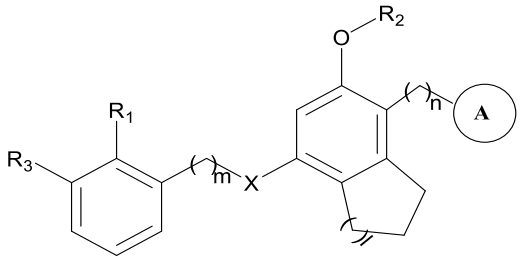
antibody-mimic functions and are advantageous over antibody for their chemically synthetic nature, low immunogenicity, and efficient tissue penetration (Lai W.Y.et al., Mol. Therapy - Nucl. Acids, 2016, 5: e397). Small molecule inhibitors, therefore, can provide increased oral bioavailability, increased bio-efficiency and shortened half-life activity for a more controllable treatment, particularly in the case of auto-immune or other adverse events.

[0008] As discussed, the PD-1/PD-L1 inhibitory compounds have vast utility in upregulating the immune system for efficiently combating cancer. Therefore, the identification of a chemical moiety, especially small molecule inhibitors, that facilitates this inhibition is necessary. Therefore, the identification and development of new PD-1/PD-L1 inhibitor compounds treating cancer and other diseases or conditions associated with activation of PD-1/PD-L1 would open new opportunities in the realm of cancer treatment.

SUMMARY

[0009] In an aspect of the present disclosure there is provided a compound of Formula (I):



Formula (I)

their stereoisomers, an N-oxide or pharmaceutically acceptable salts thereof;

wherein,

X is selected from O or NR′;

Ring A is selected from C_{6-10} aryl, C_{3-10} cycloalkyl, C_{7-16} alkylaryl, C_{2-10} heteroaryl, C_{2-20} heterocyclyl, -CO-C_{2-20} heterocyclyl, or –C(O)NR_4-C_{2-20} heterocyclyl; wherein, C_{6-10} aryl, C_{3-10} cycloalkyl, C_{7-16} alkylaryl, C_{2-10} heteroaryl, C_{2-20} heterocyclyl, -CO-C_{2-20} heterocyclyl, or –C(O)NR_4-C_{2-20} heterocyclyl is

optionally substituted with one or more groups selected from halogen, hydroxy, C_{1-10} alkyl, C_{1-10} alkoxy, C_{1-10} haloalkyl, C_{2-10} alkylalkoxy, $-CH_2-NR_aC(O)R_b$, $-CR_aR_b-OR_c$, $-CR_aR_b-NR_cR_d$, or $-CH_2-NHC(O)NR_aR_b$; wherein, R_a, R_b, R_c, and R_d are independently selected from hydrogen, halogen, C_{1-10} alkyl, -C(O)R", C_{3-10} cycloalkyl C_{1-10} haloalkyl, or C_{1-10} alkoxy;

R′ is selected from hydrogen or C_{1-10} alkyl;

R_1 is selected from hydrogen, cyano or C_{1-10} alkyl;

R_2 is selected from hydrogen, C_{1-10} alkyl, C_{6-10} aryl, C_{3-10} cycloalkyl, C_{1-10} haloalkyl, C_{7-16} alkylaryl, C_{2-10} heteroaryl, C_{3-20} alkyl heteroaryl, C_{2-20} heterocyclyl, or C_{3-20} alkyl heterocyclyl; wherein, C_{1-10} alkyl, C_{6-10} aryl, C_{3-10} cycloalkyl, C_{1-10} haloalkyl, C_{7-16} alkylaryl, C_{2-10} heteroaryl, C_{3-20} alkyl heteroaryl, C_{2-20} heterocyclyl, or C_{3-20} alkyl heterocyclyl, is optionally substituted with one or more groups selected from halogen, cyano, hydroxy, $-C(O)NH_2$, C_{1-10} alkyl, or C_{6-10} aryl;

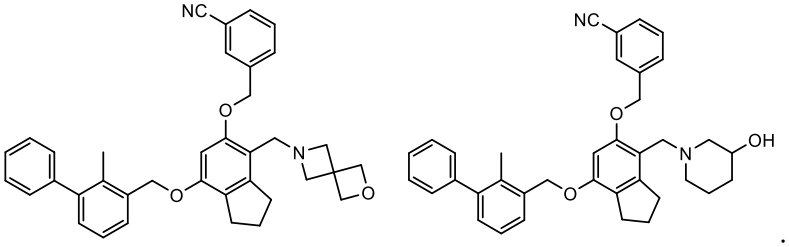
R_3 is selected from halogen, C_{6-10} aryl, or C_{2-10} heteroaryl; wherein, C_{6-10} aryl, or C_{2-10} heteroaryl, is optionally substituted with one or more groups selected from halogen, haloalkyl, cyano, hydroxy, amino, C_{1-10} alkyl, OR", C_{6-10} aryl, C_{2-20} heterocyclyl, or C_{2-10} heteroaryl;

wherein, R" is selected from hydrogen, halogen, C_{1-10} alkyl, or C_{1-10} haloalkyl;

R_4 is selected from hydrogen or C_{1-10} alkyl;

m is 1 to 5; n is 0 to 5; and l is 1 to 5,

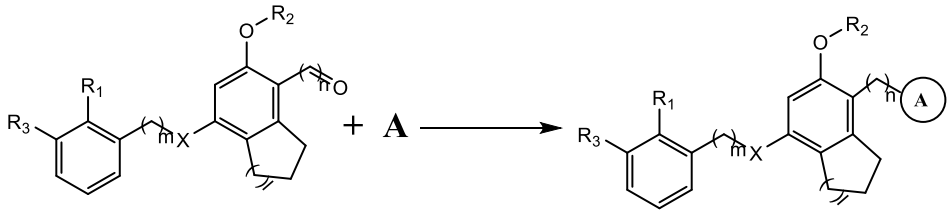
provided that the compound of Formula (I) is not:



.

