Compounds of the general formula (I) their tautomeric forms, their stereoisomers, their analogs, their prodrugs, their isomers, their N-oxides, their metabolites, their pharmaceutically acceptable salts, polymorphs, solvates, optical isomers, clathrates, co-crystals, combinations with suitable medicament, pharmaceutical compositions containing them, methods of making of the above compounds, and their use as antiviral candidate, more specifically as anti-HCV are disclosed.
FIELD OF THE INVENTION:

The present invention is related to novel compounds of the general formula I,

their tautomeric forms, their stereoisomers, their analogs, their prodrugs, their isotopes, their N-oxides, their metabolites, their pharmaceutically acceptable salts, polymorphs, solvates, optical isomers, clathrates, co-crystals, combinations with suitable medicament, pharmaceutical compositions containing them, methods of making of the above compounds, and their use as antiviral candidate, more specifically as anti-HCV.

BACKGROUND OF THE INVENTION

Persistent hepatitis C virus (HCV) infection is a major health problem globally affecting ~3% of the world population and is an important contributor to chronic liver disease culminating with liver cirrhosis, hepatocellular carcinoma and liver failure [Szabo E, Lotz G, et al., Pathol. Oncol. Res. 2003, 9, 215-221; Hoofnagle JH., Hepatology 1997, 26, 15S-20]. An estimated 170 million chronic carriers worldwide are at risk of developing liver disease. In the United States alone ~3 million are chronically infected with HCV and the number of HCV related deaths is increasing significantly over the years [Barnes E., WHO factsheet 2010. Available at: http://www.who.int/vaccine_research/diseases/viral_cancers/en/index2.html]. Clinically, chronic infection is often asymptomatic with latent periods lasting for decades before manifestation by which time extensive liver damage has occurred. HCV is spread primarily by unscreened blood transfusions and use of contaminated needles and syringes; the highest risk groups are intravenous drug users and people who received blood transfusions (mainly haemophiliacs) before 1990 when screening for HCV was introduced. Factors that have been reported to influence the rate of HCV disease progression include age (increasing age is associated with more rapid progression), gender (males have more rapid disease progression than females), alcohol consumption (associated with an
increased rate of disease progression), HIV co-infection (associated with a markedly increased rate of disease progression), and fatty liver.

Despite significant efforts, no vaccine exists for HCV and until a year ago the standard therapy for HCV was a combination of pegylated interferon (PEG-IFN) a and weight based ribavarin (RBV), which was inadequate for majority of the patients and therapy associated side effects such as pancytopenia, flu-like symptoms or depression were commonly observed leading to early treatment discontinuation [Fried MW, et al., N Engl J Med. 2002, 347, 975-982]. The approval of two direct acting agents (DAA) i.e. 1st generation protease inhibitors, Incivek and Victrelis in May 2011 ushered in the era of specifically targeted HCV therapy[Jesudian AB, Gambarin-Gelwan M and Jacobson IM., Gastroenterology Hepatol. 2012, 8, 91-101.

The combination of above mentioned DAAs, Peg-IFN and RBV (triple therapy) substantially increases the rate of sustained virologic response in treatment naïve and experienced patients. However, a number of issue restrict the usage of these drugs - i) complex treatment algorithms issued by the regulatory bodies; ii) they are restricted to genotype 1; iii) low barrier to resistance mutations and iv) increased cost of therapy leading to limited access to care. Hence, there exists a need for alternative therapeutic strategies that ensure broader genotype coverage, better efficacy, better tolerance and limited selection of resistant HCV variants.

The sequence diversity of HCV is complex with the virus organized into 6 distinct genotypes and over 100 subtypes. Additionally, HCV exists as many closely related viral sequences, termed as quasi-species, in the infected individual, making specific pharmaceutical targeting of HCV proteins challenging due to the rapid evolution of escape mutants. It is increasingly evident that a broad collection of specific, pan genotypic antiviral drugs targeting multiple essential viral functions, in addition to the current viral therapies will be required for effective global control of HCV.

SUMMARY OF THE INVENTION

According to one aspect of the present invention there is provided a novel compound of the general formula (I), its tautomeric forms, its stereoisomers, its analogs, its prodrugs, its
isotopes, its N-oxides, its metabolites, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates, or its co-crystals,

wherein, R₁⁻ and R₃ to R₁², m, n, Y, ring D and ring A are as defined hereinbelow.

In another aspect, the present invention provides a pharmaceutical composition, containing the compound of the general formula (I) as defined herein, its tautomeric forms, its stereoisomers, its analogs, its prodrugs, its isotopes, its N-oxides, its metabolites, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates, or its co-crystals in combination with the usual pharmaceutically employed carriers, diluents and the like are useful for the treatment of HCV infection.

DESCRIPTION OF THE INVENTION

HCV is a member of the Flaviviridae family of enveloped, positive stranded RNA viruses belonging to the genus Hepacivirus. The genome is a single ~9.6 kb strand of RNA and consists of one open reading frame that encodes for a polyprotein of ~3000 amino acids flanked by untranslated regions at both 5' and 3' ends. This precursor polyprotein is then processed by viral and cellular proteases to yield 10 separate mature viral proteins critical for replication and assembly of progeny viral particles. The organization of the structural and non-structural proteins in the HCV polyprotein is as follows: C-E1-E2-P7-NS2-NS3-NS4a-NS4b-NS5a-NS5b. The three structural proteins C, E1 and E2 are involved in packaging of the virus and the infectivity cycle. The function of the p7 protein is unknown. Of the non-structural proteins, NS2 is a zinc dependent metalloproteasein that functions in conjunction with a part of NS3 protein. NS3 protein has two catalytic activities associated with it: a serine protease at the N-terminal end which requires NS4A as a cofactor, and an ATPase dependent helicase activity at the C-terminal end. NS5A is a membrane anchored phosphoprotein that is present in basally phosphorylated (56kDa) and hyperphosphorylated (58kDa) forms. Its precise role has not been determined but it has
been shown to play a role in RNA binding, multiple host protein interactions, and interferon resistance. Additionally recent evidence suggests that NS5A plays an important role in replication and infectivity of HCV. The NS5B protein encodes an RNA dependent RNA polymerase activity, key to the generation of progeny viruses. While the pathology of HCV infection mainly affects the liver, the virus is found in other cell types in the body including peripheral blood lymphocytes [Thomson BJ et al., Clin Microbial Infect. 2005, 11, 86-94; Moriishi K et al., Antivir. Chem. Chemother. 2003, 14, 285-297]. Characterization of the replicase machinery required for HCV RNA synthesis has defined the protease/helicase NS3 protein, the NS4A cofactor, the NS4B integral membrane protein, the NS5A protein and the RNA dependent RNA polymerase NS5B as being its essential components.

Hence, one of the aspects of the present invention is provision of novel compounds of the general formula I,

![Chemical Structure](image)

their tautomeric forms, their isomers, their isotopes, their metabolites, their prodrugs, their pharmaceutically acceptable salts, pharmaceutical compositions containing them, methods of making of the above compounds, and their use as antiviral compounds;

wherein,

Ring 'A' is a saturated carbocycle, which may be a monocyclic system or may be a fused carbocycle or may be a bridged carbocycle, the said ring A may contain 5 to 10 carbons;

Ring 'D' is selected from 5 to 10 membered carbocycle and 5 to 10 membered heterocycle, the ring 'D' may be monocyclic, fused bicyclic, bridged bicyclic or spiro bicyclic;

Y is selected from -CH(R^2a)- and -N(R^3)-;

R^1 is selected from the group consisting of R^{13a}C(=0)N(R^{14})-, R^{13a}OC(=0)N(R^{14})-, R^{13}(R^{14})N-, R^{13}(R^{14})NC(=0)N(R^{15})-, R^{13a}S0_2N(R^{14})-, R^{13a}OC(=0)N(R^{14})CR^a(R^b)C(=0)N(R^{15})-,
R_{13a}OC\{0\}(N(R_{14}^{1})CR_{13b}^{1}(R_{15}^{1}))C(R_{14}^{1})C(=0)N(R_{15}^{1})-,
R_{13}^{1}(R_{14}^{1})NC(=0)N(R_{14}^{1})CR_{13b}^{1}(R_{15}^{1})C(=0)N(R_{15}^{1})-,
R_{13}^{1}(R_{14}^{1})NC(=0)N(R_{14}^{1})CR_{13b}^{1}(R_{15}^{1})C(=0)N(R_{15}^{1})-;
R_{13}^{1} is selected independently at each occurrence from the group consisting of halogen, 5
substituted- or unsubstituted- Ci-6 alkyl, R_{13a}^{13a}C(=0)-, R_{13b}^{13b}O-, R_{13a}^{13a}OC(=0)-, 10
R_{13a}^{13a}C(=0)0-, and R_{13}^{13} (R_{14}^{1})NC(=0)-,
R_{2}^{2} is selected independently at each occurrence from the group consisting of substituted- or 15
unsubstituted- Ci-6 alkyl, R_{13a}^{13a}C(=0)-, R_{13b}^{13b}SO_{2}-, R_{13a}^{13a}OC(=0)-, R_{13}^{13} (R_{14}^{1})NC(=0)-,
R_{13a}^{13a}OC(=0)N(R_{14}^{1})C(R_{14}^{1})(R_{15}^{1})C(=0)-, R_{13a}^{13a}OC(=0)N(R_{14}^{1})C(R_{14}^{1})(R_{15}^{1})C(R_{15}^{1})C(=0)-,
R_{13}^{13} (R_{14}^{1})NC(=0)N(R_{15}^{1})C(R_{15}^{1})(R_{14}^{1})C(=0)-, R_{13}^{13} (R_{14}^{1})NC(=0)N(R_{15}^{1})C(R_{15}^{1})(R_{14}^{1})(R_{15}^{1})C(=0)-, 20
R_{13}^{13} SO_{2}N(R_{14}^{1})C(R_{15}^{1})(R_{15}^{1})C(=0)-, R_{13}^{13} SO_{2}N(R_{14}^{1})C(R_{15}^{1})(R_{15}^{1})C(R_{15}^{1})(R_{15}^{1})C(=0)-, and
R_{13a}^{13a}OC(=0)N(R_{14}^{1})C(R_{14}^{1})(R_{15}^{1})SO_{2}-;
R_{2}^{2} a is selected independently at each occurrence from the group consisting of 25
R_{13a}^{13a}C(=0)N(R_{14}^{1})- R_{13a}^{13a}OC(=0)N(R_{14}^{1})- R_{13}^{13} (R_{14}^{1})N- R_{13}^{13} (R_{14}^{1})NC(=0)N(R_{15}^{1})-,
R_{13a}^{13a}SO_{2}N(R_{14}^{1})-, R_{13a}^{13a}OC(=0)N(R_{14}^{1})C(R_{14}^{1})(R_{15}^{1})C(=0)N(R_{15}^{1})-,
R_{13a}^{13a}OC(=0)N(R_{14}^{1})C(R_{14}^{1})(R_{15}^{1})(R_{15}^{1})C(=0)N(R_{15}^{1})-,
R_{13}^{13} (R_{14}^{1})NC(=0)N(R_{14}^{1})C(R_{14}^{1})(R_{15}^{1})C(=0)N(R_{15}^{1})-; and
R_{13}^{13} (R_{14}^{1})NC(=0)N(R_{14}^{1})C(R_{14}^{1})(R_{15}^{1})C(R_{15}^{1})(R_{15}^{1})C(=0)N(R_{15}^{1})-;
R_{3} is independently selected from O and N(R_{18});
R_{4} is selected independently at each occurrence from CR_{6}(R_{1}^{1}), O and N(R_{14}); such that, 30
when n = 2 and R_{4} is selected as CR_{6}(R_{1}^{1}) for both the occurrences, two R_{4}s together can
form a bond to form an alkylene linkage or two R_{4}s and two R_{4}s together can form bonds to
form alkylene linkage;
R_{5}, R_{6}, R_{7}, R_{8}, R_{9} and R_{10} are independently selected as hydrogen, or R_{5} and R_{6} together,
R_{7} and R_{10} together, or R_{6} and R_{9} together independently along with the carbon atoms to
which they are attached forming 5 to 8 membered substituted- or unsubstituted-
carbocycle, 5 to 8 membered substituted- or unsubstituted- heterocycle, 6 membered
substituted- or unsubstituted- aryl, or 5 to 6 membered substituted- or unsubstituted-
heteroaryl;
with a proviso that the compound of formula I must have at least one cyclic system formed out of either \( R^5 \) and \( R^6 \), \( R^8 \), \( R^9 \), or \( R^7 \) and \( R^{10} \); also provided that \( R^7 \) and \( R^{10} \) take part in formation of cyclic system only when \( n \) is 0;

\( R^{11} \) and \( R^{12} \) are independently selected from a group consisting of hydrogen, halogen, substituted- or unsubstituted- \( \text{C}_{1-6} \) alkyl, \( R^{13b} \text{O}^- \), and \( (R^{13})(R^{14}) \text{N}^- \);

wherein, \( R^{13} \), \( R^{14} \), \( R^{14a} \) and \( R^{15} \) are independently selected from hydrogen, substituted- or unsubstituted- \( \text{C}_{1-6} \) alkyl, substituted- or unsubstituted- aryl, substituted- or unsubstituted- heteroaryl, substituted- or unsubstituted- cycloalkyl, and substituted- or unsubstituted- heterocyclyl;

\( R^{13a} \) is selected from substituted- or unsubstituted- \( \text{C}_{1-6} \) alkyl, perhaloalkyl, substituted- or unsubstituted- aryl, substituted- or unsubstituted- heteroaryl, substituted- or unsubstituted- cycloalkyl, and substituted- or unsubstituted- heterocyclyl;

\( R^{13b} \) is selected from hydrogen, substituted- or unsubstituted- \( \text{C}_{1-6} \) alkyl, perhaloalkyl, substituted- or unsubstituted- aryl, substituted- or unsubstituted- heteroaryl, substituted- or unsubstituted- cycloalkyl, and substituted- or unsubstituted- heterocyclyl;

\( R^{16} \) is selected from hydrogen or substituted- or unsubstituted alkyl group;

\( R^a \), \( R^b \), \( R^c \) and \( R^d \) are independently selected from hydrogen, halogen, substituted- or unsubstituted- \( \text{C}_{1-6} \) alkyl, substituted- or unsubstituted- aryl, substituted- or unsubstituted- heteroaryl, substituted- or unsubstituted- cycloalkyl, and substituted- or unsubstituted- heterocyclyl, or \( R^a \), \( R^b \), \( R^c \) and \( R^d \) together with the carbon atom(s) to which they are attached forming substituted- or unsubstituted- carbocycle, substituted- or unsubstituted- heterocycle;

\( m \) is an integer ranging between 0 to 2, selected independently at each occurrence;

\( n \) is an integer ranging between 0 and 2;

‘alkyl’ may be substituted with 1 to 4 substituents selected from the group consisting of halogen, oxo, \( \text{C}_{1-6} \) alkyl, haloalkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, \( R^{17a} \text{C} (=0) \text{-} \), \( R^{17a} \text{SO}_2 \text{-} \), \( R^{17b} \text{O}^- \), \( R^{17a} \text{OC} (=0) \text{-} \), \( R^{17a} \text{C} (=0) \text{O}^- \), \( (R^{17})(R^{18}) \text{NC} (=0) \text{-} \), \( (R^{17a}) \text{C} (=0) \text{N} (R^{18}) \text{-} \), \( (R^{17})(R^{18}) \text{N}^- \), \( (R^{17})(R^{18}) \text{NC} (=0) \text{N} (R^{19}) \text{-} \), and \( R^{17a} \text{SO}_2 \text{N} (R^{18}) \text{-} \);
'cycloalkyl', 'cycloalkenyl' and 'carbocycle' may be substituted with 1 to 2 substituents selected from the group consisting of halogen, oxo, C_i^2 alkyl, haloalkyl, R'^{17a}C(=0)-, R'^{17b}S0_2-, R'^{17b}OC(=0)-, R'^{17a}OC(=0)-, (R'^{17})(R'^{18})NC(=0)-, (R'^{17a})C(=0)N(R'^{18})-, (R'^{17})(R'^{18})N-, (R'^{17})(R'^{18})NC(=0)N(R'^{19})- and R'^{17a}S0_2N(R'^{18})-;

5 'aryl' may be substituted with 1 to 2 substituents selected from the group consisting of halogen, nitro, cyano, hydroxy, alkyl, perhaloalkyl, alkyl-O-, perhaloalkyl-O-, alkyl(H)N-, alkyl(alkyl)N-, H_2N-, alkyl-S0_2-, alkyl-C(=0)(H)N-, alkyl-C(=0)(alkyl )N-, alkyl(H)NC(=0)-, alkyl(alkyl)NC(=0)-, H_2NC(=0)-, alkyl(H)NS0_2-; alkyl(alkyl)NS0_2-; and H_2NS0_2-;

'heteroaryl' may be substituted with 1 to 2 substituents selected from the group consisting of halogen, nitro, cyano, hydroxy, alkyl, perhaloalkyl, alkyl-O-, perhaloalkyl-O-, alkyl-S0_2-, H_2N-, alkyl(H)N-, alkyl(alkyl)N-, alkyl-C(=0)(H)N-, alkyl-C(=0)(alkyl )N-, NH_2C(=0)-, alkyl(H)NC(=0)-, alkyl(alkyl)NC(=0)-, NH_2S0_2-, alkyl(H)NS0_2- and alkyl(alkyl)NS0_2-;

ring carbon(s) of 'heterocycle' may be substituted with 1 to 2 substituents selected from the group consisting of halogen, nitro, cyano, oxo, alkyl, R'^{17b}O-, R'^{17b}OC(=0)-, R'^{17b}C(=0)0-, R'^{17}(H)NC(=0)-, R'^{17}(alkyl)NC(=0)-, R'^{17}(H)N-, R'^{17}(alkyl)N-, R'^{17a}C(=0)(H)N-, R'^{17}(H)NC(=0)(H)N-, and R'^{17}(alkyl)NC(=0)N)-; the substituents on ring nitrogen(s) of 'heterocycle' are selected from the group consisting of alkyl, R'^{17a}S0_2-, R'^{17a}C(=0)-, R'^{17a}OC(=0)-, R'^{17}(H)NC(=0)-, and R'^{17}(alkyl)NC(=0);

R'^{17}, R'^{18} and R'^{19} are independently selected from hydrogen and alkyl;

20 R'^{17a} is selected from alkyl and perhaloalkyl;

R'^{17b} is selected from the group consisting of hydrogen, alkyl, and perhaloalkyl;

Whenever a range of the number of atoms in a structure is indicated (e.g., a C_{1-2}, Cl_{8-1}, Cl_{6}, or C_{1-4} alkyl, alkylamino, etc.), it is specifically contemplated that any sub-range or individual number of carbon atoms falling within the indicated range also can be used.

Thus, for instance, the recitation of a range of 1-8 carbon atoms (e.g., CrC_1^3), 1-6 carbon atoms (e.g., CrC_1^2), 1-4 carbon atoms (e.g., CrC_1^1), 1-3 carbon atoms (e.g., CrC_1^0), or 2-8 carbon atoms (e.g., C_2^5C_2^0) as used with respect to any chemical group (e.g., alkyl, alkylamino, etc.) referenced herein encompasses and specifically describes 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, and/or 12 carbon atoms, as appropriate, as well as any sub-range thereof.
(e.g., 1-2 carbon atoms, 1-3 carbon atoms, 1-4 carbon atoms, 1-5 carbon atoms, 1-6 carbon atoms, 1-7 carbon atoms, 1-8 carbon atoms, 1-9 carbon atoms, 1-10 carbon atoms, 1-11 carbon atoms, 1-12 carbon atoms, 2-3 carbon atoms, 2-4 carbon atoms, 2-5 carbon atoms, 2-6 carbon atoms, 2-7 carbon atoms, 2-8 carbon atoms, 2-9 carbon atoms, 2-10 carbon atoms, 2-11 carbon atoms, 2-12 carbon atoms, 3-4 carbon atoms, 3-5 carbon atoms, 3-6 carbon atoms, 3-7 carbon atoms, 3-8 carbon atoms, 3-9 carbon atoms, 3-10 carbon atoms, 3-11 carbon atoms, 3-12 carbon atoms, 4-5 carbon atoms, 4-6 carbon atoms, 4-7 carbon atoms, 4-8 carbon atoms, 4-9 carbon atoms, 4-10 carbon atoms, 4-11 carbon atoms, and/or 4-12 carbon atoms, etc., as appropriate).

One of the embodiments of the present invention is compound of formula (I) as described above, wherein, ring A is particularly selected as cyclopentane;

In any of the embodiments of the invention described above, Y is particularly selected as - N(R²)-;

In any of the embodiments of the invention described above, R¹ is particularly selected as R²OC(=0)N(R³)CR⁴(R⁵)C(=0)N(R⁶)-;

In any of the embodiments of the invention described above, m is particularly selected as 0 at all the occurrences;

In any of the embodiments of the invention described above, R² is particularly selected as R²OC(=0)N(R³)CR⁴(R⁵)C(=0)-;

In any of the embodiments of the invention described above, R³ is particularly selected from NH and O;

In any of the embodiments of the invention described above, n is particularly selected as 0;

In any of the embodiments of the invention described above, R⁵ and R⁶ are independently selected from hydrogen and halogen, or R⁵ and R⁶ together with the carbon atoms to which they are attached form a six membered carbocycle;

In any of the embodiments of the invention described above, R⁷ and R¹⁰ are particularly selected as hydrogen, or R⁷ and R¹⁰ together with the carbon atoms to which they are
attached form a five or six membered carbocycle, the said carbocycle is unsubstituted or substituted with one or two alkyl groups;

In any of the embodiments of the invention described above, R⁵ and R⁸ are particularly selected as hydrogen, or R⁵ and R⁸ together with the carbon atoms to which they are attached form a six or seven membered carbocycle, or R⁹ and R⁸ together with the carbon atoms to which they are attached form a seven membered heterocycle containing one heteroatom;

In any of the embodiments of the invention described above, R¹¹ and R¹² are particularly selected as hydrogen;

In any of the embodiments of the invention described above, ring D is particularly selected as

\[
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\end{align*}
\]

In any of the embodiments of the invention described above, ring A is particularly selected as cyclopentane, ring D is particularly selected as

\[
\begin{align*}
\text{\includegraphics[width=0.2\textwidth]{image.png}}
\end{align*}
\]

R¹ is particularly selected as R¹³OC(=0)N(R¹⁴)CR¹⁰(R¹⁰)C(=0)N(R¹⁵)⁻, m is particularly selected as 0 at all the occurrences, R³ is particularly selected from NH and O, n is particularly selected as 0, R⁵ and R⁶ are independently selected from hydrogen and halogen, or R⁵ and R⁶ together with the carbon atoms to which they are attached form a six membered carbocycle, R⁷ and R¹⁰ are particularly selected as hydrogen, or R⁷ and R¹⁰ together with the carbon atoms to which they are attached form a five or six membered carbocycle, the said carbocycle is unsubstituted or substituted with one or two alkyl groups, R⁹ and R⁸ are particularly selected as hydrogen, or R⁹ and R⁸ together with the carbon atoms to which they are attached form a six or seven membered carbocycle, or R⁹ and R⁸ together with the carbon atoms to which they are attached form a seven membered heterocycle containing one heteroatom, R¹¹ and R¹² are particularly selected as hydrogen, such that at least one cyclic system is formed out of either R⁵ and R⁶, R⁸ and R⁹, or R⁷ and R¹⁰;
General terms used in formula can be defined as follows; however, the meaning stated should not be interpreted as limiting the scope of the term per se.

The term "alkyl", as used herein, means a straight chain or branched hydrocarbon containing from 1 to 20 carbon atoms. Preferably the alkyl chain may contain 1 to 10 carbon atoms. More preferably alkyl chain may contain up to 6 carbon atoms. Representative examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl, iso-butyl, tert-butyl, n-pentyl, isopentyl, neopentyl, and n-hexyl.

'Alkyl' as defined hereinabove may be substituted with one or more substituents selected independently from the group comprising of halogen, oxo, C_{1-6} alkyl, haloalkyl, aryl, heteroaryl, cycloalkyi, heterocyclyl, R^{17a}C(=0)-, R^{17a}SO_2^-, R^{17b}O-, R^{17a}OC(=0)-, R^{17a}C(=0)O-, (R^{17})(R^{18})NC(=0)-, (R^{17a})C(=0)N(R^{18})-, (R^{17})(R^{18})N-, (R^{17})(R^{18})NC(=0)N(R^{19})-, and R^{17a}SO_2 N(R^{18})-; wherein, R^{17}, R^{18} and R^{19} are independently selected from hydrogen and alkyl, R^{17a} is selected from alkyl and perhaloalkyl, R^{17b} is selected from the group consisting of hydrogen, alkyl, and perhaloalkyl.

The term "haloalkyl" used herein means an alkyl group as defined hereinabove wherein at least one of the hydrogen atoms of the said alkyl group is substituted with halogen. The haloalkyl group is exemplified by monofluoromethyl, 1,2-dichloroethyl and the like. The term "perhaloalkyl" means an alkyl group as defined hereinabove wherein all the hydrogen atoms of the said alkyl group are substituted with halogen. The perhaloalkyl group is exemplified by trifluoromethyl, pentafluoroethyl and the like.

The term "cycloalkyi" as used herein, means a monocyclic, bicyclic, or tricyclic non-aromatic ring system containing from 3 to 14 carbon atoms, preferably monocyclic cycloalkyi ring containing 3 to 6 carbon atoms. Examples of monocyclic ring systems include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl. Bicyclic ring systems are also exemplified by a bridged monocyclic ring system in which two non-adjacent carbon atoms of the monocyclic ring are linked by an alkyylene bridge. Representative examples of bicyclic ring systems include, but are not limited to,
bicyclo[3.1.1]heptane, bicyclo[2.2.1]heptane, bicyclo[2.2.2]octane, bicyclo[3.2.2]nonane, bicyclo[3.3.1]nonane, and bicyclo[4.2.1]nonane, bicyclo[3.3.2]decane, bicyclo[3.1.0]hexane, bicyclo[410]heptane, bicyclo[3.2.0]heptanes, octahydro-1 H-indene. Tricyclic ring systems are also exemplified by a bicyclic ring system in which two non-adjacent carbon atoms of the bicyclic ring are linked by a bond or an alkylene bridge. Representative examples of tricyclic-ring systems include, but are not limited to, tricyclo[3.3.1.0^3.7]nonane and tricyclo[3.3.1.0^3.7]decane (adamantane). The term cycloalkyl also include spiro systems wherein one of the ring is annulated on a single carbon atom such ring systems are exemplified by spiro[2.5]octane, spiro[4.5]decane, spiro[bicyclo[4.1.0]heptane-2,1'-cyclopentane], hexahydro-2'H-spiro[cyclopropane-1,1'-pentalen].

