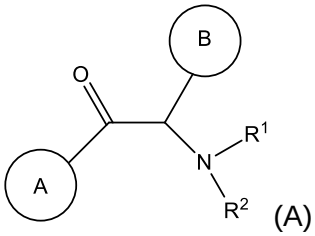
The present disclosure furthermore relates to the use of such compounds as medicines and to their use for the manufacture of medicaments for treating and/or preventing viral infections, in particular with viruses belonging to the family of the Flaviviruses, and yet more particularly infections with Dengue viruses or yellow fever virus, in animals or mammals, more in particular in humans. The disclosure also relates to methods for the preparation of all such compounds and to pharmaceutical compositions comprising them in an effective amount.

The present disclosure also relates to a method of treatment or prevention of viral infections in humans by the administration of one or more such compounds, optionally in combination with one or more other medicines, to a patient in need thereof. Particularly, the present disclosure also relates to a method of treatment or prevention of viral infections, especially Flaviviral infections, in humans by the administration of an effective amount of one or more such compounds or a pharmaceutically acceptable salt thereof, optionally in combination with one or more other medicines, to a patient in need thereof. More particularly, the present disclosure also relates to a method of treatment or prevention of infections by the Dengue virus or yellow fever virus in humans by the administration of an effective amount of one or more such compounds or a pharmaceutically acceptable salt thereof, optionally in combination with one or more other medicines, to a patient in need thereof.

The present disclosure relates to the provision of new compounds of formula (A),



(A)

wherein,

- cycle A is a heterocycle, which can be unsubstituted or substituted with one or more Z^1;
- cycle B is selected from aryl; and heterocycle; wherein said aryl and heterocycle can be unsubstituted or substituted with one or more Z^{1a};
- R^1 is selected from cycloalkyl; cycloalkenyl; cycloalkynyl; aryl; heterocycle; arylalkyl; arylalkenyl; arylalkynyl; heterocycle-alkyl; heterocycle-alkenyl; heterocycle-alkynyl; arylheteroalkyl; arylheteroalkenyl; arylheteroalkynyl; heterocycle-heteroalkyl; heterocycle-heteroalkenyl; heterocycle-heteroalkynyl;

  and wherein said cycloalkyl; cycloalkenyl; cycloalkynyl; aryl, heterocycle, arylalkyl, arylalkenyl, arylalkynyl, heterocycle-alkyl, heterocycle-alkenyl, heterocycle-alkynyl, arylheteroalkyl, arylheteroalkenyl, arylheteroalkynyl, heterocycle-heteroalkyl, heterocycle-heteroalkenyl and heterocycle-heteroalkynyl can be unsubstituted or substituted with one or more Z^{1b};
- R^2 is selected from hydrogen; alkyl; alkenyl; alkynyl; heteroalkyl; heteroalkenyl; and

alkynyl, hydroxyl, =O, halogen, -SH, =S, trifluoromethyl, -O-alkyl, -OCF_3, cyano, nitro, -C(O)OH or NH_2;

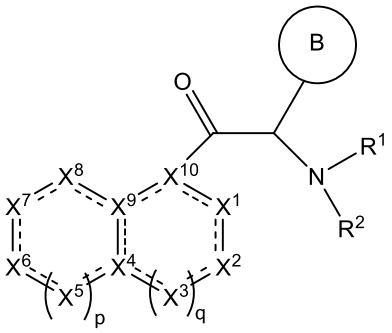
- each Z^4 and Z^5 is independently selected from hydrogen; alkyl; alkenyl; alkynyl; heteroalkyl; heteroalkenyl; heteroalkynyl; aryl; heterocycle; arylalkyl; arylalkenyl; arylalkynyl; arylheteroalkyl; arylheteroalkenyl; arylheteroalkynyl; heterocycle-alkyl; heterocycle-alkenyl; heterocycle-alkynyl; heterocycle-heteroalkyl; heterocycle-heteroalkenyl; or heterocycle-heteroalkynyl;

wherein said alkyl, alkenyl, alkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, aryl, heterocycle, arylalkyl, arylalkenyl, arylalkynyl, arylheteroalkyl, arylheteroalkenyl, arylheteroalkynyl, heterocycle-alkyl, heterocycle-alkenyl, heterocycle-alkynyl, heterocycle-heteroalkyl, heterocycle-heteroalkenyl, or heterocycle-heteroalkynyl can be unsubstituted or substituted with one or more substituents selected from alkyl, alkenyl, alkynyl, hydroxyl, =O, halogen, -SH, =S, trifluoromethyl, -O-alkyl, -OCF_3, cyano, nitro, -C(O)OH or NH_2;

and wherein Z^4 and Z^5 can be taken together in order to form a (5-, 6-, or 7-membered) heterocycle which can be unsubstituted or substituted with alkyl, alkenyl, alkynyl, hydroxyl, halogen, -SH, trifluoromethyl, -O-alkyl, -OCF_3, cyano, nitro, -C(O)OH or -NH_2;

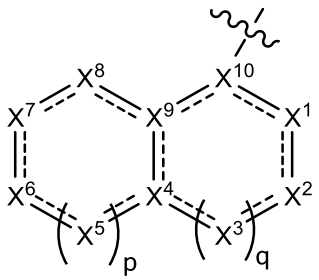
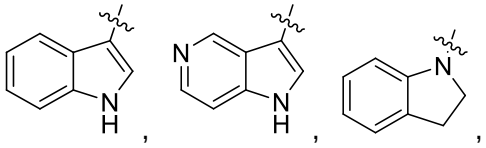
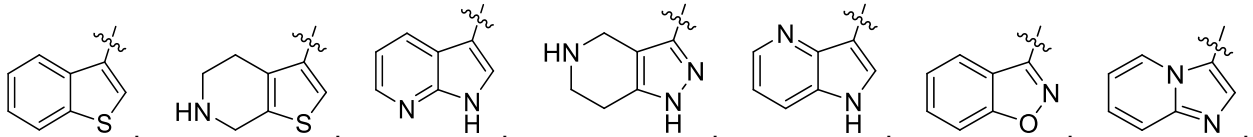
and isomers (in particular stereo-isomers or tautomers), solvates, salts (in particular pharmaceutically acceptable salts) or prodrugs thereof.

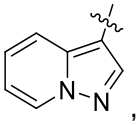
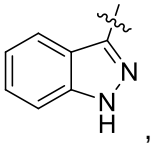
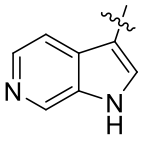
In one aspect, the present disclosure refers to a compound of formula (B),