[0010] In another aspect of the present disclosure, there is provided a process for the preparation of compounds of Formula (I), their stereoisomers, an N-oxide or pharmaceutically acceptable salts thereof, comprising the steps of: (a) reacting

compounds of Formula (Ia) with a compound A in the presence of a reducing agent and a solvent to obtain compounds of Formula (I):



Formula (Ia) **Formula (I)**

[0011] In yet another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound of Formula (I) or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

[0012] In another example of the present disclosure, there is provided a method for the treatment and/or prevention of a condition mediated by PD-1/PD-L1 or a proliferative disorder or cancer, comprising administering to a subject suffering from the condition mediated by PD-1/PD-L1 or the proliferative disorder or cancer, a therapeutically effective amount of the compound of Formula (I) or the pharmaceutical composition as disclosed herein.

[0012a] In another aspect, there is provided the use of the compound as defined above or or the pharmaceutical composition as defined above, in the manufacture of a medicament for the treatment and/or prevention of a condition mediated by PD-1/PD-L1 or a proliferative disorder or cancer.

[0013] In another example of the present disclosure, there is provided a compound of Formula (I) or the pharmaceutical composition as disclosed herein, for use in the manufacture of a medicament for inhibiting PD-1/PD-L1 enzymes in a cell.

[0013a] In another aspect, there is provided a compound as defined above or the pharmaceutical composition as defined above for use in inhibiting PD-1/PD-L1 interaction in a cell.

[0014] In yet another example of the present disclosure, there is provided a compound of Formula (I) or the pharmaceutical composition as disclosed herein, for use in the treatment and/or prevention of a condition mediated by PD-1/PD-L1 or a proliferative disorder or cancer, comprising administering to a subject suffering from the condition mediated by PD-1/PD-L1 or the proliferative disorder or cancer.

[0014a] In another aspect, there is provided a compound as defined above or the pharmaceutical composition as defined above for use in the treatment and/or prevention of a condition mediated by PD-1/PD-L1 interaction or a proliferative disorder or cancer.

[0015] In one more example of the present disclosure, there is provided use of the compounds of Formula (I), or the pharmaceutical composition, for the treatment

or prevention of diseases or proliferative disorder or cancer together with other clinically relevant cytotoxic agents or non-cytotoxic agents.

[0015a] In another aspect, there is provided the use of a compound as defined above or the pharmaceutical composition as defined above, with other clinically relevant cytotoxic agents or non-cytotoxic agents to a subject in need thereof, in the manufacture of a medicament for the treatment or prevention of disease or proliferative disorder or cancer.

[0016] In a further example of the present disclosure, there is provided a method for the treatment of cancer, said method comprising administering a combination of the compounds of Formula (I) or the pharmaceutical composition as disclosed herein, with other clinically relevant cytotoxic agents or non-cytotoxic agents to a subject in need thereof.

[0016a] In another aspect, there is provided the use of the compounds as defined above, or the pharmaceutical composition as defined above, in the manufacture of a medicament for the treatment or prevention of various diseases or proliferative disorder or cancer; together with other clinically relevant cytotoxic agents or non-cytotoxic agents.

[0016b] In another aspect, there is provided the use of the compounds as defined above or the pharmaceutical composition as defined above, with other clinically relevant cytotoxic agents or non-cytotoxic agents to a subject in need thereof, in the manufacture of a medicament for the treatment of cancer.

[0016c] In another aspect, there is provided the use of a combination of the compounds as defined above, or the pharmaceutical composition as defined above, with other clinically relevant immune modulators agents to a subject in need of thereof, in the manufacture of a medicament for the treatment of cancer.

[0017] These and other features, examples, and advantages of the present subject matter will become better understood with reference to the following description. This summary is provided to introduce a selection of concepts in a simplified form. This summary is not intended to identify key features or essential features of the disclosure, nor is it intended to be used to limit the scope of the subject matter.

DETAILED DESCRIPTION OF THE INVENTION

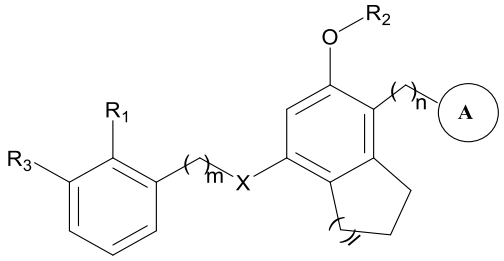
[0018] Those skilled in the art will be aware that the present invention is subject to variations and modifications other than those specifically described. It is to be understood that the present invention includes all such variations and modifications. The invention also includes all such steps, features, compositions and compounds referred to or indicated in this specification, individually or collectively, and any and all combinations of any or more of such steps or features.

