-cycloalkyl, oxo, -CN, $-OR^9$, $-NO_2$, $-NR^9R^{10}$, $N(R^9)(CO)R^{10}$, $N(R^9)(CO)OR^{10}$, $N(R^9)(CO)NR^9R^{10}$, $-C(=Y)R^9$ (wherein Y is O or S), $-(CO)NR^9R^{10}$, $-O(CO)R^9$, $-O(CO)NR^9R^{10}$, $-COOR^9$, $-SR^9$, $S(O)_mR^9$, $SO_2NR^9R^{10}$; SO_3H, $NHSO_2R^9$, $P(O)R^9R^{10}$; or R^a and R^b may be joined together along with the nitrogen atom to which they are attached to form a heterocyclic or heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N, the ring formed may optionally be substituted with one or more substituents selected from hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, oxo, CN, $-OR^9$, $-CF_3$, $-OCF_3$ CH_2CF_3, CF_2CF_3, $-NO_2$, $-NR^9R^{10}$, $N(R^9)(CO)R^{10}$, $N(R^9)(CO)OR^{10}$, $N(R^9)(CO)NR^9R^{10}$, $-C(=Y)R^9$ (wherein Y is O or S), $-(CO)NR^9R^{10}$, $-O(CO)C_1$-C_{12}alkyl, $-O(CO)NR^9R^{10}$, $-COOR^9$, $-SR^9$, $S(O)_mR^9$, $SO_2NR^9R^{10}$; SO_3H, $NHSO_2R^9$, $P(O)R^9R^{10}$; the ring thus formed may further be fused with 3 to 7 membered unsaturated or saturated ring, which may contain from one to three heteroatoms independently selected from O, S or N, the fused ring may optionally be substituted with one or more substituents R^c or $R^{c'}$;

R^c or $R^{c'}$ is independently selected from the group consisting of but not limited to (1) hydrogen, (2) halogen, (3) C_{1-12} alkyl which is linear or branched and which can be unsubstituted or substituted with 1-5 halogens or phenyl, which is unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl ,wherein the CO_2C_{1-6} alkyl is linear or branched (4) aryl which can be unsubstituted or substituted with 1-5 substituents independently selected from

halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl, wherein the CO_2C_{1-6} alkyl is linear or branched (5) a 5 or 6 membered heterocyclyl which may be saturated or unsaturated comprising 1-4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1-3 substituents independently selected from oxo, OH, halogen, C_{1-6} alkyl, and OC_{1-6} alkyl, wherein the C_{1-6} alkyl and OC_{1-6} alkyl are linear or branched and optionally substituted with 1-5 halogens; (6) $(CH_2)_n$-cycloalkyl, (7) $(CH_2)_n$-heterocyclyl, (8) $(CH_2)_n$-aryl, (9) $(CH_2)_n$-heteroaryl, (10) C_{1-12} alkylcarbonyl, (11) C_{1-12} alkoxycarbonyl, (12) CN, (13) $-OR^9$, (14) $-OCF_3$, (15) $-NO_2$, (16) $=NOR^{10}$, (17) $-NR^9R^{10}$, (18) $N(R^9)(CO)R^{10}$, (19) $N(R^9)(CO)OR^{10}$, (20) $N(R^9)(CO)NR^9R^{10}$, (21) $C(=Y)R^9$ (wherein Y is O or S), (22) $-(CO)NR^9R^{10}$, (23) $-O(CO)R^9$, (24) $-O(CO)NR^9R^{10}$,(25) $-COOR^9$, (26) $-SR^9$, (27) $S(O)_mR^9$, (28) $SO_2NR^9R^{10}$; (29) SO_3H, (30) $NHSO_2R^9$, (31) $P(O)R^9R^{10}$, (32) C_{2-12} alkenyl, (33) C_{2-12} alkynyl, (34) C_{1-12} haloalkyl, (35) C_{2-12} haloalkenyl, (36) C_{2-12} haloalkynyl, (37) C_{1-12} alkoxy, (38) C_{1-12} haloalkoxy, (39) C_{3-8} cycloalkyl, (40) heteroaryl;

with a proviso that when R^1 and R^3 together with the nitrogen atom to which R^1 is attached form an imidazole ring, R^c or $R^{c'}$ cannot be CO_2H.

or

with a proviso that when R^1 and R^3 together with the nitrogen atom to which R^1 is attached forms a heterocyclic or heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N, R^c or $R^{c'}$ cannot be CO_2H.

R^9 and R^{10} are independently selected from hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, each of which may be optionally substituted with halogen, hydroxyl or C_{1-6} alkoxy, or $R^9$and R^{10} may be joined together to form a heterocyclic or heteroaryl ring which may contain from one to three heteroatoms independently selected from O, S and N, which may optionally be substituted with one or more substituents independently selected from R^c or $R^{c'}$;

R^{12} is C_{1-6} alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 groups independently selected from halogen, CO_2H, and CO_2C_{1-6} alkyl, wherein the CO_2C_{1-6} alkyl is linear or branched;

X is selected from the group consisting of N and CR^{11};

R^{11} is selected from the group consisting of R^c or $R^{c'}$;

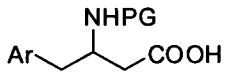
m can be 1 or 2;

n can be 1, 2, 3 or 4;

r can be 1, 2, 3 or 4.

comprising,

a) coupling a compound of Formula II,



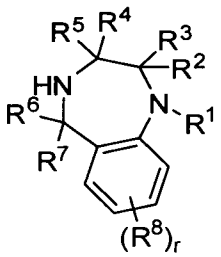
Formula II

wherein

Ar is as defined above; and

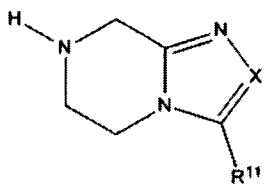
PG is an amino protecting groups selected from acetyl, trifluoroacetyl, benzyloxycarbonyl (CBz), t-butoxycarbonyl (Boc), 9-fluorenylmethyloxycarbonyl (Fmoc), 2,2,2-trichloroethyloxycarbonyl, allyloxycarbonyl and the like;

with a compound of Formula VIII or IX or their salts respectively,



Formula VIII

OR



Formula IX

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^{11}, X and r are as defined above;

using 1,1- carbonyl diimidazole, in a solvent and optionally in the presence of a base;

b) removing the protecting group (PG) from the compound obtained in step (a) using deprotecting agents, and

c) optionally converting the product obtained in step (b) to a salt.

Examples of solvent (s) that can be used in the present invention can be selected form the group comprising Dimethylfomamide (DMF), Dimethyl acetamide (DMAc), Dichloromethane (DCM), acetonitrile (ACN) , toluene, tetrahydrofuran (THF) or mixtures thereof.

In a preferred embodiment, the solvent is acetonitrile and/or Dimethylformamide.

Examples of base (s) that can be used in the present invention can be selected form the group comprising *N*-methylmorpholine (NMM), *N,N*-diisopropylethylamine (DIPEA) and triethylamine (TEA) or mixtures thereof.

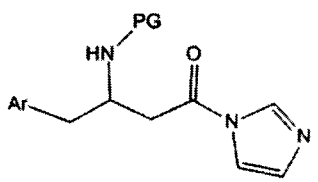
In a preferred embodiment, the base is *N,N*-diisopropylethylamine.

Examples of deprotecting agent that can be used in the present invention can be selected form the group comprising trifluoroacetic acid, hydrochloric acid, phosphoric acid, p-toluenesulphonic acid, piperidine, palladium on charcoal and platinum.

In a preferred embodiment, the deprotecting agent is hydrochloric acid.

The process steps of the present invention can be carried out without the need for isolating the intermediates.

In yet another embodiment the present invention relates to a compound of formula IV, their pharmaceutically acceptable derivatives, tautomeric forms, stereoisomers including R and S isomers, prodrugs, metabolites, salts or solvates thereof:



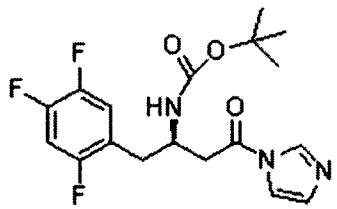
Formula IV

wherein, Ar and PG are as defined above.

The compound of formula IV is formed as an intermediate in the process of the present invention. The compound of formula IV is formed as a result of the

reaction between the compound of formula II with 1,1-carbonyldinidazole, which is then reacted with the compound of formula III or VIII or IX. This said intermediate compound can be optionally isolated or can be used *in-situ* during the progression of the process.

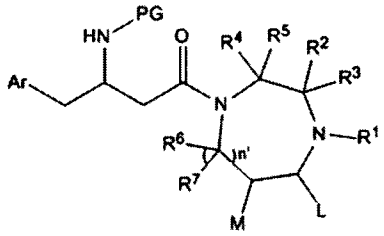
In a preferred embodiment, the present invention relates to a compound of formula V, its pharmaceutically acceptable derivatives, tautomeric forms, stereoisomers including R and S isomers, prodrugs, metabolites, salts or solvates thereof:



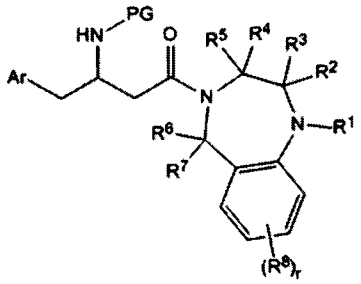
Formula V

The compound of formula IV and V can exist in the various physical forms say amorphous and crystalline form and also in the form of a single diastereoisomer, racemate, racemic mixture or diastereoisomeric mixture, all of which fall within the scope of compound of Formula IV in accordance with the present invention. The racemic mixtures can be resolved if desired at appropriate stages by methods known to those skilled in the art such as crystallization, chromatography, salt formation or enzymatic resolution to obtain the respective individual enantiomers.