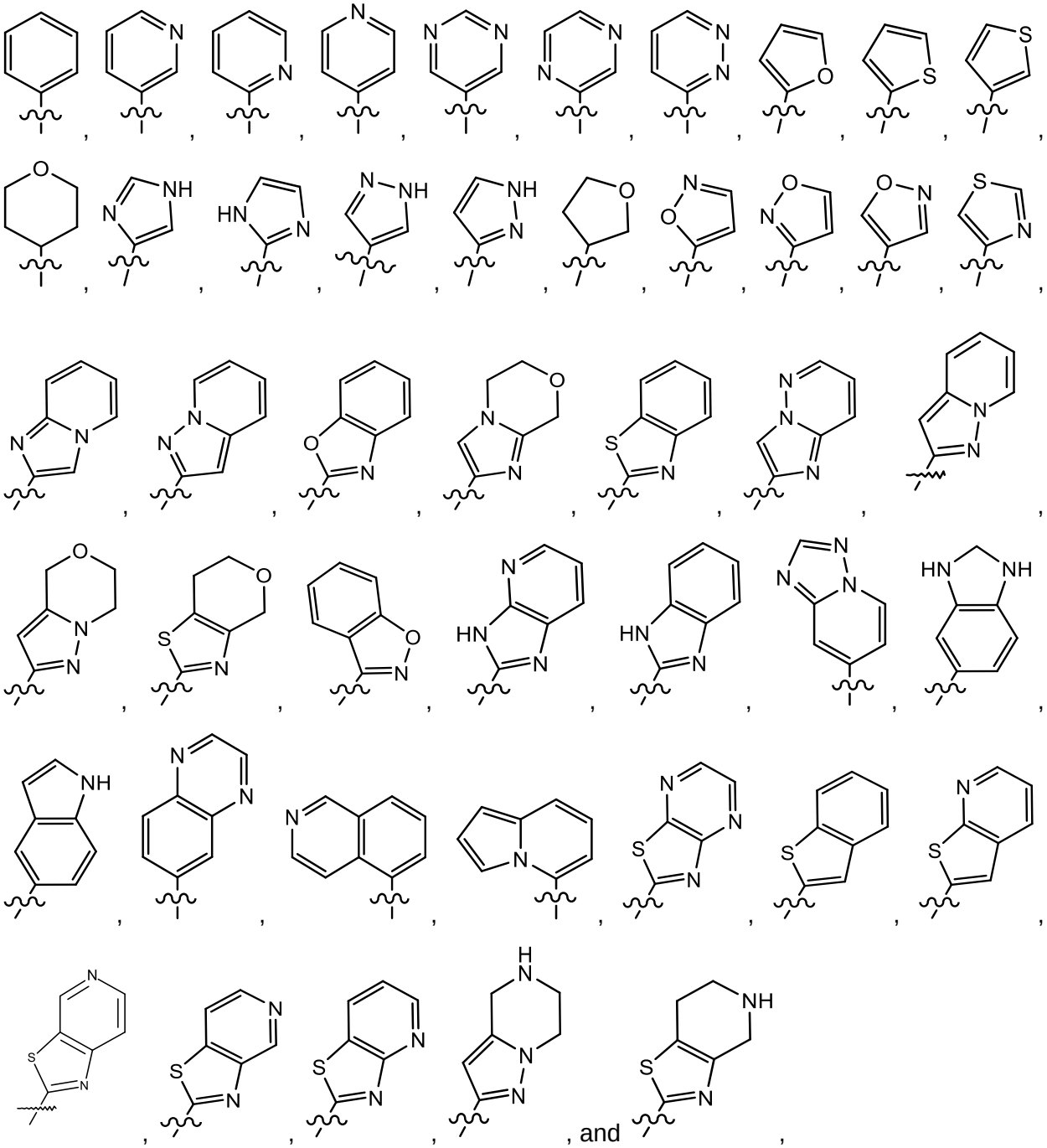
(B)

wherein

- the moiety  is selected from , ,

, , and ; wherein the wavy line (〰) indicates the point of attachment to the carbonyl of the main formula (B); wherein said moiety is unsubstituted;

- cycle B is selected from



wherein the wavy line (〰) indicates the point of attachment to the carbon atom of the main formula (B), and wherein the depicted cycles may be optionally substituted with one, two, or three Z^{1a};

- R^1 is selected from C_{3-7}cycloalkyl, aryl, heterocycle;

and wherein said C_{3-7}cycloalkyl, aryl, and heterocycle, are optionally substituted with one, two, or three Z^{1b};

- R^2 is hydrogen;

- each Z^{1a} is independently selected from the group consisting of halogen, hydroxyl, sulfhydryl, $-OZ^2$, $-O-C(=O)Z^3$, =O, $-SZ^2$, =S, $-S(=O)Z^2$, $-S(=O)_2Z^3$, $-S(=O)_2NZ^4Z^5$, trifluoromethoxy, nitro, $-NZ^4Z^5$, $-NZ^4S(=O)_2Z^2$, $-NZ^4C(=O)Z^2$, $-NZ^4C(=O)NZ^4Z^5$, cyano, $-C(=O)Z^3$, $-C(=O)OZ^2$, $-C(=O)NZ^4Z^5$, -C(=O)H, heteroC_{1-6}alkyl, aryl, heterocycle, and heterocycle-C_{1-6}alkyl;

and wherein said heteroC_{1-6}alkyl, aryl, heterocycle, and heterocycle-C_{1-6}alkyl, are optionally substituted with one, two, or three substituents selected from hydroxyl, =O, halogen, -SH, =S, trifluoromethyl, $-OCF_3$, -O-C(O)Me, cyano, nitro, -C(O)OH, $-C(O)OC_{1-6}$alkyl, $-NH_2$, $-NHCH_3$; $-N(CH_3)_2$, -NH-C(=O)O-C_{1-4}alkyl; $-S(O)_2C_{1-4}$alkyl, and –O-C_{1-6}alkyl;

- each Z^{1b} is independently selected from the group consisting of halogen, hydroxyl, sulfhydryl, $-OZ^2$, $-O-C(=O)Z^3$, =O, $-SZ^2$, =S, $-S(=O)Z^2$, $-S(=O)_2Z^3$, $-S(=O)_2NZ^4Z^5$, trifluoromethyl, trifluoromethoxy, nitro, $-NZ^4Z^5$, $-NZ^4C(=O)NZ^4Z^5$, cyano, $-C(=O)Z^3$, $-C(=O)OZ^2$, -C(=O)H, C_{1-6}alkyl, heteroC_{1-6}alkyl, aryl, and heterocycle;

and wherein said C_{1-6}alkyl, heteroC_{1-6}alkyl, aryl, and heterocycle, are optionally substituted with one, two, or three substituents selected from hydroxyl, halogen, -SH, =S, trifluoromethyl, $-OCF_3$, -O-C(O)Me, cyano, nitro, -C(O)OH, $-C(O)OC_{1-6}$alkyl, $-NH_2$, $-NHCH_3$; $-N(CH_3)_2$, -NH-C(=O)O-C_{1-4}alkyl; $-S(O)_2C_{1-4}$alkyl, and –O-C_{1-6}alkyl;

- each Z^2 is independently selected from C_{1-6}alkyl, aryl, and heterocycle;

wherein said C_{1-6}alkyl, aryl, heterocycle, are optionally substituted with one, two, or three substituents selected from hydroxyl, =O, halogen, -SH, =S, trifluoromethyl, difluoromethyl, -O-C_{1-6}alkyl, $-OCF_3$, $-S(=O)_2C_{1-4}$alkyl, cyano, nitro, -C(=O)OH, -C(=O)O-C_{1-4}alkyl, $-NH_2$, and $-N(CH_3)_2$, pyrrolidinyl, piperidinyl, and piperazinyl;

- each Z^3 is independently selected from hydroxyl, C_{1-6}alkyl, aryl, and heterocycle;

wherein said C_{1-6}alkyl, aryl, and heterocycle are optionally substituted with one, two, or three substituents selected from C_{1-6}alkyl and $-N(CH_3)_2$;

- each Z^4 and Z^5 is independently selected from hydrogen, C_{1-6}alkyl, aryl, C_{3-7}cycloalkyl, and heterocycle;

or 1-(1H-indol-4-yl)-2-(3-methoxyanilino)-2-phenyl-ethanone;

or 1-(4-isoquinolyl)-2-(3-methoxyanilino)-2-phenyl-ethanone;

or 1-(1H-indol-3-yl)-2-(3-methoxy-N-methyl-anilino)-2-phenyl-ethanone;

or 3-[[2-(1H-indol-3-yl)-2-oxo-1-phenyl-ethyl]amino]-N,N-dimethyl-benzamide;

or 2-[2-furylmethyl(methyl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone;

or N-[2-(1H-indol-3-yl)-2-oxo-1-phenyl-ethyl]-2-(dimethylamino)-N-(3-methoxyphenyl)acetamide;

and stereo-isomers or tautomers, solvates, or salts in particular pharmaceutically acceptable salts thereof;

wherein the term “alkyl” as used herein means a normal, secondary, or tertiary, linear or cyclic or a combination of linear and cyclic, branched or straight hydrocarbon with no site of unsaturation,

wherein the term “heteroalkyl” as used herein refers to an acyclic alkyl wherein one or more carbon atoms are replaced by an oxygen, nitrogen or sulphur atom, with the proviso that said chain may not contain two adjacent O atoms or two adjacent S atoms;

wherein the term “heterocycle” means a saturated, unsaturated, or aromatic ring system of 3 to 18 atoms including at least one N, O, S or P;

the term “aryl” means an aromatic hydrocarbon radical of 6-20 carbon atoms derived by the removal of hydrogen from a carbon atom of a parent aromatic ring system,

with the proviso that compound per se of formula (B) is not:

3-(2-(1H-indol-3-yl)-2-oxo-1-phenylethylamino)benzenesulfonamide (CAS nr. 1211427-21-2);

2-(3,4-dihydro-2H-benzo[b][1,4]dioxepin-7-ylamino)-1-(1H-indol-3-yl)-2-phenylethanone (CAS nr. 1090733-87-1);

1-(1H-indol-3-yl)-2-phenyl-2-(m-tolylamino)ethanone (CAS nr. 1252467-88-1);