Definitions

[0019] For convenience, before further description of the present invention, certain terms employed in the specification, and examples are collected here. These definitions should be read in the light of the remainder of the invention and understood as by a person of skill in the art. The terms used herein have the meanings recognized and known to those of skill in the art, however, for convenience and completeness, particular terms and their meanings are set forth below.

We Claim:

1. A compound of Formula (I):



Formula (I)

their stereoisomers, an N-oxide or pharmaceutically acceptable salts thereof;

wherein,

X is selected from O or NR′;

Ring A is selected from C_{6-10} aryl, C_{3-10} cycloalkyl, C_{7-16} alkylaryl, C_{2-10} heteroaryl, C_{2-20} heterocyclyl, -CO-C_{2-20} heterocyclyl, or –C(O)NR_4-C_{2-20} heterocyclyl; wherein, C_{6-10} aryl, C_{3-10} cycloalkyl, C_{7-16} alkylaryl, C_{2-10} heteroaryl, C_{2-20} heterocyclyl, -CO-C_{2-20} heterocyclyl, or –C(O)NR_4-C_{2-20} heterocyclyl is optionally substituted with one or more groups selected from halogen, hydroxy, C_{1-10} alkyl, C_{1-10} alkoxy, C_{1-10} haloalkyl, C_{2-10} alkylalkoxy, -CH_2-$NR_aC(O)R_b$, -CR_aR_b-OR_c, -CR_aR_b-NR_cR_d, or -CH_2-$NHC(O)NR_aR_b$; wherein, R_a, R_b, R_c, and R_d are independently selected from hydrogen, halogen, C_{1-10} alkyl, -C(O)R", C_{3-10} cycloalkyl, C_{1-10} haloalkyl, or C_{1-10} alkoxy;

R′ is selected from hydrogen or C_{1-10} alkyl;

R_1 is selected from hydrogen, cyano or C_{1-10} alkyl;

R_2 is selected from hydrogen, C_{1-10} alkyl, C_{6-10} aryl, C_{3-10} cycloalkyl, C_{1-10} haloalkyl, C_{7-16} alkylaryl, C_{2-10} heteroaryl, C_{3-20} alkyl heteroaryl, C_{2-20} heterocyclyl, or C_{3-20} alkyl heterocyclyl; wherein, C_{1-10} alkyl, C_{6-10} aryl, C_{3-10} cycloalkyl, C_{1-10} haloalkyl, C_{7-16} alkylaryl, C_{2-10} heteroaryl, C_{3-20} alkyl heteroaryl, C_{2-20} heterocyclyl, or C_{3-20} alkyl heterocyclyl, is optionally substituted with one or more groups selected from halogen, cyano, hydroxy, -C(O)NH_2, C_{1-10} alkyl, or C_{6-10} aryl;

R_3 is selected from halogen, C_{6-10} aryl, or C_{2-10} heteroaryl; wherein, C_{6-10} aryl, or C_{2-10} heteroaryl, is optionally substituted with one or more groups selected from

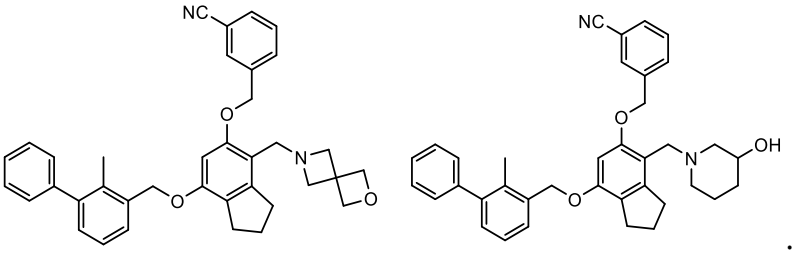
halogen, haloalkyl, cyano, hydroxy, amino, C_{1-10} alkyl, OR", C_{6-10} aryl, C_{2-20} heterocyclyl, or C_{2-10} heteroaryl;

R" is selected from hydrogen, halogen, C_{1-10} alkyl, or C_{1-10} haloalkyl;

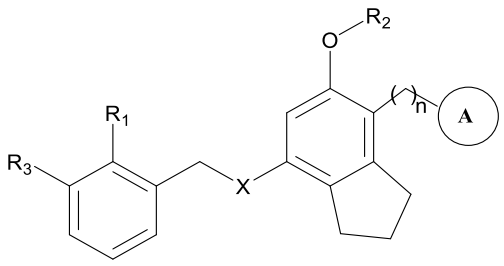
R_4 is selected from hydrogen or C_{1-10} alkyl;

m is 1 to 5; n is 0 to 5; and l is 1 to 5,

provided that the compound of Formula (I) is not:



2. The compound as claimed in claim 1, having compound of Formula (IA):



Formula (IA)

their stereoisomers, an N-oxide or pharmaceutically acceptable salts thereof;

wherein,

X is selected from O;