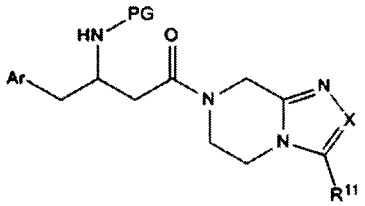
In a further embodiment, the present invention relates to compounds of formula X, XI and XII and their pharmaceutically acceptable derivatives, tautomeric forms, stereoisomers including R and S isomers, prodrugs, metabolites, salts or solvates thereof:



Formula X



Formula XI



Formula XII

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^{11}, M, L, X, n', r, Ar and PG are as defined above.

The compound of formula X, XI and XII are formed by the reaction of the intermediate compound of formula IV with compound of formula III, VIII and IX respectively.

EXAMPLES

The invention is explained in detail in the following examples which are given solely for the purpose of illustration only and therefore should not be construed to limit the scope of the invention. All of the starting materials are either commercially available or can be prepared by procedures that would be well known to one of ordinary skill in organic chemistry.

Solvents were dried prior to use wherever necessary by standard methods (Perrin, D.D.; Armarego, W.L.F. Purification of Laboratory Chemicals, Pergamon Press: Oxford, 1988). Mass spectra (MS) were obtained by electron spray ionization (ESI) eV using Applied biosystem 4000 Q TRAP. ^{1}H NMR were recorded on Bruker 400 MHz Avance II NMR spectrometer. Chemical shifts are reported as δ values in parts per million (ppm), relative to TMS as internal standard. All coupling constants (*J*) values are given in Hz.

ABBREVIATIONS

The following abbreviations are employed in the examples and elsewhere herein:

^{1}H NMR	Proton nuclear magnetic resonance
BOP	(benzotriazolyl-1-yloxy)-*tris*(dimethylamine)phosphonium hexafluoro phosphate
C	centigrade
DCM	dichloromethane
DIPEA	diisopropylethylamine
DMF	dimethylformamide
DMSO	dimethylsulfoxide
EDC	*N*-(3-dimethylaminopropyl)-*N*-ethylcarbodiiimide hydrochloride
ESIMS	electron spray ionization mass Spectroscopy
g	gram(s)
h	hour(s)
HOBT	1-hydroxybenzotriazole
HPLC	High performance liquid chromatography

Hz	Hertz
IPA	Isopropyl alcohol
J	coupling constant
m	multiplet
mg	milligram
min	minutes
mL	milliliter
mmol	millimoles
mp	melting point
$NaHCO_3$	sodium bicarbonate
NMR	Nuclear magnetic resonance
PG	Protecting Group
ppm	parts per million
r. t.	room temperature
s	singlet
THF	tetrahydrofuran

Example-1: Synthesis of *tert*-butyl (R)-1-(2,4,5-trifluorophenyl)-4-(1H-imidazol-1-yl)-4-oxobutan-2-ylcarbamate (compound of Formula V)

To a solution of (R)-3-[(*tert*-butyloxycarbonyl)amino]-4-(2,4,5-trifluorophenyl)-butanoic acid (1 g, 0.003 mol) (synthesized in accordance with the procedure given in WO-2009093269, which is incorporated in its entirety herein by reference) in acetonitrile (20 ml), was added N,N-Diisopropylethylamine (1.4 ml, 0.010 mol) and 1,1-Carbonyl diimidazole (0.73 g, 0.004 mol) at room temperature. The reaction mixture was stirred for 1 h at 40°C. After completion of the reaction water (25 ml) was added and extracted twice with ethyl acetate (2 x 50 ml). The combined ethyl acetate layers was evaporated to obtain 0.54 gm of *tert*-butyl (R)-1-(2,4,5-trifluorophenyl)-4-(1H-imidazol-1-yl)-4-oxobutan-2-ylcarbamate as a white solid.

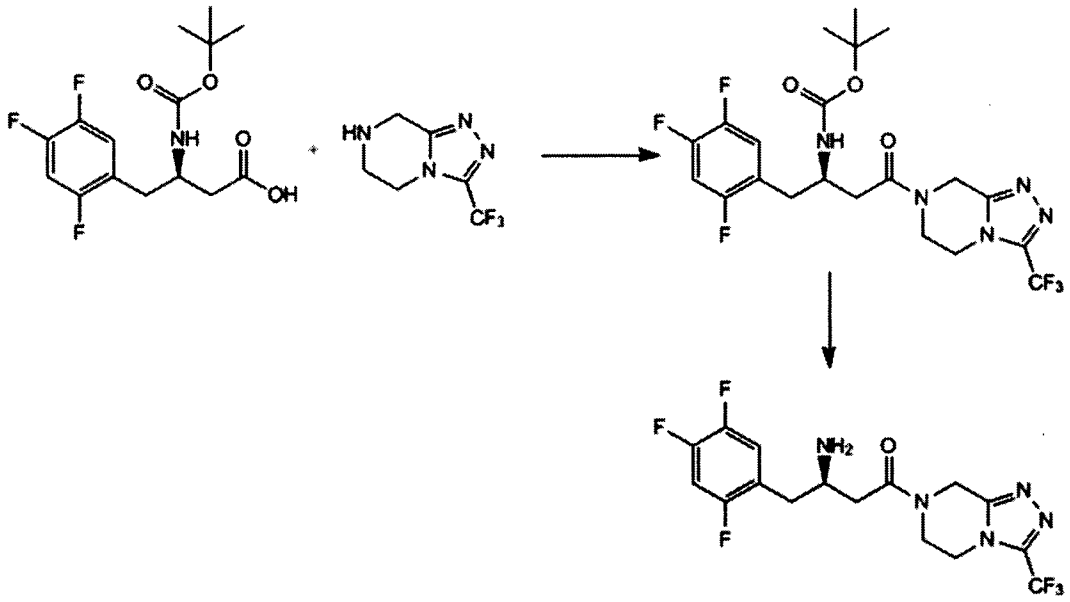
^1H NMR (400 MHz, DMSO-d6): δ 8.39 (d,*J* = 15 Hz, 1H), 7.69-7.63 (m, 1H), 7.49-7.43 (m, 1H) 7.39-7.32 (m, 1H), 7.06 (s, 1H), 6.91 (d, *J* = 9.6 Hz, 1H, D_2O

exchangeable), 4.16 (m, 1H), 3.18-3.16 (m, 1H), 2.93-2.88 (m, 1H), 2.70-2.65 (m, 1H), 1.18 (s, 9 H).
ESIMS (m/z): 384.8 (M+1)

Example 2: Synthesis of Hydrochloric acid salt of (2R)-4-oxo-(3-trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-α]pyrazin-7(8H)-yl]-1-(2,4,5-trifluoro-phenyl)butan-2-amine (Sitagliptin hydrochloride)

To a solution of (R)-3-[(*tert*-butyloxycarbonyl)amino]-4-(2,4,5-trifluorophenyl)-butanoic acid (1.36 g, 4.080 mmol) in acetonitrile (20 ml) was added Diisopropylethylamine (2.47 g, 19.12 mmol) and 1,1-Carbonyl diimidazole (0.94 g, 5.82 mmol) at room temperature. The reaction mixture was stirred for 30 min at room temperature. 3-(Trifluoromethyl)-5,6,7,8-tetrahydro-1,2,3-triazolo[4,3-α]pyrazine (0.750 g, 3.88 mmol) was added to the above reaction mixture at room temperature. The reaction mixture was heated to 65-70°C for 22 h. After completion of the reaction, the mixture was concentrated under vacuum and the crude mass was dissolved in ethyl acetate (15 ml) and washed with 5% aqueous $NaHCO_3$ solution followed by twice with water (2 x 30 ml). The ethyl acetate layer was concentrated under reduced pressure to get crude mass and recrystallized from mixture of 10 % ethyl acetate and petroleum ether (50 ml) to get 1.5 g (82%) of tert-butyl{(1R)-3-oxo-1-(2,4,5-trifluorobenzyl)-3-[3-(trifluoromethyl)-5-6-dihydro[1,2,4] triazole[4,3-α]pyrazin-7(8H)-yl]propyl}carbamate.
The above obtained solid was treated with Hydrochloric acid to get Hydrochloric acid salt of (2R)-4-oxo-(3-trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-α]pyrazin-7(8H)-yl]-1-(2,4,5-trifluoro-phenyl)butan-2-amine (Sitagliptin Hydrochloride).

The process can be represented schematically as given below:



Example 3: Synthesis of Hydrochloric acid salt of 4-[(R)-3-amino-4-(2,4,5-trifluorophenyl)-butyryl]-1,3,4,5-tetrahydro-benzo[e][1,4]diazipin-2-one.