2-(4-ethoxy-3-(hydroxymethyl)phenylamino)-1-(1H-indol-3-yl)-2-phenylethanone (CAS nr. 1241127-58-1);

1-(1H-indol-3-yl)-2-[(6-methoxy-3-pyridinyl)amino]-2-phenyl-ethanone (CAS nr. 1181884-55-8);

1-(1H-indol-3-yl)-2-[(1-methyl-1H-pyrazol-3-yl)amino]-2-phenyl-ethanone (CAS nr. 1134766-19-0);

2-[(3,5-dimethoxyphenyl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 1030232-46-2);

1-(1H-indol-3-yl)-2-phenyl-2-(phenylamino)-ethanone (CAS nr. 1030214-83-5);

1-(1H-indol-3-yl)-2-[[6-(4-morpholinyl)-3-pyridinyl]amino]-2-phenyl-ethanone (CAS nr. 1030212-41-9);

2-(3-(difluoromethoxy)-4-methoxyphenylamino)-1-(1H-indol-3-yl)-2-phenylethanone (CAS nr. 1015662-06-2);

1-(1H-indol-3-yl)-2-phenyl-2-[(3,4,5-trimethoxyphenyl)amino]-ethanone (CAS nr. 1014535-82-0);

2-[(4-fluorophenyl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 1014493-63-0);

2-[(4-ethoxy-3-methoxyphenyl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 1014422-80-0);

1-[4-[[2-(1H-indol-3-yl)-2-oxo-1-phenylethyl]amino]-2-methoxyphenyl]-2-pyrrolidinone (CAS nr.

1011119-79-1);
2-[(1-acetyl-2,3-dihydro-1H-indol-5-yl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 949443-90-7);
1-(1H-indol-3-yl)-2-phenyl-2-[(1-propyl-4-piperidinyl)amino]-ethanone (CAS nr. 941047-24-1);
2-(cyclopentylamino)-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 931079-25-3);
1-(1H-indol-3-yl)-2-[(4-methylphenyl)amino]-2-phenyl-ethanone (CAS nr. 931016-79-4);
2-(cyclopropylamino)-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 931000-99-6);
2-[(3,4-dihydro-2H-1-benzothiopyran-4-yl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 924713-60-0)**;**
2-[(3,4-dimethoxyphenyl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 924712-67-4)**;**
2-ethoxy-5-[[2-(1H-indol-3-yl)-2-oxo-1-phenylethyl]amino]-N,N-dimethyl-benzenesulfonamide (CAS nr. 920883-17-6);
6-[[2-(1H-indol-3-yl)-2-oxo-1-phenylethyl]amino]-2-methyl-2H-1,4-benzoxazin-3(4H)-one (CAS nr. 920834-07-7);
2-[(3,4-dihydro-2H-1-benzopyran-4-yl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 920819-87-0)**;**
4-[[2-(1H-indol-3-yl)-2-oxo-1-phenylethyl]amino]-benzeneacetonitrile (CAS nr. 920669-36-9)**;**
1-(1H-indol-3-yl)-2-[(4-methoxyphenyl)amino]-2-phenyl-ethanone (CAS nr. 920601-77-0)**;**
1-(1H-indol-3-yl)-2-phenyl-2-(1,1-dioxotetrahydrothiophen-3-ylamino)ethanone (CAS nr. 878619-92-2);
2-[[3-(hydroxymethyl)phenyl]amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 875166-36-2)**;**
2-[(2,3-dihydro-1,4-benzodioxin-6-yl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 874669-99-5)**;**
1-(1H-indol-3-yl)-2-(morpholino(phenyl)methylamino)-2-phenylethanone;
2-(4-(dimethylamino)benzylamino)-1-(1H-indol-3-yl)-2-phenylethanone;
1-(1H-indol-3-yl)-2-(2-methoxybenzylamino)-2-phenylethanone;
1-(1H-indol-3-yl)-2-(3-methoxybenzylamino)-2-phenylethanone;
2-(2-(dimethylamino)-1-phenylethylamino)-1-(1H-indol-3-yl)-2-phenylethanone;
2-(3,4-dimethoxyphenethylamino)-1-(1H-indol-3-yl)-2-phenylethanone;
1-(1H-indol-3-yl)-2-(1-(2-methoxyphenyl)ethylamino)-2-phenylethanone;
1-(1H-indol-3-yl)-2-(4-methoxybenzylamino)-2-phenylethanone;
2-(benzylamino)-1-(1H-indol-3-yl)-2-phenylethanone;
2-[4-[[2-(1H-indol-3-yl)-2-oxo-1-phenyl-ethyl]amino]phenyl]-N,N-dimethyl-acetamide;
4-[[2-(1H-indol-3-yl)-2-oxo-1-phenyl-ethyl]amino]-1,5-dimethyl-2-phenyl-pyrazol-3-one;
(2S)-2-(1,3-benzodioxol-5-ylamino)-1-(1H-indol-3-yl)-2-phenylethanone;
(2S)-2-(2,3-dihydro-1,4-benzodioxin-6-ylamino)-1-(1H-indol-3-yl)-2-phenylethanone;

(2S)-2-anilino-1-(1H-indol-3-yl)-2-phenylethanone;

(2S)-1-(1H-indol-3-yl)-2-(3-methylanilino)-2-phenylethanone;

(2S)-1-(1H-indol-3-yl)-2-(3-methoxyanilino)-2-phenylethanone;

(2S)-1-(1H-indol-3-yl)-2-(4-methylanilino)-2-phenylethanone;

(2S)-1-(1H-indol-3-yl)-2-(4-methoxyanilino)-2-phenylethanone;

Methyl 4-[[(1S)-2-(1H-indol-3-yl)-2-oxo-1-phenylethyl]amino]benzoate;

(2S)-1-(1H-indol-3-yl)-2-phenyl-2-(3,4,5-trimethoxyanilino)ethanone;

(2S)-2-(4-ethoxy-3-methoxyanilino)-1-(1H-indol-3-yl)-2-phenylethanone;

2-[4-[[(1S)-2-(1H-indol-3-yl)-2-oxo-1-phenylethyl]amino]phenyl]acetonitrile;

(2S)-2-(4-fluoroanilino)-1-(1H-indol-3-yl)-2-phenylethanone;

(2R)-2-[(1-acetyl-2,3-dihydroindol-5-yl)amino]-1-(1H-indol-3-yl)-2-phenylethanone;

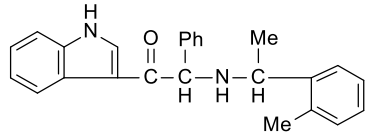
(2S)-2-(3,4-dihydro-2H-1,5-benzodioxepin-7-ylamino)-1-(1H-indol-3-yl)-2-phenylethanone

(2R)-2-(4-fluoroanilino)-1-(1H-indol-3-yl)-2-phenyl-ethanone;

3,4-dihydro-6-[[2-(1H-indol-3-yl)-2-oxo-1-phenylethyl]amino]-2(1H)-quinolinone (CAS nr. 1277962-26-1);

2-[(3-(hydroxymethyl)-4-methoxyphenyl)amino]-1-(1H-indol-3-yl)-2-phenylethanone;

2-(1,3-benzodioxol-5-ylamino)-1-(1H-indol-3-yl)-2-phenylethanone; or



.

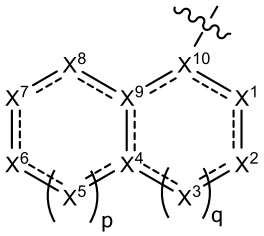
In one aspect, the present disclosure refers to any one of the compounds as disclosed herein, for use as a medicine.

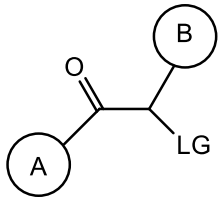
In one aspect, the present disclosure refers to any one of the compounds as disclosed herein, for use in the prevention or treatment of a flavivirus infection in an animal, mammal or human.

In one aspect, the present disclosure refers to use of any one of the compounds as disclosed herein, in the manufacture of a medicament for prevention or treatment of a Flaviviral infection in an animal, mammal or human.