The term "cycloalkenyl" as used herein, means a cycloalkyl group as defined above containing at least one double bond.

The term "carbocycle" as used herein, means a cyclic system made up of carbon atoms, which includes cycloalkyl, cycloalkenyl and aryl.

Cycloalkyl, cycloalkenyl and carbocycle as defined hereinabove may be substituted with one or more substituents selected independently from the group comprising of halogen, oxo, C1-6 alkyl, haloalkyl, R^{17a}C(=0)-, R^{17a}SO_2-, R^{17b}O-, R^{17a}OC(=0)-, R^{17a}C(=0)O-, (R^{17})(R^{18})NC(=0)-, (R^{17a})C(=0)N(R^{18})-, (R^{17})(R^{18})N-, (R^{17})(R^{18})NC(=0)N(R^{19})-, and R^{17a}SO_2N(R^{18})-; wherein, R^{17}, R^{18} and R^{19} are independently selected from hydrogen and alkyl, R^{17a} is selected from alkyl and perhaloalkyl, R^{17b} is selected from the group consisting of hydrogen, alkyl, and perhaloalkyl.

The term "aryl" refers to a monovalent monocyclic, bicyclic or tricyclic aromatic hydrocarbon ring system. Examples of aryl groups include phenyl, naphthyl, anthracenyl, fluorenyl, indenyl, azulenyl, and the like. Aryl group also include partially saturated bicyclic and tricyclic aromatic hydrocarbons such as tetrahydro-naphthalene. The said aryl group also includes aryl rings fused with heteroaryl or heterocyclic rings such as 2,3-dihydrobenzo[1,4]dioxin-6-yl, 2,3-dihydro-benzo[1,4]dioxin-5-yl, 2,3-dihydro-benzofuran-5-yl, 2,3-dihydro-benzofuran-4-yl, 2,3-dihydro-benzofuran-6-yl, 2,3-dihydro-benzofuran-6-yl, 2,3-
dihydro-1 H-indol-5-yl, 2,3-dihydro-1 H-indol-4-yl, 2,3-dihydro-1 H-indol-6-yl, 2,3-dihydro-1 H-indol-7-yl, benzo[1,3]dioxol-4-yl, benzo[1,3]dioxol-5-yl, 1,2,3,4-tetrahydroquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, 2,3-dihydrobenzothien-4-yl, 2-oxoindolin-5-yl.

Aryl as defined hereinabove may be substituted with one or more substituents selected independently from the group consisting of halogen, nitro, cyano, hydroxy, alkyl, perhaloalkyl, alkyl-O-, perhaloalkyl-O-, alkyl(H)N-, alkyl(alkyl)N-, H₂N-, alkyl-S0₂-, alkyl-C(=0)(H)N-, alkyl-C(=0)(alkyl)N-, alkyl(H)NC(=0)-, alkyl(alkyl)NC(=0)-, H₂NC(=0)-, alkyl(H)NS0₂-, alkyl(alkyl)NS0₂-, and H₂NS0₂-.

The term "heteroaryl" refers to a 5-14 membered monocyclic, bicyclic, or tricyclic ring system having 1-4 ring heteroatoms selected from O, N, or S, and the remainder ring atoms being carbon (with appropriate hydrogen atoms unless otherwise indicated), wherein at least one ring in the ring system is aromatic. Heteroaryl groups may be optionally substituted with one or more substituents. In one embodiment, 0, 1, 2, 3, or 4 atoms of each ring of a heteroaryl group may be substituted by a substituent. Examples of heteroaryl groups include pyridyl, 1-oxo-pyridyl, furanyi, thiényl, pyrrolyl, oxazolyl, oxadiazolyl, imidazolyl, thiazolyl, isoxazolyl, quinolinyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, triazolyl, thiadiazolyl, isoquinolinyl, benzoxazolyl, benzofuranyl, indolizinyi, imidazopyridyl, tetrazolyl, benzimidazolyl, benzoazolyl, benzothiadiazolyl, benzoxadiazolyl, indolyl. azindolyl, imidazopyridyl. quinazolinyl, purinyl, pyrrolo[2,3]pyrimidinyi, pyrazino[3,4]pyrimidinyi, and benzo(b)thienyl, 2,3-thiadiazolyl, 1H-pyrazoio[5,1-c]-1,2,4-triazolyl, pyrrolo[3,4-d]-1,2,3-triazolylLCyclopentauriazolylL 3H-pyrroio[3,4-c] isoxazolyl and the like.

Heteroaryl as defined hereinabove may be substituted with one or more substituents selected independently from the group consisting of halogen, nitro, cyano, hydroxy, alkyl, perhaloalkyl, alkyl-O-, perhaloalkyl-O-, alkyl-S0₂-, H₂N-, alkyl(H)N-, alkyl(alkyl)N-, alkyl-C(=0)(H)N-, alkyl-C(=0)(alkyl)N-, NH₂C(=0)-, alkyl(H)NC(=0)-, alkyl(alkyl)NC(=0)-, NH₂S0₂-, alkyl(H)NS0₂-, and alkyl(alkyl)NS0₂-.

The term "heterocycle" or "heterocyclic" as used herein, means a 'cycloalkyl' group wherein one or more of the carbon atoms replaced by -0-, -S-, -S(0₂)-, -S(O)-, -N(Rᵐ)-,
Si(R\textsuperscript{m})R\textsuperscript{n}, where R\textsuperscript{m} and R\textsuperscript{n} are independently selected from hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, and heterocyclyl. The heterocycle may be connected to the parent molecular moiety through any carbon atom or any nitrogen atom contained within the heterocycle. Representative examples of monocyclic heterocycle include, but are not limited to, azetidinyl, azepanyl, aziridinyl, diazepanyl, 1,3-dioxanyl, 1,3-dioxolanly, 1,3-dithiolanyl, 1,3-dithianyl, imidazolinyl, imidazolidinyl, isothiazolinyl, isothiazolidinyl, isoxazolinyl, isoxazolidinyl, morpholinyl, oxadiazolinyl, oxadiazolidinyl, oxazolinyl, oxazolidinyl, piperazinyl, piperidinyl, pyranyl, pyrazolinyl, pyrazolidinyl, pyrrolinyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydrothienyl, thiadiazolinyl, thiadiazolidinyl, thiazolinyl, thiazolidinyl, thiomorpholinyl, 1,1-dioxidothiomorpholinyl (thiomorpholine sulfone).

The tetrahydroquinolinyl, thiazolidinyl, selected pyrrolidinyl,

Heterocyclyl group may be substituted on ring carbons with one or more substituents selected independently from the group consisting of halogen, nitro, cyano, oxo, alkyl, R\textsuperscript{17b}O=, R\textsuperscript{17a}OC(=0)-, R\textsuperscript{17a}C(=0)=O-, R\textsuperscript{17}(H)NC(=0)-, R\textsuperscript{17}(alkyl)NC(=0)-, R\textsuperscript{17}(H)N-, R\textsuperscript{17}(alkyl)N-, R\textsuperscript{17a}C(=0)(H)N-, R\textsuperscript{17}(H)NC(=0)(H)N-, and R\textsuperscript{17}(alkyl)NC(=0)(H)N-; wherein, R\textsuperscript{17} is selected from hydrogen and alkyl, R\textsuperscript{17a} is selected from alkyl and perhaloalkyl, R\textsuperscript{17b} is selected from the group consisting of hydrogen, alkyl, and perhaloalkyl.

Heterocyclyl group may further be substituted on ring nitrogen(s) with substituents selected from the group comprising of alkyl, R\textsuperscript{17a}SO\textsuperscript{2-}, R\textsuperscript{17a}C(=0)-, R\textsuperscript{17a}OC(=0)-, R\textsuperscript{17}(H)NC(=0)-, and R\textsuperscript{17}(alkyl)NC(=0)-; wherein, R\textsuperscript{17} is selected from hydrogen and alkyl, R\textsuperscript{17a} is selected from alkyl and perhaloalkyl.

The term ‘oxo’ means a divalent oxygen (=0) attached to the parent group. For example oxo attached to carbon forms a carbonyl, oxo substituted on cyclohexane forms a cyclohexanone, and the like.
The term 'annulated' means the ring system under consideration is either annulated with another ring at a carbon atom of the cyclic system or across a bond of the cyclic system as in the case of fused or spiro ring systems.

The term 'bridged' means the ring system under consideration contain an alkylene bridge having 1 to 4 methylene units joining two non adjacent ring atoms.

A compound its stereoisomers, racemates, pharmaceutically acceptable salt thereof as described hereinabove wherein the compound of general formula I is selected from:

1. methyl ((2S)-1-(((2-(5-(4-(2-(((S)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-2-yl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

2. methyl ((2S)-1-(((2-(5-(4-(2-(((S)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-2-yl)pyrrolidin-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

3. methyl ((2S)-1-(((2-(5-(4-(2-(((S)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-2-yl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

4. methyl ((S)-1-(((1 R,2S)-2-(5-(4-(2-(((S)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methylbutanoyl)pyrrolidin-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

5. methyl ((S)-1-(((1 R,2S)-2-(5-(4-(2-(((S)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methylbutanoyl)pyrrolidin-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

6. methyl ((S)-1-(((1 R,2S)-2-(5-(4-(2-(((S)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-benzo[2,3]oxepino[4,5-d]imidazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

7. methyl ((S)-1-(((1S,2R)-2-(5-(4-((2-(((S)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-benzo[2,3]oxepino[4,5-d]imidazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.
8. methyl (((S)-1-(((1S,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)pyrrolidin-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

9. methyl (((S)-1-(((1S,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)pyrrolidin-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

10. methyl (((S)-1-(((1S,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

11. methyl (((S)-1-(((1S,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

12. methyl (((S)-1-(((1R,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

13. methyl (((S)-1-(((1R,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

14. methyl (((S)-1-(((1R,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

15. methyl (((S)-1-(((1S,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.
16. methyl ((S)-1 -(((1 R,2R)-2-(5-(4-(2-((S)-1 -((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1 H-naphtho[1 ,2-d]imidazol-7-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

17. methyl ((S)-1 -(((1 S,2R)-2-(5-(4-(2-((S)-1 -((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1 H-naphtho[1 ,2-d]imidazol-7-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

18. methyl ((S)-1 -(((1 S,2S)-2-(5-(4-(2-((S)-1 -((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1 H-naphtho[1 ,2-d]imidazol-7-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

19. methyl ((S)-1 -(((1 S,2R)-2-(5-(4-(2-((S)-1 -((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4-chloro-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

20. methyl ((S)-1 -(((1 S,2S)-2-(5-(4-(2-((S)-1 -((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4-chloro-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.


22. methyl ((S)-1 -(((1 S,2S)-2-(5-(4-(2-((S)-1 -((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydrobenzo[2,3]oxepino[4,5-d]oxazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

23. methyl ((S)-1 -(((1 R,2S)-2-(5-(4-(2-((S)-1 -((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydrobenzo[2,3]oxepino[4,5-d]oxazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

24. methyl ((S)-1 -(((1 S,2S)-2-(7-(4-(2-((S)-1 -((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1 H-naphtho[1 ,2-d]imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

25. methyl ((S)-1 -(((1 S,2R)-2-(7-(4-(2-((S)-1 -((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1 H-naphtho[1 ,2-d]imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.
naphtho[1,2-d]imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

26. methyl ((S)-1-(((1S,2R)-2-(7-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-5-yl)phenyl)-1H-naphtho[1,2-d]imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

27. methyl ((S)-1-(((1S,2S)-2-(7-(4-(2-((S)-1-((S)-2-amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-5-yl)phenyl)-1H-naphtho[1,2-d]imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

28. methyl ((S)-1-(((1S,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)(ethyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

29. methyl ((S)-1-(((1S,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)(methyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

30. methyl ((S)-1-(((1S,2S)-2-(5-(7-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-5-yl)-9H-fluoren-2-yl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

According to a feature of the present invention, the compounds of general formula I where all the symbols are as defined earlier, can be prepared by methods given in Schemes given below or example. Representative procedures are shown below, however; the disclosure should not be construed to limit the scope of the invention arriving at compound of formula I as disclosed hereinabove.

Scheme 1: Halogenation of synthon 1 (could be prepared by methods well known in the art, Tetrahedron, 2000, 56, 5225-5240) may be achieved leading to the formation of 2 which could be coupled to the protected (P = Boc, Cbz) β-aminocyclopentane carboxylic acid 3 (individual isomers RR, SS, RS and SR could be made by methods known in the
literature, Tet. Lett., 2002, 43, 5401-5404; J. Am. Chem. Soc, 1999, 121, 7574-7581; Tet. Asymm., 2008, 19, 2796-2803) using an appropriate base like triethylamine, 4-methylmorpholine, diisopropylethyamine and solvents like DMF, 1,4-dioxane, THF, acetonitrile to yield 4. Cyclization of 4 using NH₄OAc could lead to the formation of 5 which may be deprotected and coupled with (S)-2-((methoxycarbonyl)amino)-3-methylbutanoic acid using amide coupling reagents like carbodiimides, phosphonium salts, uronium salts, carbonyldiimidazole in presence of a mild base like triethylamine, 4-methylmorpholine, diisopropylethyamine in a solvent like DMF, 1,4-dioxane, THF, dichloromethane leading to the formation of 6. Alternatively, de-protected form of 5 can be coupled to similar moieties by methods known in the literature to furnish compounds of formula I.

![Scheme 1](image)

**Scheme 1:**

**Scheme 2:** Reduction of 7, could be prepared by methods known in the literature, using either of Pd/C, Pt0₂ or Raney Ni, Fe/HCl, tin(II) chloride, titanium(III) chloride or zinc/AcOH could lead to the formation of 8. Diazotization followed by Sandmeyer reaction of 8 might lead to the formation of 9 which on acidic/basic hydrolysis might result in formation of 10. One carbon homologation followed by halogenations might lead to formation of 11 from 10. Intermediate 11 could further be O-alkylated with 3 in presence of a suitable base and solvent and cyclized using NH₄OAc to yield 13. Pd-catalyzed C-C coupling of 13 with 14 (ref WO2009102318 A1) might lead to the formation of 15 which on de-protection and
coupling with (S)-2-((methoxycarbonyl)amino)-3-methylbutanoic acid or similar moieties might lead to the synthesis of 16 or compounds of formula I.

Scheme 2: Diazotization followed by Sandmeyer reaction on synthon 17 may lead to the formation of 18. Synthesis of 19 may be accomplished by halogenation of 18 with suitable halogenating agents. O-alkylation of 19 with Boc-L-proline using an appropriate base like triethylamine, 4-methylmorpholine, diisopropylethylamine and solvent like DMF, 1,4-dioxane, THF, acetonitrile might lead to the formation of 20. Cyclization of intermediate 20 with NH₄OAc might lead to the formation of tricyclic system 21. Synthon 25 might be synthesized from 22 wherein 22 could be O-alkylated with 3 followed by cyclization using NH₄OAc and finally generation of boronate/boronic acid via Pd-catalysis. Synthons 21 and 25 could be linked through C-C coupling method using Pd catalysts to obtain 26. Synthesis of the compound 27 or compounds of formula I may be accomplished by de-protection of 26 and coupling the de-protected amine to (S)-2-((methoxycarbonyl)amino)-3-methylbutanoic acid or similar moieties using a suitable combination of coupling reagents, bases and solvents.
Scheme 3: In another process, Wittig reaction on m-halo substituted benzaldehyde using the appropriate base and solvent might lead to the formation of which on reduction with Pt-based reagents amongst others may lead to the formation of acid which under acidic conditions may lead to the formation of . Alternatively, could also be synthesized from the phenol which on alkylation might lead to the formation of which on acidic/basic hydrolysis could lead to the formation of the acid . Cyclization of under acidic conditions might lead to the formation of . (J. Med. Chem., 2000, 43, 2049-2063; ibid, 2005, 48, 7351-7362; WO2009102633 A1). On treatment with isoamyl nitrite in an appropriate solvent, oxime might be generated from which upon reaction with Boc-L-prolinal under basic conditions may lead to formation of . Treatment of with triethyl phosphite might lead to the formation of either or . Pd-catalyzed C-C coupling of either or with followed by de-protection and coupling with (S)-2-((methoxycarbonyl)amino)-3-methylbutanoic acid might lead to the formation of or .

Symmetrical compounds could be prepared by coupling (generated from ) with the boronate/boronic acid of through the use of Pd catalyzed C-C coupling reactions to yield or compounds of formula I.
Scheme 5: Acetophenone 45, which is readily available or prepared from suitable reagents, could be protected with a suitable protecting group to get 46 which could be then halogenated and O-alkylated to possibly yield 48. Cyclization of 48 might be accomplished using ammonium acetate to yield 49 which upon de-protection of benzylic hydroxyl group...
followed by alkylation under basic conditions with either synthon 37 or 38 might lead to the synthesis of 50. De-protection of 50 under acidic conditions and sequential coupling with (S)-2-((methoxycarbonyl)amino)-3-methylbutanoic acid or similar moieties might lead to the formation of 51 or compounds of formula I.
Compounds of the present invention were prepared using synthetic schemes provided below:

Compounds 1 to 3 were prepared by following the route provided in Scheme I.
Compounds 4 to 15 were prepared by following the route provided in Scheme II

Compounds 16 to 20 were prepared by following the route provided in Scheme III
Compounds 21 to 23 were prepared by following the route provided in Scheme IV.

Compounds 24 to 27 were prepared by following the route provided in Scheme V.
Compounds 28 and 29 were prepared by following the route provided in Scheme VI.
Compounds 30 to 32 were prepared by following the route provided in Scheme VII

Scheme VII

A further embodiment of the present invention includes pharmaceutical compositions comprising any single compound, a combination of two or more compounds delineated herein, or a pharmaceutically acceptable salt thereof, with a pharmaceutically acceptable carrier or excipient.

Yet a further embodiment of the present invention is a pharmaceutical composition comprising any single compound or a combination of two or more compounds delineated herein, or a pharmaceutically acceptable salt thereof, in combination with one or more agents known in the art, with a pharmaceutically acceptable carrier or excipient.

It will be further appreciated that compounds of the present invention can be administered as the sole active pharmaceutical agent, or used in combination with one or more agents...
to treat or prevent hepatitis C infections or the symptoms associated with HCV infection. Other agents to be administered in combination with a compound or combination of compounds of the present invention include therapies for diseases caused by HCV infection that suppresses HCV viral replication by direct or indirect mechanisms. These agents include, but not limited to, host immune modulators (for example, interferon-alpha, pegylated interferon-alpha, consensus interferon, interferon-beta, interferon-gamma, CpG oligonucleotides and the like); antiviral compounds that inhibit host cellular functions such as inosine monophosphate dehydrogenase (for example, ribavirin and the like); cytokines that modulate immune function (for example, interleukin 2, interleukin 6, and interleukin 12); a compound that enhances the development of type 1 helper T cell response; interfering RNA; anti-sense RNA; vaccines comprising HCV antigens or antigen adjuvant combinations directed against HCV; agents that interact with host cellular components to block viral protein synthesis by inhibiting the internal ribosome entry site (IRES) initiated translation step of HCV viral replication or to block viral particle maturation and release with agents targeted toward the viroporin family of membrane proteins such as, for example, HCV P7 and the like; and any agent or combination of agents that inhibit the replication of HCV by targeting other proteins of the viral genome involved in the viral replication and/or interfere with the function of other viral targets, such as inhibitors of NS3/NS4A protease, NS3 helicase, NS5B polymerase, NS4A protein and NS5A protein.

According to yet another embodiment, the pharmaceutical compositions of the present invention may further comprise inhibitor(s) of other targets in the HCV life cycle, including, but not limited to, helicase, polymerase, metalloprotease, NS4A protein, NS5A protein, and internal ribosome entry site (IRES).

Accordingly, one embodiment of the present invention is directed to a method for treating or preventing an infection caused by an RNA-containing virus comprising co-administering to a patient in need of such treatment one or more agents selected from the group consisting of a host immune modulator and a second or more antiviral agents, or a combination thereof, with a therapeutically effective amount of a compound or combination of compounds of the present invention, or a pharmaceutically acceptable salt thereof.

Examples of the host immune modulator are, but not limited to, interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine, and a vaccine comprising an antigen and an adjuvant, and said second antiviral agent inhibits
replication of HCV either by inhibiting host cellular functions associated with viral replication or by targeting proteins of the viral genome. Example of the RNA-containing virus includes, but not limited to, hepatitis C virus (HCV).

A further embodiment of the present invention is directed to a method of treating or preventing infection caused by an RNA-containing virus comprising co-administering to a patient in need of such treatment an agent or combination of agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of the liver, with a therapeutically effective amount of a compound or combination of compounds of the present invention, or a pharmaceutically acceptable salt thereof. Example of the RNA-containing virus includes, but not limited to, hepatitis C virus (HCV).

Yet another embodiment of the present invention provides a method of treating or preventing infection caused by an RNA-containing virus comprising co-administering to a patient in need of such treatment one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, with a therapeutically effective amount of a compound or a combination of compounds of the present invention, or a pharmaceutically acceptable salt thereof. An agent that treats patients for disease caused by hepatitis B (HBV) infection may be for example, but not limited thereto, L-deoxythymidine, adefovir, lamivudine or tenofovir, or any combination thereof. Example of the RNA-containing virus includes, but not limited to, hepatitis C virus (HCV).

A further embodiment of the present invention provides a method of treating or preventing infection caused by an RNA-containing virus comprising co-administering to a patient in need of such treatment one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, with a therapeutically effective amount of a compound or a combination of compounds of the present invention, or a pharmaceutically acceptable salt thereof. The agent that treats patients for disease caused by human immunodeficiency virus (HIV) infection may include, but is not limited thereto, ritonavir, lopinavir, indinavir, nelfmavir, saquinavir, amprenavir, atazanavir, tipranavir, TMC-114, fosamprenavir, zidovudine, lamivudine, didanosine, stavudine, tenofovir, zalcitabine, abacavir, efavirenz, nevirapine, delavirdine, TMC-125, L-870812, S-1 360, enfuvirtide (T-20) or T-1249, or any combination thereof. Example of the RNA-containing virus includes, but not limited to, hepatitis C virus (HCV).
It can occur that a patient may be co-infected with hepatitis C virus and one or more other viruses, including but not limited to human immunodeficiency virus (HIV), hepatitis A virus (HAV) and hepatitis B virus (HBV). Thus also contemplated is combination therapy to treat such co-infections by co-administering a compound according to the present invention with at least one of an HIV inhibitor, an HAV inhibitor and an HBV inhibitor.

In addition, the present invention provides the use of a compound or a combination of compounds of the invention, or a therapeutically acceptable salt thereof, and one or more agents selected from the group consisting of a host immune modulator and a second or more antiviral agents, or a combination thereof, to prepare a medicament for the treatment of an infection caused by an RNA-containing virus in a patient, particularly hepatitis C virus. Examples of the host immune modulators include, but are not limited to, interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine, and a vaccine comprising an antigen and an adjuvant, and said second antiviral agent inhibits replication of HCV either by inhibiting host cellular functions associated with viral replication or by targeting proteins of the viral genome.

When used in the above or other treatments, combination of compound or compounds of the present invention, together with one or more agents as defined herein above, can be employed in pure form or, where such forms exist, in pharmaceutically acceptable salt thereof. Alternatively, such combination of therapeutic agents can be administered as a pharmaceutical composition containing a therapeutically effective amount of the compound or combination of compounds of interest, or their pharmaceutically acceptable salt thereof, in combination with one or more agents as defined herein above, and a pharmaceutically acceptable carrier. Such pharmaceutical compositions can be used for inhibiting the replication of an RNA-containing virus, particularly Hepatitis C virus (HCV), by contacting said virus with said pharmaceutical composition. In addition, such compositions are useful for the treatment or prevention of an infection caused by an RNA-containing virus, particularly Hepatitis C virus (HCV).

Hence, a still further embodiment of the invention is directed to a method of treating or preventing infection caused by an RNA-containing virus, particularly a hepatitis C virus (HCV), comprising administering to a patient in need of such treatment a pharmaceutical composition comprising a compound or combination of compounds of the invention or a
pharmaceutically acceptable salt thereof, and one or more agents as defined hereinabove, with a pharmaceutically acceptable carrier.

When administered as a combination, the therapeutic agents can be formulated as separate compositions which are given at the same time or within a predetermined period of time, or the therapeutic agents can be given as a single unit dosage form.

Antiviral agents contemplated for use in such combination therapy include agents (compounds or biologicals) that are effective to inhibit the formation and/or replication of a virus in a mammal, including but not limited to agents that interfere with either host or viral mechanisms necessary for the formation and/or replication of a virus in a mammal. Such agents can be selected from another anti-HCV agent; an HIV inhibitor; an HAV inhibitor; and an HBV inhibitor.

Other agents to be administered in combination with a compound of the present invention include a cytochrome P450 monooxygenase inhibitor, which is expected to inhibit metabolism of the compounds of the invention. Therefore, the cytochrome P450 monooxygenase inhibitor would be in an amount effective to inhibit metabolism of the compounds of the present invention. Accordingly, the CYP inhibitor is administered in an amount such that the bioavailability of the compounds of the present invention is increased in comparison to the bioavailability in the absence of the CYP inhibitor.

The term ‘room temperature’ used in the specification denotes any temperature ranging between about 20 °C to about 40 °C, except and otherwise it is specifically mentioned in the specification.