To a solution of (R)-3-[(*tert*-butyloxycarbonyl)amino]-4-(2,4,5-trifluorophenyl)-butanoic acid (0.927 g, 2.78 mmol) in acetonitrile (15 ml) was added Diisopropylethylamine (2.84 g, 22.02 mmol) and 1,1-Carbonyl diimidazole (0.615 g, 3.797 mmol) at room temperature. The reaction mixture was stirred for 30 min at room temperature. 1,3,4,5-Tetrahydro-benzo[e][1,4]diazepin-2-one hydrochloride (0.5 g, 2.531 mmol) (synthesized in accordance with the procedure given in WO-2009093269, which is incorporated in its entirety herein by reference) was added to the above reaction mixture at room temperature. The reaction mixture was heated to 65-70°C for 22 h. After completion of the reaction, the mixture was concentrated under vacuum and the crude mass was dissolved in ethyl acetate (15 ml) and washed twice with water (2 x 30 ml). The ethyl acetate layer was concentrated under reduced pressure to get crude mass and was purified by column chromatography using mixture of 2% methanol in dichloromethane (500 ml) to get 0.679 g (65%) of [(R)-3-oxo-3-(2-oxo-1,2,3,5-tetrahydro-benzo[e][1,4]diazepin-4-yl)-1-(2,4,5-trifluoro-benzyl)-propyl]-carbamic acid tert-butyl ester.

The above obtained solid was treated with Hydrochloric acid to get the Hydrochloric acid salt of (R)-4-[3-amino-4-(2,4,5-trifluorophenyl)-butyryl]-1,3,4,5-tetrahydro-benzo[e][1,4]diazipin-2-one.

Example 4: Synthesis of Hydrochloric acid salt of (R)-4-(3-amino-4-(2,4,5-trifluorophenyl)-butanoyl)-7-methoxy-4,5-dihydro-1H-benzo[e][1,4]diazipin-2(3H)-one.

To a solution of (R)-3-[(*tert*-butyloxycarbonyl)amino]-4-(2,4,5-trifluorophenyl)-butanoic acid (0.241 g, 2.197 mmol) in acetonitrile (15 ml) was added Diisopropylethylamine (2.47 g,19.12 mmol) and 1,1-Carbonyl diimidazole (0.534 g, 3.296 mmol) at room temperature. The reaction mixture was stirred for 30 min at room temperature. 7-methoxy-1,3,4,5-tetrahydro-benzo[e][1,4]diazepin-2-one hydrochloride (0.5 g, 2.197 mmol) (synthesized in accordance with the procedure given in WO-2009093269, which is incorporated in its entirety herein by reference) was added to the above reaction mixture at room temperature. The reaction mixture was heated to 65-70°C for 22 h. After completion of the reaction, the mixture was concentrated under vacuum and the crude mass was dissolved in ethyl acetate (15 ml) and washed twice with water (2 x 30 ml). The ethyl acetate layer was concentrated under reduced pressure to get crude mass and which was purified by column chromatography using mixture of 2% methanol in dichloromethane (500 ml) to get 0.9 g (92%) of (R)-[3-(7-methoxy-2-oxo-1,2,3,5-tetrahydro-benzo[e][1,4]diazepine-4-yl)-3-oxo-1-(2,4,5-trifluorophenyl-propyl]-carbamic acid *tert*-butyl ester.

The above obtained solid was treated with Hydrochloric acid to get the Hydrochloric acid salt of (R)-4-(3-amino-4-(2,4,5-trifluorophenyl)-butanoyl)-7-methoxy-4,5-dihydro-1H-benzo[e][1,4] diazipin-2(3H)-one.

Example 5: Synthesis of Hydrochloride salt of (R)-3-amino-1-(9-fluoro-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-yl)-4-(2,4,5-trifluoro-phenyl)-butan-1-one.

To a solution of (R)-3-[(*tert*-butyloxycarbonyl)amino]-4-(2,4,5-trifluorophenyl)-butanoic acid (2.91 g, 0.0087 mol) in acetonitrile (24 ml) was added Diisopropylethylamine (3.22 g, 0.024 mol) and 1,1-Carbonyl diimidazole (1.755 g, 0.0108 mol) at room temperature. The reaction mixture was stirred for 30 min at room temperature. 9-Fluoro-5,6-dihydro-4H-2,3,5,10 β-tetraaza-benzo[e]azulene hydrochloride (2.0 g, 0.0083 mol) (synthesized in accordance with the procedure given in WO-2009093269, which is incorporated in its entirety herein by reference) dissolved in a mixture of acetonitrile (20 ml) and diisopropylethylamine (3.23 g, 0.0249 mol), was added to the above reaction mixture at room temperature. The reaction mixture was heated to 65-70°C for 22 h. After completion of the reaction, the mixture was concentrated under vacuum and the crude mass was dissolved in ethyl acetate (40 ml) and washed twice with water (2 x 20 ml). The ethyl acetate layer was concentrated under reduced pressure to get crude mass and which was recrystallized from methyl isobutyl ketone (10 ml) to get 3.3 g (76%) of [3-(9-fluoro-4H,6H-2,3,5,10b-tetraaza-benzo[e]-azulen-5-yl)-3-oxo-1-(2,4,5-trifluoro-benzyl)-propyl]-carbamic acid-tert-butyl ester.

The above obtained solid was treated with Hydrochloric acid to give the Hydrochloride salt of (R)-3-amino-1-(9-fluoro-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-yl)-4-(2,4,5-trifluoro-phenyl)-butan-1-one.

Example 6: Synthesis of Hydrochloric acid salt of (R)-4-(3-amino-4-(2,4,5-trifluorophenyl)-butanoyl)-8-Fluoro-4,5-dihydro-1H-benzo[e][1,4]diazipin-2(3H)-one.

To a solution of (R)-3-[(*tert*-butyloxycarbonyl)amino]-4-(2,4,5-trifluorophenyl)-butanoic acid (1.17 g, 3.537 mmol) in acetonitrile (15 ml) was added Diisopropylethylamine (3.505 g, 23.67 mmol) and 1,1-Carbonyl diimidazole (0.661 g, 4.0 mmol) at room temperature. The reaction mixture was stirred for 30 min at 40°C. The 8-Fluoro-1,3,4,5-tetrahydrobenzo(e)[1,4]diazepin-2-one trifluoro acetate (0.5 g, 27.21 mmol) (synthesized in accordance with the procedure given in WO-2009093269, which is incorporated in its entirety herein by reference) was added to the above reaction mixture at 40°C. The reaction mixture was heated to

65-70°C for 22 h. After completion of the reaction, the mixture was concentrated under vacuum and the crude mass was dissolved in ethyl acetate (15 ml), washed with saturated sodium bi carbonate solution (15 ml) and washed twice with water (2 x 30 ml). The ethyl acetate layer was concentrated under reduced pressure to get 0.55 g of (R)-*tert*-butyl-4-(8-fluoro-2oxo-2,3-dihydro-1H-benzo[e][1,4]diazepin-4-oxo-1-(2,4,5-triflurophenyl) butan-2-ylcarbamate.

The above obtained solid was treated with Hydrochloric acid to get the Hydrochloric acid salt of(R)-4-(3-amino-4-(2,4,5-trifluorophenyl)-butanoyl)-8-Fluoro-4,5-dihydro-1H-benzo[e][1,4]diazipin-2(3H)-one.

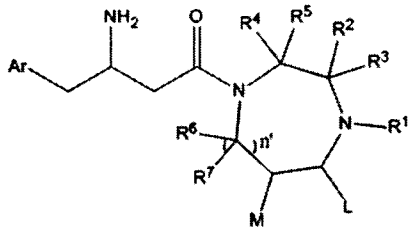
Example 7: Synthesis of Hydrochloric acid salt of 4-[(R)-3-amino-4-(2,4,5-trifluorophenyl)-butyryl]-1-methyl-8-Fluoro-1,3,4,5-tetrahydro-benzo[e][1,4]diazepin-2-one.

To a solution of (R)-3-[(*tert*-butyloxycarbonyl)amino]-4-(2,4,5-trifluorophenyl)-butanoic acid (1.24 g, 3.749 mmol) in acetonitrile (25 ml) was added Diisopropylethylamine (4.01 g, 31.07 mmol) and 1,1-Carbonyl diimidazole (0.867 g, 5.357 mmol) at room temperature. The reaction mixture was stirred for 30 min at 40°C. 8-Fluoro-1-methyl-1,3,4,5-tetrahydrobenzo (e)[1,4]diazepin-2-one trifluoro acetate (1.10 g, 3.571 mmol) (synthesized in accordance with the procedure given in WO-2009093269, which is incorporated in its entirety herein by reference) was added to the above reaction mixture at 40°C. The reaction mixture was heated to 65-70°C for 24 h. After completion of the reaction, the mixture was concentrated under vacuum and the crude mass was dissolved in ethyl acetate (30 ml) and washed twice with water (2 x 30 ml). The ethyl acetate layer was concentrated under reduced pressure to get crude mass and which was purified by column chromatography using mixture of 30% Ethyl acetate in petroleum ether (1000 ml) to get 1.43 g (79%) of 2-[3-(1-methyl-8-fluoro-2-oxo-1,2,3,5-tetrahydro-benzo[e][1,4]diazepin-4-yl)-3-oxo-(R)-1-(2,4,5-trifluro-benzyl)-propyl]-carbamicacid *tert*-butyl ester.