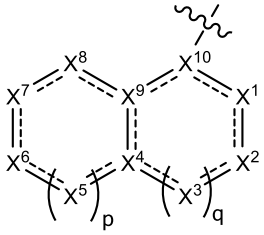
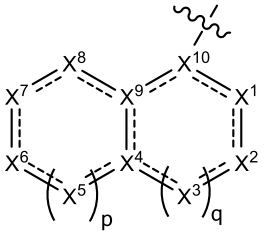
In one aspect, the present disclosure refers to a pharmaceutical composition comprising a pharmaceutically acceptable carrier, and as active ingredient an effective amount of any one the compounds as disclosed herein or a pharmaceutically acceptable salt thereof.

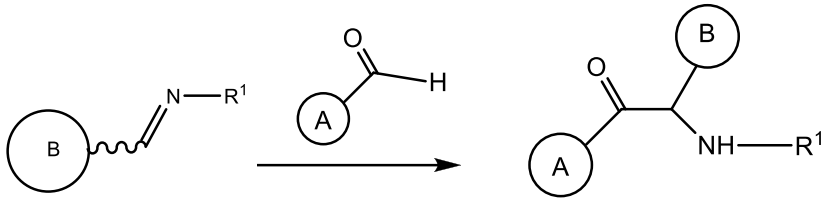
In one aspect, the present disclosure refers to a method for the preparation of any one the compounds as disclosed herein comprising the step of

- reacting compound of formula (X1) with the amine R^1R^2NH in a suitable solvent, wherein cycle A corresponds to moiety  of formula (B) as defined herein, cycle B, R^1, and R^2 have the meaning as defined herein, and LG is a leaving group, preferably selected from chlorine, bromine, and iodine; or



(X1)

- reacting the imine of formula (X2) with an aldehyde of formula (X3) in the presence of a catalyst and a suitable solvent to obtain compound of formula (A1), wherein cycle A of formula  corresponds to moiety  of formula (B) as defined herein, cycle B, and R^1, have the meaning as defined herein, and provided that in cycle A of formulae (X3) and (A1), a carbon atom is binding to the carbonyl.



(X2) (X3) (A1)

In one aspect, the present disclosure refers to use of an effective amount of any one of the compounds as disclosed herein or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for treatment or prevention of Flaviviral infections in humans, wherein the medicament is to be optionally administered in combination with one or more other medicines, to a patient in need thereof.

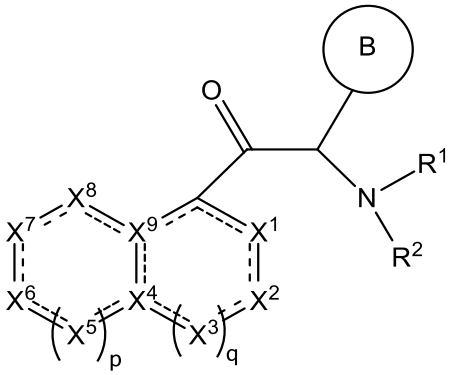
DETAILED DESCRIPTION OF THE FIGURES

Figure 1: Kaplan Meier plot of dengue virus induced mortality/euthanasia in AG129 mice and the effect of treatment with Celgosivir and CPD-242. The red dotted line indicates end of treatment.

DETAILED DESCRIPTION OF THE INVENTION

The present invention will be described with respect to particular embodiments but the invention is not limited thereto.

A first embodiment of the present invention relates to a compound according to formula (D),



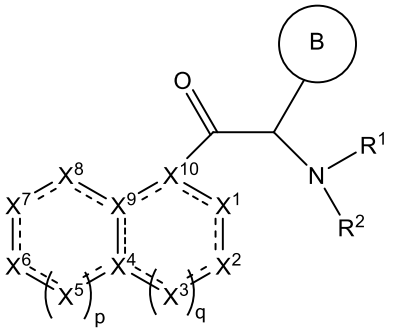
(D)

wherein

- each dotted line represents an optional double bond whereby maximally 6 non-adjacent dotted

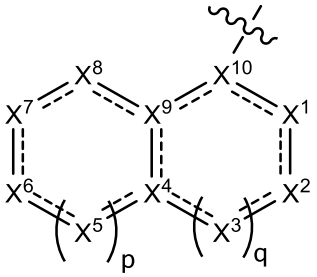
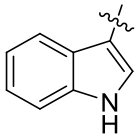
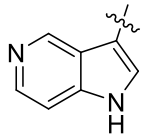
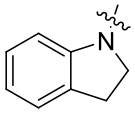
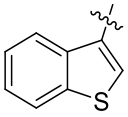
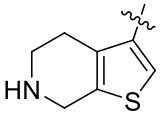
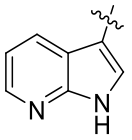
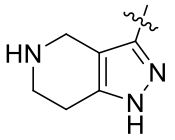
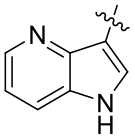
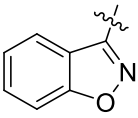
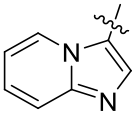
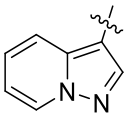
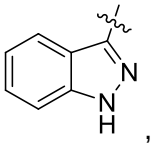
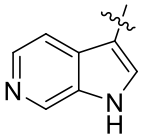
CLAIMS

1. A compound, characterized for being of formula (B),

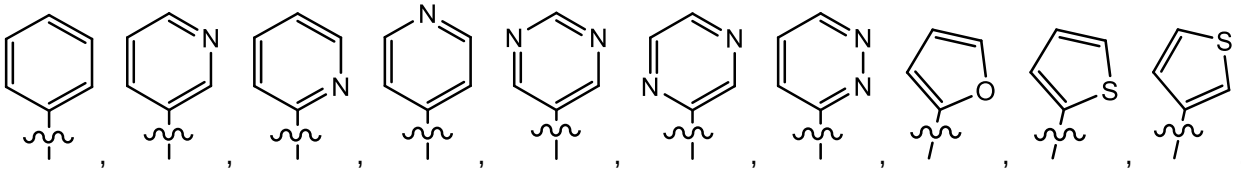


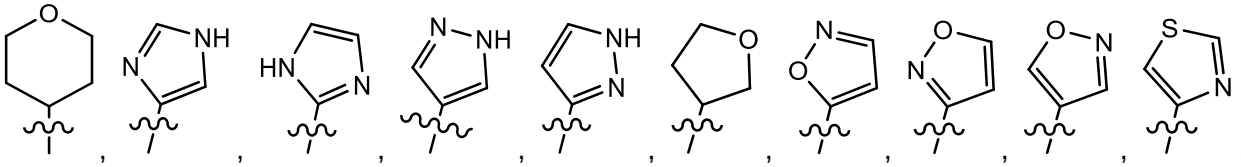
(B)