The intermediates and the compounds of the present invention may obtained in pure form in a manner known per se, for example, by distilling off the solvent in vacuum and recrystallizing the residue obtained from a suitable solvent, such as pentane, diethyl ether, isopropyl ether, chloroform, dichloromethane, ethyl acetate, acetone or their combinations or subjecting it to one of the purification methods, such as column chromatography (e.g., flash chromatography) on a suitable support material such as alumina or silica gel using eluent such as dichloromethane, ethyl acetate, hexane, methanol, acetone and their
combinations. Preparative LC-MS method is also used for the purification of molecules described herein.

Salts of compound of formula I can be obtained by dissolving the compound in a suitable solvent, for example in a chlorinated hydrocarbon, such as methyl chloride or chloroform or a low molecular weight aliphatic alcohol, for example, ethanol or isopropanol, which was then treated with the desired acid or base as described in Berge S.M. et al. "Pharmaceutical Salts, a review article in Journal of Pharmaceutical sciences volume 66, page 1-19 (1977)" and in handbook of pharmaceutical salts properties, selection, and use by P.H.Einrich Stahland Camille G.wermuth, Wiley- VCH (2002). Lists of suitable salts can also be found in Remington's Pharmaceutical Sciences, 18th ed., Mack Publishing Company, Easton, PA, 1990, p. 1445, and Journal of Pharmaceutical Science, 66, 2-19 (1977). For example, they can be a salt of an alkali metal (e.g., sodium or potassium), alkaline earth metal (e.g., calcium), or ammonium of salt.

The compound of the invention or a composition thereof can potentially be administered as a pharmaceutically acceptable acid-addition, base neutralized or addition salt, formed by reaction with inorganic acids, such as hydrochloric acid, hydrobromic acid, perchloric acid, nitric acid, thiocyanic acid, sulfuric acid, and phosphoric acid, and organic acids such as formic acid, acetic acid, propionic acid, glycolic acid, lactic acid, pyruvic acid, oxalic acid, malonic acid, succinic acid, maleic acid, and fumaric acid, or by reaction with an inorganic base, such as sodium hydroxide, potassium hydroxide. The conversion to a salt is accomplished by treatment of the base compound with at least a stoichiometric amount of an appropriate acid. Typically, the free base is dissolved in an inert organic solvent such as diethyl ether, ethyl acetate, chloroform, ethanol, methanol, and the like, and the acid is added in a similar solvent. The mixture is maintained at a suitable temperature (e.g., between 0 °C and 50 °C). The resulting salt precipitates spontaneously or can be brought out of solution with a less polar solvent.

The stereoisomers of the compounds of formula I of the present invention may be prepared by stereospecific syntheses or resolution of the achiral compound using an optically active amine, acid or complex forming agent, and separating the diastereomeric salt/complex by fractional crystallization or by column chromatography.
The term "prodrug" denotes a derivative of a compound, which derivative, when administered to warm-blooded animals, e.g. humans, is converted into the compound (drug). The enzymatic and/or chemical hydrolytic cleavage of the compounds of the present invention occurs in such a manner that the proven drug form (parent carboxylic acid drug) is released, and the moiety or moieties split off remain nontoxic or are metabolized so that nontoxic metabolic products are produced. For example, a carboxylic acid group can be esterified, e.g., with a methyl group or ethyl group to yield an ester. When an ester is administered to a subject, the ester is cleaved, enzymatically or non-enzymatically, reductively, oxidatively, or hydrolytically, to reveal the anionic group. An anionic group can be esterified with moieties (e.g., acyloxyethyl esters) which are cleaved to reveal an intermediate compound which subsequently decomposes to yield the active compound.

The prodrugs can be prepared in situ during the isolation and purification of the compounds, or by separately reacting the purified compound with a suitable derivatizing agent. For example, hydroxy groups can be converted into esters via treatment with a carboxylic acid in the presence of a catalyst. Examples of cleavable alcohol prodrug moieties include substituted or unsubstituted, branched or unbranched lower alkyl ester moieties, e.g., ethyl esters, di-lower alkylamino lower-alkyl esters, e.g., dimethylaminoethyl ester, acylamino lower alkyl esters, acyloxy lower alkyl esters (e.g., pivaloyloxyethyl ester), aryl esters, e.g., phenyl ester, aryl-lower alkyl esters, e.g., benzyl ester, optionally substituted, e.g., with methyl, halo, or methoxy substituents aryl and aryl-lower alkyl esters, amides, lower-alkyl amides, di-lower alkyl amides, and hydroxy amides.

Thus the present invention further provides a pharmaceutical composition, containing the compounds of the general formula (I) as defined above, its tautomeric forms, its stereoisomers, its analogues, its prodrugs, its isotopically substituted analogues, its metabolites, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates and its co-crystals in combination with the usual pharmaceutically acceptable carriers, diluents and the like.

The pharmaceutically acceptable carrier (or excipient) is preferably one that is chemically inert to the compound of the invention and one that has no detrimental side effects or
toxicity under the conditions of use. Such pharmaceutically acceptable carriers preferably include saline (e.g., 0.9% saline), Cremophor EL (which is a derivative of castor oil and ethylene oxide available from Sigma Chemical Co., St. Louis, MO) (e.g., 5% Cremophor EL/5% ethanol/90% saline, 10% Cremophor EL/90% saline, or 50% Cremophor EL/50% ethanol), propylene glycol (e.g., 40% propylene glycol/10% ethanol/50% water), polyethylene glycol (e.g., 40% PEG 400/60% saline), and alcohol (e.g., 40% ethanol/60% water). A preferred pharmaceutical carrier is polyethylene glycol, such as PEG 400, and particularly a composition comprising 40% PEG 400 and 60% water or saline. The choice of carrier will be determined in part by the particular compound chosen, as well as by the particular method used to administer the composition. Accordingly, there is a wide variety of suitable formulations of the pharmaceutical composition of the present invention.

The following formulations for oral, aerosol, parenteral, subcutaneous, intravenous, intraarterial, intramuscular, interperitoneal, rectal, and vaginal administration are merely exemplary and are in no way limiting.

The pharmaceutical compositions can be administered parenterally, e.g., intravenously, intraarterially, subcutaneously, intradermal^, intrathecal^, or intramuscularly. Thus, the invention provides compositions for parenteral administration that comprise a solution of the compound of the invention dissolved or suspended in an acceptable carrier suitable for parenteral administration, including aqueous and non-aqueous, isotonic sterile injection solutions.

Overall, the requirements for effective pharmaceutical carriers for parenteral compositions are well known to those of ordinary skill in the art. See *Pharmaceutics and Pharmacy Practice*, J.B. Lippincott Company, Philadelphia, PA, Banker and Chalmers, eds., pages 238-250 (1982), and *ASHP Handbook on Injectable Drugs*, Toissel, 4th ed., pages 622-630 (1986). Such compositions include solutions containing anti-oxidants, buffers, bacteriostats, and solutes that render the formulation isotonic with the blood of the intended recipient, and aqueous and non-aqueous sterile suspensions that can include suspending agents, solubilizers, thickening agents, stabilizers, and preservatives. The compound can be administered in a physiologically acceptable diluent in a pharmaceutical carrier, such as a sterile liquid or mixture of liquids, including water, saline, aqueous...
dextrose and related sugar solutions, an alcohol, such as ethanol, isopropanol (for example in topical applications), or hexadecyl alcohol, glycols, such as propylene glycol or polyethylene glycol, dimethylsulfoxide, glycerol ketals, such as 2,2-dimethyl-1,3-dioxolane-4-methanol, ethers, such as poly(ethylene glycol) 400, an oil, a fatty acid, a fatty acid ester or glyceride, or an acetylated fatty acid glyceride with or without the addition of a pharmaceutically acceptable surfactant, such as a soap or a detergent, suspending agent, such as pectin, carboxomers, methylcellulose, hydroxypropylmethylcellulose, or carboxymethylcellulose, or emulsifying agents and other pharmaceutical adjuvants.

Oils useful in parenteral formulations include petroleum, animal, vegetable, and synthetic oils. Specific examples of oils useful in such formulations include peanut, soybean, sesame, cottonseed, corn, olive, petrolatum, and mineral oil. Suitable fatty acids for use in parenteral formulations include oleic acid, stearic acid, and isostearic acid. Ethyl oleate and isopropyl myristate are examples of suitable fatty acid esters.

Suitable soaps for use in parenteral formulations include fatty alkali metal, ammonium, and triethanolamine salts, and suitable detergents include (a) cationic detergents such as, for example, dimethyl dialkyl ammonium halides, and alkyl pyridinium halides, (b) anionic detergents such as, for example, alkyl, aryl, and olefin sulfonates, alkyl, olefin, ether, and monoglyceride sulfates, and sulfosuccinates, (c) nonionic detergents such as, for example, fatty amine oxides, fatty acid alkanolamides, and polyoxyethylene polypropylene copolymers, (d) amphoteric detergents such as, for example, alkyl-β-aminopropionates, and 2-alkyl-imidazoline quaternary ammonium salts, and (e) mixtures thereof.

The parenteral formulations typically will contain from about 0.5% or less to about 25% or more by weight of a compound of the invention in solution. Preservatives and buffers can be used. In order to minimize or eliminate irritation at the site of injection, such compositions can contain one or more nonionic surfactants having a hydrophilic-lipophilic balance (HLB) of from about 12 to about 17. The quantity of surfactant in such formulations will typically range from about 5% to about 15% by weight. Suitable surfactants include polyethylene sorbitan fatty acid esters, such as sorbitan monooleate and the high molecular weight adducts of ethylene oxide with a hydrophobic base, formed by the condensation of propylene oxide with propylene glycol. The parenteral formulations
can be presented in unit-dose or multi-dose sealed containers, such as ampoules and vials, and can be stored in a freeze-dried (lyophilized) condition requiring only the addition of the sterile liquid excipient, for example, water, for injections, immediately prior to use. Extemporaneous injection solutions and suspensions can be prepared from sterile powders, granules, and tablets.

Topical formulations, including those that are useful for transdermal drug release, are well known to those of skill in the art and are suitable in the context of the present invention for application to skin.

Formulations suitable for oral administration can consist of (a) liquid solutions, such as an effective amount of a compound of the invention dissolved in diluents, such as water, saline, or orange juice; (b) capsules, sachets, tablets, lozenges, and troches, each containing a pre-determined amount of the compound of the invention, as solids or granules; (c) powders; (d) suspensions in an appropriate liquid; and (e) suitable emulsions. Liquid formulations can include diluents, such as water and alcohols, for example, ethanol, benzyl alcohol, and the polyethylene alcohols, either with or without the addition of a pharmaceutically acceptable surfactant, suspending agent, or emulsifying agent. Capsule forms can be of the ordinary hard- or soft-shelled gelatin type containing, for example, surfactants, lubricants, and inert fillers, such as lactose, sucrose, calcium phosphate, and cornstarch. Tablet forms can include one or more of lactose, sucrose, mannitol, corn starch, potato starch, alginic acid, microcrystalline cellulose, acacia, gelatin, guar gum, colloidal silicon dioxide, croscarmellose sodium, talc, magnesium stearate, calcium stearate, zinc stearate, stearic acid, and other excipients, colorants, diluents, buffering agents, disintegrating agents, moistening agents, preservatives, flavoring agents, and pharmacologically compatible excipients. Lozenge forms can comprise the compound ingredient in a flavor, usually sucrose and acacia or tragacanth, as well as pastilles comprising a compound of the invention in an inert base, such as gelatin and glycerin, or sucrose and acacia, emulsions, gels, and the like containing, in addition to the compound of the invention, such excipients as are known in the art.

An compound of the present invention, alone or in combination with other suitable components, can be made into aerosol formulations to be administered via inhalation. A
compound or epimer of the invention is preferably supplied in finely divided form along with a surfactant and propellant. Typical percentages of the compounds of the invention can be about 0.01% to about 20% by weight, preferably about 1% to about 10% by weight. The surfactant must, of course, be nontoxic, and preferably soluble in the propellant. Representative of such surfactants are the esters or partial esters of fatty acids containing from 6 to 22 carbon atoms, such as caproic, octanoic, lauric, palmitic, stearic, linoleic, linolenic, olesteric and oleic acids with an aliphatic polyhydric alcohol or its cyclic anhydride. Mixed esters, such as mixed or natural glycerides can be employed. The surfactant can constitute from about 0.1% to about 20% by weight of the composition, preferably from about 0.25% to about 5%. The balance of the composition is ordinarily propellant. A carrier can also be included as desired, e.g., lecithin, for intranasal delivery. These aerosol formulations can be placed into acceptable pressurized propellants, such as dichlorodifluoromethane, propane, nitrogen, and the like. They also can be formulated as pharmaceuticals for non-pressured preparations, such as in a nebulizer or an atomizer. Such spray formulations can be used to spray mucosa.

Additionally, the compound of the invention can be made into suppositories by mixing with a variety of bases, such as emulsifying bases or water-soluble bases. Formulations suitable for vaginal administration can be presented as pessaries, tampons, creams, gels, pastes, foams, or spray formulas containing, in addition to the compound ingredient, such carriers as are known in the art to be appropriate.

The concentration of the compound in the pharmaceutical formulations can vary, e.g., from less than about 1% to about 10%, to as much as 20% to 50% or more by weight, and can be selected primarily by fluid volumes, and viscosities, in accordance with the particular mode of administration selected.

For example, a typical pharmaceutical composition for intravenous infusion could be made up to contain 250 ml of sterile Ringer's solution, and 100 mg of at least one compound of the invention. Actual methods for preparing parenterally administrable compounds of the invention will be known or apparent to those skilled in the art and are described in more detail in, for example, *Remington's Pharmaceutical Science* (17th ed., Mack Publishing Company, Easton, PA, 1985).
It will be appreciated by one of ordinary skill in the art that, in addition to the aforedescribed pharmaceutical compositions, the compound of the invention can be formulated as inclusion complexes, such as cyclodextrin inclusion complexes, or liposomes. Liposomes can serve to target a compound of the invention to a particular tissue, such as lymphoid tissue or cancerous hepatic cells. Liposomes can also be used to increase the half-life of a compound of the invention. Many methods are available for preparing liposomes, as described in, for example, Szoka et al., *Ann. Rev. Biophys. Bioeng.*, 9, 467 (1980) and U.S. Patents 4,235,871, 4,501,728, 4,837,028, and 5,019,369.

The present invention also provides a pharmaceutical composition, containing the compounds of the general formula (I) as defined above, its tautomeric forms, its stereoisomers, its analogs, its prodrugs, its isotopes, its metabolites, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates and its co-crystals in combination with the usual pharmaceutically employed carriers, diluents and the like, and for use in any of the methods described herein.

The compounds of the invention can be administered in a dose sufficient to treat the disease, condition or disorder. Such doses are known in the art (see, for example, the *Physicians’ Desk Reference* (2004)). The compounds can be administered using techniques such as those described in, for example, Wasserman et al., *Cancer*, 36, pp. 1258-1268 (1975) and *Physicians’ Desk Reference*, 58th ed., Thomson PDR (2004).

Suitable doses and dosage regimens can be determined by conventional range-finding techniques known to those of ordinary skill in the art. Generally, treatment is initiated with smaller dosages that are less than the optimum dose of the compound of the present invention. Thereafter, the dosage is increased by small increments until the optimum effect under the circumstances is reached. The present method can involve the administration of about 0.1 µg to about 50 mg of at least one compound of the invention per kg body weight of the individual. For a 70 kg patient, dosages of from about 10 µg to about 200 mg of the compound of the invention would be more commonly used, depending on a patient's physiological response.
By way of example and not intending to limit the invention, the dose of the pharmaceutically active agent(s) described herein for methods of treating or preventing a disease or condition as described above can be about 0.001 to about 1 mg/kg body weight of the subject per day, for example, about 0.001 mg, 0.005 mg, 0.010 mg, 0.015 mg, 0.020 mg, 0.025 mg, 0.050 mg, 0.075 mg, 0.1 mg, 0.15 mg, 0.2 mg, 0.25 mg, 0.5 mg, 0.75 mg, or 1 mg/kg body weight per day. The dose of the pharmaceutically active agent(s) described herein for the described methods can be about 1 to about 1000 mg/kg body weight of the subject being treated per day, for example, about 1 mg, 2 mg, 5 mg, 10 mg, 15 mg, 0.020 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 250 mg, 500 mg, 750 mg, or 1000 mg/kg body weight per day.

In accordance with embodiments, the present invention provides methods of treating, preventing, ameliorating, and/or inhibiting a hepatitis C virus infection comprising administering a compound of formula (I) or a salt thereof.

It should also be understood that the compounds of the present invention can inhibit multiple genotypes of HCV. In one of the embodiment compound of the present invention are active against the 1a, 1b, 2a, 2b, 3a, 4a and 5a genotypes.

The terms "treat," "prevent," "ameliorate," and "inhibit," as well as words stemming therefrom, as used herein, do not necessarily imply 100% or complete treatment, prevention, amelioration, or inhibition. Rather, there are varying degrees of treatment, prevention, amelioration, and inhibition of which one of ordinary skill in the art recognizes as having a potential benefit or therapeutic effect. In this respect, the inventive methods can provide any amount of any level of treatment, prevention, amelioration, or inhibition of the disorder in a mammal. For example, a disorder, including symptoms or conditions thereof, may be reduced by, for example, 100%, 90%, 80%, 70%, 60%, 50%, 40%, 30%, 20%, or 10%. Furthermore, the treatment, prevention, amelioration, or inhibition provided by the inventive method can include treatment, prevention, amelioration, or inhibition of one or more conditions or symptoms of the disorder, e.g., cancer. Also, for purposes herein, "treatment," "prevention," "amelioration," or "inhibition" can encompass delaying the onset of the disorder, or a symptom or condition thereof.
In accordance with the invention, the term subject includes an "animal" which in turn includes a mammal such as, without limitation, the order Rodentia, such as mice, and the order Lagomorpha, such as rabbits. It is preferred that the mammals are from the order Carnivora, including Felines (cats) and Canines (dogs). It is more preferred that the mammals are from the order Artiodactyla, including Bovines (cows) and Swine (pigs) or of the order Perssodactyla, including Equines (horses). It is most preferred that the mammals are of the order Primates, Ceboids, or Simoids (monkeys) or of the order Anthropoids (humans and apes). An especially preferred mammal is the human.

The term "viral infection" refers to the introduction of a virus into cells or tissues, e.g., hepatitis C virus (HCV). In general, the introduction of a virus is also associated with replication. Viral infection may be determined by measuring virus antibody titer in samples of a biological fluid, such as blood, using, e.g., enzyme immunoassay. Other suitable diagnostic methods include molecular based techniques, such as RT-PCR, direct hybrid capture assay, nucleic acid sequence based amplification, and the like. A virus may infect an organ, e.g., liver, and cause disease, e.g., hepatitis, cirrhosis, chronic liver disease and hepatocellular carcinoma.

The term "immune modulator" refers to any substance meant to alter the working of the humoral or cellular immune system of a subject. Such immune modulators include inhibitors of mast cell mediated inflammation, interferons, interleukins, prostaglandins, steroids, cortico-steroids, colony-stimulating factors, chemotactic factors, etc.

Following are the abbreviations used and meaning thereof in the specification:

Bis(diphenylphosphino)ferrocene dichloropalladium(II) complex with dichloromethane.

pet-ether: petroleum ether. TFA: trifluoroacetic acid. THF: Tetrahydrofuran

The following examples are provided to further illustrate the present invention and therefore should not be construed in any way to limit the scope of the present invention. All $^1$H-NMR spectra were determined in the solvents indicated and chemical shifts are reported in δ units downfield from the internal standard tetramethylsilane (TMS) and interproton coupling constants are reported in Hertz (Hz). In case of mixture of the isomers, the peak values given are for the dominant isomer (rotamer/tautomer).

Example 1: Preparation of methyl ((2S)-1-(((2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (mixture of trans isomers) (Compound 1):

Step 1: 2-(4-bromophenyl)-2-oxoethyl-2-((tert-butoxycarbonyl)amino)cyclopentancarboxilate (trans isomers) (1a):

![HN-Boc](image)

To a stirred solution of trans-2-((tert-butoxycarbonyl)amino)cyclopentancarboxylic acid (0.8 g, 3.49 mmol) [synthesized as described in J. Org. Chem., 2001, 66 (16), 5629-5632] and 2-bromo-1-(4-bromophenyl)ethanone (0.97 g, 3.49 mmol) in acetonitrile (50 mL) DIPEA (0.61 mL, 3.49 mmol) was added and the reaction was stirred at rt for 2 h. The contents were concentrated under reduced pressure and water (100 mL) was added and extracted with ethyl acetate (2 x 50mL). The combined organic layers were washed with brine, dried over anhydrous Na$_2$SO$_4$ and concentrated under reduced pressure to get pale yellow colored oily liquid (1.3 g, 87 %) that was used in the next step without further purification. $^1$H-NMR (400 MHz, CDCl$_3$), δ 7.81-7.79 (m, 2H), 7.67-7.65 (m, 2H), 5.61 (bs,
1H), 5.42-5.20 (m, 2H), 4.30-4.22 (m, 1H), 3.19-3.14 (m, 1H), 2.15-1.65 (m, 6H), 1.47 (s, 9H); m/z 426.30 (M+1).

**Step 2:** tert-butyl (2-(5-(4-bromophenyl)-1H-imidazol-2-yl)cyclopentyl)carbamate (trans isomers)(1b):

To the stirred solution of 2-(4-bromophenyl)-2-oxoethyl-2-((tert-butoxycarbonyl)amino)cyclopentanecarboxylate (1.3 g, 3.05 mmol) from the previous step in toluene (20 mL), ammonium acetate (4.70 g, 61.0 mmol) was added and the contents were heated at 110 °C for 15 h. The reaction mixture was poured into 100 mL water and extracted with ethyl acetate (2 x 50 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄ and purified by flash column chromatography (45% EtOAc/hexane) to get orange colored solid (1.0 g, 81%). ¹H-NMR (400 MHz, CDCl₃), δ 7.57-7.47 (m, 4H), 7.21 (s, 1H), 5.14-4.95 (m, 1H), 4.35-4.15 (m, 1H), 3.39-3.15 (m, 1H), 2.14-1.65 (m, 6H), 1.43 (s, 9H); m/z 406.1 (M+1).

**Step 3:** tert-butyl (2-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)carbamate (trans isomers) (1c):

A mixture of tert-butyl (2-(5-(4-bromophenyl)-1H-imidazol-2-yl)cyclopentyl)carbamate (1 g, 2.46 mmol) from the previous step, potassium acetate (0.68 g, 6.90 mmol) and 4,4',4'',5,5,5''-octamethyl-2,2''-bi(1,3,2-dioxaborolane) (1.3 g, 4.92 mmol) in dioxane (10 mL) was de-gassed with nitrogen for 30 min after which Pd(PPh₃)₄ (0.08 g, 0.07 mmol) was added and the reaction mixture was irradiated with microwaves at 120 °C for 40 min.
The contents were taken up in EtOAc (20 mL) and passed through a celite bed. The celite bed was thoroughly rinsed with EtOAc (20 mL). The combined organic layers were washed with brine, dried over sodium sulphate and purified by flash chromatography (50% ethylacetate/hexane) to yield a pale yellow coloured solid (0.7 g, 62%). $^1$H-NMR (400 MHz, CDCl$_3$), $\delta$ 7.79-7.77 (d, J = 8.0 Hz, 2H), 7.61 -7.59 (d, J = 8.0 Hz, 2H), 7.32 (s, 1H), 5.20-5.10 (m, 1H), 4.30-4.25 (m, 1H), 3.39-3.30 (m, 1H), 2.14-1.60 (m, 6H), 1.36 (s, 12H), 1.30 (s, 9H); m/z 454.28 (M$^+$+1).

**Step 4**: (2S)-tert-butyl 2-(7-(4-(2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (trans isomers) (1d):

![Chemical Structure](image)

The solution of (S)-tert-butyl 2-(7-bromo-4,5-dihydro-1H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (0.2 g, 0.48 mmol) [synthesized as reported in ref. WO2009/102633] and tert-butyl (2-(5-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)carbamate (0.26 g, 0.57 mmol) [from the previous step] in a mixture of DME-H$_2$O (3:1, 4 mL) was degassed using nitrogen gas for 15 min. Potassium carbonate (0.33 g, 2.40 mmol) and Pd(PPh$_3$)$_4$ (0.055 g, 0.048 mmol) were added and irradiated using microwaves at 120 °C for 40 min. The contents were taken up in ethyl acetate and washed with water. The organic layer was dried over Na$_2$SO$_4$ and concentrated under reduced pressure to obtain the crude compound which was purified by flash chromatography (80% EtOAc/hexane) to get a pale yellow solid (0.16 g, 50%). $^1$H-NMR (400 MHz, CDCl$_3$), $\delta$ 7.85-7.40 (m, 7H), 7.12-6.90 (m, 1H), 5.07-4.86 (m, 2H), 4.40-4.20 (m, 2H), 3.50-3.33 (m, 3H), 3.15-2.80 (m, 4H), 2.45-1.80 (m, 8H), 1.60-1.51 (m, 18H); m/z 665.40 (M$^+$+1).
Step 5: methyl ((2S)-1-((2-(5-(4-((2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (mixture of trans isomers) (Compound 1):

(2S)-tert-butyl 2-(7-(4-(2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (0.1 g, 0.15 mmol) [from previous step] was dissolved in DCM (4 mL) and TFA (0.2 mL) was added to the reaction mixture at 5-10 °C. After completion of addition, the mixture was stirred at rt for 2 h. The mixture was evaporated to dryness and triturated with diethyl ether to obtain the product as a TFA salt which was used in the next step without any further purification. (S)-2-((methoxycarbonyl)amino)-3-methylbutanoic acid (0.05 g, 0.30 mmol) [synthesized as reported in ref. WO201 0/132538 A1] was added to acetonitrile (10 mL) followed by EDCI hydrochloride (0.06 g, 0.30 mmol), HOBt (0.05 g, 0.30 mmol) and DIPEA (0.18 mL, 0.9 mmol) and stirred for 20 min. Subsequently crude TFA salt from previous step (0.070 g) was added and stirred overnight at rt. The reaction mixture was evaporated to dryness and the required amide was precipitated out by adding water (20 mL) and filtered. The pale yellow solid was purified by preparative HPLC (0.023 g, 20 %). 1H NMR (DMSO-D6, 400 MHz), δ 12.10-1.55 (m, 2H), 7.82-7.29 (m, 9H), 7.05-6.60 (m, 2H), 5.10-5.05 (m, 1H), 4.40-4.32 (m, 2H), 4.11-4.07 (m, 2H), 3.87-3.81 (m, 4H), 3.51-3.45 (s, 6H), 3.02-2.67 (m, 4H), 2.25-1.65 (m, 10H), 0.99-0.51 (m, 12H); m/z 779.50 (M^+1). m.p.: 148-150 °C.
Example 2: methyl ((2S)-1-((2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (mixture of cis isomers) (Compound 2):

**Step 1:** 2-(4-bromophenyl)-2-oxoethyl-2-((tert-butoxycarbonyl)amino)cyclopentanecarboxylate (cis isomers) (2a):

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 1 of Example 1 using c/s-2-((tert-butoxycarbonyl)amino)cyclopentanecarboxylic acid [synthesized as described in Tetrahedron: Asymmetry, 2008, 19, 2796-2803]. $^1$H-NMR (400 MHz, CDCl$_3$), $\delta$ 7.85-7.79 (m, 2H), 7.70-7.65 (m, 2H), 5.65 (bs, 1H), 5.35-5.20 (m, 2H), 4.35-4.22 (m, 1H), 3.25-3.14 (m, 1H), 2.20-1.65 (m, 6H), 1.47 (s, 9H); m/z 426.30 (M$^+$+1).