The above obtained solid was treated with Hydrochloric acid to get Hydrochloric acid salt of 4-[(R)-3-amino-4-(2,4,5-trifluorophenyl)-butyryl]-8-fluoro-1-methyl-1,3,4,5-tetrahydro-benzo [e][1,4]diazepin-2-one.

Claims

1. A process for preparing a compound of general formula I, their pharmaceutically acceptable derivatives, tautomeric forms, stereoisomers including R and S isomers, prodrugs, metabolites, salts or solvates thereof:



Formula I

wherein,

Ar represents aryl which may be phenyl, which may be unsubstituted or optionally substituted at any available position by R^8 or by one or more substituents selected from but not limited to halogen, CN, hydroxyl, NH_2, C_{1-12} alkyl or C_{1-12} alkoxy, wherein each of C_{1-12} alkoxy and C_{1-12} alkyl may be linear or branched and can be unsubstituted or optionally substituted with 1-5 halogens;

R^1 is selected from the group consisting of but not limited to $(CH_2)_nCONR^aR^b$, $(CH_2)_nCOOR^a$, $(CH_2)_nNR^aR^b$, $(CH_2)_nNR^aCOR^b$, $(CH_2)_nC(=Y)R^a$ (wherein Y is O or S), $(CH_2)_nOR^a$ (wherein each methylene group may be substituted by one or more halogen atoms), $-(CO)R^a$, $-(CO)NR^aR^b$, hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, each of which may be optionally substituted at any available position by one or more substituents selected from but not limited to hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, oxo, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one

or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^2 and R^3 together represents a single oxygen or sulphur atom which is linked to the diazepine ring by a double bond; or R^1 and R^2 together forms a double bond in the diazepine ring and R^3 represents the group $-NR^aR^b$; or R^1 and R^3 together with the nitrogen atom to which R^1 is attached forms a heterocyclic or heteroaryl ring which may additionally contain from one to three hetero atoms independently selected from O, S and N; the ring formed may optionally be substituted with one or more substituents selected from R^c or $R^{c'}$ and R^2 represent hydrogen or a double bond;

R^4 and R^5 are independently selected from the group consisting of hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^6 and R^7 are independently selected from the group consisting of hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$,

$N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^8 is independently selected from hydrogen, halogen, CN, C_{1-12} alkyl, C_{1-12} haloalkyl, C_{1-12} alkoxy, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-CF_3$, $-OCF_3$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-6} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^a and R^b are independently selected from hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl; each of which may be optionally substituted with halogen, hydroxyl, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, C_{3-8} cycloalkyl, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, aryl, heterocyclyl, heteroaryl, $(CH_2)_n$-aryl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-heteroaryl, $(CH_2)_n$-cycloalkyl, oxo, -CN, $-OR^9$, $-NO_2$, $-NR^9R^{10}$, $N(R^9)(CO)R^{10}$, $N(R^9)(CO)OR^{10}$, $N(R^9)(CO)NR^9R^{10}$, $-C(=L)R^9$ (wherein L is O or S), $-(CO)NR^9R^{10}$, $-O(CO)R^9$, $-O(CO)NR^9R^{10}$, $-COOR^9$, $-SR^9$, $S(O)_mR^9$, $SO_2NR^9R^{10}$; SO_3H, $NHSO_2R^9$, $P(O)R^9R^{10}$; or R^a and R^b may be joined together

along with the nitrogen atom to which they are attached to form a heterocyclic or heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N, the ring formed may optionally be substituted with one or more substituents selected from hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, oxo, CN, $-OR^9$, $-CF_3$, $-OCF_3$ CH_2CF_3, CF_2CF_3, $-NO_2$, $-NR^9R^{10}$, $N(R^9)(CO)R^{10}$, $N(R^9)(CO)OR^{10}$, $N(R^9)(CO)NR^9R^{10}$, $-C(=Y)R^9$ (wherein Y is O or S), $-(CO)NR^9R^{10}$, $-O(CO)C_1$-C_{12}alkyl, $-O(CO)NR^9R^{10}$, $-COOR^9$, $-SR^9$, $S(O)_mR^9$, $SO_2NR^9R^{10}$; SO_3H, $NHSO_2R^9$, $P(O)R^9R^{10}$; the ring thus formed may further be fused with 3 to 7 membered unsaturated or saturated ring, which may contain from one to three heteroatoms independently selected from O, S or N, the fused ring may optionally be substituted with one or more substituents R^c or $R^{c'}$;

R^c or $R^{c'}$ is independently selected from the group consisting of but not limited to (1) hydrogen, (2) halogen, (3) C_{1-12} alkyl which is linear or branched and which can be unsubstituted or substituted with 1-5 halogens or phenyl , which is unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl ,wherein the CO_2C_{1-6} alkyl is linear or branched ; (4) aryl which can be unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl ,wherein the CO_2C_{1-6} alkyl is linear or branched (5) a 5 or 6 membered heterocyclyl which may be saturated or unsaturated comprising 1-4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1-3 substituents independently selected from oxo, OH, halogen, C_{1-6}alkyl, and OC_{1-6}alkyl, wherein the C_{1-6} alkyl and OC_{1-6} alkyl are linear or branched and optionally substituted with 1-5 halogens; (6) $(CH_2)_n$-cycloalkyl; (7) $(CH_2)_n$-heterocyclyl, (8) $(CH_2)_n$-aryl, (9) $(CH_2)_n$-heteroaryl, (10) C_{1-12} alkylcarbonyl, (11) C_{1-12} alkoxycarbonyl, (12) CN, (13) $-OR^9$, (14) $-OCF_3$, (15) $-NO_2$, (16) $=NOR^{10}$, (17) $-NR^9R^{10}$, (18) $N(R^9)(CO)R^{10}$, (19) $N(R^9)(CO)OR^{10}$, (20) $N(R^9)(CO)NR^9R^{10}$, -(21) $C(=Y')R^9$ (wherein Y is O or S), (22) $-(CO)NR^9R^{10}$,

(23) -O(CO)R^9, (24)*-O(CO)NR^9R^{10}, (25) -$COOR^9$, (26) -SR^9, (27) $S(O)_mR^9$, (28) $SO_2NR^9R^{10}$; (29) SO_3H, (30) $NHSO_2R^9$, (31) $P(O)R^9R^{10}$, (32) C_{2-12} alkenyl, (33) C_{2-12} alkynyl, (34) C_{1-12} haloalkyl, (35) C_{2-12} haloalkenyl, (36) C_{2-12} haloalkynyl, (37) C_{1-12} alkoxy, (38) C_{1-12} haloalkoxy, (39) C_{3-8} cycloalkyl, (40) heteroaryl;

with a proviso that when R^1 and R^3 together with the nitrogen atom to which R^1 is attached forms a heterocyclic or heteroaryl ring which may additionally contain from one to three hetero atoms independently selected from O, S and N , then R^c or $R^{c'}$ cannot be CO_2H.

R^9 and R^{10} are independently selected from hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, each of which may be optionally substituted with halogen, hydroxyl or C_{1-6} alkoxy, or $R^9$and R^{10} may be joined together to form a heterocyclic or heteroaryl ring which may contain from one to three heteroatoms independently selected from O, S and N, which may optionally be substituted with one or more substituents independently selected from R^c or $R^{c'}$;

R^{12} is C_{1-6} alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 groups independently selected from halogen, CO_2H, and CO_2C_{1-6} alkyl, wherein the CO_2C_{1-6} alkyl is linear or branched;

M and L independently represent a hydrogen atom or they may join together to form a ring,

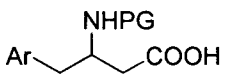
n' is 0 or 1

m can be 1 or 2;

n can be 1, 2, 3 or 4;

comprising:

a) coupling a compound of Formula II,

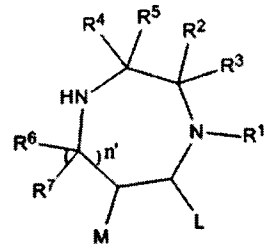


Formula II

wherein

Ar is as defined above and PG is an amino protecting groups selected from acetyl, trifluoroacetyl, benzyloxycarbonyl (CBz), t-butoxycarbonyl (Boc), 9-fluorenylmethyloxycarbonyl (Fmoc), 2,2,2-trichloroethyloxycarbonyl and allyloxycarbonyl;

with a compound of Formula III or its salt



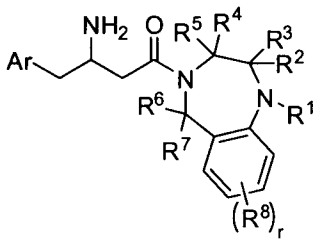
Formula III

using 1,1- carbonyl diimidazole, in a solvent and optionally in the presence of a base;

b) removing the protecting group (PG) from the compound obtained in step (a) using deprotecting agent; and

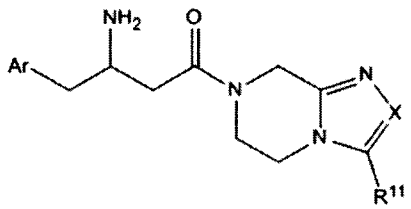
c) optionally converting the product obtained in step (b) to a salt.