Ring A is selected from C_{2-20} heterocyclyl, -CO-C_{2-20} heterocyclyl, or –C(O)NR_4-C_{2-20} heterocyclyl; wherein, C_{2-20} heterocyclyl, -CO-C_{2-20} heterocyclyl, or –C(O)NR_4-C_{2-20} heterocyclyl is optionally substituted with one or more groups selected from halogen, hydroxy, C_{1-10} alkyl, -CH_2-$NR_aC(O)R_b$, -CR_aR_b-ORc, -CR_aR_b-NR_cR_d, or -CH_2-$NHC(O)NR_aR_b$; wherein, R_a, R_b, R_c, and R_d are independently selected from hydrogen, C_{1-10} alkyl, or -C(O)R";

R_1 is selected from cyano or C_{1-10} alkyl;

R_2 is selected from C_{6-10} aryl, C_{1-10} haloalkyl, C_{7-16} alkylaryl, C_{3-20} alkyl heteroaryl or C_{3-20} alkyl heterocyclyl; wherein, C_{6-10} aryl, C_{1-10} haloalkyl, C_{7-16} alkylaryl, C_{3-}

$_{20}$ alkyl heteroaryl, or C_{3-20} alkyl heterocyclyl, is optionally substituted with one or more groups selected from cyano, hydroxy, -C(O)NH_2, or C_{1-10} alkyl;

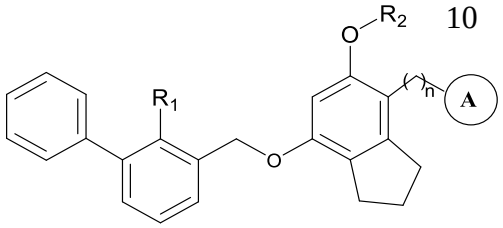
R_3 is selected from halogen, C_{6-10} aryl, or C_{2-10} heteroaryl; wherein, C_{6-10} aryl, or C_{2-10} heteroaryl, is optionally substituted with one or more groups selected from halogen, haloalkyl, hydroxy, amino, C_{1-10} alkyl, OR" or C_{2-20} heterocyclyl;

R" is selected from C_{1-10} alkyl, or C_{1-10} haloalkyl;

R_4 is hydrogen; and

n is 0 to 1.

3. The compound as claimed in claim 1, having compound of Formula (IB):



Formula (IB)

their stereoisomers, an N-oxide or pharmaceutically acceptable salts thereof;

wherein,

Ring A is selected from C_{6-10} aryl, C_{3-10} cycloalkyl, C_{7-16} alkylaryl, C_{2-10} heteroaryl, C_{2-20} heterocyclyl, -CO-C_{2-20} heterocyclyl, or –C(O)NR_4-C_{2-20} heterocyclyl; wherein, C_{6-10} aryl, C_{3-10} cycloalkyl, C_{7-16} alkylaryl, C_{2-10} heteroaryl, C_{2-20} heterocyclyl, -CO-C_{2-20} heterocyclyl, or –C(O)NR_4-C_{2-20} heterocyclyl is optionally substituted with one or more groups selected from halogen, hydroxy, C_{1-10} alkyl, C_{1-10} alkoxy, C_{1-10} haloalkyl, C_{2-10} alkylalkoxy, -CH_2-$NR_aC(O)R_b$, -CR_aR_b-OR_c, -CR_aR_b-NR_cR_d,, or -CH_2-$NHC(O)NR_aR_b$; wherein, R_a, R_b, R_c, and R_d are independently selected from hydrogen, halogen, C_{1-10} alkyl, -C(O)R", C_{3-10} cycloalkyl, C_{1-10} haloalkyl, or C_{1-10} alkoxy;

R_1 is selected from hydrogen, cyano or C_{1-10} alkyl;

R_2 is selected from hydrogen, C_{1-10} alkyl, C_{6-10} aryl, C_{3-10} cycloalkyl, C_{1-10} haloalkyl, C_{7-16} alkylaryl, C_{2-10} heteroaryl, C_{3-20} alkyl heteroaryl, C_{2-20} heterocyclyl, or C_{3-20} alkyl heterocyclyl; wherein, C_{1-10} alkyl, C_{6-10} aryl, C_{3-10} cycloalkyl, C_{1-10}

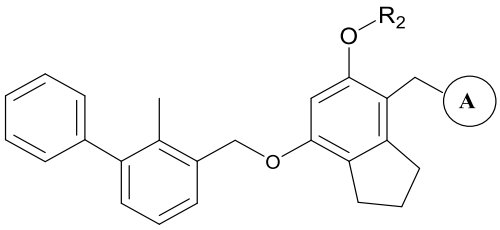
haloalkyl, C_{7-16} alkylaryl, C_{2-10} heteroaryl, C_{3-20} alkyl heteroaryl, C_{2-20} heterocyclyl, or C_{3-20} alkyl heterocyclyl, is optionally substituted with one or more groups selected from halogen, cyano, hydroxy, -$C(O)NH_2$, C_{1-10} alkyl, or C_{6-10} aryl;

R" is selected from hydrogen, halogen, C_{1-10} alkyl, or C_{1-10} haloalkyl;

R_4 is selected from hydrogen or C_{1-10} alkyl; and

n is 0 to 1.