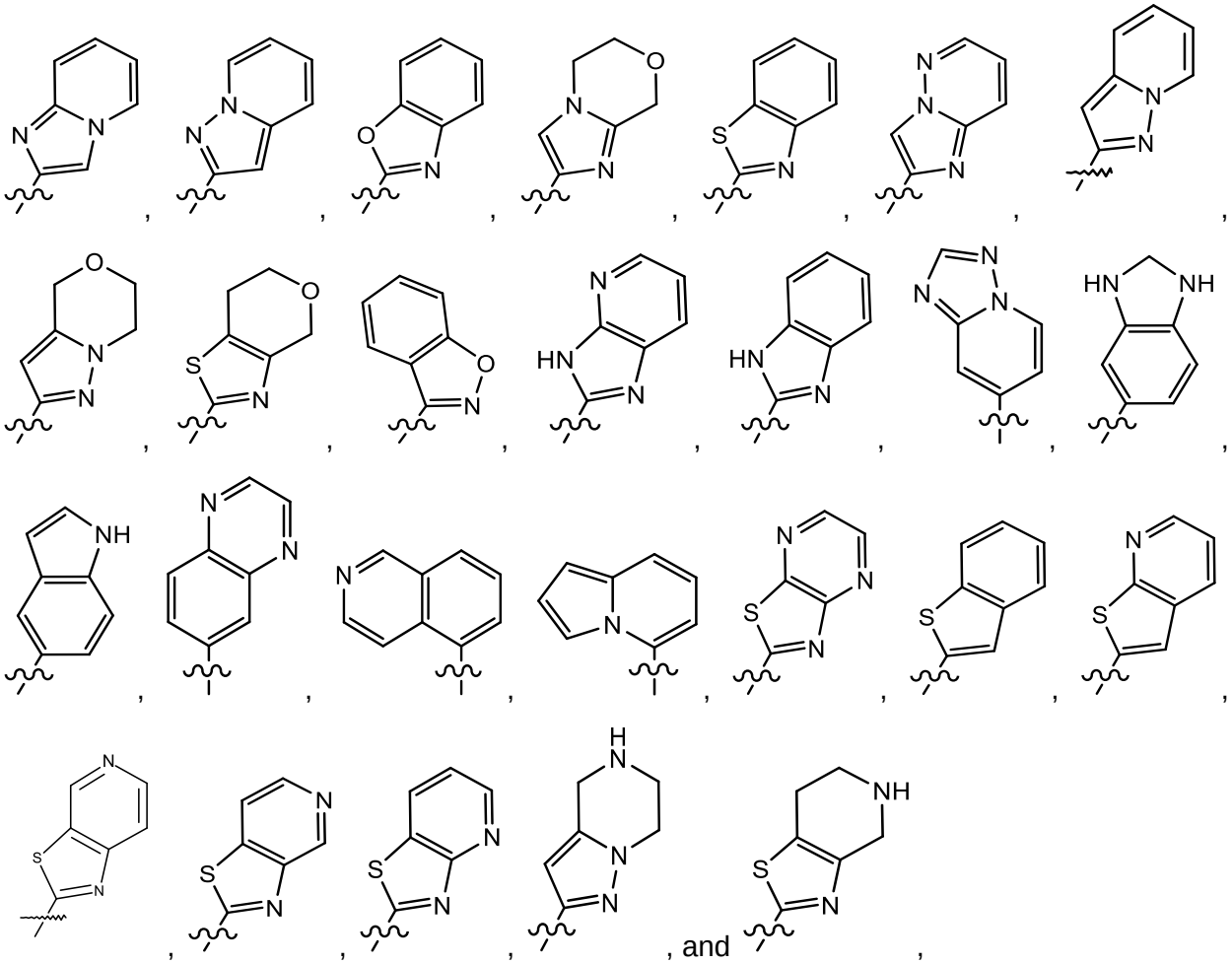
wherein

- the moiety  is selected from , , , , , , , , , , , , and ; wherein the wavy line (〰) indicates the point of attachment to the carbonyl of the main formula (B); wherein said moiety is unsubstituted;

- cycle B is selected from







wherein the wavy line (〰) indicates the point of attachment to the carbon atom of the main formula (B), and wherein the depicted cycles may be optionally substituted with one, two, or three Z^{1a};

- R^1 is selected from C_{3-7}cycloalkyl, aryl, heterocycle;

and wherein said C_{3-7}cycloalkyl, aryl, and heterocycle, are optionally substituted with one, two, or three Z^{1b};

- R^2 is hydrogen;

- each Z^{1a} is independently selected from the group consisting of halogen, hydroxyl, sulfhydryl, -OZ^2, -O-C(=O)Z^3, =O, -SZ^2, =S, -S(=O)Z^2, -$S(=O)_2Z^3$, -$S(=O)_2NZ^4Z^5$, trifluoromethoxy, nitro, -NZ^4Z^5, -$NZ^4S(=O)_2Z^2$, -$NZ^4C(=O)Z^2$, -$NZ^4C(=O)NZ^4Z^5$, cyano, -C(=O)Z^3, -C(=O)OZ^2, -C(=O)NZ^4Z^5, -C(=O)H, heteroC_{1-6}alkyl, aryl, heterocycle, and heterocycle-C_{1-6}alkyl;

and wherein said heteroC_{1-6}alkyl, aryl, heterocycle, and heterocycle-C_{1-6}alkyl, are optionally substituted with one, two, or three substituents selected from hydroxyl, =O, halogen, -SH, =S, trifluoromethyl, -OCF_3, -O-C(O)Me, cyano, nitro, -C(O)OH, -C(O)OC_{1-6}alkyl, -NH_2, -$NHCH_3$; -$N(CH_3)_2$, -NH-C(=O)O-C_{1-4}alkyl; -$S(O)_2C_{1-4}$alkyl, and –O-C_{1-6}alkyl;

- each Z^{1b} is independently selected from the group consisting of halogen, hydroxyl, sulfhydryl, -OZ^2, -O-C(=O)Z^3, =O, -SZ^2, =S, -S(=O)Z^2, -$S(=O)_2Z^3$, -$S(=O)_2NZ^4Z^5$, trifluoromethyl, trifluoromethoxy, nitro, -NZ^4Z^5, -$NZ^4C(=O)NZ^4Z^5$, cyano, -C(=O)Z^3, -C(=O)OZ^2, -C(=O)H, C_{1-6}alkyl, heteroC_{1-6}alkyl, aryl, and heterocycle;

and wherein said C_{1-6}alkyl, heteroC_{1-6}alkyl, aryl, and heterocycle, are optionally substituted with one, two, or three substituents selected from hydroxyl, halogen, -SH, =S, trifluoromethyl, -OCF_3, -O-C(O)Me, cyano, nitro, -C(O)OH, -C(O)OC_{1-6}alkyl, -NH_2, -$NHCH_3$; -$N(CH_3)_2$, -NH-C(=O)O-C_{1-4}alkyl; -$S(O)_2C_{1-4}$alkyl, and –O-C_{1-6}alkyl;

- each Z^2 is independently selected from C_{1-6}alkyl, aryl, and heterocycle;

wherein said C_{1-6}alkyl, aryl, heterocycle, are optionally substituted with one, two, or three substituents selected from hydroxyl, =O, halogen, -SH, =S, trifluoromethyl, difluoromethyl, -O-C_{1-6}alkyl, -OCF_3, -$S(=O)_2C_{1-4}$alkyl, cyano, nitro, -C(=O)OH, -C(=O)O-C_{1-4}alkyl, -NH_2, and -$N(CH_3)_2$, pyrrolidinyl, piperidinyl, and piperazinyl;

- each Z^3 is independently selected from hydroxyl, C_{1-6}alkyl, aryl, and heterocycle;

wherein said C_{1-6}alkyl, aryl, and heterocycle are optionally substituted with one, two, or three substituents selected from C_{1-6}alkyl and -$N(CH_3)_2$;

- each Z^4 and Z^5 is independently selected from hydrogen, C_{1-6}alkyl, aryl, C_{3-7}cycloalkyl, and heterocycle;

or 1-(1H-indol-4-yl)-2-(3-methoxyanilino)-2-phenyl-ethanone;

or 1-(4-isoquinolyl)-2-(3-methoxyanilino)-2-phenyl-ethanone;

or 1-(1H-indol-3-yl)-2-(3-methoxy-N-methyl-anilino)-2-phenyl-ethanone;

or 3-[[2-(1H-indol-3-yl)-2-oxo-1-phenyl-ethyl]amino]-N,N-dimethyl-benzamide;

or 2-[2-furylmethyl(methyl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone;

or N-[2-(1H-indol-3-yl)-2-oxo-1-phenyl-ethyl]-2-(dimethylamino)-N-(3-methoxyphenyl)acetamide;

and stereo-isomers or tautomers, solvates, or salts in particular pharmaceutically acceptable salts thereof;

wherein the term “alkyl” as used herein means a normal, secondary, or tertiary, linear or cyclic or a combination of linear and cyclic, branched or straight hydrocarbon with no site of unsaturation,

wherein the term “heteroalkyl” as used herein refers to an acyclic alkyl wherein one or more carbon atoms are replaced by an oxygen, nitrogen or sulphur atom, with the proviso that said chain may not contain two adjacent O atoms or two adjacent S atoms;

wherein the term “heterocycle” means a saturated, unsaturated, or aromatic ring system of 3 to

18 atoms including at least one N, O, S or P;

the term “aryl” means an aromatic hydrocarbon radical of 6-20 carbon atoms derived by the removal of hydrogen from a carbon atom of a parent aromatic ring system,

with the proviso that compound per se of formula (B) is not:

3-(2-(1H-indol-3-yl)-2-oxo-1-phenylethylamino)benzenesulfonamide (CAS nr. 1211427-21-2);

2-(3,4-dihydro-2H-benzo[b][1,4]dioxepin-7-ylamino)-1-(1H-indol-3-yl)-2-phenylethanone (CAS nr. 1090733-87-1);

1-(1H-indol-3-yl)-2-phenyl-2-(m-tolylamino)ethanone (CAS nr. 1252467-88-1);