**Step 2:** tert-butyl (2-(5-(4-bromophenyl)-1 H-imidazol-2-yl)cyclopentyl)carbamate (cis isomers) (2b):

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 2 of Example 1 using intermediate (2a) from the previous step. $^1$H-NMR (400 MHz, CDCl$_3$), $\delta$ 7.60-7.45 (m, 4H), 7.23 (s, 1H), 5.20-4.95 (m, 1H), 4.37-4.15 (m, 1H), 3.40-3.17 (m, 1H), 2.20-1.70 (m, 6H), 1.50 (s, 9H); m/z 406.1 1 (M$^+$+1).
Step 3: tert-butyl \((2-(5-(4-(4,4,5,5\text{-}\text{tetramethyl\text{-}1,3,2\text{-}dioxaborol\text{-}2\text{-}yl)phenyl})-1\text{H-imidazol\text{-}2\text{-}yl})cyclopentyl)amatamte)\) (cis isomers) (2c):

![Chemical structure](image)

Title compound was synthesized by following the procedure as described in Step 3 of Example 1 using intermediate (2b) from the previous step. \(^1\)H-NMR (400 MHz, CDCl\(_3\)), \(\delta\) 7.79-7.77 (m, 2H), 7.70-7.67 (m, 2H), 7.30 (s, 1H), 5.20-5.10 (m, 1H), 4.30-4.25 (m, 1H), 3.39-3.32 (m, 1H), 2.14-1.60 (m, 6H), 1.36 (s, 12H), 1.30 (s, 9H); \(m/z\) 454.20 (M\(^+\) + 1).

Step 4: (2S)-tert-butyl \(2-(8-(4-(2-(2-(\text{tert\text{-}butoxycarbonyl)amino)cyclopentyl})-1\text{H-imidazol-5-yl})phenyl)-1,4,5,6\text{-}\text{tetrahydrobenzo[3,4\text{-}cyclohepta[1,2-d]imidazol-2-yl})pyrrolidine-1-carboxylate\) (2d):

![Chemical structure](image)

Title compound was synthesized by following the procedure as described in Step 4 of Example 1 using intermediate (2c) from the previous step and (S)-tert-butyl \(2-(8\text{-bromo-3,4,5,6\text{-}tetrahydrobenzo[3,4\text{-}cyclohepta[1,2-d]imidazol-2-yl})pyrrolidine-1\)-carboxylate [synthesized as described in WO2009/1 02633]. \(^1\)H-NMR (400 MHz, CDCl\(_3\)), \(\delta\) 7.83-7.45 (m, 8H), 5.07-4.86 (m, 2H), 4.40-4.20 (m, 2H), 3.50-3.43 (m, 3H), 3.10-2.80 (m, 4H), 2.45-1.80 (m, 10H), 1.60-1.51 (m, 18H), \(m/z\) 679.40 (M\(^+\) + 1).

Step 5: methyl \(((2S)-1-((2-(5-(4-(4-(4\text{-methoxycarbonyl)amino}-3\text{-methylbutanoyl)pyrrolidin-2-yl})-1,4,5,6\text{-}\text{tetrahydrobenzo[3,4\text{-}cyclohepta[1,2-d]imidazol-8-yl}]phenyl)-1\text{H-imidazol-2-yl})cyclopentyl)amino)-3-methyl-1\text{-oxobutan-2-yl})\) carbamate (mixture of cis isomers) (Compound 2)
Title compound was synthesized by following the procedure as described in Step 5 of Example 1 using intermediate (2d) from the previous step. ¹H NMR (DMSO-δ6, 400 MHz), δ 11.88-1.55 (m, 2H), 8.15-8.00 (m, 2H), 7.82-7.29 (m, 9H), 5.15-5.02 (m, 1H), 4.40-4.32 (m, 2H), 4.11-4.07 (m, 2H), 3.87-3.81 (m, 4H), 3.51 (s, 6H), 2.94-2.80 (m, 4H), 2.14-1.65 (m, 10H), 0.97-0.59 (m, 14H); m/z 793.50 (M+1). m.p.: 155-157 °C.

Example 3: Preparation of methyl ((2S)-1-((2-(5-(4-(2-((S)-1-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (mixture of cis isomers) (Compound 3):

Step 1: (2S)-tert-butyl 2-(7-(4-(2-((S)-2-(tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (cis isomers) (3a):

Title compound was synthesized by following the procedure as described in Step 4 of Example 1, using intermediate 2c from Example 2, Step 3 and (S)-tert-butyl 2-(7-bromo-4,5-dihydro-1H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate [synthesized as described in WO2009/1 02633]. ¹H-NMR (400 MHz, CDCl3), δ 7.85-7.40 (m, 7H), 7.12-6.90 (m, 1H), 5.07-4.86 (m, 2H), 4.40-4.20 (m, 2H), 3.50-3.33 (m, 3H), 3.15-2.80 (m, 4H), 2.45-1.80 (m, 8H), 1.60-1.51 (m, 18H); m/z 665.40 (M+1).
Step 2: methyl \([(2S)-1-(2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate\] (mixture of cis isomers): (Compound 3)

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 5 of Example 1 using intermediate \((3a)\) from the previous step. \(^1\)H NMR \((\text{DMSO-}\delta_6, 400 \text{ MHz}), \delta 11.88-1.55 (m, 2H), 7.88-7.28 (m, 9H), 7.02-6.87 (m, 2H), 5.15-5.02 (m, 1H), 4.40-4.32 (m, 2H), 4.11-4.07 (m, 2H), 3.87-3.81 (m, 2H), 3.51-3.45 (m, 6H), 3.02-2.67 (m, 4H), 2.20-1.55 (m, 12H), 1.10-0.55 (m, 12H); \(m/z\) 779.50 \((\text{M}^+ + 1)\). m.p.: 140 °C.

Example 4: Preparation of methyl \([(S)-1-(((1R,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate\] (Compound 4):

Step 1: \((1S,2R)-2-(4-bromophenyl)-2-oxoethyl-2-((tert-butoxycarbonyl)amino)cyclopentanecarboxylate\) \((4a)\):

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 1 of Example 1 using 2-bromo-1-(4-bromophenyl)ethanone and \((1S,2R)-2-((\text{tert}-\text{butoxycarbonyl})\text{amino})\text{cyclopentanecarboxylic acid}\) [synthesized as described in \textit{Tetrahedron: Asymmetry}, 2008, 19, 2796-2803] as starting materials. \(^1\)H-NMR \((400 \text{ MHz}, 48\)
Step 2: tert-butyl ((1R,2S)-2-(4-(4-bromophenyl)-1H-imidazol-2-yl)cyclopentyl)carbamate (4b):

\[
\text{CDCl}_3 \quad \delta \quad 7.79 \text{ (d, } J = 8 \text{ Hz, 2H)}, \quad 7.66 \text{ (d, } J = 8 \text{ Hz, 2H)}, \quad 5.60 \text{ (bs, 1H)}, \quad 5.40-5.20 \text{ (m, 2H)}, \quad 4.35-4.30 \text{ (m, 1H)}, \quad 3.20-3.15 \text{ (m, 1H)}, \quad 2.20-1.60 \text{ (m, 6H)}, \quad 1.40 \text{ (s, 9H)}. \quad \text{LC-MS: } m/z \quad 326.0 \quad [(M^+1) - 100] \text{ (value observed for the de-Boc product).}
\]

Step 3: tert-butyl ((1R,2S)-2-(5-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)carbamate (4c):

\[
\text{CDCl}_3 \quad \delta \quad 7.79-7.77 \text{ (m, 2H)}, \quad 7.70-7.67 \text{ (m, 2H)}, \quad 7.30 \text{ (s, 1H)}, \quad 5.20-5.10 \text{ (m, 1H)}, \quad 4.30-4.25 \text{ (m, 1H)}, \quad 3.39-3.32 \text{ (m, 1H)}, \quad 2.14-1.60 \text{ (m, 6H)}, \quad 1.36 \text{ (s, 12H)}, \quad 1.30 \text{ (s, 9H)}; \quad m/z \quad 406.10 \quad (M^+1).
\]

Step 4: (S)-tert-butyl 2-(7-(4-(2-((1S,2R)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (4d):

\[
\text{CDCl}_3 \quad \delta \quad 7.79 \text{ (d, } J = 8 \text{ Hz, 2H}), \quad 7.66 \text{ (d, } J = 8 \text{ Hz, 2H}), \quad 5.60 \text{ (bs, 1H)}, \quad 5.40-5.20 \text{ (m, 2H)}, \quad 4.35-4.30 \text{ (m, 1H)}, \quad 3.20-3.15 \text{ (m, 1H)}, \quad 2.20-1.60 \text{ (m, 6H)}, \quad 1.40 \text{ (s, 9H)}. \quad \text{LC-MS: } m/z \quad 326.0 \quad [(M^+1) - 100] \text{ (value observed for the de-Boc product).}
\]
Title compound was synthesized by following the procedure as described in Step 4 of Example 1 using the intermediate 4c and and (S)-tert-butyl 2-(7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate [synthesized as described in WO2009102633]. ¹H-NMR (400 MHz, CDCl₃) δ 7.83-7.45 (m, 7H), 7.20-7.10 (m, 1H), 5.07-4.86 (m, 2H), 4.40-4.20 (m, 2H), 3.50-3.43 (m, 3H), 3.15-3.05 (m, 2H), 2.97-2.80 (m, 2H), 2.45-1.80 (m, 8H), 1.60-1.51 (m, 18H), m/z 665.40 (M⁺+1).

**Step 5:** methyl ((S)-1-(((1R,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 4).

---

Title compound was synthesized by following the procedure as described in Step 5 of Example 1 using the intermediate (4d) from previous step. ¹H NMR (DMSO-d₆, 400 MHz), δ 12.10-1.55 (m, 2H), 7.82-7.29 (m, 9H), 7.05-6.60 (m, 2H), 5.10-5.05 (m, 1H), 4.40-4.32 (m, 2H), 4.11-4.07 (m, 2H), 3.87-3.81 (m, 4H), 3.51-3.45 (s, 6H), 3.02-2.67 (m, 4H), 2.20-1.65 (m, 10H), 0.99-0.51 (m, 12H), m/z 779.50 (M⁺+1). m.p.: 162-165 °C.

**Example 5:** Preparation of methyl ((S)-1-(((1R,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Example 5):

**Step 1:** (S)-tert-butyl 2-(8-(4-(2-(((1S,2R)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-8-yl)phenyl)-1H-imidazol-2-yl)pyrrolidine-1-carboxylate (5a):
Title compound was synthesized by following the procedure as described in Step 4 of Example 1 using the intermediates from Step 2 of Example 4 (4b) and (S)-tert-butyl 2-(8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate [synthesized as described in WO2009102633].

\[ \delta 7.83-7.45 (m, 8H), 5.07-4.86 (m, 2H), 4.40-4.20 (m, 2H), 3.50-3.43 (m, 3H), 3.10-2.80 (m, 4H), 2.45-1.80 (m, 10H), 1.60-1.51 (m, 18H), m/z 679.40 (M^+1). \]

**Step 2**: methyl ((S)-1-(((1R,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-2-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 5):

\[ \delta 11.88-11.55 (m, 2H), 8.04-7.29 (m, 11H), 5.15-5.02 (m, 1H), 4.40-4.32 (m, 2H), 4.11-4.07 (m, 2H), 3.87-3.70 (m, 4H), 3.51-3.45 (m, 6H), 2.94-2.80 (m, 4H), 2.20-1.65 (m, 12H), 0.97-0.71 (m, 12H), m/z 793.50 (M^+1). \]
Example 6: Preparation of methyl ([(S)-1-(((1 R,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1 H-benzo[2,3]oxepino[4,5-d]imidazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 6):

**Step 1:** (S)-tert-butyl 2-(8-(4-(2-((1 S,2R)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1 H-imidazol-5-yl)phenyl)-4,5-dihydro-1 H-benzo[2,3]oxepino[4,5-d]imidazol-2-yl)pyrrolidine-1-carboxylate (6a):

![Chemical Structure of 6a](image)

Title compound was synthesized by following the procedure as described in Step 4 of Example 1 using the intermediates from Step 2 of Example 4 (4b) and (S)-tert-butyl 2-(8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4,5-dihydro-1 H-benzo[2,3]oxepino[4,5-d]imidazol-2-yl)pyrrolidine-1-carboxylate [synthesized using procedures described in WO2009102633]. ^1H-NMR (400 MHz, CDCl₃) δ 11.00 (bs, 1H), 10.30 (bs, 1H), 7.83-7.40 (m, 8H), 5.07-4.90 (m, 2H), 4.40-4.20 (m, 3H), 3.50-3.43 (m, 3H), 3.25-3.10 (m, 2H), 2.95-2.90 (m, 1H), 2.45-1.72 (m, 8H), 1.65-1.51 (m, 18H), m/z 681.40 (M+1).

**Step 2:** methyl ([(S)-1-(((1 R,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1 H-benzo[2,3]oxepino[4,5-d]imidazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 6):

![Chemical Structure of 6a](image)
Title compound was synthesized by following the procedure as described in Step 5 of Example 1 using HATU, DMF and the intermediate (6a) from previous step. \( ^1\)H NMR (DMSO-D6, 400 MHz), \( \delta \) 12.00-1.70 (m, 2H), 8.14-6.90 (m, 11H), 5.05-5.02 (m, 1H), 4.40-4.10 (m, 4H), 3.90-3.70 (m, 4H), 3.60 (s, 6H), 3.15-3.00 (m, 2H), 2.14-1.55 (m, 12H), 0.97-0.71 (m, 12H), m/z 795.50 (M+1). m.p.: 191 °C.

**Example 7**: methyl ((S)-1-((1S,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1 H-benzo[2,3]oxepino[4,5-d]imidazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 7):

**Step 1:** (1R,2S)-2-(4-bromophenyl)-2-oxoethyl-2-((tert-butoxycarbonyl)amino)cyclopentanecarboxylate (7a):

![Chemical Structure 7a](image)

Title compound was synthesized by following the procedure as described in Step 1 of Example 1 using 2-bromo-1-(4-bromophenyl)ethanone and (1R,2S)-2-((tert-butoxycarbonyl)amino)cyclopentanecarboxylic acid [synthesized by following the procedures described in *Tetrahedron: Asymmetry*, 2008, 19, 2796-2803]. \( ^1\)H-NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.80 (d, \( J = 8 \) Hz, 2H), 7.67 (d, \( J = 8 \) Hz, 2H), 5.6 (bs, 1H), 5.40-5.20 (m, 2H), 4.35-4.30 (m, 1H), 3.19-3.15 (m, 1H), 2.20-1.60 (m, 6H), 1.40 (s, 9H); m/z 326.2 [(M+1) - 100] (value observed for the de-Boc product).

**Step 2**: tert-butyl- (1S,2R)-2-(4-(4-bromophenyl)-1 H-imidazol-2-yl)cyclopentyl)carbamate (7b):

![Chemical Structure 7b](image)
Title compound was synthesized by following the procedure as described in Step 2 of Example 1, using the intermediate (7a) from the previous step. $^1$H-NMR (400 MHz, CDCl$_3$) δ 7.60-7.56 (m, 2H), 7.49-7.47 (m, 2H), 7.20 (s, 1H), 5.05-4.95 (m, 1H), 4.40-4.31 (m, 1H), 3.40-3.35 (m, 1H), 2.40-1.60 (m, 6H), 1.33/1.26 (s, 9H); m/z 406.0 (M$^+$+1).

**Step 3**: tert-butyl ((1S,2R)-2-(5-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)carbamate (7c):

$$
\text{Boc} \quad \text{HN} \quad \text{(S)}
\begin{array}{c}
\text{O} \\
\text{B} \\
\text{N}
\end{array}
\begin{array}{c}
\text{O} \\
\text{B} \\
\text{N}
\end{array}
\begin{array}{c}
\text{O} \\
\text{B} \\
\text{N}
\end{array}
\begin{array}{c}
\text{O} \\
\text{B} \\
\text{N}
\end{array}
\begin{array}{c}
\text{O} \\
\text{B} \\
\text{N}
\end{array}
\begin{array}{c}
\text{O} \\
\text{B} \\
\text{N}
\end{array}
$$

1H-NMR (400 MHz, CDCl$_3$) δ 7.85-7.78 (m, 2H), 7.65-7.60 (m, 2H), 7.30 (s, 1H), 5.15-5.10 (m, 1H), 4.35-4.25 (m, 1H), 3.45-3.30 (m, 1H), 2.19-1.60 (m, 6H), 1.40 (s, 12H), 1.35 (s, 9H); m/z 454.28 (M$^+$+1).

**Step 4**: (S)-tert-butyl 2-(8-(4-(2-((1R,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-4,5-dihydro-1H-benzo[2,3]oxepino[4,5-d]imidazol-2-yl)pyrrolidine-1-carboxylate (7d):

$$
\text{Boc} \quad \text{HN} \quad \text{(S)}
\begin{array}{c}
\text{O} \\
\text{B} \\
\text{N}
\end{array}
\begin{array}{c}
\text{O} \\
\text{B} \\
\text{N}
\end{array}
\begin{array}{c}
\text{O} \\
\text{B} \\
\text{N}
\end{array}
\begin{array}{c}
\text{O} \\
\text{B} \\
\text{N}
\end{array}
\begin{array}{c}
\text{O} \\
\text{B} \\
\text{N}
\end{array}
$$

1H-NMR (400 MHz, CDCl$_3$) δ 7.78-7.48 (m, 8H), 5.07-4.86 (m, 2H), 4.40-4.20 (m, 2H), 3.70-3.43 (m, 3H), 3.05-2.90 (m, 4H), 2.45-1.90 (m, 10H), 1.50-1.31 (m, 18H), m/z 681.40 (M$^+$+1).
**Step 5**: methyl ((S)-1-(((1S,2R)-2-(5-(4-(2-(((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-benzo[2,3]oxepino[4,5-d]imidazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 7):

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 2 of Example 6 using the intermediate (7d) from the previous step. $^1$H NMR (DMSO-d$_6$, 400 MHz), $\delta$ 12.10-1.80 (m, 2H), 8.14-6.90 (m, 11 H), 5.05-5.02 (m, 1H), 4.40-4.10 (m, 4H), 3.90-3.70 (m, 4H), 3.60 (s, 6H), 3.15-3.00 (m, 2H), 2.14-1.95 (m, 12H), 0.97-0.71 (m, 12H), m/z 795.30 (M$^+$+1). m.p.: 218 °C.

**Example 8**: Preparation of methyl ((S)-1-(((1S,2R)-2-(5-(4-(2-(((1R,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 8):

**Step 1**: (S)-tert-butyl 2-(8-(4-(2-((1 R,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (8a):

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 4 of Example 1 using the intermediates from Step 2 Example 7 (7b) and (S)-tert-butyl 2-(8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate [synthesized as described in WO20091 02633].
**Step 2**: methyl \(((S)-1-(((1S,2R)-2-(5-((4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate**

(Compound 8):

![methyl ((S)-1-(((1S,2R)-2-(5-((4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate](image)

Title compound was synthesized by following the procedure as described in Step 5 of Example 1 using the intermediate (8a) from the previous step. \(^1\)H NMR (DMSO-\(d_6\), 400 MHz), \(\delta\) 11.08-1.55 (m, 2H), 8.31-6.99 (m, 11 H), 5.15-5.02 (m, 1H), 4.40-4.32 (m, 2H), 4.11-4.07 (m, 2H), 3.87-3.81 (m, 4H), 3.51-3.45 (s, 6H), 2.94-2.80 (m, 4H), 2.10-1.40 (m, 12H), 0.95-0.54 (m, 12H), \(m/z\) 793.50 (M\(^+\)+1). m.p.: 162-164 °C.

**Example 9**: Preparation of methyl \(((S)-1-(((1S,2S)-2-(5-((4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate** (Compound 9):

**Step 1**: (1S,2S)-2-(4-bromophenyl)-2-oxoethyl-2-((tertbutoxycarbonyl)amino)
cyclopentanecarboxylate (9a):
Title compound was synthesized by following the procedure as described in Step 1 of Example 1 using 2-bromo-1-(4-bromophenyl)ethanone and (1S,2S)-2-((tert-butoxycarbonyl)amino)cyclopentanecarboxylic acid [synthesized as described in J. Org. Chem., 2001, 66 (16), 5629-5632]. $^1$H NMR (DMSO-$d_6$, 400 MHz), $\delta$ 7.90-7.87 (m, 2H), 7.78-7.76 (m, 2H), 7.06-7.03 (m, 1H), 5.45-5.30 (m, 2H), 4.05-3.95 (m, 1H), 2.80-2.75 (m, 1H), 1.90-1.40 (m, 6H), 1.35 (s, 9H); m/z 326.0 [(M$^+$1) - 100] (value observed for the de-Boc product).

**Step 2:** tert-butyl ((1S,2S)-2-(4-(4-bromophenyl)-1H-imidazol-2-yl)cyclopentyl)carbamate (9b):

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 2 of Example 1 using the intermediate (9a) from the previous step. $^1$H-NMR (DMSO-$d_6$, 400 MHz), $\delta$ 7.68 (d, $J$ = 8.0 Hz, 2H), 7.57-7.54 (m, 1H), 7.48 (d, $J$ = 8.0 Hz, 2H), 6.95 (d, $J$ = 8.0 Hz, 1H), 4.05-3.90 (m, 1H), 3.10-3.02 (m, 1H), 2.10-1.40 (m, 6H), 1.35 (s, 9H); m/z 406.0 (M$^+$1).

**Step 3:** tert-butyl ((1S,2S)-2-(5-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)carbamate (9c):

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 3 of Example 1 using the intermediate (9b) from the previous step. $^1$H-NMR (400 MHz, CDCl$_3$), $\delta$ 7.85-7.78 (m, 2H), 7.65-7.60 (m, 2H), 7.30 (s, 1H), 5.30-5.10 (m, 1H), 4.30-4.20 (m, 1H), 3.45-3.30 (m, 1H), 2.25-1.60 (m, 6H), 1.40 (s, 12H), 1.35 (s, 9H); m/z 454.28 (M$^+$1).
Step 4: (S)-tert-butyl 2-(8-(4-(2-((1S,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (9d):

Title compound was synthesized by following the procedure as described in Step 4 of Example 1 using the intermediates 9c and (S)-tert-butyl 2-(8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate [synthesized as described in WO2009102633]. \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 11.00 (bs, 1H), 10.50 (bs, 1H), 7.83-7.45 (m, 8H), 4.95-4.86 (m, 2H), 4.25-4.15 (m, 2H), 3.50-3.43 (m, 3H), 3.20-2.80 (m, 4H), 2.45-1.80 (m, 10H), 1.60-1.51 (m, 18H), m/z 679.40 (M\(^+\)+1).

Step 5: methyl ((S)-1-(((1S,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 9):

Title compound was synthesized by following the procedure as described in Step 5 of Example 1 using the intermediate (9d) from the previous step. \(^1\)H NMR (DMSO-d\(_6\), 400 MHz), \(\delta\) 11.88-11.55 (m, 2H), 8.31-6.99 (m, 11H), 5.15-5.02 (m, 1H), 4.40-4.32 (m, 2H), 4.1-4.07 (m, 2H), 3.87-3.81 (m, 4H), 3.51-3.45 (s, 6H), 2.94-2.80 (m, 4H), 2.14-1.50 (m, 12H), 0.97-0.70 (m, 12H), m/z 793.50 (M\(^+\)+1). m.p.: 147 °C.
Example 10: Preparation of methyl ((S)-1-(((1S,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1 H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 10):

**Step 1:** (S)-tert-butyl 2-(7-(4-(2-((1S,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1 H-imidazol-5-yl)phenyl)-4,5-dihydro-1 H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (10a)

Title compound was synthesized by following the procedure as described in Step 4 of Example 1 using the intermediates from Step 2 of Example 9 (9b) and (S)-tert-butyl 2-(7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4,5-dihydro-1 H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate [synthesized as described in WO2009102633]. m/z 665.3 (M+1).