4. The compound as claimed in claim 1, having compound of Formula (IC):



Formula (IC)

their stereoisomers, an N-oxide or pharmaceutically acceptable salts thereof;

wherein,

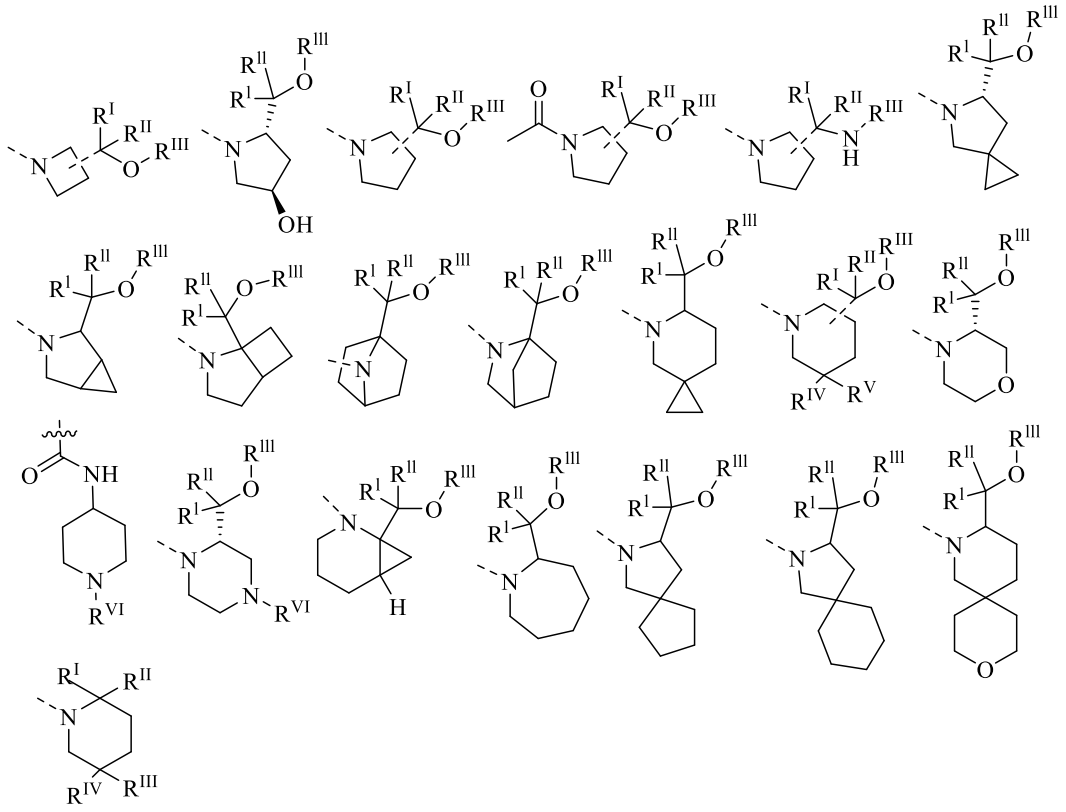
Ring A is selected from C_{6-10} aryl, C_{3-10} cycloalkyl, C_{7-16} alkylaryl, C_{2-10} heteroaryl, C_{2-20} heterocyclyl, -CO-C_{2-20} heterocyclyl, or –$C(O)NR_4$-C_{2-20} heterocyclyl; wherein, C_{6-10} aryl, C_{3-10} cycloalkyl, C_{7-16} alkylaryl, C_{2-10} heteroaryl, C_{2-20} heterocyclyl, -CO-C_{2-20} heterocyclyl, or –$C(O)NR_4$-C_{2-20} heterocyclyl is optionally substituted with one or more groups selected from halogen, hydroxy, C_{1-10} alkyl, C_{1-10} alkoxy, C_{1-10} haloalkyl, C_{2-10} alkylalkoxy, -CH_2-$NR_aC(O)R_b$, -CR_aR_b-OR_c, -CR_aR_b-NR_cR_d, or -CH_2-$NHC(O)NR_aR_b$; wherein, R_a, R_b, R_c, and R_d are independently selected from hydrogen, halogen, C_{1-10} alkyl, -C(O)R", C_{3-10} cycloalkyl, C_{1-10} haloalkyl, or C_{1-10} alkoxy;

R_2 is selected from hydrogen, C_{1-6} alkyl, C_{6-10} aryl, C_{3-10} cycloalkyl, C_{1-6} haloalkyl, C_{7-16} alkylaryl, C_{2-10} heteroaryl, C_{3-20} alkyl heteroaryl, C_{2-20} heterocyclyl, or C_{3-20} alkyl heterocyclyl; wherein, C_{1-6} alkyl, C_{6-10} aryl, C_{3-10} cycloalkyl, C_{1-6} haloalkyl, C_{7-16} alkylaryl, C_{2-10} heteroaryl, C_{3-20} alkyl heteroaryl, C_{2-20} heterocyclyl, or C_{3-20} alkyl heterocyclyl, is optionally substituted with one or more groups selected from halogen, cyano, hydroxy, -$C(O)NH_2$, C_{1-10} alkyl, or C_{6-10} aryl;

R" is selected from hydrogen, halogen, C_{1-10} alkyl, or C_{1-10} haloalkyl; and

R_4 is selected from hydrogen or C_{1-6} alkyl.

5. The compound as claimed in claim 1, their stereoisomers, an N-oxide or pharmaceutically acceptable salts thereof; wherein A is selected from:



wherein, "----" is —— or ····· or ▬ ;

R^{I}, R^{II}, R^{III}, R^{IV}, R^{V} and R^{VI} are independently selected from hydrogen, C_{1-10} alkyl, -C(O)R", -C(O)NH-R", $-CH_2$-OR", halogen or C_{1-10} haloalkyl.