2. A process for preparing compounds of formula VI or VII, their pharmaceutically acceptable derivatives, tautomeric forms, stereoisomers including R and S isomers, prodrugs, metabolites, salts or solvates thereof:



Formula VI

OR



Formula VII

wherein,

Ar represents aryl which may be phenyl, which may be unsubstituted or optionally substituted at any available position by one or more substituents selected from but not limited to halogen, CN, hydroxyl, NH_2, C_{1-12} alkyl or C_{1-12} alkoxy, wherein

each of C_{1-12} alkoxy and C_{1-12} alkyl may be linear or branched and can be unsubstituted or optionally substituted with 1-5 halogens;

R^1 is selected from the group consisting of but not limited to $(CH_2)_nCONR^aR^b$, $(CH_2)_nCOOR^a$, $(CH_2)_nNR^aR^b$, $(CH_2)_nNR^aCOR^b$, $(CH_2)_nC(=Y)R^a$ (wherein Y is O or S), $(CH_2)_nOR^a$ (wherein each methylene group may be substituted by one or more halogen atoms), $-(CO)R^a$, $-(CO)NR^aR^b$, hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, each of which may be optionally substituted at any available position by one or more substituents selected from but not limited to hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, oxo, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^2 and R^3 together represents a single oxygen or sulphur atom which is linked to the diazepine ring by a double bond; or R^1 and R^2 together forms a double bond in the diazepine ring and R^3 represents the group $-NR^aR^b$; or R^1 and R^3 together with the nitrogen atom to which R^1 is attached forms a heterocyclic or heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N; the ring formed may optionally be substituted with one or more substituents selected from R^c or $R^{c'}$ and R^2 represent hydrogen or a double bond;

R^4 and R^5 are independently selected from the group consisting of hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^6 and R^7 are independently selected from the group consisting of hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^8 is independently selected from hydrogen, halogen, CN, C_{1-12} alkyl, C_{1-12} haloalkyl, C_{1-12} alkoxy, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-CF_3$, $-OCF_3$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-6} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more

substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^a and R^b are independently selected from hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl; each of which may be optionally substituted with halogen, hydroxyl, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, C_{3-8} cycloalkyl, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, aryl, heterocyclyl, heteroaryl, $(CH_2)_n$-aryl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-heteroaryl, $(CH_2)_n$-cycloalkyl, oxo, -CN, $-OR^9$, $-NO_2$, $-NR^9R^{10}$, $N(R^9)(CO)R^{10}$, $N(R^9)(CO)OR^{10}$, $N(R^9)(CO)NR^9R^{10}$, $-C(=Y)R^9$ (wherein Y is O or S), $-(CO)NR^9R^{10}$, $-O(CO)R^9$, $-O(CO)NR^9R^{10}$, $-COOR^9$, $-SR^9$, $S(O)_mR^9$, $SO_2NR^9R^{10}$; SO_3H, $NHSO_2R^9$, $P(O)R^9R^{10}$; or R^a and R^b may be joined together along with the nitrogen atom to which they are attached to form a heterocyclic or heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N, the ring formed may optionally be substituted with one or more substituents selected from hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, oxo, CN, $-OR^9$, $-CF_3$, $-OCF_3$ CH_2CF_3, CF_2CF_3, $-NO_2$, $-NR^9R^{10}$, $N(R^9)(CO)R^{10}$, $N(R^9)(CO)OR^{10}$, $N(R^9)(CO)NR^9R^{10}$, $-C(=Y)R^9$ (wherein Y is O or S), $-(CO)NR^9R^{10}$, $-O(CO)C_1$-C_{12}alkyl, $-O(CO)NR^9R^{10}$, $-COOR^9$, $-SR^9$, $S(O)_mR^9$, $SO_2NR^9R^{10}$; SO_3H, $NHSO_2R^9$, $P(O)R^9R^{10}$; the ring thus formed may further be fused with 3 to 7 membered unsaturated or saturated ring, which may contain from one to three heteroatoms independently selected from O, S or N, the fused ring may optionally be substituted with one or more substituents R^c or $R^{c'}$;

R^c or $R^{c'}$ is independently selected from the group consisting of but not limited to (1) hydrogen, (2) halogen, (3) C_{1-12} alkyl which is linear or branched and which can be unsubstituted or substituted with 1-5 halogens or phenyl , which is unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl ,wherein the CO_2C_{1-6} alkyl is linear or branched (4) aryl which can be unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl, wherein the CO_2C_{1-6} alkyl is linear or branched (5) a 5 or 6 membered heterocyclyl which may be saturated or unsaturated comprising 1-4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1-3 substituents independently selected from oxo, OH, halogen, C_{1-6}alkyl, and OC_{1-6}alkyl, wherein the C_{1-6}alkyl and OC_{1-6}alkyl are linear or branched and optionally substituted with 1-5 halogens; (6) $(CH_2)_n$-cycloalkyl, (7) $(CH_2)_n$-heterocyclyl, (8) $(CH_2)_n$-aryl, (9) $(CH_2)_n$-heteroaryl, (10) C_{1-12} alkylcarbonyl, (11) C_{1-12} alkoxycarbonyl, (12) CN, (13) $-OR^9$, (14) $-OCF_3$, (15) $-NO_2$, (16) $=NOR^{10}$, (17) $-NR^9R^{10}$, (18) $N(R^9)(CO)R^{10}$, (19) $N(R^9)(CO)OR^{10}$, (20) $N(R^9)(CO)NR^9R^{10}$, (21) $C(=Y)R^9$ (wherein Y is O or S), (22) $-(CO)NR^9R^{10}$, (23) $-O(CO)R^9$, (24) $-O(CO)NR^9R^{10}$,(25) $-COOR^9$, (26) $-SR^9$, (27) $S(O)_mR^9$, (28) $SO_2NR^9R^{10}$; (29) SO_3H, (30) $NHSO_2R^9$, (31) $P(O)R^9R^{10}$, (32) C_{2-12} alkenyl, (33) C_{2-12} alkynyl, (34) C_{1-12} haloalkyl, (35) C_{2-12} haloalkenyl, (36) C_{2-12} haloalkynyl, (37) C_{1-12} alkoxy, (38) C_{1-12} haloalkoxy, (39) C_{3-8} cycloalkyl, (40) heteroaryl;

with a proviso that when R^1 and R^3 together with the nitrogen atom to which R^1 is attached form an imidazole ring, R^c or $R^{c'}$ cannot be CO_2H.

or

with a proviso that when R^1 and R^3 together with the nitrogen atom to which R^1 is attached forms a heterocyclic or heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N, R^c or $R^{c'}$ cannot be CO_2H.

R^9 and R^{10} are independently selected from hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl,

each of which may be optionally substituted with halogen, hydroxyl or C_{1-6} alkoxy, or $R^9$and R^{10} may be joined together to form a heterocyclic or heteroaryl ring which may contain from one to three heteroatoms independently selected from O, S and N, which may optionally be substituted with one or more substituents independently selected from R^c or $R^{c'}$;

R^{12} is C_{1-6} alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 groups independently selected from halogen, CO_2H, and CO_2C_{1-6} alkyl, wherein the CO_2C_{1-6} alkyl is linear or branched;

X is selected from the group consisting of N and CR^{11};

R^{11} is selected from the group consisting of R^c or $R^{c'}$;

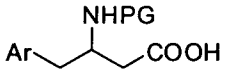
m can be 1 or 2;

n can be 1, 2, 3 or 4;

r can be 1, 2, 3 or 4.

comprising,

a) coupling a compound of Formula II,



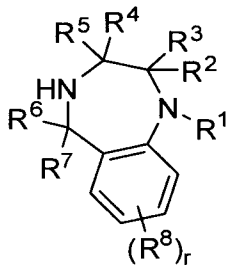
Formula II

wherein

Ar is as defined above; and

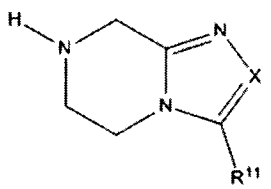
PG is an amino protecting groups selected from acetyl, trifluoroacetyl, benzyloxycarbonyl (CBz), t-butoxycarbonyl (Boc), 9-fluorenylmethyloxycarbonyl (Fmoc), 2,2,2-trichloroethyloxycarbonyl, allyloxycarbonyl and the like;

with a compound of Formula VIII or IX or their salts respectively,



Formula VIII

OR



Formula IX

using 1,1- carbonyl diimidazole, in a solvent and optionally in the presence of a base;

b) removing the protecting group (PG) from the compound obtained in step (a) using deprotecting agents, and

c) optionally converting the product obtained in step (b) to a salt.

3. A process according to claim 1 or 2 wherein the solvent used in step (a) is selected form the group comprising Dimethylfomamide (DMF), Dimethyl acetamide (DMAc), Dichloromethane (DCM), acetonitrile (ACN), toluene, tetrahydrofuran (THF) or mixtures thereof.