**Step 2:** methyl ((S)-1-(((1S,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1 H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 10):

Title compound was synthesized by following the procedure as described in Step 5 of Example 1 using the intermediate (10a) from the previous step. $^1$H NMR (DMSO-$d_6$, 400 MHz), $\delta$ 12.10-1.55 (m, 2H), 8.08-6.96 (m, 11H), 5.10-5.05 (m, 1H), 4.40-4.32 (m, 2H), 4.1-4.07 (m, 2H), 3.87-3.81 (m, 4H), 3.51-3.45 (s, 6H), 3.02-2.67 (m, 4H), 2.20-1.45 (m, 10H), 0.97-0.68 (m, 12H), m/z 779.50 (M+1). m.p.: 181 ºC.
Example 11: Preparation of methyl ((S)-1-(((1S,2S)-2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-benzo[2,3]oxepino[4,5-d]imidazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 11):

**Step 1**: (S)-tert-butyl 2-(8-(4-((1S,2S)-2-(tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-4,5-dihydro-1H-benzo[2,3]oxepino[4,5-d]imidazol-2-yl)pyrrolidine-1-carboxylate (11a):

![Structure of 11a]

Title compound was synthesized by following the procedure as described in Step 4 of Example 1 using the intermediates from Step 2 of Example 9 (9b) and (S)-tert-butyl 2-(8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4,5-dihydro-1H-benzo[2,3]oxepino[4,5-d]imidazol-2-yl)pyrrolidine-1-carboxylate [synthesized as described in WO2009102633].

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 11.00 (bs, 1H), 10.30 (bs, 1H), 7.90-7.30 (m, 8H), 5.07-4.90 (m, 2H), 4.40-4.10 (m, 3H), 3.50-3.43 (m, 2H), 3.25-3.10 (m, 3H), 2.95-2.90 (m, 1H), 2.45-1.72 (m, 8H), 1.65-1.51 (m, 18H), m/z 681.40 (M$^+$+1).

**Step 2**: methyl ((S)-1-(((1S,2S)-2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-benzo[2,3]oxepino[4,5-d]imidazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 11):

![Structure of 11]

Title compound was synthesized by following the procedure as described in Step 2 of Example 6 using the intermediate (11a) from the previous step. $^1$H NMR (DMSO-$d_6$, 400 MHz, CDCl$_3$) $\delta$...
Example 12: Preparation of methyl (S)-1-(((1R,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-2-yl)carbonyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 12):

Step 1: (1R, 2R)-2-(4-bromophenyl)-2-oxoethyl-2-((tert-butoxycarbonyl)amino)cyclopentane carboxylate (12a):

\[
\begin{align*}
\text{Br} & \quad \text{O} \\
(\text{R}) & \quad \text{Boc} \\
\end{align*}
\]

Title compound was synthesized by following the procedure as described in Step 1 of Example 1 using 2-bromo-1-(4-bromophenyl)ethanone and (1R,2R)-2-((tert-butoxycarbonyl)amino)cyclopentanecarboxylic acid [synthesized by following the procedures provided in J. Org. Chem., 2001, 66 (16), 5629-5632]. \(^1\)H-NMR (400 MHz, CDCl\textsubscript{3}), \(\delta\) 7.79 (d, J = 8 Hz, 2H), 7.66 (d, J = 8 Hz, 2H), 5.40-5.20 (m, 1H), 4.25-4.18 (m, 1H), 2.85-2.80 (m, 1H), 2.20-2.00 (m, 3H), 1.82-1.76 (m, 2H), 1.60-1.50 (m, 1H), 1.40 (s, 9H), m/z 326.0 ([M\textsuperscript{+}]+100) (value observed for the de-Boc product).

Step 2: tert-butyl (1R,2R)-2-(4-(bromophenyl)-1H-imidazol-2-yl)cyclopentyl)carbamate (12b):

\[
\begin{align*}
\text{Br} & \quad \text{HN} \\
(\text{R}) & \quad \text{HN-Boc} \\
\end{align*}
\]

Title compound was synthesized by following the procedure as described in Step 2 of Example 1 using intermediate (12a) from the previous step. \(^1\)H-NMR (400 MHz, CDCl\textsubscript{3}), \(\delta\) 7.60-7.56 (m, 2H), 7.49-7.47 (m, 2H), 7.26 (s, 1H), 5.00-4.90 (m, 1H), 4.17-4.10 (m, 1H), 3.17-3.12 (m, 1H), 2.38-2.10 (m, 4H), 1.80-1.55 (m, 2H), 1.50 (s, 9H); m/z 405.85 (M\textsuperscript{+}+1).
Step 3: tert-butyl ((1 R,2R)-2-(5-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)carbamate (12c):

Title compound was synthesized by following the procedure as described in Step 3 of Example 1 using intermediate (12b) from the previous step. 1H-NMR (400 MHz, CDCl₃), δ 7.85-7.78 (m, 2H), 7.70-7.60 (m, 2H), 7.35 (s, 1H), 5.25-5.10 (m, 1H), 4.30-4.25 (m, 1H), 3.45-3.30 (m, 1H), 2.19-1.60 (m, 6H), 1.45 (s, 12H), 1.35 (s, 9H); m/z 454.28 (M⁺+1).

Step 4: (S)-tert-butyl 2-(8-(4-(2-(1 R,2R)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (12d):

Title compound was synthesized by following the procedure as described in Step 4 of Example 1 using the intermediates 12c and (S)-tert-butyl 2-(8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate [synthesized as described in WO2009102633]. 1H-NMR (400 MHz, CDCl₃), δ 7.83-7.30 (m, 8H), 5.07-4.86 (m, 2H), 4.25-4.15 (m, 2H), 3.50-3.43 (m, 2H), 3.20-2.90 (m, 5H), 2.45-1.70 (m, 10H), 1.60-1.51 (m, 18H), m/z 679.40 (M⁺+1).

Step 5: methyl ((S)-1-(((1 R,2R)-2-(5-(4-(2-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 12):
Title compound was synthesized by following the procedure as described in Step 5 of Example 1 using the intermediate (12d) from the previous step. $^1$H NMR (DMSO-$d_6$, 400 MHz), $\delta$ 11.88-1.55 (m, 2H), 8.20-8.02 (m, 2H), 7.78-7.29 (m, 8H), 7.08-7.05 (m, 1H), 5.15-5.02 (m, 1H), 4.40-4.32 (m, 2H), 4.11-4.07 (m, 2H), 3.87-3.81 (m, 2H), 3.87-3.81 (m, 4H), 3.51-3.45 (s, 6H), 2.97-2.94 (m, 4H), 2.14-1.55 (m, 12H), 0.97-0.79 (m, 12H), m/z 793.50 (M$^+$+1). m.p.: 157-162 °C.

Example 13: Preparation of methyl ((S)-1-(((1R,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1 H-benzo[2,3]oxepino[4,5-d]imidazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutano-2-yl)carbamate (Compound 13):

Step 1: (S)-tert-butyl 2-(8-(4-(2-((1R,2R)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1 H-imidazol-5-yl)phenyl)-4,5-dihydro-1 H-benzo[2,3]oxepino[4,5-d]imidazol-2-yl)pyrrolidine-1-carboxylate (13a):

Title compound was synthesized by following the procedure as described in Step 4 of Example 1 using the intermediates from Step 2 of Example 12 (12b) and (S)-tert-butyl 2-(8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4,5-dihydro-1 H-benzo[2,3]oxepino[4,5-d]imidazol-2-yl)pyrrolidine-1 -carboxylate [synthesized following the procedures provided in WO20091 02633]. $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 7.83-7.40 (m, 8H), 5.07-4.90 (m, 2H), 4.40-4.20 (m, 3H), 3.50-3.43 (m, 2H), 3.25-3.10 (m, 3H), 2.95-2.90 (m, 1H), 2.45-1.72 (m, 8H), 1.65-1.51 (m, 18H), m/z 681.40 (M$^+$+1).
Step 2: methyl ((S)-1-(((1R,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-benzo[2,3]oxepino[4,5-d]imidazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 13):

Title compound was synthesized by following the procedure as described in Step 2 of Example 6 using the intermediate (13a) from the previous step. 

\[ ^1 \text{H-NMR} \text{ (DMSO-}_d^6, \text{ 400 MHz), } \delta 12.10-11.80 \text{ (m, 2H), } 8.14-7.00 \text{ (m, 11 H), } 5.05-5.02 \text{ (m, 1H), } 4.40-4.10 \text{ (m, 5H), } 3.90-3.70 \text{ (m, 3H), } 3.55-3.50 \text{ (m, 6H), } 3.15-3.10 \text{ (m, 2H), } 2.14-1.95 \text{ (m, 12H), } 0.97-0.71 \text{ (m, 12H), } m/z 795.40 \text{ (M}^+\text{+1). m.p.:} 162-165 ^\circ \text{C.} \]

Example 14: Preparation of methyl ((S)-1-(((1R,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 14):

Step 1: (S)-tert-butyl 2-(7-(4-2-((1R,2R)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (14a):

Title compound was synthesized by following the procedure as described in Step 4 of Example 1 using the intermediates from Step 2 of Example 12 (12b) and (S)-tert-butyl 2-(7-(4,4,5,5-tetramethyl-3,2-dioxaborolan-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate [synthesized following the procedures described in WO20091 02633]. 

\[ ^1 \text{H-NMR} \text{ (400 MHz, CDCl}_3\text{), } \delta 7.83-7.35 \text{ (m, 8H), } 5.07-4.86 \text{ (m, 2H), } \]
4.20-4.10 (m, 2H), 3.50-3.43 (m, 3H), 3.19-3.10 (m, 2H), 2.97-2.80 (m, 2H), 2.45-1.80 (m, 8H), 1.60-1.51 (m, 18H), m/z 665.40 (M+1).

**Step 2:** methyl ((S)-1-(((1R,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 14):

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 5 of Example 1 using the intermediate (14a) from the previous step. 1H NMR (DMSO-d6, 400 MHz), δ 12.10-1.55 (m, 2H), 8.20-8.14 (m, 1H), 7.80-6.96 (m, 10H), 5.10-5.05 (m, 1H), 4.40-4.32 (m, 2H), 4.11-4.07 (m, 2H), 3.87-3.81 (m, 4H), 3.51-3.45 (s, 6H), δ 3.02-2.67 (m, 4H), 2.20-1.45 (m, 10H), 0.99-0.75 (m, 12H), m/z 779.50 (M+1). m.p.: 142-145 °C.

**Example 15:** Preparation of methyl ((S)-1-(((1S,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 15):

**Step 1:** (S)-tert-butyl 2-(7-(4-((1R,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-4,5-dihydro-1 H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (15a):

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 4 of Example 1 using the intermediates from Step 2 of Example 7 (7b) and (S)-tert-butyl 2-(7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4,5-dihydro-1 H-naphtho[1,2-d]imidazol-2-yl)pyrrolidin-1-carboxylate (15a)
yl)pyrrolidine-1-carboxylate [synthesized by following procedures provided in WO2009102633]. 1H-NMR (400 MHz, CDCl₃) δ 11.00 (bs, 1H), 10.50 (bs, 1H), 7.83-7.45 (m, 7H), 7.20-7.10 (m, 1H), 5.07-4.86 (m, 2H), 4.40-4.20 (m, 2H), 3.50-3.43 (m, 3H), 3.29-3.26 (m, 2H), 2.97-2.80 (m, 2H), 2.45-1.80 (m, 8H), 1.60-1.51 (m, 18H), m/z 665.40 (M⁺+1).

**Step 2**: methyl ((S)-1-(((1S,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 15):

**Example 16**: Preparation of methyl ((S)-1-(((1R,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 16):

**Step 1**: (S)-tert-butyl 2-(7-bromo-3H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (16a):
DDQ (0.41 g, 1.79 mmol) was added to the solution of (S)-tert-butyl 2-(7-bromo-4,5-dihydro-3H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate [synthesized by following the procedures provided in WO2009102633] (0.5 g, 1.19 mmol) in benzene (10 mL) and stirred at 80 °C for 3 h. Benzene was evaporated under reduced pressure and the residue was purified by column chromatography (60% EtOAc/hexane) to afford the title compound (0.3 g, 60%). \[\text{1}\text{H-NMR (400 MHz, CDCl}_3\text{):} \delta 8.05-8.03 (m, 1 H), 7.62-7.50 (m, 4H), 5.24-5.23 (m, 1 H), 3.61-3.50 (m, 1 H), 3.15-3.10 (m, 1 H), 2.29-2.19 (m, 2H), 2.09-2.01 (m, 2H), 1.54-1.34 (m, 9H), m/z 416.09 (M+1).

**Step 2**: (S)-tert-butyl 2-(7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (16b):

In a 5-20 mL microwave vial, 1,4-Dioxane (15 mL) was purged with nitrogen for 10 min and (S)-tert-butyl 2-(7-bromo-3H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (16a) (0.4 g, 0.96 mmol), bis(pinacolato)diboron (0.49 g, 1.92 mmol), PCy\(_3\) (0.03 g, 0.1 mmol), KOAc (0.38 g, 3.84 mmol) were added and purged with nitrogen. Finally, PdCl\(_2\)(dpdf)-CH\(_2\)Cl\(_2\) adduct (0.08 g, 0.1 mmol) was added & purged with nitrogen and irradiated with microwaves at 115 °C for 45 min. The reaction mixture was poured into water and extracted with ethyl acetate. The organic layer was washed with saturated brine solution, dried over anhydrous sodium sulphate and purified by column chromatography (70% EtOAc/hexane) to afford the title compound (0.3 g, 67%). \[\text{1}\text{H-NMR (400 MHz, CDCl}_3\text{):} \delta 8.46 (s, 1 H), 7.97-7.95 (m, 1 H), 7.71-7.47 (m, 3 H), 5.23-5.22 (br s, 1 H), 3.48-3.41 (m, 1 H), 3.20-3.23 (m, 1 H), 2.26-2.19 (m, 2 H), 2.61-2.41 (m, 2 H), 1.41 (s, 9 H), 1.30-1.22 (m, 12 H), m/z 464.26 (M+1).

**Step 3**: (S)-tert-butyl 2-(7-(4-(2-((1 R,2R)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-1H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (16c):
The title compound was synthesized by following the procedure as described in Step 4 of Example 1 using the intermediates (16b) from the previous step and from Step 2 of Example 12. $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 8.15-7.32 (m, 9H), 7.20-7.10 (m, 1H), 5.40-5.10 (m, 2H), 4.40-4.20 (m, 1H), 3.55-3.50 (m, 2H), 3.35-3.10 (m, 2H), 2.45-1.80 (m, 8H), 1.60-1.51 (m, 18H), m/z 663.40 (M$^+$+1).

**Step 4:** methyl ((S)-1-(((1S,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 16):

Title compound was synthesized by following the procedure as described in Step 5 of Example 1 using the intermediate (16c) from the previous step. $^1$H NMR (DMSO-$d_6$, 400 MHz), $\delta$ 13.02-1.85 (m, 2H), 8.50-8.30 (m, 2H), 8.10-7.65 (m, 8H), 7.37-7.25 (m, 1H), 7.10-6.90 (m, 1H), 5.30-5.28 (m, 1H), 4.40-4.32 (m, 2H), 4.11-4.07 (m, 2H), 3.87-3.81 (m, 4H), 3.51-3.45 (s, 6H), 2.20-1.50 (m, 10H), 0.99-0.81 (m, 12H), m/z 777.30 (M$^+$+1). m.p.: 158-161 °C.

**Example 17:** Preparation of methyl ((S)-1-(((1S,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 17):

**Step 1:** (S)-tert-butyl 2-(7-(4-(2-((1S,2R)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-1H-naphtho[1,2-d]imidazol-2-yl)carboxylic acid (17a):
The title compound was synthesized by following the procedure as described in Step 4 of Example 1 using the intermediates from the Step 2 of Example 16 (16b) and Step 2 of Example 7 (7b). \(^\text{1}^H\text{-NMR (400 MHz, CDCl}_3\) \(\delta \): 7.83-7.52 (m, 10H), 5.30-5.20 (m, 2H), 4.35-4.25 (m, 2H), 3.55-3.35 (m, 2H), 3.29-3.26 (m, 1H), 2.60-1.72 (m, 8H), 1.65-1.51 (m, 18H), \(m/z \): 663.40 (M\(^+\)+1).

**Step 2:** methyl ((S)-1-(((1S,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 17):

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 2 of Example 6 using the intermediate (17a) from the previous step. \(^\text{1}^H\text{NMR (DMSO-}\delta_6\): 13.02-1.85 (m, 2H), 8.50-8.30 (m, 2H), 8.10-7.65 (m, 8H), 7.37-7.25 (m, 1H), 7.10-6.90 (m, 1H), 5.30-5.28 (m, 1H), 4.40-4.32 (m, 2H), 4.11-4.07 (m, 2H), 3.87-3.81 (m, 4H), 3.51-3.45 (s, 6H), 2.14-1.65 (m, 10H), 0.99-0.51 (m, 12H), \(m/z \): 777.30 (M\(^+\)+1). m.p.: 210 \(^\circ\)C.

**Example 18:** Preparation of methyl ((S)-1-(((1S,2S)-2-((4-(2-(((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 18):

**Step 1:** (S)-tert-butyl 2-(7-(4-2-(((1S,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-1H-naphtho-[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (18a):
The title compound was synthesized by following the procedure as described in Step 4 of Example 1 using the intermediates from the Step 2 of Example 16 (16b) and from Step 2 of Example 9 (9b). $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 7.83-7.52 (m, 10H), 5.30-5.20 (m, 2H), 4.35-4.25 (m, 2H), 3.55-3.35 (m, 2H), 3.29-3.26 (m, 1H), 2.60-1.72 (m, 8H), 1.65-1.51 (m, 18H), $m/z$ 663.40 (M$^+$+1).

**Step 2:** methyl ((S)-1-(((1S,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 18):

![Chemical Structure of Compound 18](image)

Title compound was synthesized by following the procedure as described in Step 5 of Example 1 using the intermediate (18a) from the previous step. $^1$H NMR (DMSO-$d_6$, 400 MHz), $\delta$ 13.02-1.85 (m, 2H), 8.45-7.06 (m, 13H), 5.30-5.25 (m, 1H), 4.44-4.32 (m, 2H), 4.1-4.07 (m, 2H), 3.87-3.81 (m, 4H), 3.51-3.45 (s, 6H), 3.1-3.1 (m, 6H), 2.14-1.50 (m, 9H), 0.99-0.51 (m, 12H), $m/z$ 777.30 (M$^+$+1). m.p.: 171°C.

**Example 19: Preparation of methyl ((S)-1-(((1S,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)phenyl)-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-4-chloro-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 19):**

**Step 1:** tert-butyl ((1S,2R)-2-(5-(4-bromophenyl)-4-chloro-1H-imidazol-2-yl)cyclopentyl)carbamate (19a):
To the stirred solution of tert-butyl ((1S,2R)-2-(5-(4-bromophenyl)-1H-imidazol-2-yl)cyclopentyl)carbamate (0.15 g, 0.369 mmol) [7b] in DMF (2 mL) was added NCS (0.074 g, 0.55 mmol) at room temperature and the reaction was warmed to 50°C and stirred for 20 min. The contents were diluted by water and extracted by ethyl acetate. The organic layer was separated, dried over sodium sulphate, evaporated under reduced pressure to get crude product which was used in the next step without further purification (0.1 g, 62%).

\[ \text{1H-NMR (400 MHz, CDCl}_3\text{)} \delta \text{7.58-7.51 (m, 4H), 4.75-4.70 (m, 1H), 4.40-4.30 (m, 1H), 3.35-3.25 (m, 1H), 2.40-1.60 (m, 6H), 1.50/1.30 (s, 9H); m/z 440.10 (M}^++\text{1).}
\]

**Step 2:** (S)-tert-butyl 2-(7-(4-(2-((1R,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-4-chloro-1H-imidazol-5-yl)phenyl)-1H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (19b):

The title compound was synthesized by following the procedure as described in Step 4 of Example 1 using the intermediates (19a) from the previous step and intermediate from Step 2 of Example 16 (16b). \[ \text{1H-NMR (400 MHz, CDCl}_3\text{)} \delta \text{8.20-7.52 (m, 9H), 5.40-5.30 (m, 1H), 4.83-4.75 (m, 1H), 4.40-4.35 (m, 2H), 3.55-3.35 (m, 2H), 3.30-3.26 (m, 2H), 2.45-1.72 (m, 8H), 1.55-1.31 (s, 18H), m/z 697.40 (M}^++\text{1).}
\]

**Step 3:** methyl ((S)-1-(((1S,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino)-3-methylbutanoyl)pyrrolidin-2-yl)-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-4-chloro-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 19).
Title compound was synthesized by following the procedure as described in Step 2 of Example 6 using the intermediate (19b) from the previous step. $^1$H NMR (DMSO-$d_6$, 400 MHz), $\delta$ 13.10-1.20 (m, 2H), 8.50-8.30 (m, 2H), 8.10-7.65 (m, 7H), 7.35-7.30 (m, 1H), 6.82-6.80 (m, 1H), 5.45-5.30 (m, 1H), 4.55-4.32 (m, 2H), 4.10-4.07 (m, 2H), 3.87-3.81 (m, 4H), 3.51-3.45 (s, 6H), 2.40-1.65 (m, 10H), 0.99-0.51 (m, 12H), $m/z$ 811.40 (M$^+$+1). m.p.: 255-257 °C.

Example 20: Preparation of methyl ((S)-1-(((1S,2S)-2-(5-(4-chloro-1H-imidazol-2-yl)cyclopentyl)amino)-3-methylbutanoyl)pyrrolidin-2-yl)-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-4-chloro-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutane-2-yl)carbamate (Compound 20):

Step 1: tert-butyl ((1S,2S)-2-(5-(4-bromophenyl)-4-chloro-1H-imidazol-2-yl)cyclopentyl)carbamate (20a):

To the stirred solution of tert-butyl ((1S,2S)-2-(5-(4-bromophenyl)-4-chloro-1H-imidazol-2-yl)cyclopentyl)carbamate (0.15 g, 0.369 mmol) (9b) in DMF (2 mL) was added NCS (0.074 g, 0.55 mmol) at room temperature and the reaction was warmed to 50 °C and stirred for 20 min. The contents were diluted by water and extracted by ethyl acetate. The organic layer was separated, dried over sodium sulphate, evaporated under reduced pressure to get crude product which was used in the next step without further purification (0.1 g, 62%). $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 12.07 (bs, 1H), 7.69-7.67 (m 2H), 7.56-7.51 (m, 2H), 4.90-
4.89 (m, 1H), 3.10-3.00 (m, 1H), 2.36-2.33 (m, 1H), 2.21 -2.18 (m, 2H), 1.83-1.78 (m, 3H), 1.57-1.53 (m, 9H). m/z 440.04 (M⁺+1).

**Step 2**: (S)-tert-butyl 2-(7-(4-(2-((1S,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-4-chloro-1H-imidazol-5-yl)phenyl)-1H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (20b):

![Chemical structure of (S)-tert-butyl 2-(7-(4-(2-((1S,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-4-chloro-1H-imidazol-5-yl)phenyl)-1H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (20b).]

Title compound was synthesized by following the procedure as described in Step 4 of Example 1 using the intermediate (20a) from the previous step and Step 2 of Example 16 (16b). m/z 697.26 (M⁺+1).

**Step 3**: methyl ((S)-1-(((1S,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-4-chloro-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 20):

![Chemical structure of methyl ((S)-1-(((1S,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-4-chloro-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 20).]