2-(4-ethoxy-3-(hydroxymethyl)phenylamino)-1-(1H-indol-3-yl)-2-phenylethanone (CAS nr. 1241127-58-1);

1-(1H-indol-3-yl)-2-[(6-methoxy-3-pyridinyl)amino]-2-phenyl-ethanone (CAS nr. 1181884-55-8);

1-(1H-indol-3-yl)-2-[(1-methyl-1H-pyrazol-3-yl)amino]-2-phenyl-ethanone (CAS nr. 1134766-19-0);

2-[(3,5-dimethoxyphenyl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 1030232-46-2);

1-(1H-indol-3-yl)-2-phenyl-2-(phenylamino)-ethanone (CAS nr. 1030214-83-5);

1-(1H-indol-3-yl)-2-[[6-(4-morpholinyl)-3-pyridinyl]amino]-2-phenyl-ethanone (CAS nr. 1030212-41-9);

2-(3-(difluoromethoxy)-4-methoxyphenylamino)-1-(1H-indol-3-yl)-2-phenylethanone (CAS nr. 1015662-06-2);

1-(1H-indol-3-yl)-2-phenyl-2-[(3,4,5-trimethoxyphenyl)amino]-ethanone (CAS nr. 1014535-82-0);

2-[(4-fluorophenyl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 1014493-63-0);

2-[(4-ethoxy-3-methoxyphenyl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 1014422-80-0);

1-[4-[[2-(1H-indol-3-yl)-2-oxo-1-phenylethyl]amino]-2-methoxyphenyl]-2-pyrrolidinone (CAS nr. 1011119-79-1);

2-[(1-acetyl-2,3-dihydro-1H-indol-5-yl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 949443-90-7);

1-(1H-indol-3-yl)-2-phenyl-2-[(1-propyl-4-piperidinyl)amino]-ethanone (CAS nr. 941047-24-1);

2-(cyclopentylamino)-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 931079-25-3);

1-(1H-indol-3-yl)-2-[(4-methylphenyl)amino]-2-phenyl-ethanone (CAS nr. 931016-79-4);

2-(cyclopropylamino)-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 931000-99-6);

2-[(3,4-dihydro-2H-1-benzothiopyran-4-yl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 924713-60-0)**;**

2-[(3,4-dimethoxyphenyl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 924712-67-4)**;**

2-ethoxy-5-[[2-(1H-indol-3-yl)-2-oxo-1-phenylethyl]amino]-N,N-dimethyl-benzenesulfonamide (CAS nr. 920883-17-6);

6-[[2-(1H-indol-3-yl)-2-oxo-1-phenylethyl]amino]-2-methyl-2H-1,4-benzoxazin-3(4H)-one (CAS

nr. 920834-07-7);

2-[(3,4-dihydro-2H-1-benzopyran-4-yl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 920819-87-0)**;**

4-[[2-(1H-indol-3-yl)-2-oxo-1-phenylethyl]amino]-benzeneacetonitrile (CAS nr. 920669-36-9)**;**

1-(1H-indol-3-yl)-2-[(4-methoxyphenyl)amino]-2-phenyl-ethanone (CAS nr. 920601-77-0)**;**

1-(1H-indol-3-yl)-2-phenyl-2-(1,1-dioxotetrahydrothiophen-3-ylamino)ethanone (CAS nr. 878619-92-2);

2-[[3-(hydroxymethyl)phenyl]amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 875166-36-2)**;**

2-[(2,3-dihydro-1,4-benzodioxin-6-yl)amino]-1-(1H-indol-3-yl)-2-phenyl-ethanone (CAS nr. 874669-99-5)**;**

1-(1H-indol-3-yl)-2-(morpholino(phenyl)methylamino)-2-phenylethanone;

2-(4-(dimethylamino)benzylamino)-1-(1H-indol-3-yl)-2-phenylethanone;

1-(1H-indol-3-yl)-2-(2-methoxybenzylamino)-2-phenylethanone;

1-(1H-indol-3-yl)-2-(3-methoxybenzylamino)-2-phenylethanone;

2-(2-(dimethylamino)-1-phenylethylamino)-1-(1H-indol-3-yl)-2-phenylethanone;

2-(3,4-dimethoxyphenethylamino)-1-(1H-indol-3-yl)-2-phenylethanone;

1-(1H-indol-3-yl)-2-(1-(2-methoxyphenyl)ethylamino)-2-phenylethanone;

1-(1H-indol-3-yl)-2-(4-methoxybenzylamino)-2-phenylethanone;

2-(benzylamino)-1-(1H-indol-3-yl)-2-phenylethanone;

2-[4-[[2-(1H-indol-3-yl)-2-oxo-1-phenyl-ethyl]amino]phenyl]-N,N-dimethyl-acetamide;

4-[[2-(1H-indol-3-yl)-2-oxo-1-phenyl-ethyl]amino]-1,5-dimethyl-2-phenyl-pyrazol-3-one;

(2S)-2-(1,3-benzodioxol-5-ylamino)-1-(1H-indol-3-yl)-2-phenylethanone;

(2S)-2-(2,3-dihydro-1,4-benzodioxin-6-ylamino)-1-(1H-indol-3-yl)-2-phenylethanone;

(2S)-2-anilino-1-(1H-indol-3-yl)-2-phenylethanone;

(2S)-1-(1H-indol-3-yl)-2-(3-methylanilino)-2-phenylethanone;

(2S)-1-(1H-indol-3-yl)-2-(3-methoxyanilino)-2-phenylethanone;

(2S)-1-(1H-indol-3-yl)-2-(4-methylanilino)-2-phenylethanone;

(2S)-1-(1H-indol-3-yl)-2-(4-methoxyanilino)-2-phenylethanone;

Methyl 4-[[(1S)-2-(1H-indol-3-yl)-2-oxo-1-phenylethyl]amino]benzoate;

(2S)-1-(1H-indol-3-yl)-2-phenyl-2-(3,4,5-trimethoxyanilino)ethanone;

(2S)-2-(4-ethoxy-3-methoxyanilino)-1-(1H-indol-3-yl)-2-phenylethanone;

2-[4-[[(1S)-2-(1H-indol-3-yl)-2-oxo-1-phenylethyl]amino]phenyl]acetonitrile;

(2S)-2-(4-fluoroanilino)-1-(1H-indol-3-yl)-2-phenylethanone;

(2R)-2-[(1-acetyl-2,3-dihydroindol-5-yl)amino]-1-(1H-indol-3-yl)-2-phenylethanone;

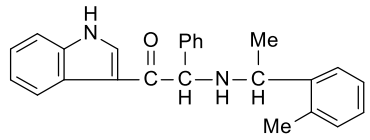
(2S)-2-(3,4-dihydro-2H-1,5-benzodioxepin-7-ylamino)-1-(1H-indol-3-yl)-2-phenylethanone

(2R)-2-(4-fluoroanilino)-1-(1H-indol-3-yl)-2-phenyl-ethanone;

3,4-dihydro-6-[[2-(1H-indol-3-yl)-2-oxo-1-phenylethyl]amino]-2(1H)-quinolinone (CAS nr. 1277962-26-1);

2-[(3-(hydroxymethyl)-4-methoxyphenyl)amino]-1-(1H-indol-3-yl)-2-phenylethanone;

2-(1,3-benzodioxol-5-ylamino)-1-(1H-indol-3-yl)-2-phenylethanone; or



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2. The compound according to claim 1, wherein

- each Z^{1a} is independently selected from the group consisting of halogen, hydroxyl, $-OZ^2$, $-O-C(=O)Z^3$, =O, $-S(=O)_2Z^3$, $-S(=O)_2NZ^4Z^5$, trifluoromethoxy, $-NZ^4Z^5$, $-NZ^4C(=O)Z^2$, cyano, $-C(=O)Z^3$, $-C(=O)OZ^2$, $-C(=O)NZ^4Z^5$, heteroC_{1-6}alkyl, aryl, heterocycle, and heterocycle-C_{1-6}alkyl;
  and wherein said aryl, and heterocycle are optionally substituted with one, two, or three substituents selected from hydroxyl, =O, -O-C(O)Me, cyano, -C(O)OH, $-C(O)OC_{1-6}$alkyl, $-NH_2$, $-NHCH_3$; $-N(CH_3)_2$, -NH-C(=O)O-C_{1-4}alkyl; $-S(O)_2C_{1-4}$alkyl, and $-O-C_{1-6}$alkyl;