4. A process according to claim 3, wherein the solvent is acetonitrile and/or Dimethylformamide.

5. A process according to claim 1 or 2, wherein the base used in step (a) is selected form the group comprising *N*-methylmorpholine (NMM), *N,N*-diisopropylethylamine (DIPEA) and triethylamine (TEA) or mixtures thereof.

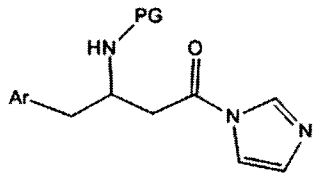
6. A process according to claim 5, wherein the base is *N,N*-diisopropylethylamine.

7. A process according to claim 1 or 2, wherein the deprotecting agent used in step (b) is selected form the group comprising trifluoroacetic acid, hydrochloric acid, phosphoric acid, p-toluenesulphonic acid, piperidine, palladium on charcoal and platinum.

8. A process according to claim 7, wherein the deprotecting agent is hydrochloric acid.

9. A process according to claim 1 or 2, wherein the process steps are carried out without isolating the intermediates.

10. A compound of formula IV and its pharmaceutically acceptable derivatives, tautomeric forms, stereoisomers including R and S isomers, prodrugs, metabolites, salts or solvates thereof:



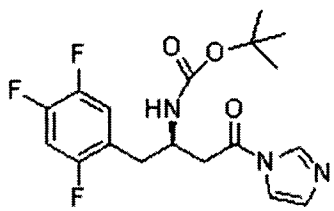
Formula IV

wherein

Ar represents aryl which may be phenyl, which may be unsubstituted or optionally substituted at any available position by one or more substituents selected from but not limited to halogen, CN, hydroxyl, NH_2, C_{1-12} alkyl or C_{1-12} alkoxy, wherein each of C_{1-12} alkoxy and C_{1-12} alkyl may be linear or branched and can be unsubstituted or optionally substituted with 1-5 halogens; and

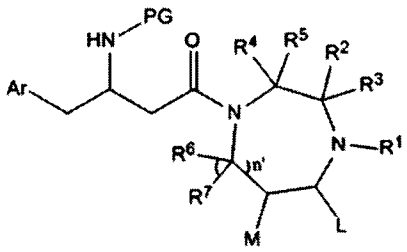
PG is an amino protecting groups selected from acetyl, trifluoroacetyl, benzyloxycarbonyl (CBz), t-butoxycarbonyl (Boc), 9-fluorenylmethyloxycarbonyl (Fmoc), 2,2,2-trichloroethyloxycarbonyl and allyloxycarbonyl.

11. A compound of formula V, its pharmaceutically acceptable derivatives, tautomeric forms, stereoisomers including R and S isomers, prodrugs, metabolites, salts or solvates thereof:



Formula V

12. A compound of formula X and its pharmaceutically acceptable derivatives, tautomeric forms, stereoisomers including R and S isomers, prodrugs, metabolites, salts or solvates thereof:



Formula X

wherein

Ar represents aryl which may be phenyl, which may be unsubstituted or optionally substituted at any available position by one or more substituents selected from but not limited to halogen, CN, hydroxyl, NH_2, C_{1-12} alkyl or C_{1-12} alkoxy, wherein each of C_{1-12} alkoxy and C_{1-12} alkyl may be linear or branched and can be unsubstituted or optionally substituted with 1-5 halogens;

R^1 is selected from the group consisting of but not limited to $(CH_2)_nCONR^aR^b$, $(CH_2)_nCOOR^a$, $(CH_2)_nNR^aR^b$, $(CH_2)_nNR^aCOR^b$, $(CH_2)_nC(=Y)R^a$ (wherein Y is O or S), $(CH_2)_nOR^a$ (wherein each methylene group may be substituted by one or more halogen atoms), $-(CO)R^a$, $-(CO)NR^aR^b$, hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, each of which may be optionally substituted at any available position by one or more substituents selected from but not limited to hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, oxo, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at

any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^2 and R^3 together represents a single oxygen or sulphur atom which is linked to the diazepine ring by a double bond; or R^1 and R^2 together forms a double bond in the diazepine ring and R^3 represents the group $-NR^aR^b$; or R^1 and R^3 together with the nitrogen atom to which R^1 is attached forms a heterocyclic or heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N; the ring formed may optionally be substituted with one or more substituents selected from R^c or $R^{c'}$ and R^2 represent hydrogen or a double bond;

R^4 and R^5 are independently selected from the group consisting of hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^6 and R^7 are independently selected from the group consisting of hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl

which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^a and R^b are independently selected from hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl; each of which may be optionally substituted with halogen, hydroxyl, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, C_{3-8} cycloalkyl, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, aryl, heterocyclyl, heteroaryl, $(CH_2)_n$-aryl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-heteroaryl, $(CH_2)_n$-cycloalkyl, oxo, -CN, $-OR^9$, $-NO_2$, $-NR^9R^{10}$, $N(R^9)(CO)R^{10}$, $N(R^9)(CO)OR^{10}$, $N(R^9)(CO)NR^9R^{10}$, $-C(=Y)R^9$ (wherein Y is O or S), $-(CO)NR^9R^{10}$, $-O(CO)R^9$, $-O(CO)NR^9R^{10}$, $-COOR^9$, $-SR^9$, $S(O)_mR^9$, $SO_2NR^9R^{10}$; SO_3H, $NHSO_2R^9$, $P(O)R^9R^{10}$; or R^a and R^b may be joined together along with the nitrogen atom to which they are attached to form a heterocyclic or heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N, the ring formed may optionally be substituted with one or more substituents selected from hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, oxo, CN, $-OR^9$, $-CF_3$, $-OCF_3$ CH_2CF_3, CF_2CF_3, $-NO_2$, $-NR^9R^{10}$, $N(R^9)(CO)R^{10}$, $N(R^9)(CO)OR^{10}$, $N(R^9)(CO)NR^9R^{10}$, $-C(=Y)R^9$ (wherein Y is O or S), $-(CO)NR^9R^{10}$, $-O(CO)C_1$-C_{12}alkyl, $-O(CO)NR^9R^{10}$, $-COOR^9$, $-SR^9$, $S(O)_mR^9$, $SO_2NR^9R^{10}$; SO_3H, $NHSO_2R^9$, $P(O)R^9R^{10}$; the ring thus formed may further be fused with 3 to 7 membered unsaturated or saturated ring, which may contain from one to three heteroatoms independently selected from O, S or N, the fused ring may optionally be substituted with one or more substituents R^c or $R^{c'}$;

R^c or $R^{c'}$ is independently selected from the group consisting of but not limited to (1) hydrogen, (2) halogen, (3) C_{1-12} alkyl which is linear or branched and which can be unsubstituted or substituted with 1-5 halogens or phenyl , which is

unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl ,wherein the CO_2C_{1-6} alkyl is linear or branched (4) aryl which can be unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl, wherein the CO_2C_{1-6} alkyl is linear or branched (5) a 5 or 6 membered heterocyclyl which may be saturated or unsaturated comprising 1-4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1-3 substituents independently selected from oxo, OH, halogen, C_{1-6}alkyl, and OC_{1-6}alkyl, wherein the C_{1-6}alkyl and OC_{1-6}alkyl are linear or branched and optionally substituted with 1-5 halogens; (6) $(CH_2)_n$-cycloalkyl, (7) $(CH_2)_n$-heterocyclyl, (8) $(CH_2)_n$-aryl, (9) $(CH_2)_n$-heteroaryl, (10) C_{1-12} alkylcarbonyl, (11) C_{1-12} alkoxycarbonyl, (12) CN, (13) $-OR^9$, (14) $-OCF_3$, (15) $-NO_2$, (16) $=NOR^{10}$, (17) $-NR^9R^{10}$, (18) $N(R^9)(CO)R^{10}$, (19) $N(R^9)(CO)OR^{10}$, (20) $N(R^9)(CO)NR^9R^{10}$, (21) $C(=Y)R^9$ (wherein Y is O or S), (22) $-(CO)NR^9R^{10}$, (23) $-O(CO)R^9$, (24) $-O(CO)NR^9R^{10}$,(25) $-COOR^9$, (26) $-SR^9$, (27) $S(O)_mR^9$, (28) $SO_2NR^9R^{10}$; (29) SO_3H, (30) $NHSO_2R^9$, (31) $P(O)R^9R^{10}$, (32) C_{2-12} alkenyl, (33) C_{2-12} alkynyl, (34) C_{1-12} haloalkyl, (35) C_{2-12} haloalkenyl, (36) C_{2-12} haloalkynyl, (37) C_{1-12} alkoxy, (38) C_{1-12} haloalkoxy, (39) C_{3-8} cycloalkyl, (40) heteroaryl;

with a proviso that when R^1 and R^3 together with the nitrogen atom to which R^1 is attached form an imidazole ring, R^c or $R^{c'}$ cannot be CO_2H.

or

with a proviso that when R^1 and R^3 together with the nitrogen atom to which R^1 is attached forms a heterocyclic or heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N, R^c or $R^{c'}$ cannot be CO_2H.