Title compound was synthesized by following the procedure as described in Step 2 of Example 6 using the intermediate (20b) from the previous step. ¹H NMR- (400 MHz, MeOD), δ 8.46-8.43 (m, 1H), 8.30-8.25 (m, 1H), 8.10 (s, 1H), 7.96-7.94 (m, 1H), 7.88-7.87 (m, 3H), 7.83-7.80 (m, 1H), 7.73-7.67 (m, 1H), 5.38-5.37 (m, 1H), 4.50-4.49 (m, 1H), 4.30-4.29 (m, 1H), 4.15-4.10 (m, 1H), 4.01-4.00 (m, 1H), 3.7 (s, 6H), 3.32-3.30 (m, 2H), 3.10-3.02 (m, 1H), 2.60-2.50 (m, 1H), 2.40-2.15 (m, 6H), 2.10-1.85 (m, 7H), 1.80-1.71 (m, 2H), 1.10-0.95 (m, 6H), 0.91-0.82 (m, 6H); m/z 811.4 (M⁺+1). m.p.: 185-187 °C.
Example 21: Preparation of methyl ((S)-1-(((1R,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-5,6-dihydro-4H-benzo[3,4]cyclohepta[1,2-d]oxazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 21):

**Step 1:** (S)-tert-butyl 2-(8-bromo-5,6-dihydro-4H-benzo[3,4]cyclohepta[1,2-d]oxazol-2-yl)pyrrolidine-1-carboxylate (21a):

To the stirred solution of (2S)-2-(2-bromo-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulen-6-yl) 1-tert-butyl pyrrolidine-1,2-dicarboxylate (3.2 g, 7.04 mmol) [synthesized using procedures described in WO2009/102633] in xylene (25 mL), ammonium acetate (1.086 g, 141 mmol) was added at room temperature and the reaction mass was heated at 130 °C for 15 h. The reaction mixture was poured into water (100 mL) and the compound was extracted with ethyl acetate (100 mL x 2), dried over sodium sulphate, concentrated under reduced pressure and purified by flash column chromatography (45-55% Ethylacetate/Hexane) to get the title compound as side product, orange colored solid (0.7 g, 23 % yield) along with (S)-tert-butyl 2-(8-bromo-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate as the major compound. $^1$H NMR (CDCl$_3$, 400 MHz): δ 7.52-7.50 (m, 1H), 7.37-7.28 (m, 2H), 4.88-4.85 (m, 1H), 3.60-3.40 (m, 2H), 2.95-2.80 (m, 4H), 2.40-1.90 (m, 6H), 1.45/1.25 (s, 9H); m/z 433.05 (M$^+$+1)

**Step 2:** (S)-tert-butyl 2-(8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydro-4H-benzo[3,4]cyclohepta[1,2-d]oxazol-2-yl)pyrrolidine-1-carboxylate (21 b):
Title compound was synthesized by following the procedure as described in Step 3 of Example 1 using intermediate (21a) from the previous step. \( ^1 \text{H NMR (CDCl}_3, 400 \text{ MHz)}: \delta 7.80-7.60 \text{ (m, 2H), 7.56-7.53 (m, 1H), 4.90-4.80 (m, 1H), 3.80-3.50 (m, 2H), 2.95-2.80 (m, 4H), 2.40-1.90 (m, 6H), 1.48/1.44 (s, 9H), 1.25 (m, 12H); } m/z 480.90 (M^+1) \)

**Step 3**: (S)-tert-butyl 2-(8-((1S,2R)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-5,6-dihydro-4H-benzo[3,4]cyclohepta[1,2-d]oxazol-2-yl)pyrrolidine-1-carboxylate (21c):

\[
\text{\includegraphics{image}}
\]

**Step 4**: methyl ((S)-1-(((1R,2S)-2-(5-((4-((2-(methoxycarbonyl)amino)-3-methylbutanoyl)pyrrolidin-2-yl)-5,6-dihydro-4H-benzo[3,4]cyclohepta[1,2-d]oxazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 21):

\[
\text{\includegraphics{image}}
\]

Title compound was synthesized by following the procedure as described in Step 5 of Example 1 using the intermediate (21c) from the previous step. \( ^1 \text{H NMR (DMSO-\text{d}_6, 400 MHz)}: \delta 11.85-1.70 \text{ (m, 1H), 7.82-7.03 (m, 11H), 5.1 5-5.02 (m, 1H), 4.44-4.32 (m, 2H), } \]
Example 22: Preparation of methyl ((S)-1-(((1S,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydrobenzo[2,3]oxepino[4,5-d]oxazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 22):

Step 1: (S)-tert-butyl 2-(8-bromo-4,5-dihydrobenzo[2,3]oxepino[4,5-d]oxazol-2-yl)pyrrolidine-1-carboxylate (22a):

Title compound was synthesized by following the procedure described in Step 1 of Example 21 using (2S)-2-(8-bromo-5-oxo-2,3,4,5-tetrahydrobenzo[b]oxepin-4-yl) 1-tert-butyl pyrrolidine-1,2-dicarboxylate [synthesized as described in WO2009/102633] as the starting material. $^1$H NMR (DMSO-$d_6$, 400 MHz): $\delta$ 7.57-7.53 (m, 1H), 7.38-7.35 (m, 1H), 7.30-7.28 (m, 1H), 4.90-4.82 (m, 1H), 4.30-4.26 (m, 2H), 3.50-3.45 (m, 1H), 3.00-2.95 (m, 2H), 2.40-2.20 (m, 1H), 2.05-1.90 (m, 4H), 1.38/1.5 (s, 9H); m/z 435.00 (M$^+$+1)

Step 2: (S)-tert-butyl 2-(8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4,5-dihydrobenzo[2,3]oxepino[4,5-d]oxazol-2-yl)pyrrolidine-1-carboxylate (22b):

Title compound was synthesized by following the procedure as described in Step 3 of Example 1 using intermediate (22a) from the previous step. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.66-7.63 (m, 1H), 7.56-7.53 (m, 2H), 5.07-4.90 (m, 1H), 4.29-4.21 (m, 2H), 3.70-3.60 (m,
1H), 3.15-3.05 (m, 2H), 2.40-1.70 (m, 5H), 1.48/1.44 (s, 9H), 1.25 (m, 12H); m/z 482.98 (M+1)

**Step 3**: (S)-tert-butyl 2-((8-(4-(2-((1S,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-4,5-dihydrobenzo[2,3]oxepino[4,5-d]oxazol-2-yl)pyrrolidine-1-carboxylate (22c): 

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 4 of Example 1 using the intermediates from Step 2 of Example 9 (9b) and the boronate (22b) from the previous step. ¹H-NMR (400 MHz, CDCl₃) δ 7.83-7.35 (m, 8H), 5.07-4.90 (m, 2H), 4.40-4.20 (m, 3H), 3.75-3.40 (m, 4H), 3.25-3.10 (m, 2H), 2.45-1.72 (m, 8H), 1.65-1.51 (m, 18H), m/z 682.40 (M+1).

**Step 4**: methyl ((S)-1-(((1S,2S)-2-((5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydrobenzo[2,3]oxepino[4,5-d]oxazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 22): 

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 2 of Example 6 using the intermediate (22c) from the previous step. ¹H NMR (DMSO-d₆, 400 MHz), δ 12.10-1.80 (m, 1H), 8.14-6.90 (m, 11 H), 5.15-5.10 (m, 1H), 4.40-4.30 (m, 4H), 4.15-4.10 (m, 1H), 3.95-3.70 (m, 3H), 3.55-3.50 (m, 6H), 3.10-2.95 (m, 2H), 2.14-1.95 (m, 12H), 0.97-0.71 (m, 12H), m/z 796.50 (M+1). m.p.: 220-222 °C.
Example 23: Preparation of methyl (S)-1-(((1 R,2S)-2-(5-(4-(2-(((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydrobenzo[2,3]oxepino[4,5-d]oxazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 23):

5 Step 1: (S)-tert-butyl 2-(8-(4-(2-((1 S,2R)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-4,5-dihydrobenzo[2,3]oxepino[4,5-d]oxazol-2-yl)pyrrolidine-1-carboxylate (23a):

Title compound was synthesized by following the procedure as described in Step 4 of Example 1, using the intermediates from Step 2 of Example 4 (4b) and the intermediate from step 2 of Example 22 (22b). 1H-NMR (400 MHz, CDCl3) δ 7.83-7.35 (m, 8H), 5.07-4.90 (m, 2H), 4.40-4.20 (m, 3H), 3.75-3.40 (m, 4H), 3.25-3.10 (m, 2H), 2.45-1.72 (m, 8H), 1.65-1.51 (m, 18H), m/z 682.40 (M+1).

Step 2: methyl (S)-1-(((1 R,2S)-2-(5-(4-(2-(((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydrobenzo[2,3]oxepino[4,5-d]oxazol-8-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 23):

Title compound was synthesized by following the procedure as described in Step 2 of Example 6 using the intermediate (23a) from the previous step. 1H NMR (DMSO-d6, 400 MHz), δ 12.1 0-1 1.80 (m, 1H), 8.14-6.90 (m, 11 H), 5.1 5-5.10 (m, 1H), 4.40-4.30 (m, 4H), 4.15-4.1 0 (m, 1H), 3.95-3.70 (m, 3H), 3.55-3.50 (m, 6H), 3.1 0-2.95 (m,2H), 2.14-1.95 (m, 12H), 0.97-0.71 (m, 12H), m/z 796.50 (M+1). m.p.:166-168 °C.
Example 24: Preparation of methyl ((S)-1-(((1S,2S)-2-(7-(4-((2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1 H-imidazol-5-yl)phenyl)-4,5-dihydro-1 H-naphtho[1,2-d]imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 24):

**Step 1:** (1S,2S)-6-bromo-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl 2-((tert-butoxycarbonyl)amino)cyclopentanecarboxylate (24a):

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 1 of Example 1 using 2,6-dibromo-3,4-dihydronaphthalen-1 (2H)-one [synthesized using procedures described in WO2010/17635A1] and (1S,2S)-2-((tert-butoxycarbonyl)amino)cyclopentanecarboxylic acid [synthesized using procedures described in J. Org. Chem., 2001, 66 (16), 5629-5632] as starting materials. $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 8.09-8.07 (m, 1H), 7.85-7.81 (m, 1H), 7.55-7.50 (m, 2H), 5.56-5.50 (m, 1H), 4.30-4.05 (m, 2H), 3.30-3.05 (m, 4H), 2.45-2.10 (m, 6H), 1.40 (s, 9H); m/z 352.10 [(M$^+$+1) - 100] (value observed for the de-Boc product).

**Step 2:** tert-butyl ((1S,2S)-2-(7-bromo-4,5-dihydro-3H-naphtho[1,2-d]imidazol-2-yl)cyclopentyl)carbamate (24b):

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 2 of Example 1, using the intermediate (24a) from the previous step. $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 7.34-7.30 (m, 3H), 4.90-4.87 (m, 1H), 4.19-4.12 (m, 1H), 3.15-3.13 (m, 1H), 3.05-2.85 (m, 4H), 2.45-2.10 (m, 2H), 1.90-1.60 (m, 4H), 1.50 (s, 9H); m/z 432.10 (M$^+$+1).
Step 3: (S)-tert-butyl 2-(5-(4-(2-((1S,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)pyrrolidine-1-carboxylate (24c).

Title compound was synthesized by following the procedure as described in Step 4 of Example 1, using the intermediates (24b) from the previous step and (S)-tert-butyl 2-(5-(4,4,5,5-tetramethyl-1,3-dioxaborolan-2-yl)phenyl)-1H-imidazol-2-yl)pyrrolidine-1-carboxylate [synthesized using procedures described in ref. WO2010/99527A1] as starting materials. \(^1^H\)NMR (400 MHz, CDCl\(_3\)) \(\delta\) 11.00 (bs, 1H), 10.50 (bs, 1H), 7.85-7.40 (m, 7H), 7.20-7.10 (m, 1H), 5.07-4.86 (m, 2H), 4.40-4.20 (m, 2H), 3.50-3.43 (m, 2H), 3.17-3.09 (m, 3H), 2.93-2.89 (m, 2H), 2.45-1.80 (m, 8H), 1.60-1.51 (m, 18H); m/z 665.40 (M\(^{+}\) + 1).

Step 4: methyl (S)-1-(((1S,2S)-2-(7-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino)-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-5-yl)phenyl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 24):

Title compound was synthesized by following the procedure as described in Step 5 of Example 1 using the intermediate (24c) from the previous step. \(^1^H\) NMR (DMSO-\(d_6\), 400 MHz), \(\delta\) 12.10-1.55 (m, 2H), 8.13-7.46 (m, 9H), 7.31-7.29 (m, 1H), 7.04-7.01 (m, 1H), 5.10-5.05 (m, 1H), 4.40-4.32 (m, 2H), 4.11-4.07 (m, 2H), 3.87-3.81 (m, 4H), 3.51-3.45 (s, 6H), 3.02-2.67 (m, 1H), 2.14-1.55 (m, 10H), 0.99-0.51 (m, 12H), m/z 779.30 (M\(^{+}\) + 1). m.p.: 181-183 °C.
Example 25: Preparation of methyl ((S)-1-(((1S,2R)-2-(7-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1 H-imidazol-5-yl)phenyl)-4,5-dihydro-1 H-naphtho[1,2-d]imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 25):

Step 1: (1R,2S)-6-bromo-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl 2-((tert-butoxycarbonyl)amino)cyclopentanecarboxylate (25a):

Title compound was synthesized by following the procedure as described in Step 1 of Example 1, using 2,6-dibromo-3,4-dihydronaphthalen-1 (2H)-one [synthesized using procedures described in WO2010/17635A1] and (1R,2S)-2-((tert-butoxycarbonyl)amino)cyclopentanecarboxylic acid [synthesized using procedures described in Tetrahedron: Asymmetry, 2008, 19, 2796-2803] as starting materials. 1H-NMR (400 MHz, CDCl₃) δ 8.09-8.07 (m, 1H), 7.85-7.81 (m, 1H), 7.55-7.50 (m, 2H), 5.56-5.50 (m, 1H), 4.30-4.05 (m, 2H), 3.30-3.05 (m, 4H), 2.45-1.60 (m, 6H), 1.40 (s, 9H); m/z 352.10 [(M⁺+1) - 100] (value observed for the de-Boc product).

Step 2: tert-butyl ((1S,2R)-2-(7-bromo-4,5-dihydro-3H-naphtho[1,2-d]imidazol-2-yl)cyclopentyl)carbamate (25b):

Title compound was synthesized by following the procedure as described in Step 2 of Example 1, using the intermediate (25a) from the previous step. 1H-NMR (400 MHz, CDCl₃) δ 7.34-7.30 (m, 3H), 5.19-5.16 (m, 1H), 4.90-4.87 (m, 1H), 4.40-4.30 (m, 1H), 3.36-3.31 (m, 1H), 3.05-2.80 (m, 4H), 2.45-2.10 (m, 2H), 1.90-1.60 (m, 4H), 1.50/1.43 (s, 9H); m/z 431.85 (M⁺+1).
**Step 3**: (S)-tert-butyl 2-(5-(4-(2-((1R,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)pyrrolidine-1-carboxylate (25c):

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 4 of Example 1, using the intermediates (25b) from the previous step and (S)-tert-butyl 2-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1H-imidazol-2-yl)pyrrolidine-1-carboxylate [synthesized using procedures described in ref. WO2010/99527A1] as starting materials. $^1$H-NMR (400 MHz, CDCl$_3$) δ 11.00 (bs, 1H), 10.50 (bs, 1H), 7.85-7.40 (m, 7H), 7.20-7.10 (m, 1H), 5.07-4.86 (m, 2H), 4.40-4.20 (m, 2H), 3.50-3.43 (m, 2H), 3.17-3.09 (m, 3H), 2.93-2.89 (m, 2H), 2.45-1.80 (m, 8H), 1.60-1.51 (m, 18H), m/z 665.40 (M$^+$+1).

**Step 4**: methyl ((S)-1-(((1S,2R)-2-(7-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino)-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-5-yl)phenyl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 25):

![Chemical Structure](image)

Title compound was synthesized following the procedure as described in Step 2 of Example 6 using the intermediate (25c) from the previous step. $^1$H NMR (DMSO-$d_6$, 400 MHz), δ 12.10-1.55 (m, 2H), 8.13-7.46 (m, 8H), 7.41-7.29 (m, 2H), 7.04-6.90 (m, 1H), 5.10-5.05 (m, 1H), 4.40-4.32 (m, 2H), 4.11-4.07 (m, 2H), 3.87-3.81 (m, 4H), 3.51-3.45 (s, 6H), 3.02-2.67 (m, 4H), 2.14-1.50 (m, 10H), 0.99-0.51 (m, 12H), m/z 779.30 (M$^+$+1). m.p.: 224 °C.
Example 26: Preparation of methyl \(((S)-1-(((1S,2R)-2-(7-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-5-yl)phenyl)-1H-naphtho[1,2-d]imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 26):

**Step 1:** (S)-tert-butyl 2-(5-(4-(2-((1R,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-2-yl)phenyl)-1H-imidazol-7-yl)pyrrolidine-1-carboxylate (26a):

Title compound was synthesized by following the procedure as described in Step 1 of Example 16, using the intermediate from Step 3 of Example 25 (25c). \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.10-7.45 (m, 9H), 7.26 (s, 1H), 5.15-5.03 (m, 2H), 4.55-4.35 (m, 1H), 3.75-3.35 (m, 2H), 3.25-3.15 (m, 2H), 2.55-1.60 (m, 8H), 1.51-1.30 (m, 18H), m/z 663.40 (M\(^{+}\)+1).

**Step 2:** methyl \(((S)-1-(((1S,2R)-2-(7-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-5-yl)phenyl)-1H-naphtho[1,2-d]imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 26):

Title compound was synthesized by following the procedure as described in Step 2 of Example 6 using the intermediate (26a) from the previous step. \(^1\)H NMR (DMSO-\(d_6\), 400 MHz), \(\delta\) 12.1 0-1.55 (m, 2H), 8.60-7.50 (m, 11H), \(\delta\) 7.31-7.29 (m, 1H), 7.1 0-6.85 (m, 1H), 5.10-5.05 (m, 1H), 4.55-4.40 (m, 2H), 4.11-4.07 (m, 2H), 3.87-3.81 (m, 4H), 3.51-3.45 (s, 6H), 2.40-1.50 (m, 10H), 0.99-0.51 (m, 12H), m/z 777.30 (M\(^{+}\)+1). m.p.: 238-240 °C.
Example 27: Preparation of methyl $((S)-1-(((1S,2S)-2-(7-(4-(2-((S)-1-((S)-2-amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-5-yl)phenyl)-1H-naphtho[1,2-d]imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate$ (Compound 27):

Step 1: (S)-tert-butyl 2-(5-(4-(2-((1S,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)pyrrolidine-1-carboxylate (27a):

Title compound was synthesized by following the procedure as described in Step 1 of Example 16, using the intermediate from Step 3 of Example 24 (24c) as starting material. 

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 8.10-7.45 (m, 9H), 7.26 (s, 1H), 5.15-5.03 (m, 2H), 4.60-4.35 (m, 1H), 3.75-3.35 (m, 2H), 3.25-3.15 (m, 2H), 2.55-1.60 (m, 8H), 1.51-1.30 (m, 18H), m/z 663.40 (M$^+$+1).

Step 2: methyl $((S)-1-(((1S,2S)-2-(7-(4-(2-((S)-1-((S)-2-amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-5-yl)phenyl)-1H-naphtho[1,2-d]imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate$ (Compound 27):

Title compound was synthesized by following the procedure as described in Step 2 of Example 6 using the intermediate (27a) from the previous step. 

$^1$H NMR (400 MHz, MeOD), $\delta$ 8.55-8.47 (m, 2H), 8.20-7.75 (m, 8H), 7.42-7.30 (m, 2H), 5.30-5.27 (m, 2H), 4.65-4.60 (m, 2H), 4.27-4.15 (m, 2H), 3.95-3.85 (m, 3H), 3.70-3.65 (m, 6H), 2.70-1.95 (m, 10H), 0.99-0.80 (m, 12H), m/z 777.30 (M$^+$+1).
Example 28: Preparation of methyl \(((S)-1-(((1S,2S)-2-\text{(5-(4-(2-((S)-1-((S)-2-\text{(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1 H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl}(ethyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 28):

5 Step 1: (1S,2S)-ethyl-2-(ethylamino)cyclopentanecarboxylate (28a):

To a solution of \((1S,2S)\)-ethyl 2-aminocyclopentanecarboxylate (0.2 g, 1.27 mmol) [synthesized using procedures described in J. Org. Chem., 2001, 66 (16), 5629-5632] in THF (10 mL), acetic acid (0.07 mL, 1.27 mmol) and acetaldehyde (0.07 mL, 1.27 mmol) were added and stirred for 1 h at room temperature after which sodium triacetoxyborohydride (0.4 g, 1.91 mmol) was added and stirred at room temperature for 16 h. After completion, the mixture was added to saturated NaHCO₃ solution and extracted with EtOAc (2 x 35 mL). The organic layer was washed with brine, dried over Na₂SO₄ and concentrated under reduced pressure to get colorless oil (0.14 g, 59%) which was taken to next step without any purification. ¹H-NMR (400 MHz, CDCl₃), δ 4.20-4.10 (m, 2H), 3.56 (q, \(J = 7.2\) Hz, 1H), 2.72 (q, \(J = 7.2\) Hz, 1H), 2.62-2.50 (m, 2H), 1.94-1.50 (m, 6H), 1.28-1.23 (t, \(J = 7.2\) Hz, 3H), 1.05-1.02 (t, \(J = 7.2\) Hz, 3H); m/z 186 (M⁺+1).

Step 2: (1S,2S)-ethyl 2-((tert-butoxycarbonyl)(ethyl)amino)cyclopentanecarboxylate (28b):

To a stirred solution of (1S, 2S)-ethyl-2-(ethylamino)cyclopentanecarboxylate (28a) (0.22 g, 1.19 mmol) in 1,4-Dioxane (10 mL) was added a solution of NaHCO₃ (0.35 g, 4.16 mmol) in water (10 mL) till the solution turned basic. To this Boc anhydride (0.33 mL, 1.43 mmol) was added. The resultant mixture was stirred at room temperature for 16 h. The
reaction mixture was poured into water and extracted with ethyl acetate (2 × 15 ml). The combined organic layers were dried over sodium sulfate and concentrated under reduced pressure to get white solid (0.2 g, 59%) which was used in the next step without any further purification. ¹H-NMR (400 MHz, CDCl₃), δ 4.25 (bs, 1H), 4.16-4.11 (m, 1H), 3.20-3.19 (m, 2H), 2.93 (q, J = 7.2 Hz, 2H), 2.05-1.70 (m, 6H), 2.00-1.65 (m, 6H), 1.47 (s, 9H), 1.13 (t, J = 7.2 Hz, 3H); m/z 285.2 (M⁺).

**Step 3**: (1S,2S)-2-((tert-butoxycarbonyl)(ethyl)amino)cyclopentanecarboxylic acid (28c):

To a stirred solution of (1S, 2S)-ethyl-2-((tert-butoxycarbonyl)(ethyl)amino)cyclopentanecarboxylate (28b) (1.3 g, 4.56 mmol) in Tetrahydrofuran (10 ml), Ethanol (10 mL) and Water (10 mL) lithium hydroxide (0.44 g, 18.22 mmol) was added. The reaction mixture was stirred at room temperature for 4 h. The reaction mixture was concentrated under reduced pressure and diluted with water and extracted with ethyl acetate (2 × 35 mL). The aqueous layer was acidified by 1N HCl, and extracted with ethyl acetate (2 × 10 mL) and the combined organic layers were washed with brine, dried over sodium sulfate and concentrated under reduced pressure to yield a white solid (0.7 g, 59%) which was used in the next step without any purification. ¹H-NMR (400 MHz, CDCl₃), δ 4.33-4.29 (m, 1H), 3.28-3.18 (m, 1H), 3.00-2.90 (m, 2H), 2.00-1.65 (m, 6H), 1.47 (s, 9H), 1.13 (t, J = 7.2 Hz, 3H); m/z 257.18 (M⁺).

**Step 4**: (1S, 2S)-2-(4-bromophenyl)-2-oxoethyl 2-((tert-butoxycarbonyl)(ethyl) amino)cyclopentane carboxylate (28d):
To a stirred solution of (1S,2S)-2-((tert-butoxycarbonyl)(ethyl)amino)cyclopentanecarboxylic acid (28c) (0.7 g, 2.72 mmol) in ACN (20 mL), 2-bromo-1-(4-bromophenyl)ethanone (0.76 g, 2.72 mmol) and DIPEA (0.35 g, 2.72 mmol) were added and stirred for 3 h at room temperature. The contents were concentrated under reduced pressure and water (50 mL) was added to it and extracted with DCM (20 mL x 2). The combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated under reduced pressure to get white foam (0.9 g, 73%) that was used in the next step without any further purification, m/z 354 [(M⁺) - 100].

Step 5: tert-butyl ((1S,2S)-2-(5-(4-bromophenyl)-1H-imidazol-2-yl)cyclopentyl)(ethyl)carbamate (28e):

![Chemical Structure]

To a stirred solution of (1S,2S)-2-(4-bromophenyl)-2-oxoethyl-2-((tert-butoxycarbonyl)(ethyl)amino)cyclopentanecarboxylate (28d) (0.900 g, 1.98 mmol) in toluene (12 mL) ammonium acetate (4.58 g, 59.4 mmol) was added and heated for 18 hr at 110 °C. The mixture was added to water (100 mL) and extracted with DCM (70 mL x 2). The combined organic layers were washed with brine and dried over Na₂SO₄, concentrated under reduced pressure and purified by flash chromatography using 5% EtOAc / pet-ether to get yellow solid (0.22 g, 26%). ¹H-NMR (400 MHz, CDCl₃): δ 7.70-7.60 (m, 1H), 7.48-7.46 (m, 3H), 7.16 (bs, 1H), 4.90-4.80 (m, 1H), 3.30-3.20 (m, 2H), 3.10-3.00 (m, 1H), 2.50-2.40 (m, 1H), 2.00-1.70 (m, 5H), 1.50 (s, 9H), 1.18-1.13 (m, 3H); m/z 434.98 (M⁺+1).

Step 6: (S)-tert-butyl 2-(7-(4-(2-((1S,2S)-2-((tert-butoxycarbonyl)(ethyl)amino)cyclopentyl)-1 H-imidazol-5-yl)phenyl)-4,5-dihydro-1 H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (28f):
Title compound was synthesized by following the procedure as described in Step 4 of Example 1 using intermediate (28e) from the previous step and (S)-tert-butyl 2-((7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate [synthesized using procedures described in WO2009/102633].

\[ \text{m/z 693.50 (M+1).} \]

\[ \text{1H-NMR (400 MHz, CDCl}_3\text{):} \delta 11.00 \text{ (bs, 1H), 10.50 (bs, 1H), 7.83-7.52 (m, 8H), 5.07-4.86 (m, 2H), 3.50-3.43 (m, 3H), 3.2-3.26 (m, 2H), 3.08-3.03 (m, 2H), 2.97-2.90 (m, 2H), 2.50-2.40 (m, 2H), 2.25-1.72 (m, 8H), 1.60-1.51 (m, 18H), 1.20-1.15 (m, 3H), m/z 693.50 (M+1).} \]

**Step 7:** methyl ((S)-1-(((1S,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)(ethyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 28):

\[ \text{m/z 807.50 (M+1). m.p.: 193-195 °C.} \]

Title compound was synthesized by following the procedure as described in Step 5 (Example 1) using intermediate (28f) from the previous step. \[ \text{1H NMR (DMSO-\text{d}_6, 400 MHz),} \delta 11.80-1.75 \text{ (bs, 2H), 8.14-7.92 (m, 6H), 7.34-7.31 (m, 1H), 6.99-6.96 (m, 1H), 5.17-4.99 (m, 4H), 4.20-3.85 (m, 5H), 3.55-3.50 (m, 6H), 3.15-2.85 (m, 4H), 2.14-1.50 (m, 12H), 0.99-0.51 (m, 15H), m/z 807.50 (M+1). m.p.: 193-195 °C.} \]
Example 29: Preparation of methyl (S)-1-(((1S,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1 H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)(methyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 29):

Step 1: (1S, 2S)-ethyl 2-(methylamino)cyclopentanecarboxylate (29a):

To a solution of (1S,2S)-ethyl 2-aminocyclopentanecarboxylate (2 g, 12.72 mmol) in ethanol (30 mL), formaldehyde solution (37% v/v, 0.385 mL, 14 mmol) was added and stirred for 1 h. Then, 10% Pd-C (2.03 g, 19.1 mmol) was added to the mixture and stirred for 2 h under H₂ atmosphere. After completion of reaction, the mixture was filtered through a pad of celite. The celite bed was washed with ethanol (20 mL). The combined organic layers were evaporated under reduced pressure and the residue (1.4 g, 64%) was taken to next step without any purification. ¹H-NMR (400 MHz, CDCl₃), δ 4.20-4.10 (m, 2H), 3.07 (q, J = 7.6 Hz, 1H), 2.70 (q, J = 7.2 Hz, 1H), 2.26 (s, 3H), 1.94-1.50 (m, 6H), 1.27 (t, J = 7.2 Hz, 3H); m/z 171.23 (M⁺)

Step 2: (1S, 2S)-ethyl 2-((tert-butoxycarbonyl)(methyl)amino) cyclopentanecarboxylate (29b):

Title compound was synthesized by following the procedure as described in Step 2 of Example 28, using intermediate (29a) from the previous step. ¹H-NMR (400 MHz, CDCl₃), δ 4.60-4.50 (m, 1H), 4.19-4.10 (m, 2H), 2.56 (q, J = 7.2 Hz, 1H), 2.05-1.70 (m, 6H), 3.27 (s, 3H), 1.47-1.44 (m, 9H), 1.25 (t, J = 7.2 Hz, 3H); m/z 271.29 (M⁺)
**Step 3**: (1S, 2S)-2-((tert-butoxycarbonyl)(methyl)amino)cyclopentanecarboxylic acid (29c):

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 3 of Example 28, using intermediate 29b as starting material. $^1$H-NMR (400 MHz, CDCl$_3$), $\delta$ 4.61-4.59 (m, 1H), 3.28-3.18 (m, 1H), 2.81 (s, 3H), 2.00-1.65 (m, 6H), 1.47 (s, 9H); m/z 244.08 (M$^+$+1).