6. A compound selected from:

Example No.	IUPAC Name
1	(S)-5-(((4-((2-(hydroxymethyl)piperidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
2	(S)-3-(((4-((2-(hydroxymethyl)piperidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)benzonitrile;
3	(S)-5-(((7-((2-cyano-[1,1'-biphenyl]-3-yl)methoxy)-4-((2-(hydroxymethyl)pyrrolidin-1-yl)methyl)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;

4	(S)-3-(((6-((3-cyanobenzyl)oxy)-7-((2-(hydroxymethyl)pyrrolidin-1-yl)methyl)-2,3-dihydro-1H-inden-4-yl)oxy)methyl)-[1,1'-biphenyl]-2-carbonitrile;
5	(S)-5-(((7-((2-cyano-[1,1'-biphenyl]-3-yl)methoxy)-4-((2-(hydroxymethyl)piperidin-1-yl)methyl)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
6	(5-(((4-(((2S,4R)-4-hydroxy-2-(hydroxymethyl)pyrrolidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
7	(S)-3-(((4-((2-(hydroxymethyl)pyrrolidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)benzonitrile;
8	(S)-5-(((4-((2-(hydroxymethyl)pyrrolidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
9	(R)-5-(((4-((3-(hydroxymethyl)morpholino)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
10	5-(((4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
11	5-(((4-((6-(hydroxymethyl)-5-azaspiro[2.5]octan-5-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
12	5-(((4-((5,5-difluoro-2-(hydroxymethyl)piperidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
13	5-(((4-((2-(hydroxymethyl)-4-methylpiperazin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
14	5-(((4-((3-(hydroxymethyl)azetidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
15	(R)-5-(((4-((3-(hydroxymethyl)pyrrolidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
16	(S)-5-(((4-((3-(hydroxymethyl)piperidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;

17	5-(((4-((4-(hydroxymethyl)piperidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
18	(S)-5-(((4-((3-(hydroxymethyl)pyrrolidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
19	(R)-5-(((4-((2-(hydroxymethyl)pyrrolidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
20	5-(((4-((2-(hydroxymethyl)azepan-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
21	(R)-5-(((4-((3-(hydroxymethyl)piperidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile 2,2,2-trifluoroacetate;
22	5-(((4-((2,2-bis(hydroxymethyl)piperidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile 2,2,2-trifluoroacetate;
23	(S)-3-(((7-((2-(hydroxymethyl)piperidin-1-yl)methyl)-6-(2,2,2-trifluoroethoxy)-2,3-dihydro-1H-inden-4-yl)oxy)methyl)-[1,1'-biphenyl]-2-carbonitrile;
24	(S)-(1-((7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-5-(2,2,2-trifluoroethoxy)-2,3-dihydro-1H-inden-4-yl)methyl)piperidin-2-yl)methanol;
25	(S)-5-(((4-((6-(hydroxymethyl)-5-azaspiro[2.4]heptan-5-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
26	(S)-5-(((7-((2-cyano-[1,1'-biphenyl]-3-yl)methoxy)-4-((6-(hydroxymethyl)-5-azaspiro[2.4]heptan-5-yl)methyl)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
27	(S)-(1-((5-(2-fluoroethoxy)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-4-yl)methyl)piperidin-2-yl)methanol;
28	(S)-(1-((5-(2-fluoroethoxy)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-4-yl)methyl)pyrrolidin-2-yl)methanol;
29	(S)-3-(((6-(2-fluoroethoxy)-7-((2-(hydroxymethyl)piperidin-1-yl)methyl)-2,3-dihydro-1H-inden-4-yl)oxy)methyl)-[1,1'-biphenyl]-2-carbonitrile;

30	(S)-(1-((5-((5-fluoropentyl)oxy)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-4-yl)methyl)piperidin-2-yl)methanol;
31	(S)-(1-((5-(4-fluorobutoxy)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-4-yl)methyl)piperidin-2-yl)methanol;
32	(S)-(1-((5-(3-fluoropropoxy)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-4-yl)methyl)piperidin-2-yl)methanol
33	(S)-(1-((5-(4-fluorobutoxy)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-4-yl)methyl)azetidin-2-yl)methanol;
34	3-(((4-((1-(hydroxymethyl)-2-azabicyclo[4.1.0]heptan-2-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)benzonitrile;
35	5-(((4-((1-(hydroxymethyl)-2-azabicyclo[4.1.0]heptan-2-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
36	3-(((6-((3-cyanobenzyl)oxy)-7-((1-(hydroxymethyl)-2-azabicyclo[4.1.0]heptan-2-yl)methyl)-2,3-dihydro-1H-inden-4-yl)oxy)methyl)-[1,1'-biphenyl]-2-carbonitrile;
37	(S)-5-(((4-((2-(hydroxymethyl)piperidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinamide;
38	(S)-3-(((4-((2-(hydroxymethyl)pyrrolidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)benzamide;
39	(S)-(1-((5-((1-methyl-1H-pyrazol-4-yl)methoxy)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-4-yl)methyl)piperidin-2-yl)methanol;
40	(1-((7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-5-(thiazol-4-ylmethoxy)-2,3-dihydro-1H-inden-4-yl)methyl)azetidin-2-yl)methanol;
41	(1-((5-((1-methyl-1H-imidazol-4-yl)methoxy)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-4-yl)methyl)azetidin-2-yl)methanol;
42	(1-((7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-5-(pyrimidin-5-ylmethoxy)-2,3-dihydro-1H-inden-4-yl)methyl)azetidin-2-yl)methanol;