R^9 and R^{10} are independently selected from hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, each of which may be optionally substituted with halogen, hydroxyl or C_{1-6} alkoxy, or $R^9$and R^{10} may be joined together to form a heterocyclic or heteroaryl ring which may contain from one to three heteroatoms independently selected

from O, S and N, which may optionally be substituted with one or more substituents independently selected from R^c or $R^{c'}$;

R^{12} is C_{1-6} alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 groups independently selected from halogen, CO_2H, and CO_2C_{1-6} alkyl, wherein the CO_2C_{1-6} alkyl is linear or branched;

M and L independently represent a hydrogen atom or they may join together to form a ring;

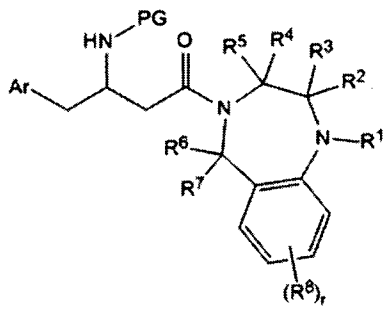
n' is 0 or 1

m can be 1 or 2;

n can be 1, 2, 3 or 4; and

PG is an amino protecting groups selected from acetyl, trifluoroacetyl, benzyloxycarbonyl (CBz), t-butoxycarbonyl (Boc), 9-fluorenylmethyloxycarbonyl (Fmoc), 2,2,2-trichloroethyloxycarbonyl and allyloxycarbonyl.

13. A compound of formula XI and its pharmaceutically acceptable derivatives, tautomeric forms, stereoisomers including R and S isomers, prodrugs, metabolites, salts or solvates thereof:



Formula XI

wherein

Ar represents aryl which may be phenyl, which may be unsubstituted or optionally substituted at any available position by one or more substituents selected from but not limited to halogen, CN, hydroxyl, NH_2, C_{1-12} alkyl or C_{1-12} alkoxy, wherein each of C_{1-12} alkoxy and C_{1-12} alkyl may be linear or branched and can be unsubstituted or optionally substituted with 1-5 halogens;

R^1 is selected from the group consisting of but not limited to $(CH_2)_nCONR^aR^b$, $(CH_2)_nCOOR^a$, $(CH_2)_nNR^aR^b$, $(CH_2)_nNR^aCOR^b$, $(CH_2)_nC(=Y)R^a$ (wherein Y is O or S), $(CH_2)_nOR^a$ (wherein each methylene group may be substituted by one or more halogen atoms), $-(CO)R^a$, $-(CO)NR^aR^b$, hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, each of which may be optionally substituted at any available position by one or more substituents selected from but not limited to hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, oxo, $-OR^a$, $-SR^a$, $-NO_2$, $-NR^aR^b$, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, $-(CO)R^a$, $-(CO)NR^aR^b$, $-O(CO)R^a$, $-O(CO)NR^aR^b$, $-COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^2 and R^3 together represents a single oxygen or sulphur atom which is linked to the diazepine ring by a double bond; or R^1 and R^2 together forms a double bond in the diazepine ring and R^3 represents the group $-NR^aR^b$; or R^1 and R^3 together with the nitrogen atom to which R^1 is attached forms a heterocyclic or heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N; the ring formed may optionally be substituted with one or more substituents selected from R^c or $R^{c'}$ and R^2 represent hydrogen or a double bond;

R^4 and R^5 are independently selected from the group consisting of hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12}

alkoxycarbonyl, -OR^a, -SR^a, -NO_2, -NR^aR^b, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, -$(CO)R^a$, -$(CO)NR^aR^b$, -$O(CO)R^a$, -$O(CO)NR^aR^b$, -$COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^6 and R^7 are independently selected from the group consisting of hydrogen, halogen, CN, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, -OR^a, -SR^a, -NO_2, -NR^aR^b, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, -$(CO)R^a$, -$(CO)NR^aR^b$, -$O(CO)R^a$, -$O(CO)NR^aR^b$, -$COOR^a$, C_{3-8} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^8 is independently selected from hydrogen, halogen, CN, C_{1-12} alkyl, C_{1-12} haloalkyl, C_{1-12} alkoxy, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, -OR^a, -SR^a, -CF_3, -OCF_3, -NO_2, -NR^aR^b, $N(R^a)(CO)R^b$, $N(R^a)(CO)OR^b$, $N(R^a)(CO)NR^aR^b$, -$(CO)R^a$, -$(CO)NR^aR^b$, -$O(CO)R^a$, -$O(CO)NR^aR^b$, -$COOR^a$, C_{3-6} cycloalkyl, $S(O)_mR^a$, $SO_2NR^aR^b$; cycloalkyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; aryl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$; heteroaryl which may be optionally substituted at any

available position by one or more substituents independently selected from R^c or $R^{c'}$; or heterocyclyl which may be optionally substituted at any available position by one or more substituents independently selected from R^c or $R^{c'}$;

R^a and R^b are independently selected from hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl; each of which may be optionally substituted with halogen, hydroxyl, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} alkoxy, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, C_{3-8} cycloalkyl, C_{1-12} haloalkyl, C_{1-12} haloalkoxy, C_{2-12} haloalkenyl, aryl, heterocyclyl, heteroaryl, $(CH_2)_n$-aryl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-heteroaryl, $(CH_2)_n$-cycloalkyl, oxo, -CN, $-OR^9$, $-NO_2$, $-NR^9R^{10}$, $N(R^9)(CO)R^{10}$, $N(R^9)(CO)OR^{10}$, $N(R^9)(CO)NR^9R^{10}$, $-C(=Y)R^9$ (wherein Y is O or S), $-(CO)NR^9R^{10}$, $-O(CO)R^9$, $-O(CO)NR^9R^{10}$, $-COOR^9$, $-SR^9$, $S(O)_mR^9$, $SO_2NR^9R^{10}$; SO_3H, $NHSO_2R^9$, $P(O)R^9R^{10}$; or R^a and R^b may be joined together along with the nitrogen atom to which they are attached to form a heterocyclic or heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N, the ring formed may optionally be substituted with one or more substituents selected from hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{2-12} haloalkynyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, C_{1-12} alkylcarbonyl, C_{1-12} alkoxycarbonyl, oxo, CN, $-OR^9$, $-CF_3$, $-OCF_3$ CH_2CF_3, CF_2CF_3, $-NO_2$, $-NR^9R^{10}$, $N(R^9)(CO)R^{10}$, $N(R^9)(CO)OR^{10}$, $N(R^9)(CO)NR^9R^{10}$, $-C(=Y)R^9$ (wherein Y is O or S), $-(CO)NR^9R^{10}$, $-O(CO)C_1$-C_{12}alkyl, $-O(CO)NR^9R^{10}$, $-COOR^9$, $-SR^9$, $S(O)_mR^9$, $SO_2NR^9R^{10}$; SO_3H, $NHSO_2R^9$, $P(O)R^9R^{10}$; the ring thus formed may further be fused with 3 to 7 membered unsaturated or saturated ring, which may contain from one to three heteroatoms independently selected from O, S or N, the fused ring may optionally be substituted with one or more substituents R^c or $R^{c'}$;

R^c or $R^{c'}$ is independently selected from the group consisting of but not limited to (1) hydrogen, (2) halogen, (3) C_{1-12} alkyl which is linear or branched and which can be unsubstituted or substituted with 1-5 halogens or phenyl, which is unsubstituted or substituted with 1-5 substituents independently selected from

halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl ,wherein the CO_2C_{1-6} alkyl is linear or branched (4) aryl which can be unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl, wherein the CO_2C_{1-6} alkyl is linear or branched (5) a 5 or 6 membered heterocyclyl which may be saturated or unsaturated comprising 1-4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1-3 substituents independently selected from oxo, OH, halogen, C_{1-6} alkyl, and OC_{1-6} alkyl, wherein the C_{1-6} alkyl and OC_{1-6} alkyl are linear or branched and optionally substituted with 1-5 halogens; (6) $(CH_2)_n$-cycloalkyl, (7) $(CH_2)_n$-heterocyclyl, (8) $(CH_2)_n$-aryl, (9) $(CH_2)_n$-heteroaryl, (10) C_{1-12} alkylcarbonyl, (11) C_{1-12} alkoxycarbonyl, (12) CN, (13) $-OR^9$, (14) $-OCF_3$, (15) $-NO_2$, (16) $=NOR^{10}$, (17) $-NR^9R^{10}$, (18) $N(R^9)(CO)R^{10}$, (19) $N(R^9)(CO)OR^{10}$, (20) $N(R^9)(CO)NR^9R^{10}$, (21) $C(=Y)R^9$ (wherein Y is O or S), (22) $-(CO)NR^9R^{10}$, (23) $-O(CO)R^9$, (24) $-O(CO)NR^9R^{10}$,(25) $-COOR^9$, (26) $-SR^9$, (27) $S(O)_mR^9$, (28) $SO_2NR^9R^{10}$; (29) SO_3H, (30) $NHSO_2R^9$, (31) $P(O)R^9R^{10}$, (32) C_{2-12} alkenyl, (33) C_{2-12} alkynyl, (34) C_{1-12} haloalkyl, (35) C_{2-12} haloalkenyl, (36) C_{2-12} haloalkynyl, (37) C_{1-12} alkoxy, (38) C_{1-12} haloalkoxy, (39) C_{3-8} cycloalkyl, (40) heteroaryl;

with a proviso that when R^1 and R^3 together with the nitrogen atom to which R^1 is attached form an imidazole ring, R^c or $R^{c'}$ cannot be CO_2H.

or

with a proviso that when R^1 and R^3 together with the nitrogen atom to which R^1 is attached forms a heterocyclic or heteroaryl ring which may additionally contain from one to three heteroatoms independently selected from O, S and N, R^c or $R^{c'}$ cannot be CO_2H.