**Step 4**: (1S,2S)-2-(4-bromophenyl)-2-oxoethyl 2-((tert-butoxycarbonyl)(methyl)amino)cyclopentanecarboxylate (29d):

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 4 of Example 28, using intermediate 29c as starting material, m/z 439.79 (M$^+$)

**Step 5**: tert-butyl ((1S,2S)-2-(5-(4-bromophenyl)-1H-imidazol-2-yl)cyclopentyl)(methyl)carbamate (29e):

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 5 of Example 28, using intermediate 29d as starting material. $^1$H-NMR (400 MHz, CDCl$_3$), $\delta$ 7.60-7.45 (m, 4H), 7.20 (bs, 1H), 4.90-4.88 (m, 1H), 3.30-3.23 (m, 1H), 2.80 (s, 3H), 2.50-2.40 (m, 1H), 2.00-1.70 (m, 5H), 1.50 (s, 9H); m/z 420.20 (M$^+$+1).

**Step 6**: (S)-tert-butyl 2-(7-(4-(2-((1S,2S)-2-((tert-butoxycarbonyl)(methyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenyl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate (29f):
Title compound was synthesized by following the procedure as described in Step 6 of Example 28, using intermediate (29e) from the previous step and (S)-tert-butyl 2-(7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-2-yl)pyrrolidine-1-carboxylate [synthesized using procedures described in WO2009/102633].

$^1$H-NMR (400 MHz, CDCl$_3$), $\delta$ 11.00 (bs, 1H), 10.50 (bs, 1H), 7.83-7.52 (m, 8H), 5.07-4.86 (m, 2H), 3.50-3.43 (m, 3H), 3.20-3.10 (m, 2H), 2.97-2.90 (m, 2H), 2.85 (s, 3H), 2.50-2.40 (m, 2H), 2.25-1.72 (m, 8H), 1.60-1.51 (m, 18H), m/z 679.50 (M$^+$+1).

**Step 7:** methyl ((S)-1-(((1S,2S)-2-(5-(4-((S)-1-(((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-2-yl)cyclopentyl)(methyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 29):

Title compound was synthesized by following the procedure as described in Step 7 of Example 28, using intermediate 29f as starting material. $^1$H-NMR (400 MHz, DMSO-$d_6$), $\delta$ 11.80-1.75 (bs, 2H), 8.14-7.92 (m, 6H), 7.34-7.31 (m, 1H), 6.99-6.96 (m, 1H), 5.17-4.99 (m, 2H), 4.20-3.85 (m, 4H), 3.55-3.50 (m, 6H), 3.15-2.85 (m, 5H), 2.14-1.50 (m, 12H), 0.99-0.51 (m, 15H), m/z 793.50 (M$^+$+1). m.p.: 162-155 °C.
Example 30: Preparation of methyl \(((S)-1-((((1S,2S)-2-(7-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1 H-imidazol-5-yl)-9H-fluoren-2-yl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 30):

**Step 1:** 1-(7-bromo-9H-fluoren-2-yl)ethanone (30a):

To a degassed solution of 2,7-dibromo-9H-fluorene (3.0 g, 9.3 mmol) and tributyl(1-ethoxyvinyl)stannane (3.3 g, 9.3 mmol) in 1,4-Dioxane (20 mL) was added Pd(PPh\textsubscript{3})\textsubscript{4} (0.56 g, 0.463 mmol) and PdCl\textsubscript{2}(dpdf) (0.34 g, 0.46 mmol) and the contents were heated at 80 °C for 5 h. The reaction mixture was cooled to room temperature and water was added and the contents were extracted with EtOAc (2 x 20 mL). The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure to yield 2-bromo-7-(1-ethoxyvinyl)-9,9 dimethyl-9H-fluorene as an orange liquid. To the above product THF (6 mL) and 2M HCl (10 mL) was added and the reaction was stirred at rt for 2 h. The contents were evaporated under reduced pressure, the residue was dissolved in water and extracted with EtOAc (2 x 20 mL). The organic contents were washed with brine, dried over sodium sulphate and purified by flash chromatography (3% EtOAc/Hexane) to yield a white colored solid (0.90g, 33.9%).

\[^{1}\text{H}-\text{NMR}\ (400 \text{ MHz}, \text{CDCl}\textsubscript{3})\]: \(\delta\ 8.15 \text{ (bs, 1H)}, 8.04-8.01 \text{ (m, 1H)}, 7.83-7.81 \text{ (m, 1H)}, 7.74-7.70 \text{ (m, 2H)}, 7.57-7.55 \text{ (m, 1H)}, 3.96 \text{ (s, 2H)}, 2.67 \text{ (s, 3H)}; m/z 286.07 (M\textsuperscript{+})\).

**Step 2:** 2,2-dibromo-1-(7-bromo-9H-fluoren-2-yl)ethanone (30b):

To a solution of 1-(7-bromo-9H-fluoren-2-yl)ethanone (30a) (0.4 g, 1.4 mmol) in chloroform (15 mL) was added bromine (0.07 mL, 1.4 mmol) at 0 °C under nitrogen atmosphere. The cooling bath was removed and the reaction mixture was warmed to rt and stirred for 2 h. Water was added to the reaction mixture and the organic contents were washed with sodium bisulphite solution, brine, dried over sodium sulphate and evaporated under
reduced pressure to yield a yellow colored solid that was used in the next step without further purification (0.550, 89%). $^1$H-NMR (400 MHz, CDCl$_3$) δ 8.27 (bs, 1H), 8.18-8.14 (m, 1H), 8.09-8.04 (m, 1H), 7.88-7.80 (m, 1H), 7.77-7.72 (m, 2H), 7.62-7.59 (m, 1H), 4.10-3.99 (m, 2H).

**Step 3**: 2-bromo-1-(7-bromo-9H-fluoren-2-yl)ethanone (30c):

![Chemical Structure](image)

To a solution of 2-bromo-1-(7-bromo-9H-fluoren-2-yl)ethanone (30b) (0.35 g, 0.96 mmol) in THF (3 mL) at 0°C was added triethylamine (0.24 mL, 1.69 mmol) and diethyl phosphite (0.22 mL, 1.69 mmol). The reaction was gradually warmed to room temperature and the mixture was stirred for 1.5 h after which excess THF was removed under reduced pressure. The crude was triturated with n-pentane to get a white solid (0.350g, 85%) that was used in the next step without further purification. $^1$H NMR (DMSO-$d_6$, 400 MHz), δ 8.29 (bs, 1H), 8.22-8.14 (m, 2H), 8.06-8.03 (m, 1H), 7.90-7.87 (m, 1H), 7.67-7.65 (m, 1H), 4.97 (s, 2H), 4.03 (s, 2H); m/z 386 (M$^+$+23).

**Step 4**: (1S,2S)-2-(7-bromo-9H-fluoren-2-yl)-2-oxoethyl-2-((tert-butoxycarbonyl)amino)cyclopentanecarboxylate (30d):

![Chemical Structure](image)

Title compound was synthesized by following the procedure as described in Step 1 of Example 1 using intermediate (30c) from the previous step and (1S,2S)-2-((tert-butoxycarbonyl)amino)cyclopentanecarboxylic acid [synthesized using procedures described in J. Org. Chem., 2001, 66 (16), 5629-5632] as starting materials. $^1$H-NMR (400 MHz, CDCl$_3$): δ 8.11-8.10 (m, 1H), 7.98-7.96 (m, 1H), 7.86-7.83 (m, 1H), 7.75-7.71 (m, 2H), 7.58-7.56 (m, 1H), 5.53-5.31 (m, 2H), 3.97 (s, 2H), 3.90-3.85 (m, 1H), 2.80-2.75 (m, 1H), 2.20-2.10 (m, 4H), 1.90-1.80 (m, 2H), 1.45 (s, 9H); m/z 414.10 [(M$^+$+1) - 100] (value observed for the de-Boc product).
Step 5: tert-butyl ((1S,2S)-2-(5-(7-bromo-9H-fluoren-2-yl)-1H-imidazol-2-yl)cyclopentyl)carbamate (30e):

Title compound was synthesized by following the procedure as described in Step 2 of Example 1 using intermediate (30d) from the previous step. 1H-NMR (400 MHz, CDCl₃): δ 7.88 (bs, 1H), 7.76-7.61 (m, 4H), 7.51-7.48 (m, 1H), 7.33 (s, 1H), 4.93-4.91 (m, 1H), 4.22-4.18 (s, 1H), 3.91 (s, 2H), 3.20-3.18 (m, 1H), 2.50-2.20 (m, 4H), 1.90-1.80 (m, 2H), 1.50 (s, 9H); m/z 493.99 (M⁺+1).

Step 6: tert-butyl ((1S,2S)-2-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-9H-fluoren-2-yl)-1H-imidazol-2-yl)cyclopentyl)carbamate (30f):

Title compound was synthesized by following the procedure as described in Step 3 of Example 1 using intermediate (30e) from the previous step. 1H-NMR (400 MHz, CDCl₃): δ 8.00 (bs, 1H), 7.85-7.77 (m, 3H), 7.71-7.66 (m, 1H), 7.58-7.47 (m, 1H), 7.36-7.32 (m, 1H), 4.89-4.87 (m, 1H), 4.20-4.15 (m, 1H), 3.93 (s, 2H), 3.27-3.20 (m, 1H), 2.40-1.60 (m, 6H), 1.40 (s, 9H), 1.34 (s, 12H); m/z 542.12 (M⁺+1).

Step 7: (S)-tert-butyl 2-(5-(7-((1S,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)-9H-fluoren-2-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-imidazol-2-yl)pyrrolidine-1-carboxylate (30g):
Title compound was synthesized following the procedure as described in Step 4 of Example 1 using the intermediates (30f) from the previous step and (S)-tert-butyl 2-(5-bromo-1-((2-(trimethylsilyl)ethoxy)methyl)-1 H-imidazol-2-yl)pyrrolidine-1-carboxylate [synthesized using procedures described in ref. WO201/096302 A1] as starting materials maintaining a temperature of 125 °C for 35 min. ¹H-NMR (400 MHz, CDCl₃), δ 12.00 (bs, 1H), 11.50 (bs, 1H), 8.05-7.05 (m, 8H), 5.70-5.35 (m, 2H), 5.25-5.05 (m, 1H), 4.95-4.80 (m, 2H), 4.30-4.10 (m, 1H), 4.05-3.90 (m, 2H), 3.75-3.30 (m, 4H), 3.25-3.10 (m, 1H), 2.45-1.72 (m, 8H), 1.65-1.51 (m, 18H), 0.95-0.80 (m, 2H), 0.01 (s, 9H); m/z 781.2 (M⁺+1).

**Step 8:** methyl ((S)-1-(((1S,2S)-2-(5-(7-(2-((1S,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1 H-imidazol-5-yl)-9H-fluoren-2-yl)-1 H-imidazol-2-yl)pyrrolidin-2-yl)-1 H-imidazol-5-yl)-9H-fluoren-2-yl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 30):

![Chemical structure of Compound 30](image)

To a stirred solution of (S)-tert-butyl 2-(5-(7-(2-((1S,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1 H-imidazol-5-yl)-9H-fluoren-2-yl)-1 H-imidazol-2-yl)pyrrolidine-1 -carboxylate (30g) (0.06 g, 0.07 mmol) in DCM (4 mL) was added TFA (0.143 mL, 1.854 mmol). The resultant mixture was stirred at 45 °C for 18 h. All the volatiles were evaporated under reduced pressure. The residue was washed with diethyl ether to get white solid [m/z 451.20 (M⁺+1)]. The solid so obtained (0.030 g, 0.063 mmol) was taken up in DMF (2 mL) and (S)-2-((methoxycarbonyl)amino)-3-methylbutanoic acid (0.024 g 0.13 mmol), DIPEA (0.06 mL, 0.3 mmol) and HATU (0.052 g, 0.13 mmol) was added and the resultant mixture was stirred at room temperature for 16 h under nitrogen atmosphere. Ice cold water was added in the reaction mixture and the off white colored precipitate was filtered off, washed with water, dried under high vacuum and purified by preparative HPLC to yield the title compound as a pale yellow solid (0.02 g, 25%). ¹H NMR (DMSO-d₆, 400 MHz): δ 11.80
(bs, 2H), 8.20-8.16 (m, 1H), 7.93-7.50 (m, 8H), 7.33-7.31 (m, 1H), 7.09-7.07 (m, 1H), 5.10-
5.05 (m, 1H), 4.40-4.32 (m, 6H), 3.55-3.45 (m, 7H), 3.20-3.15 (m, 2H),
2.20-1.50 (m, 10H), 0.99-0.51 (m, 12H), m/z 765.50 (M+ + 1).

Example 31: Preparation of methyl ((S)-1-(((1S,2S)-2-(5-(7-(2-((S)-1-((S)-2-
(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1 H-imidazol-5-yl)-9,9-
dimethyl-9H-fluoren-2-yl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-
2-yl)carbamate (Compound 31):

**Step 1:** 1-(7-bromo-9,9-dimethyl-9H-fluoren-2-yl)ethanone (31a):

Title compound was synthesized by following the procedure as described in Step 1 of
Example 30, using 2,7-dibromo-9,9-dimethyl-9H-fluorene as the starting material. 1H-NMR
(400 MHz, CDCl₃), δ 8.07-8.05 (m, 1H), 7.99-7.97 (m, 1H), 7.82-7.77 (m, 1H), 7.66 (d, J =
8 Hz, 1H), 7.61 (d, J = 1.6 Hz, 1H), 7.53-7.48 (m, 1H), 2.67 (s, 3H), 1.53 (s, 6H); m/z
316.96 (M+ + 1).

**Step 2:** 2,2-dibromo-1-(7-bromo-9,9-dimethyl-9H-fluoren-2-yl)ethanone

Title compound was synthesized by following the procedure as described in Step 2 of
Example 30 using intermediate (31a) from the previous step. 1H-NMR (400 MHz, CDCl₃), δ
8.08-8.07 (m, 1H), 7.99-7.97 (m, 1H), 7.85-7.79 (m, 1H), 7.66 (d, J = 8 Hz, 1H), 7.63-7.61
(m, 1H), 7.53-7.48 (m, 1H), 6.77 (s, 1H), 1.53 (s, 6H); m/z 470.5 (M+ + 1).

**Step 3:** 2-bromo-1-(7-bromo-9,9-dimethyl-9H-fluoren-2-yl)ethanone (31c):
Title compound was synthesized by following the procedure as described in Step 3 of Example 30, using intermediate (31b) from the previous step. $^1$H-NMR (400 MHz, CDCl$_3$), $\delta$ 8.07-8.05 (m, 1H), 7.99-7.97 (m, 1H), 7.82-7.77 (m, 1H), 7.66 (d, $J = 8$ Hz, 1H), 7.61 (d, $J = 1.6$ Hz, 1H), 7.53-7.48 (m, 1H), 4.15 (s, 2H), 1.57 (s, 6H); m/z 394.9 ($M^+ + 1$).

**Step 4:** (1S,2S)-2-(7-bromo-9,9-dimethyl-9H-fluoren-2-yl)-2-oxoethyl 2-((tert-butoxycarbonyl)amino)cyclopentanecarboxylate (31d):

![Chemical Structure Image]

Title compound was synthesized by following the procedure as described in Step 4 of Example 30, using intermediate (31c) from the previous step and (1S,2S)-2-((tert-butoxycarbonyl)amino)cyclopentanecarboxylic acid [synthesized using procedures described in J. Org. Chem., 2001, 66 (16), 5629-5632] as starting materials. $^1$H-NMR (400 MHz, CDCl$_3$), $\delta$ 8.0 (s, 1H), 7.94-7.92 (m, 1H), 7.78 (d, $J = 8$ Hz, 1H), 7.66 (d, $J = 8$ Hz, 1H), 7.62 (s, 1H), 7.58-7.53 (m, 1H), 5.59-5.53 (m, 1H), 5.40-5.36 (m, 1H), 4.95 (bs, 1H), 4.16 (s, 1H), 2.86-2.84 (m, 1H), 2.12-2.06 (m, 4H), 1.80-1.75 (m, 2H), 1.54 (s, 6H), 1.29 (s, 9H); m/z 542.5 ($M^+ + 1$).

**Step 5:** tert-buty1 ((1S,2S)-2-(5-(7-bromo-9,9-dimethyl-9H-fluoren-2-yl)-1 H-imidazol-2-yl)cyclopentyl)carbamate (31e):

![Chemical Structure Image]

Title compound was synthesized by following the procedure as described in Step 5 of Example 30, using intermediate (31d) from the previous step. $^1$H-NMR (400 MHz, CDCl$_3$), $\delta$ 7.76 (s, 1H), 7.69-7.67 (m, 2H), 7.59-7.55 (m, 2H), 7.50 (d, $J = 8$ Hz, 1H), 7.32 (s, 1H), 4.92 (bs, 1H), 4.23-4.21 (m, 1H), 3.25-3.21 (m, 1H), 2.48-2.45 (m, 1H), 2.25-1.60 (m, 5H), 1.54 (s, 6H), 1.29 (s, 9H); m/z 524.1 ($M^+ + 1$).
Step 6: tert-butyl (1S,2S)-2-((1S,2S)-2-(5-(9,9-dimethyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-9H-fluoren-2-yl)-1H-imidazol-2-yl)amino)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 31f)

Title compound was synthesized by following procedure as described in Step 6 of Example 30, using intermediate (31e) from the previous step. 1H-NMR (400 MHz, CDCl₃), δ 7.89 (s, 1H), 7.84 (m, 2H), 7.76 (m, 1H), 7.77 (s, 1H), 7.51 (m, 1H), 7.49 (s, 1H), 4.24 (m, 1H), 4.04 (m, 1H), 3.27 (m, 1H), 2.17-1.69 (m, 6H), 1.56 (s, 6H), 1.44 (s, 9H), 1.34 (s, 12H); m/z 570.2 (M⁺+1).

Step 7: (S)-tert-butyl 2-((1S,2S)-2-((S)-1-(((1S,2S)-2-((S)-1-((S)-2-(methoxycarbonyl)amino)-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-5-yl)-9,9-dimethyl-9H-fluoren-2-yl)-1H-imidazol-2-yl)pyrrolidine-1-carboxylate (31g):

Title compound was synthesized by following the procedure as described in Step 7 of Example 30, using intermediate (31f) from the previous step. 1H-NMR (400 MHz, CDCl₃), δ 7.85 (s, 1H), 7.80-7.78 (m, 2H), 7.60-7.58 (m, 1H), 7.51 (s, 1H), 7.25-7.22 (m, 1H), 7.19 (d, J = 8 Hz, 1H), 7.01-6.99 (m, 1H), 5.33 (s, 2H), 5.22-5.21 (m, 1H), 4.90-4.88 (m, 1H), 4.25-4.24 (m, 1H), 3.66-3.64 (m, 1H), 3.50-3.13 (m, 4H), 2.39-2.06 (m, 5H), 1.95-1.81 (m, 5H), 1.56 (s, 6H), 1.44 (s, 18H), 0.89-0.84 (m, 2H), 0.00 (s, 9H); m/z 809.5 (M⁺+1).

Step 8: methyl (((1S,2S)-2-((1S,2S)-2-((S)-1-(((1S,2S)-2-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-5-yl)-9,9-dimethyl-9H-fluoren-2-yl)-1H-imidazol-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 31)
Title compound was synthesized by following the procedure as described in Step 8 of Example 30, using intermediate from the previous step. $^1$H-NMR (400 MHz, CDCl$_3$), $\delta$ 8.30-7.57 (m, 5H), 7.53 (s, 1H), 7.42 (s, 1H), 6.86 (s, 1H), 5.39-5.31 (m, 3H), 4.49-4.46 (m, 2H), 4.04-4.02 (m, 1H), 3.84 (s, 6H), 3.20-3.18 (m, 2H), 3.15-3.12 (m, 1H), 2.34-1.75 (m, 12H), 1.66 (s, 6H), 1.06-0.89 (m, 12H); m/z 793.5 (M$^+$+1). m.p.: 157-158 °C.

Example 32: Preparation of methyl ((S)-1-(((1S,2S)-2-(5-(7-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-5-yl)phenanthren-2-yl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 32):

Step 1: 1-(7-bromophenanthren-2-yl)ethanone (32a):

$\text{O} \quad \text{Br}$

Title compound was synthesized by following the procedure as described in Step 1 of Example 30, using 2,7-dibromophenanthrene [Synthesized according to procedure reported in WO 2010132601 A1] as starting material. $^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 8.74 (d, $J = 9$ Hz, 1H), 8.60 (d, $J = 9$ Hz, 1H), 8.55 (s, 1H), 8.16 (d, $J = 8.8$ Hz, 1H), 8.02 (s, 1H), 7.75 (d, $J = 8.8$ Hz, 1H), 7.58-7.51 (m, 2H), 2.56 (s, 3H); LCMS: m/z = 299.0 (M$^+$).

Step 2: 2,2-dibromo-1-(7-bromophenanthren-2-yl)ethanone (32b):

$\text{O} \quad \text{Br} \quad \text{Br}$

Step 1: 1-(7-bromophenanthren-2-yl)ethanone (32a):

$\text{O} \quad \text{Br}$

Step 2: 2,2-dibromo-1-(7-bromophenanthren-2-yl)ethanone (32b):
Title compound was synthesized by following the procedure as described in Step 2 of Example 30, using intermediate (32a) from the previous step. $^1$H-NMR (400 MHz, CDCl$_3$): δ 8.74 (d, $J = 8.8$ Hz, 1H), 8.60 (d, $J = 9.6$ Hz, 1H), 8.55 (s, 1H), 7.90 (d, $J = 8.8$ Hz, 1H), 7.81 (s, 1H), 7.78 (d, $J = 9.6$ Hz, 1H), 7.45 (s, 2H), 6.83 (s, 1H).

**Step 3**: 2-bromo-1-(7-bromophenanthren-2-yl)ethanone (32c)

Title compound was synthesized by following the procedure as described in Step 3 of Example 30, using intermediate (32b) from the previous step. $^1$H-NMR (400 MHz, CDCl$_3$): δ 8.74 (d, $J = 8.8$ Hz, 1H), 8.60 (d, $J = 8.4$ Hz, 1H), 8.52 (s, 1H), 8.26 (d, $J = 8.8$ Hz, 1H), 8.09 (s, 1H), 7.85 (d, $J = 8.4$ Hz, 1H), 7.58-7.51 (m, 2H), 4.89 (s, 2H).

**Step 4**: (1S,2S)-2-(7-bromophenanthren-2-yl)-2-oxoethyl 2-((tert-butoxycarbonyl)amino)cyclopentanecarboxylate (32d):

![Chemical structure of 32d](image)

Title compound was synthesized by following the procedure as described in Step 4 of Example 30, using intermediate (32c) from the previous step. $^1$H-NMR (400 MHz, CDCl$_3$): δ 8.62-8.49 (m, 2H), 8.28 (s, 1H), 7.81-7.28 (m, 4H), 7.42-7.31 (m, 1H), 5.52-5.37 (m, 2H), 4.96 (bs, 1H), 4.32-4.27 (m, 1H), 2.92-2.86 (m, 1H), 2.32-1.76 (m, 6H), 1.38 (s, 9H). m/z 527.5 (M$^+$+1).

**Step 5**: tert-butyl ((1S,2S)-2-(5-(7-bromophenanthren-2-yl)-1H-imidazol-2-yl)cyclopentyl)carbamate (32e):

![Chemical structure of 32e](image)
Title compound was synthesized by following the procedure as described in Step 5 of Example 30, using intermediate (32d) from the previous step. \( ^1 \)H-NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.63-8.51 (m, 2H), 8.28 (s, 1H), 7.81-7.26 (m, 4H), 7.42-7.31 (m, 2H), 4.98-4.96 (bs, 1H), 4.29-4.22 (m, 1H), 3.29-3.209 (m, 1H), 2.88-1.61 (m, 6H), 1.38 (s, 9H). m/z 507.5 (M\( ^{+1} \)).

**Step 6:** tert-butyl ((1S,2S)-2-(5-(7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenanthren-2-yl)-1H-imidazol-2-yl)cyclopentyl)carbamate (32f)

Title compound was synthesized by following the procedure as described in Step 6 of Example 30, using intermediate (32e) from the previous step. \( ^1 \)H-NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.71-8.64 (m, 2H), 8.37 (s, 1H), 8.02 (s, 1H), 7.80-7.56 (m, 2H), 7.45-7.35 (m, 2H), 4.29-4.21 (m, 1H), 3.29-3.19 (m, 1H), 2.87-1.71 (m, 6H), 1.38 (s, 9H), 1.27 (s, 12H), m/z 553.7 (M\( ^{+1} \)).