43	(1-((7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-5-(oxazol-4-ylmethoxy)-2,3-dihydro-1H-inden-4-yl)methyl)azetidin-2-yl)methanol;
44	(S)-3-cyano-5-(((4-((2-(hydroxymethyl)pyrrolidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)pyridine 1-oxide;
45	(S)-3-cyano-5-(((4-((2-(hydroxymethyl)piperidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)pyridine 1-oxide;
46	(S)-5-(((7-((4'-fluoro-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4-((2-(hydroxymethyl)piperidin-1-yl)methyl)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
47	(S)-5-(((7-((4'-fluoro-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4-((6-(hydroxymethyl)-5-azaspiro[2.4]heptan-5-yl)methyl)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
48	(S)-5-(((7-((4'-fluoro-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4-((2-(hydroxymethyl)pyrrolidin-1-yl)methyl)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
49	5-((5-cyanopyridin-3-yl)methoxy)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-N-(1-methylpiperidin-4-yl)-2,3-dihydro-1H-indene-4-carboxamide;
50	(S)-5-(((4-(2-(hydroxymethyl)pyrrolidine-1-carbonyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
51	(S)-5-(((4-(3-(hydroxymethyl)pyrrolidine-1-carbonyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
52	N-((1-((5-((5-cyanopyridin-3-yl)methoxy)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-4-yl)methyl)pyrrolidin-2-yl)methyl)acetamide;
53	5-(((4-((2-(aminomethyl)pyrrolidin-1-yl)methyl)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
54	5-(((7-((3-bromo-2-methylbenzyl)oxy)-4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
55	5-(((7-((4'-hydroxy-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;

56	5-(((7-((2'-fluoro-2,5'-dimethyl-[1,1'-biphenyl]-3-yl)methoxy)-4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
57	5-(((4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-7-((2-methyl-3-(1H-pyrazol-4-yl)benzyl)oxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
58	5-(((4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-7-((4'-methoxy-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
59	5-(((4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-7-((2-methyl-3-(pyrimidin-5-yl)benzyl)oxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
60	5-(((4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-7-((2-methyl-2'-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
61	5-(((4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-7-((2-methyl-3-(6-morpholinopyridin-3-yl)benzyl)oxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
62	5-(((7-((2'-fluoro-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
63	5-(((4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-7-((4'-methoxy-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
64	5-(((7-((3'-fluoro-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
65	5-(((4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-7-((3'-methoxy-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
66	5-(((4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-7-((2-methyl-4'-(trifluoromethoxy)-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
67	5-(((7-((3'-hydroxy-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
68	5-(((4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-7-((2-methyl-3-(1-methyl-1H-pyrazol-4-yl)benzyl)oxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;

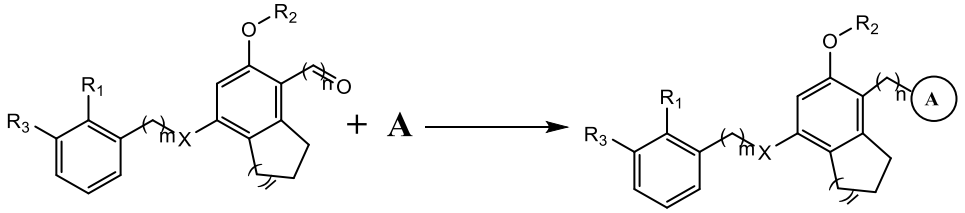
69	5-(((4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-7-((2-methyl-3-(quinolin-8-yl)benzyl)oxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
70	5-(((4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-7-((2-methyl-3-(pyridin-4-yl)benzyl)oxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
71	5-(((4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-7-((2-methyl-3-(pyridin-3-yl)benzyl)oxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
72	(S)-5-(((4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-7-((2-methyl-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)oxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
73	5-(((7-((2,4'-dimethyl-[1,1'-biphenyl]-3-yl)methoxy)-4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
74	5-(((4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-7-((2-methyl-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)oxy)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile 2,2,2-trifluoroacetate;
75	5-(((7-((4'-(tert-butyl)-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
76	5-(((7-((4'-fluoro-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
77	5-(((7-((3-(6-aminopyridin-3-yl)-2-methylbenzyl)oxy)-4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
77A	(S)-5-(((7-((3-(6-aminopyridin-3-yl)-2-methylbenzyl)oxy)-4-((2-(hydroxymethyl)azetidin-1-yl)methyl)-2,3-dihydro-1H-inden-5-yl)oxy)methyl)nicotinonitrile;
78	(1-((7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-5-phenoxy-2,3-dihydro-1H-inden-4-yl)methyl)azetidin-2-yl)methanol;
79	(1-((7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-5-(pyrazin-2-ylmethoxy)-2,3-dihydro-1H-inden-4-yl)methyl)azetidin-2-yl)methanol;
80	1-((1-((5-((5-cyanopyridin-3-yl)methoxy)-7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-2,3-dihydro-1H-inden-4-yl)methyl)pyrrolidin-2-yl)methyl)-3-methylurea formate; and

81	(1-((7-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-5-((1-methylpiperidin-4-yl)methoxy)-2,3-dihydro-1H-inden-4-yl)methyl)azetidin-2-yl)methanol.

or stereoisomers thereof, an N-oxide or a pharmaceutically acceptable salts thereof.