R^9 and R^{10} are independently selected from hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, each of which may be optionally substituted with halogen, hydroxyl or C_{1-6} alkoxy, or $R^9$and R^{10} may be joined together to form a heterocyclic or heteroaryl ring which may contain from one to three heteroatoms independently selected

from O, S and N, which may optionally be substituted with one or more substituents independently selected from R^c or $R^{c'}$;

R^{12} is C_{1-6} alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 groups independently selected from halogen, CO_2H, and CO_2C_{1-6} alkyl, wherein the CO_2C_{1-6} alkyl is linear or branched;

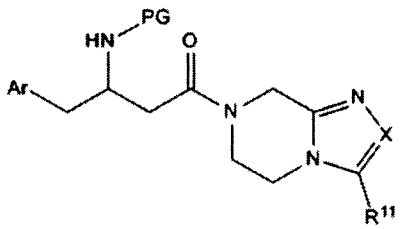
m can be 1 or 2;

n can be 1, 2, 3 or 4;

r can be 1, 2, 3 or 4; and

PG is an amino protecting groups selected from acetyl, trifluoroacetyl, benzyloxycarbonyl (CBz), t-butoxycarbonyl (Boc), 9-fluorenylmethyloxycarbonyl (Fmoc), 2,2,2-trichloroethyloxycarbonyl and allyloxycarbonyl.

14. A compound of formula XII and its pharmaceutically acceptable derivatives, tautomeric forms, stereoisomers including R and S isomers, prodrugs, metabolites, salts or solvates thereof:



Formula XII

wherein

Ar represents aryl which may be phenyl, which may be unsubstituted or optionally substituted at any available position by one or more substituents selected from but not limited to halogen, CN, hydroxyl, NH_2, C_{1-12} alkyl or C_{1-12} alkoxy, wherein each of C_{1-12} alkoxy and C_{1-12} alkyl may be linear or branched and can be unsubstituted or optionally substituted with 1-5 halogens;

X is selected from the group consisting of N and CR^{11};

R^{11} is selected from the group consisting of R^c or $R^{c'}$;

R^c or $R^{c'}$ is independently selected from the group consisting of but not limited to (1) hydrogen, (2) halogen, (3) C_{1-12} alkyl which is linear or branched and which can be unsubstituted or substituted with 1-5 halogens or phenyl , which is

unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl ,wherein the CO_2C_{1-6} alkyl is linear or branched (4) aryl which can be unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH, R^{12}, OR^{12}, $NHSO_2R^{12}$, SO_2R^{12}, CO_2H and CO_2C_{1-6} alkyl, wherein the CO_2C_{1-6} alkyl is linear or branched (5) a 5 or 6 membered heterocyclyl which may be saturated or unsaturated comprising 1-4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1-3 substituents independently selected from oxo, OH, halogen, C_{1-6}alkyl, and OC_{1-6}alkyl, wherein the C_{1-6}alkyl and OC_{1-6}alkyl are linear or branched and optionally substituted with 1-5 halogens; (6) $(CH_2)_n$-cycloalkyl, (7) $(CH_2)_n$-heterocyclyl, (8) $(CH_2)_n$-aryl, (9) $(CH_2)_n$-heteroaryl, (10) C_{1-12} alkylcarbonyl, (11) C_{1-12} alkoxycarbonyl, (12) CN, (13) $-OR^9$, (14) $-OCF_3$, (15) $-NO_2$, (16) $=NOR^{10}$, (17) $-NR^9R^{10}$, (18) $N(R^9)(CO)R^{10}$, (19) $N(R^9)(CO)OR^{10}$, (20) $N(R^9)(CO)NR^9R^{10}$, (21) $C(=Y)R^9$ (wherein Y is O or S), (22) $-(CO)NR^9R^{10}$, (23) $-O(CO)R^9$, (24) $-O(CO)NR^9R^{10}$,(25) $-COOR^9$, (26) $-SR^9$, (27) $S(O)_mR^9$, (28) $SO_2NR^9R^{10}$; (29) SO_3H, (30) $NHSO_2R^9$, (31) $P(O)R^9R^{10}$, (32) C_{2-12} alkenyl, (33) C_{2-12} alkynyl, (34) C_{1-12} haloalkyl, (35) C_{2-12} haloalkenyl, (36) C_{2-12} haloalkynyl, (37) C_{1-12} alkoxy, (38) C_{1-12} haloalkoxy, (39) C_{3-8} cycloalkyl, (40) heteroaryl;

R^9 and R^{10} are independently selected from hydrogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{1-12} haloalkyl, C_{2-12} haloalkenyl, C_{3-8} cycloalkyl, heterocyclyl, aryl, heteroaryl, $(CH_2)_n$-cycloalkyl, $(CH_2)_n$-heterocyclyl, $(CH_2)_n$-aryl, $(CH_2)_n$-heteroaryl, each of which may be optionally substituted with halogen, hydroxyl or C_{1-6} alkoxy, or $R^9$and R^{10} may be joined together to form a heterocyclic or heteroaryl ring which may contain from one to three heteroatoms independently selected from O, S and N, which may optionally be substituted with one or more substituents independently selected from R^c or $R^{c'}$;

R^{12} is C_{1-6} alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 groups independently selected from halogen, CO_2H, and CO_2C_{1-6} alkyl, wherein the CO_2C_{1-6} alkyl is linear or branched; and

PG is an amino protecting groups selected from acetyl, trifluoroacetyl, benzyloxycarbonyl (CBz), t-butoxycarbonyl (Boc), 9-fluorenylmethyloxycarbonyl (Fmoc), 2,2,2-trichloroethyloxycarbonyl and allyloxycarbonyl.

15. Use of compound of formula V for the preparation of:
(2R)-4-oxo-(3-trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-α]pyrazin-7(8H)-yl]-1-(2,4,5-trifluoro-phenyl)butan-2-amine and its pharmaceutically acceptable salts; or
4-[(R)-3-amino-4-(2,4,5-trifluorophenyl)-butyryl]-1,3,4,5-tetrahydro-benzo[e][1,4]diazipin-2-one and its pharmaceutically acceptable salts; or
(R)-4-(3-amino-4-(2,4,5-trifluorophenyl)-butanoyl)-7-methoxy-4,5-dihydro-1H-benzo[e][1,4] diazipin-2(3H)-one and its pharmaceutically acceptable salts; or
(R)-3-amino-1-(9-fluoro-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-yl)-4-(2,4,5-trifluoro-phenyl)-butan-1-one and its pharmaceutically acceptable salts; or
(R)-4-(3-amino-4-(2,4,5-trifluorophenyl)-butanoyl)-8-Fluoro-4,5-dihydro-1H-benzo[e][1,4] diazipin-2(3H)-one and its pharmaceutically acceptable salts; or
4-[(R)-3-amino-4-(2,4,5-trifluorophenyl)-butyryl]-1-methyl-8-Fluoro-1,3,4,5-tetrahydro-benzo [e][1,4]diazepin-2-one and its pharmaceutically acceptable salts.

16. Use of compound of formula X for the preparation of compound of formula I.

17. Use of compound of formula XI for the preparation of compound of formula VI.

18. Use of compound of formula XII for the preparation of compound of formula VII.

19. A process for the preparation of:
(2R)-4-oxo-(3-trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-α]pyrazin-7(8H)-yl]-1-(2,4,5-trifluoro-phenyl)butan-2-amine and its pharmaceutically acceptable salts; or
4-[(R)-3-amino-4-(2,4,5-trifluorophenyl)-butyryl]-1,3,4,5-tetrahydro-benzo[e][1,4]diazipin-2-one and its pharmaceutically acceptable salts; or
(R)-4-(3-amino-4-(2,4,5-trifluorophenyl)-butanoyl)-7-methoxy-4,5-dihydro-1H-benzo[e][1,4] diazipin-2(3H)-one and its pharmaceutically acceptable salts; or

(R)-3-amino-1-(9-fluoro-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-yl)-4-(2,4,5-trifluoro-phenyl)-butan-1-one and its pharmaceutically acceptable salts; or (R)-4-(3-amino-4-(2,4,5-trifluorophenyl)-butanoyl)-8-Fluoro-4,5-dihydro-1H-benzo[e][1,4] diazipin-2(3H)-one and its pharmaceutically acceptable salts; or 4-[(R)-3-amino-4-(2,4,5-trifluorophenyl)-butyryl]-1-methyl-8-Fluoro-1,3,4,5-tetrahydro-benzo [e][1,4]diazepin-2-one and its pharmaceutically acceptable salts; according to claims 1 or 2.