**Step 7:** (S)-tert-butyl 2-(5-(7-((1S,2S)-2-((tert-butoxycarbonyl)amino)cyclopentyl)-1H-imidazol-5-yl)phenanthren-2-yl)-1H-imidazol-2-yl)pyrrolidine-1-carboxylate (32g)

Title compound was synthesized by following procedure as described in Step 7 of Example 30, using intermediate (32f) from the previous step. m/z 795.3 (M\( ^{+1} \)).

**Step 8:** methyl ((1S,2S)-2-(5-(7-((S)-2-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1H-imidazol-5-yl)phenanthren-2-yl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (Compound 32):
Title compound was synthesized by following the procedure as described in Step 8 of Example 30, using intermediate (32g) from the previous step.

10.99-10.86 (m, 1H), 10.61-10.56 (m, 1H), 8.65-8.58 (m, 2H), 8.28 (s, 1H), 8.12-8.09 (m, 1H), 7.78-7.71 (m, 4H), 7.57-7.49 (m, 1H), 7.41-7.38 (m, 1H), 5.49-5.41 (m, 1H), 4.37-4.29 (m, 2H), 3.99-3.86 (m, 2H), 3.84-3.78 (m, 1H), 3.68 (s, 6H), 3.21-3.18 (m, 2H), 2.67-2.14 (m, 5H), 1.86-1.63 (m, 7H), 0.91 (d, 12H), m/z 777.2 (M+1), m.p.: 153-155 °C.

**Example 33: Biological Activity**

Anti-viral activity of the compounds of the invention was monitored using an HCV replicon assay. The Huh7.5/Con1/SG-Neo(l)hRluc2aUb cell line persistently expressing a bicistronic genotype 1b replicon in Huh 7.5 cells was obtained from Apath LLC. This cell line was used to test inhibition of genotype 1b replicon levels by test compound using *Renilla* luciferase enzyme activity readout as a measure of viral replication efficiency.

Briefly, 7000 cells were seeded in 96 well black clear bottom plates and allowed to adhere overnight. The next day each compound was added in triplicate to the cells at the desired concentration with a final DMSO concentration of 0.5%. Cells in media alone and cells incubated without drug with 0.5% DMSO served as controls. The plates were incubated for 72h at 37°C prior to running the luciferase assay. Enzyme activity was measured using *Renilla-Glo* Luciferase Assay kit from Promega as per the manufacturer's instructions. The following equation was used to generate the percent inhibition value for each test concentration.

\[
\text{% Inhibition} = \left(\frac{\text{Average Control (cells alone +0.5% DMSO)} - \text{Average compound value(cells + drug)}}{\text{Average Control (cells alone+0.5% DMSO)}}\right) \times 100
\]
The EC_{50} value was determined using GraphPad Prism and the following equation:

\[ Y = \text{Bottom} + \frac{(\text{Top} - \text{Bottom})}{1 + 10^{\left(\text{LogIC}_{50} - X\right) \times \text{HillSlope}}} \]

EC50 values/\% inhibitions of compounds were determined 2-3 times in the replicon assay.

Following table 1 shows EC50 values, for inhibition of genotype 1b replicon, of the compounds of the invention. Group A compounds exhibited EC50 value between 1 pM to 999 pM, Group B exhibited EC50 value between 1 nM to 999 nM, and Group C exhibited EC50 value of more than 1 µM.

**Table 1:**

<table>
<thead>
<tr>
<th>Group</th>
<th>Compound</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>8, 9, 10, 11, 15, 17, 18, 19, 20, 29, 7, 32.</td>
</tr>
<tr>
<td>B</td>
<td>1, 2, 3, 4, 5, 6, 12, 13, 14, 16, 24, 25, 26, 27, 28, 30, 31, 22.</td>
</tr>
<tr>
<td>C</td>
<td>21, 23.</td>
</tr>
</tbody>
</table>
CLAIMS

1. A compound of formula I, its tautomeric forms, its stereoisomers, its analogues, its prodrugs, its isotopically substituted analogues, its metabolites, its sulfides, its oxides, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates or its co-crystals,

![Chemical Structure](image)

wherein, in the compound of formula I,

Ring 'A' is a saturated carbocycle, which may be a monocyclic system or may be a fused carbocycle or may be a bridged carbocycle, the said ring A may contain 5 to 10 carbons;

Ring 'D' is selected from 5 to 10 membered carbocycle and 5 to 10 membered heterocycle, the ring 'D' may be monocyclic, fused bicyclic, bridged bicyclic or spiro bicyclic;

Y is selected from -CH(R²¹)- and -N(R³²)-;

R¹ is selected from the group consisting of R¹³aC(=0)N(R¹⁴)-, R¹³aOC(=0)N(R¹⁴)-, R¹³(R¹⁴)N-, R¹³(R¹⁴)NC(=0)N(R¹⁵)-, R¹³aOC(=0)N(R¹⁴)CR²¹(R²²)C(=0)N(R¹⁵)-, R¹³aOC(=0)N(R¹⁴)CR²¹(R²²)C(R²³)C(=0)N(R¹⁵)-, R¹³(R¹⁴)NC(=0)N(R¹⁴)CR²¹(R²²)C(=0)N(R¹⁵)-, and R¹³(R¹⁴)NC(=0)N(R¹⁴)CR²¹(R²²)C(R²³)C(=0)N(R¹⁵)-;

R¹² is selected independently at each occurrence from the group consisting of halogen, substituted- or unsubstituted- C⁻⁶ alkyl, R¹³aC(=0)-, R¹³bO-, R¹³aOC(=0)-, R¹³aC(=0)0-, and R¹³(R¹⁴)NC(=0)-;

R² is selected independently at each occurrence from the group consisting of substituted- or unsubstituted- C⁻⁶ alkyl, R¹³aC(=0)-, R¹³bO-, R¹³aOC(=0)-, R¹³aC(=0)0-, R¹³(R¹⁴)NC(=0)-, R¹³aOC(=0)N(R¹⁴)C(R²¹)(R²²)C(=0)-,
R^{13a}OC(=0)N(R^{14})C(R^{9})(R^{b})C(R^{o})(R^{d})C(=0)-;

R^{13}(R^{14})NC(=0)N(R^{15})C(R^{9})(R^{b})C(=0)-;

R^{13}(R^{14})NC(=0)N(R^{15})C(R^{9})(R^{b})C(R^{d})(R^{o})C(=0)-;

R^{13}S_{2}O_{2}N(R^{14})C(R^{9})(R^{b})C(R^{d})(R^{o})C(=0)-; and

R^{13a}OC(=0)N(R^{14})C(R^{9})(R^{b})S_{2}O_{2}^{-}:

R^{2}_{a} is selected independently at each occurrence from the group consisting of

R^{13a}C(=0)N(R^{14}), R^{13a}OC(=0)N(R^{14}), R^{13}(R^{14})N-, R^{13}(R^{14})NC(=0)N(R^{15}),

R^{13}S_{2}N(R^{14})-,

R^{13a}OC(=0)N(R^{14})C(R^{9})(R^{b})(R^{d})(R^{o})C(=0)N(R^{15})-,

R^{13}(R^{14a})NC(=0)N(R^{14})C(R^{9})(R^{b})C(=0)N(R^{15})-; and

R^{13}(R^{14a})NC(=0)N(R^{14})C(R^{9})(R^{b})(R^{d})(R^{o})C(=0)N(R^{15})-;

R^{2} is independently selected from O and N(R^{16});

R^{4} is selected independently at each occurrence from CR^{6}(R^{4}), O and N(R^{14}); such that, when n = 2 and R^{4} is selected as CR^{6}(R^{4}) for both the occurrences, two R^{6}s together can form a bond to form an alkenylene linkage or two R^{6}s and two R^{4}s together can form bonds to form alkynylene linkage;

R^{5}, R^{6}, R^{7}, R^{8}, R^{9} and R^{10} are independently selected as hydrogen, or R^{5} and R^{6} together, R^{7} and R^{10} together, or R^{8} and R^{9} together independently along with the carbon atoms to which they are attached forming 5 to 8 membered substituted- or unsubstituted- carbocycle, 5 to 8 membered substituted- or unsubstituted- heterocycle, 6 membered substituted- or unsubstituted- aryl, or 5 to 6 membered substituted- or unsubstituted- heteroaryl;

with a proviso that the compound of formula I must have at least one cyclic system formed out of either R^{5} and R^{6}, R^{8} and R^{9}, or R^{7} and R^{10}; also provided that R^{7} and R^{10} take part in formation of cyclic system only when n is 0;

R^{11} and R^{12} are independently selected from a group consisting of hydrogen, halogen, substituted- or unsubstituted- C_{i}^{16}_{6} alkyl, R^{13b}O-; and (R^{13})(R^{14})N-;

wherein, R^{13}, R^{14}, R^{14a} and R^{15} are independently selected from hydrogen, substituted- or unsubstituted- C_{i}^{16}_{6} alkyl, substituted- or unsubstituted- aryl, substituted- or unsubstituted- heteroaryl, substituted- or unsubstituted- cycloalkyl, and substituted- or unsubstituted- heterocyclyl;
R$^{13a}$ is selected from substituted- or unsubstituted- C$_{1-6}$ alkyl, perhaloalkyl, substituted- or unsubstituted- aryl, substituted- or unsubstituted- heteroaryl, substituted- or unsubstituted- cycloalkyl, and substituted- or unsubstituted- heterocyclyl;

R$^{13b}$ is selected from hydrogen, substituted- or unsubstituted- C$_{1-6}$ alkyl, perhaloalkyl, substituted- or unsubstituted- aryl, substituted- or unsubstituted- heteroaryl, substituted- or unsubstituted- cycloalkyl, and substituted- or unsubstituted- heterocyclyl;

R$^{16}$ is selected from hydrogen or substituted- or unsubstituted alkyl group;

R$^{a}$, R$^{b}$, R$^{c}$ and R$^{d}$, are independently selected from hydrogen, halogen, substituted- or unsubstituted- C$_{1-6}$ alkyl, substituted- or unsubstituted- aryl, substituted- or unsubstituted- heteroaryl, substituted- or unsubstituted- cycloalkyl, and substituted- or unsubstituted- heterocyclyl, or R$^{a}$, R$^{b}$, R$^{c}$ and R$^{d}$ together with the carbon atom(s) to which they are attached forming substituted- or unsubstituted- carbocycle, substituted- or unsubstituted- heterocycle;

m is an integer ranging between 0 to 2, selected independently at each occurrence;

n is an integer ranging between 0 and 2;

'alkyl' may be substituted with 1 to 4 substituents selected from the group consisting of halogen, oxo, C$_{1-6}$ alkyl, haloalkyl, aryl, heteroaryl, cycloalkyl, and heterocyclyl,

R$_{17a}^{17a}$C$_{(0)}$, R$_{17a}^{17a}$SO$_{2}^{-}$, R$_{17b}^{17b}$O$^{-}$, R$_{17a}^{17a}$OC$_{(0)}$-, R$_{17a}^{17a}$C$_{(0)=0}$, (R$_{17}^{17}$(R$_{18}^{18})$NC$_{(0)=0}$), (R$_{17a}^{17a}$C$_{(0)=0}$)N(R$_{18}^{18}$)-, (R$_{17}^{17}$(R$_{18}^{18})$N-, (R$_{17}^{17}$(R$_{18}^{18})$NC$_{(0)=0}$)N(R$_{19}^{19}$)-, and R$_{17a}^{17a}$SO$_{2}^{-}$N(R$_{18}^{18}$)-;

'cycloalkyl', 'cycloalkenyl' and 'carbocycle' may be substituted with 1 to 2 substituents selected from the group consisting of halogen, oxo, C$_{1-6}$ alkyl, haloalkyl, R$_{17a}^{17a}$C$_{(0)}$-, R$_{17a}^{17a}$SO$_{2}^{-}$, R$_{17b}^{17b}$O$^{-}$, R$_{17a}^{17a}$OC$_{(0)}$-, R$_{17a}^{17a}$C$_{(0)=0}$, (R$_{17}^{17}$(R$_{18}^{18})$NC$_{(0)=0}$), (R$_{17a}^{17a}$C$_{(0)=0}$)N(R$_{18}^{18}$)-, (R$_{17}^{17}$(R$_{18}^{18})$N-, (R$_{17}^{17}$(R$_{18}^{18})$NC$_{(0)=0}$)N(R$_{19}^{19}$)-, and R$_{17a}^{17a}$SO$_{2}^{-}$N(R$_{18}^{18}$)-;

'aryl' may be substituted with 1 to 2 substituents selected from the group consisting of halogen, nitro, cyano, hydroxy, alkyl, perhaloalkyl, alkyl-O-, perhaloalkyl-O-, alkyl(H)N-, alkyl(alkyl)N-, H$_{2}$N-, alkyl-SO$_{2}^{-}$, alkyl-C$_{(0)}$(H)N-, alkyl-C$_{(0)}$(alkyl)N-,
alkyl(H)NC(=0)-, alkyl(alkyl)NC(=0)-, H₂NC(=0)-, alkyl(H)NSO₂-, alkyl(alkyl)NSO₂-, and H₂NSO₂⁻;
'heteroaryl' may be substituted with 1 to 2 substituents selected from the group consisting of halogen, nitro, cyano, hydroxy, alkyl, perhaloalkyl, alkyl-O-, perhaloalkyl-O-, alkyl-SO₂-, H₂N-, alkyl(H)N-, alkyl(alkyl)N-, alkyl-C(=0)(H)N-, NH₂C(=0)-, alkyl(H)NC(=0)-, alkyl(alkyl)NC(=0)-, NH₂SO₂-, alkyl(H)NSO₂-, and alkyl(alkyl)NSO₂⁻;
ring carbon(s) of 'heterocycle' may be substituted with 1 to 2 substituents selected from the group consisting of halogen, nitro, cyano, oxo, alkyl, R¹⁷bO-, R¹⁷aOC(=0)-, R¹⁷aC(=0)0-, R¹⁷(H)NC(=0)-, R¹⁷(alkyl)NC(=0)-, R¹⁷(H)N-, R¹⁷(alkyl)N-, R¹⁷aC(=0)(H)N-, R¹⁷(H)NC(=0)(H)N-, and R¹⁷(alkyl)NC(=0)(H)N⁻; the substituents on ring nitrogen(s) of 'heterocycle' are selected from the group consisting of alkyl, R¹⁷aSΟ₂-, R¹⁷aC(=0)-, R¹⁷aOC(=0)-, R¹⁷(H)NC(=0)-, and R¹⁷(alkyl)NC(=0);
R¹⁷, R¹⁸ and R¹⁹ are independently selected from hydrogen and alkyl;
R¹⁷a is selected from alkyl and perhaloalkyl;
R¹⁷b is selected from the group consisting of hydrogen, alkyl, and perhaloalkyl.

2. The compound of formula I, its tautomeric forms, its stereoisomers, its analogues, its prodrugs, its isotopically substituted analogues, its metabolites, its sulfoxides, its N-oxides, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates or its co-crystals, as claimed in claim 1, wherein ring A is selected as cyclopentane.

3. The compound of formula I, its tautomeric forms, its stereoisomers, its analogues, its prodrugs, its isotopically substituted analogues, its metabolites, its sulfoxides, its N-oxides, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates or its co-crystals, as claimed in claim 1 or 2, wherein ring Y is selected as -N(R²)-.

4. The compound of formula I, its tautomeric forms, its stereoisomers, its analogues, its prodrugs, its isotopically substituted analogues, its metabolites, its sulfoxides, its...
N-oxides, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates or its co-crystals, as claimed in any one of claims 1-8, wherein R₁ is selected as \( R^{13a}OC(=0)N(R^{14})CR^bN(=0)N(R^{15}) \).

5. The compound of formula 1, its tautomeric forms, its stereoisomers, its analogues, its prodrugs, its isotopically substituted analogues, its metabolites, its sulfoxides, its N-oxides, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates or its co-crystals, as claimed in any one of claims 1-4, wherein m is selected as 0 at all the occurrences.

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6. The compound of formula 1, its tautomeric forms, its stereoisomers, its analogues, its prodrugs, its isotopically substituted analogues, its metabolites, its sulfoxides, its N-oxides, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates or its co-crystals, as claimed in any one of claims 1-5, wherein R² is selected as \( R^{13a}OC(=0)N(R^{14})CR^bN(=0) \).

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7. The compound of formula 1, its tautomeric forms, its stereoisomers, its analogues, its prodrugs, its isotopically substituted analogues, its metabolites, its sulfoxides, its N-oxides, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates or its co-crystals, as claimed in any one of claims 1-6, wherein R³ is selected from NH and O.

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8. The compound of formula 1, its tautomeric forms, its stereoisomers, its analogues, its prodrugs, its isotopically substituted analogues, its metabolites, its sulfoxides, its N-oxides, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates or its co-crystals, as claimed in any one of claims 1-7, wherein n is selected as 0.

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9. The compound of formula 1, its tautomeric forms, its stereoisomers, its analogues, its prodrugs, its isotopically substituted analogues, its metabolites, its sulfoxides, its N-oxides, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates or its co-crystals, as claimed in any one of claims 1-8, wherein \( R^5 \) and \( R^6 \) are independently selected from hydrogen and halogen, or \( R^5 \)
and \( R^6 \) together with the carbon atoms to which they are attached form a six membered carbocycle.

10. The compound of formula I, its tautomeric forms, its stereoisomers, its analogues, its prodrugs, its isotopically substituted analogues, its metabolites, its sulfoxides, its N-oxides, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates or its co-crystals, as claimed in any one of claims 1-9, wherein \( R^7 \) and \( R^{10} \) are selected as hydrogen, or \( R^7 \) and \( R^{10} \) together with the carbon atoms to which they are attached form a five or six membered carbocycle, the said carbocycle is unsubstituted or substituted with one or two alkyl groups.

11. The compound of formula I, its tautomeric forms, its stereoisomers, its analogues, its prodrugs, its isotopically substituted analogues, its metabolites, its sulfoxides, its N-oxides, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates or its co-crystals, as claimed in any one of claims 1-10, wherein \( R^5 \) and \( R^8 \) are selected as hydrogen, or \( R^5 \) and \( R^8 \) together with the carbon atoms to which they are attached form a six or seven membered carbocycle, or \( R^5 \) and \( R^8 \) together with the carbon atoms to which they are attached form a seven membered heterocycle containing one heteroatom.

12. The compound of formula I, its tautomeric forms, its stereoisomers, its analogues, its prodrugs, its isotopically substituted analogues, its metabolites, its sulfoxides, its N-oxides, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates or its co-crystals, as claimed in any one of claims 1-11, wherein \( R^{11} \) and \( R^{12} \) are selected as hydrogen.

13. The compound of formula I, its tautomeric forms, its stereoisomers, its analogues, its prodrugs, its isotopically substituted analogues, its metabolites, its sulfoxides, its N-oxides, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates or its co-crystals, as claimed in any one of claims 1-12, wherein ring \( D \) is selected as
14. The compound of formula I, its tautomeric forms, its stereoisomers, its analogues, its prodrugs, its isotopically substituted analogues, its metabolites, its sulfoxides, its N-oxides, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates or its co-crystals, as claimed in any one of claims 1-13, wherein ring A is selected as cyclopentane, ring D is selected as

\[ R^1 \text{ is selected as } R^{13a}OC(=0)N(R^{14})CR^8(R^9)C(=0)N(R^{15}), \]

m is selected as 0 at all the occurrences, \( R^3 \) is selected from NH and O, n is selected as 0, \( R^5 \) and \( R^6 \) are independently selected from hydrogen and halogen, or \( R^5 \) and \( R^6 \) together with the carbon atoms to which they are attached form a six membered carbocycle, \( R^7 \) and \( R^{10} \) are selected as hydrogen, or \( R^7 \) and \( R^{10} \) together with the carbon atoms to which they are attached form a five or six membered carbocycle, the said carbocycle is unsubstituted or substituted with one or two alkyl groups, \( R^3 \) and \( R^8 \) are selected as hydrogen, or \( R^3 \) and \( R^8 \) together with the carbon atoms to which they are attached form a six or seven membered carbocycle, or \( R^3 \) and \( R^8 \) together with the carbon atoms to which they are attached form a seven membered heterocycle containing one heteroatom, \( R^{11} \) and \( R^{12} \) are selected as hydrogen; such that at least one cyclic system is formed out of \( R^5 \) and \( R^6 \), \( R^8 \) and \( R^9 \), or \( R^7 \) and \( R^{10} \).

15. The compound of formula I, its tautomeric forms, its stereoisomers, its analogues, its prodrugs, its isotopically substituted analogues, its metabolites, its sulfoxides, its N-oxides, its pharmaceutically acceptable salts, its polymorphs, its solvates, its optical isomers, its clathrates or its co-crystals, as claimed in any one of claims 1-14, wherein the compound is selected from the group consisting of:

- methyl ((2S)-1-((2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1 H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;
methyl ((2S)-1-((2-((5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-
d]imidazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;  
methyl ((2S)-1-((2-((5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1 H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;  
methyl ((S)-1-(((1R,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1 H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;  
methyl ((S)-1-(((1R,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-
d]imidazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;  
methyl ((S)-1-(((1S,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1 H-benzo[2,3]oxepino[4,5-
d]imidazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;  
methyl ((S)-1-(((1S,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1,4,5,6-tetrahydrobenzo[3,4]cyclohepta[1,2-
d]imidazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;  
methyl ((S)-1-(((1S,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1 H-benzo[2,3]oxepino[4,5-
d]imidazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;
methyl ((S)-1-(((1S,2R)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-4,5-dihydro-1H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;
methyl ((S)-1-(((1 R,2R)-2-(5-(4-(2-((S)-1-(((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1 H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;
methyl ((S)-1-(((1R,2S)-2-(5-(4-(2-((S)-1-(3-methylbutanoyl)pyrrolidin-2-yl))-4,5-dihydrobenzo[2,3]oxepino[4,5-d]oxazol-8-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;

methyl ((S)-1-(((1S,2S)-2-(7-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl))-1 H-imidazol-5-yl)phenyl)-4,5-dihydro-1 H-naphtho[1,2-d]imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;

methyl ((S)-1-(((1S,2R)-2-(7-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl))-1 H-imidazol-5-yl)phenyl)-1 H-naphtho[1,2-d]imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;

methyl ((S)-1-(((1S,2S)-2-(7-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl))-1 H-naphtho[1,2-d]imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;

methyl ((S)-1-(((1S,2R)-2-(7-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl))-1 H-naphtho[1,2-d]imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;

methyl ((S)-1-(((1S,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl))-4,5-dihydro-1 H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)(ethyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;

methyl ((S)-1-(((1S,2S)-2-(5-(4-(2-((S)-1-((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl))-4,5-dihydro-1 H-naphtho[1,2-d]imidazol-7-yl)phenyl)-1 H-imidazol-2-yl)cyclopentyl)(methyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;
methyl ((S)-1 -(((1 S,2S)-2-(5-(7-(2-((S)-1 -((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1 H-imidazol-5-yl)-9H-fluoren-2-yl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate;
methyl ((S)-1 -(((1 S,2S)-2-(5-(7-(2-((S)-1 -((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1 H-imidazol-5-yl)-9,9-dimethyl-9H-fluoren-2-yl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate; and
methyl ((S)-1 -(((1 S,2S)-2-(5-(7-(2-((S)-1 -((S)-2-(methoxycarbonyl)amino-3-methylbutanoyl)pyrrolidin-2-yl)-1 H-imidazol-5-yl)phenanthren-2-yl)-1 H-imidazol-2-yl)cyclopentyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate.

16. A pharmaceutical composition comprising a compound or a combination of compounds according to any one of claims 1-15 or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier or excipient.

17. A method of inhibiting the replication of an RNA-containing virus comprising contacting said virus with a therapeutically effective amount of a compound or combination of compounds of any one of claims 1-15, or a pharmaceutically acceptable salt thereof.

18. A method of treating or preventing infection caused by an RNA-containing virus comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound or combination of compounds of any one of claims 1-15, or a pharmaceutically acceptable salt thereof.

19. The method of claim 18, wherein the RNA-containing virus is hepatitis C virus.

20. The method of claim 18, further comprising the step of co-administering one or more agents selected from the group consisting of a host immune modulator and an antiviral agent, or a combination thereof.

21. The method of claim 20, wherein the host immune modulator is selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, consensus interferon, a cytokine, and a vaccine.

22. The method of claim 20, wherein the antiviral agent inhibits replication of HCV by inhibiting host cellular functions associated with viral replication.
23. The method of claim 20, wherein the antiviral agent inhibits the replication of HCV by targeting proteins of the viral genome.

24. The method of claim 20, wherein said antiviral agent is an inhibitor of a HCV viral protein, a replication process or a combination thereof, wherein said targeting protein or replication process is selected from the group consisting of helicase, protease, polymerase, metalloprotease, NS4A, NS4B, NS5A, assembly, entry, and IRES.

25. The method of claim 18, further comprising the step of co-administering an agent or combination of agents that treat or alleviate symptoms of HCV infection selected from cirrhosis and inflammation of the liver.

26. The method of claim 18, further comprising the step of co-administering one or more agents that treat patients for disease caused by hepatitis B (HBV) infection.

27. The method of claim 18, further comprising the step of co-administering one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection.

28. The pharmaceutical composition of claim 16, further comprising an agent selected from interferon, pegylated interferon, ribavirin, amantadine, an HCV protease inhibitor, an HCV polymerase inhibitor, an HCV helicase inhibitor, or an internal ribosome entry site inhibitor.

29. The composition of claim 16, further comprising a cytochrome P450 monooxygenase inhibitor or a pharmaceutically acceptable salt thereof.

30. A method of treating hepatitis C infection in a subject in need thereof comprising co-administering to said subject a cytochrome P450 monooxygenase inhibitor or a pharmaceutically acceptable salt thereof, and a compound of any one of claims 1-15 or a pharmaceutically acceptable salt thereof.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D403/14 C07D413/14 C07D491/044 C07D498/04 A61K31/4178
A61K31/4184 A61K31/422 A61K31/424 A61P31/00

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal , CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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Further documents are listed in the continuation of Box C.

See patent family annex.

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A* document member of the same patent family

Date of the actual completion of the international search
20 November 2012

Date of mailing of the international search report
27/11/2012

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016

Authorized officer
Bosma, Peter

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