7. The compound as claimed in claim 1, their stereoisomers, an N-oxide or pharmaceutically acceptable salts thereof, wherein the compound acts as inhibitors for PD1/PD-L1 interaction.

8. A process for preparation of compounds of Formula (I) as claimed in claim 1, their stereoisomers, an N-oxide or pharmaceutically acceptable salts thereof, comprising the steps of: (a) reacting compounds of Formula (Ia) with a compound A in the presence of a reducing agent and a solvent to obtain compounds of Formula (I):



Formula (Ia) **Formula (I)**

9. The process as claimed in claim 8, wherein the process is carried out at a temperature in the range of 25 to 80°C for a time period in the range of 2 hours to 20 hours; the reducing agent is selected from sodium cyanoborohydride, sodium triacetoxyborohydride, or sodium borohydride and the solvent is selected from methanol, ethanol, dimethyl formamide or combinations thereof.

10. The process as claimed in claim 8, wherein the Formula (I) optionally reacted with potassium tertiary butoxide in the presence of a solvent selected from tetrahydrofuran, t-butanol or combinations thereof.

11. A pharmaceutical composition comprising a compound of Formula (I) or a pharmaceutically acceptable salt thereof as claimed in any one of the claims 1 to 6, together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

12. Use of the compound as claimed in any of claims 1 to 6 or the pharmaceutical composition as claimed in claim 11, in the manufacture of a medicament for the

treatment and/or prevention of a condition mediated by PD-1/PD-L1 or a proliferative disorder or cancer.

13. A compound as claimed in any of claims 1 to 6 or the pharmaceutical composition as claimed in claim 11 for use in inhibiting PD-1/PD-L1 interaction in a cell.

14. A compound as claimed in any of claims 1 to 6 or the pharmaceutical composition as claimed in claim 11 for use in the treatment and/or prevention of a condition mediated by PD-1/PD-L1 interaction or a proliferative disorder or cancer.

15. Use of a compound according to any one of claims 1 to 6 or the pharmaceutical composition as claimed in claim 11, with other clinically relevant cytotoxic agents or non-cytotoxic agents to a subject in need thereof, in the manufacture of a medicament for the treatment or prevention of disease or proliferative disorder or cancer.

16. Use of the compounds as claimed in any one of claims 1 to 6, or the pharmaceutical composition as claimed in claim 11, in the manufacture of a medicament for the treatment or prevention of various diseases or proliferative disorder or cancer; together with other clinically relevant cytotoxic agents or non-cytotoxic agents.

17. Use of the compounds as claimed in any of claims 1 to 6 or the pharmaceutical composition as claimed in claim 11, with other clinically relevant cytotoxic agents or non-cytotoxic agents to a subject in need thereof, in the manufacture of a medicament for the treatment of cancer.

18. Use of a combination of the compounds as claimed in any of claims 1 to 6, or the pharmaceutical composition as claimed in claim 11, with other clinically relevant immune modulators agents to a subject in need of thereof, in the manufacture of a medicament for the treatment of cancer.

19. The use as claimed in claim 18, wherein the condition mediated by PD-1/PD-L1 or a proliferative disorder or cancer is selected from metastasis cancer, breast cancer, prostate cancer, pancreatic cancer, gastric cancer, lung cancer, colon cancer, rectal cancer, esophagus cancer, duodenal cancer, tongue cancer, pharyngeal cancer, brain tumor, neurinoma, clear cell carcinoma, non-small cell lung cancer,

small cell lung cancer, liver cancer, kidney cancer, Hodgkin's lymphoma, head and neck cancer, urothelial cancer, bile duct cancer, uterine body cancer, cervical cancer, ovarian cancer, urinary bladder, skin cancer, hemangioma, malignant lymphoma, malignant melanoma, thyroid cancer, bone tumor, vascular fibroma, glioblastoma, neuroblastoma, hepatoblastoma, medulloblastoma, nephroblastoma, pancreatoblastoma, pleuropulmonary blastoma, sarcoma, neuroendocrine tumors, retinoblastoma, penile cancer, pediatric solid cancer, renal cell carcinoma, lymphoma, myeloma, leukemia, acute myelogenous leukemia (AML), chronic myelogenous leukemia (CML), chronic neutrophilic leukemia, chronic eosinophilic leukemia, chronic lymphocytic leukemia (CLL), acute lymphoblastic leukemia (ALL), hairy cell leukemia, cutaneous T-cell lymphoma (CTCL), multiple myeloma (MM), metastatic cancer, Myeloproliferative neoplasms (MPN), a disease category that includes polycythemia vera (PV), essential thrombocythemia, essential thrombocytosis (ET) and myelofibrosis (MF), chronic myelogenous leukemia (CML), chronic neutrophilic leukemia (CNL), chronic eosinophilic leukemia (CEL), cancers with mutations in specific oncogenes, EGFR, KRAS, or RET.