- each Z^{1b} is independently selected from the group consisting of halogen, hydroxyl, $-OZ^2$, $-O-C(=O)Z^3$, =O, $-S(=O)_2Z^3$, $-S(=O)_2NZ^4Z^5$, trifluoromethyl, trifluoromethoxy, $-NZ^4Z^5$, $-NZ^4C(=O)Z^2$, cyano, $-C(=O)Z^3$, $-C(=O)OZ^2$, $-C(=O)NZ^4Z^5$, C_{1-6}alkyl, heteroC_{1-6}alkyl, aryl, and heterocycle;
  and wherein said C_{1-6}alkyl, aryl, and heterocycle are optionally substituted with one, two, or three substituents selected from hydroxyl, -O-C(O)Me, cyano, -C(O)OH, $-C(O)OC_{1-6}$alkyl, $-NH_2$, $-NHCH_3$; $-N(CH_3)_2$, -NH-C(=O)O-C_{1-4}alkyl; $-S(O)_2C_{1-4}$alkyl, and $-O-C_{1-6}$alkyl;

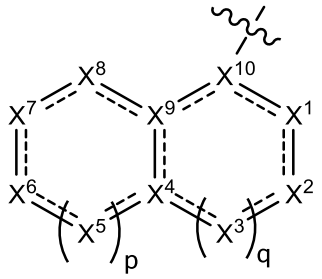
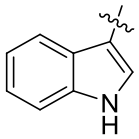
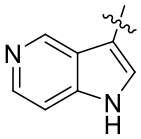
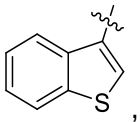
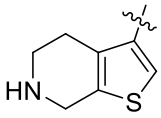
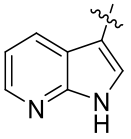
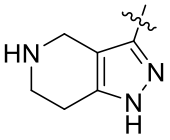
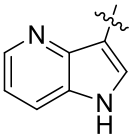
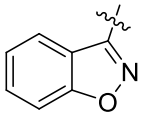
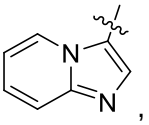
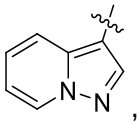
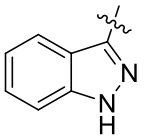
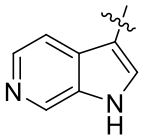
- each Z^2 is independently selected from C_{1-6}alkyl, aryl;
  wherein said C_{1-6}alkyl, and aryl, are optionally substituted with one, two, or three substituents selected from hydroxyl, halogen, difluoromethyl, $-O-C_{1-6}$alkyl, $-S(=O)_2C_{1-4}$alkyl, -C(=O)OH, -C(=O)O-C_{1-4}alkyl, $-NH_2$, and $-N(CH_3)_2$, pyrrolidinyl, piperidinyl, and piperazinyl;

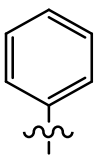
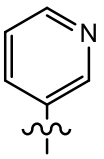
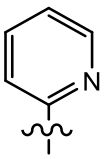
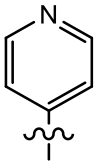
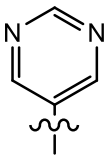
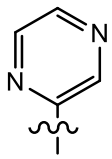
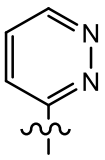
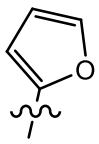
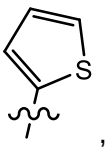
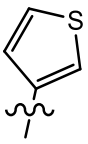
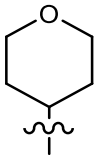
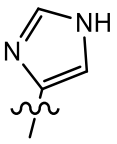
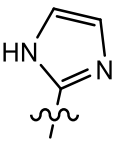
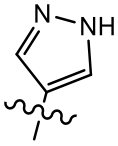
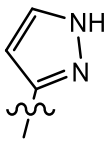
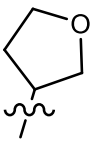
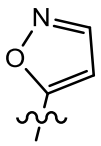
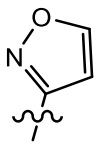
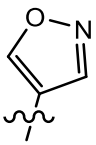
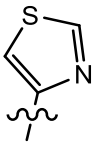
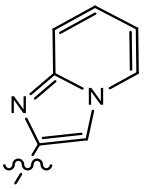
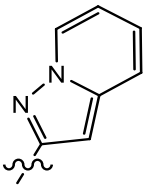
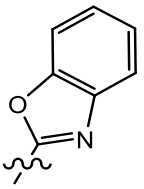
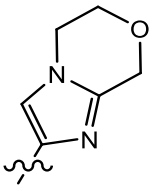
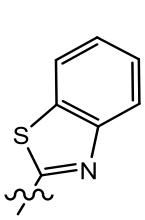
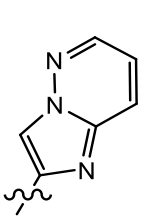
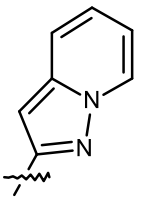
- each Z^3 is independently selected from hydroxyl, C_{1-6}alkyl, and heterocycle;
  wherein said C_{1-6}alkyl and heterocycle are optionally substituted with one, two, or three substituents selected from C_{1-6}alkyl and $-N(CH_3)_2$;

- each Z^4 and Z^5 is independently selected from hydrogen, C_{1-6}alkyl, and C_{3-7}cycloalkyl;

and stereo-isomers or tautomers, solvates, or salts in particular pharmaceutically acceptable salts thereof;

3. The compound of formula (B) according to claim 1, wherein

- the moiety  is selected from , , , , , , , , , , , and ; wherein said moiety is unsubstituted;

- cycle B is selected from , , , , , , , , , , , , , , , , , , , , , , , , , , , 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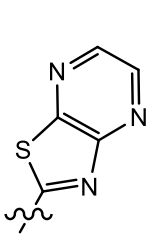
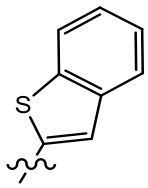
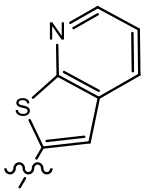
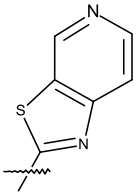
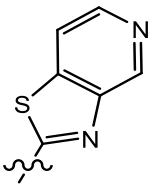
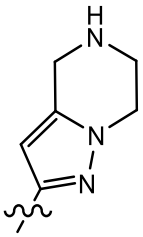
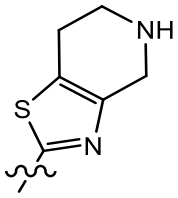
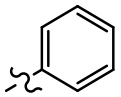
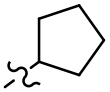
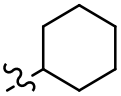
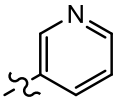
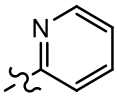
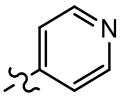
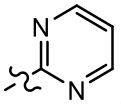
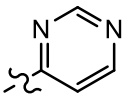
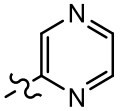
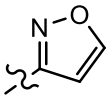
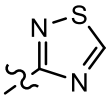
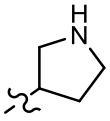
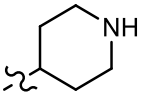
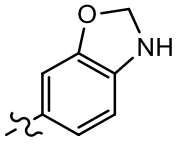
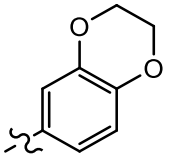
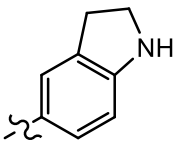
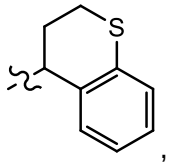
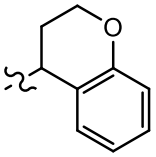
, , , , , , , and ; wherein the wavy line ( ) indicates the point of attachment to the carbon atom of the main formula (B), and wherein the depicted cycles may be optionally substituted with one, two, or three Z^{1a};

- R^1 is a moiety selected from , , , , , , , , , , , , , , , , , and ; which moiety is optionally substituted with one, two, or three Z^{1b};

- Z^{1b}, is selected from the group consisting of halogen, hydroxyl, $-OZ^2$, =O, $-S(=O)_2Z^3$, $-S(=O)_2NZ^4Z^5$, trifluoromethyl, trifluoromethoxy, $-NZ^4Z^5$, cyano, $-C(=O)Z^3$, $-C(=O)OZ^2$, C_{1-6}alkyl, aryl, and heterocycle;

  and wherein said C_{1-6}alkyl, aryl, and heterocycle are optionally substituted with one, two, or three substituents selected from hydroxyl, -O-C(O)Me, cyano, -C(O)OH,, $-NHCH_3$; $-N(CH_3)_2$, $-S(O)_2C_{1-4}$alkyl, and $-O-C_{1-6}$alkyl;

- R^2 is hydrogen;
- each Z^{1a} is independently selected from the group consisting of halogen, hydroxyl, $-OZ^2$, $-O-C(=O)Z^3$, =O, $-S(=O)_2Z^3$, $-S(=O)_2NZ^4Z^5$, trifluoromethoxy, $-NZ^4Z^5$, $-NZ^4C(=O)Z^2$, $-NZ^4C(=O)-OZ^2$, cyano, $-C(=O)Z^3$, $-C(=O)OZ^2$, $-C(=O)NZ^4Z^5$, heteroC_{1-6}alkyl, aryl, heterocycle, and heterocycle-C_{1-6}alkyl;

  wherein said aryl, and heterocycle are optionally substituted with one, two, or three

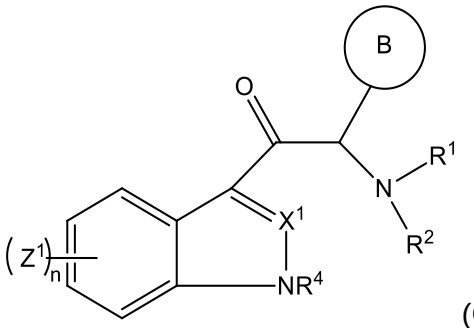
substituents selected from hydroxyl, =O, -O-C(O)Me, cyano, -C(O)OH, -C(O)OC$_{1-6}$alkyl, -NH$_2$, -NHCH$_3$; -N(CH$_3$)$_2$, -NH-C(=O)O-C$_{1-4}$alkyl, morpholinyl, -S(O)$_2$C$_{1-4}$alkyl, and –O-C$_{1-6}$alkyl;

- Z^2 is independently selected from C$_{1-6}$alkyl, and aryl;
  wherein said C$_{1-6}$alkyl, and aryl, are optionally substituted with one, two, or three substituents selected from hydroxyl, halogen, difluoromethyl, -O-C$_{1-6}$alkyl, -S(=O)$_2$C$_{1-4}$alkyl, -C(=O)OH, -C(=O)O-C$_{1-4}$alkyl, -NH$_2$, and -N(CH$_3$)$_2$, pyrrolidinyl, piperidinyl, and piperazinyl;

- Z^3 is independently selected from hydroxyl, C$_{1-6}$alkyl, and heterocycle;
  wherein said C$_{1-6}$alkyl and heterocycle are optionally substituted with one, two, or three substituents selected from C$_{1-6}$alkyl and -N(CH$_3$)$_2$;

- each Z^4 and Z^5 is independently selected from hydrogen, C$_{1-6}$alkyl, and C$_{3-7}$cycloalkyl.

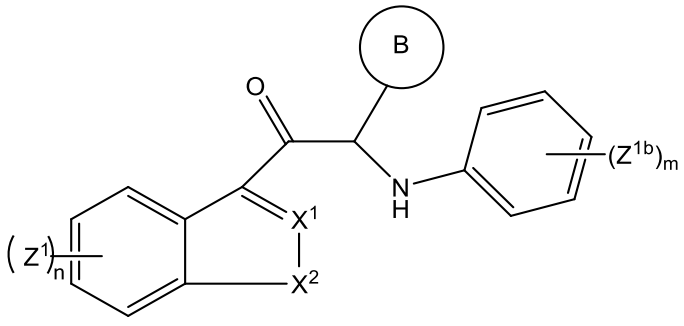
4. The compound according to any one of claims 1 or 2, wherein the compound has the structure of formula (G),



(G)

wherein cycle B, R^1, R^2, X^1, Z^1, and R^4 are as defined in any one of claims 1 or 2, R^4 is hydrogen and X^1 is N or CH, and n is selected from 0.

5. The compound according to any one of claims 1 or 2 wherein the compound has the structure of formula (H),



(H)

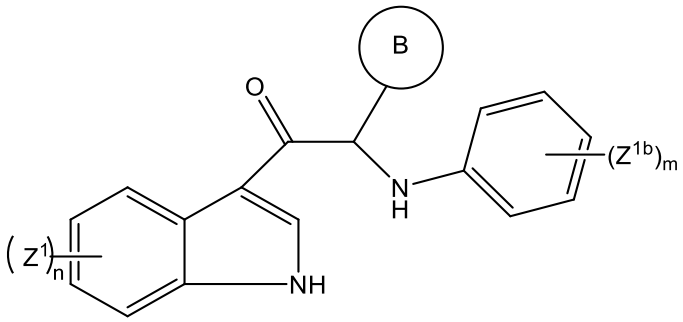
wherein

- cycle B, each Z^1 independently, and each Z^{1b} independently, are as defined in any one of claims 1 or 2;
- m is selected from 0, 1, 2, and 3;
- n is 0; and

  wherein X^2 is NH and X^1 is CH or N, or

  X^2 is S and X^1 is CH, or
- X^2 is O and X^1 is N.

6. The compound according to any one of claims 1 or 2, wherein the compound has the structure of formula (I),

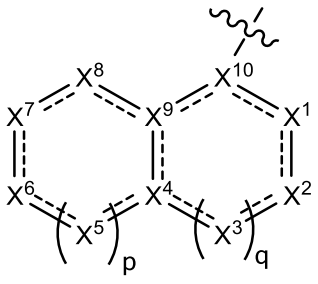


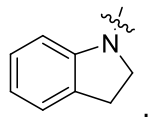
(I)

wherein

- each Z^1 independently, and each Z^{1b} independently, are as defined in any one of claims 1 or 2;
- cycle B is as defined in any one of claims 1 or 2;
- n is 0; and
- m is selected from 0, 1, 2, and 3.

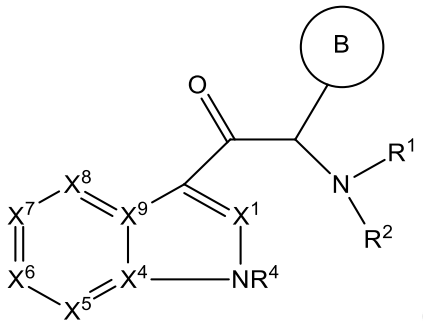
7. The compound according to claim 1, wherein

the moiety 

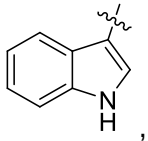
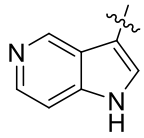
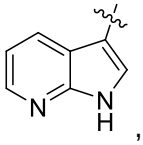
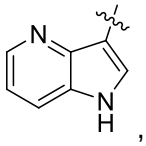
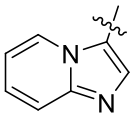
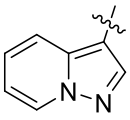
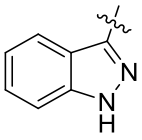
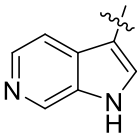
is 

.

8. The compound according to claim 1 wherein the compound has the structure of formula (F1)



(F1)

and the bicyclic moiety is selected from , , , , , , , and .

9. The compound according to any one of claims 1-8, wherein the carbon atom substituted with cycle B is in the R configuration.

10. The compound according to any one of claims 1-8, wherein the carbon atom substituted with cycle B is in the S configuration.

11. A compound according to any one of claims 1-10, for use as a medicine.

12. A compound according to any one of claims 1-10, for use in the prevention or treatment of a flavivirus infection in an animal, mammal or human.

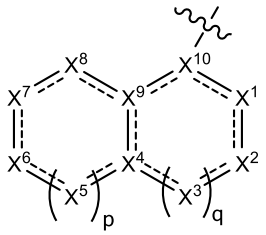
13. Use of a compound according to any one of claims 1-10, in the manufacture of a medicament for prevention or treatment of a Flaviviral infection in an animal, mammal or human.

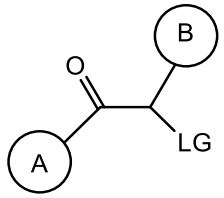
14. The compound according to claim 12 or the use according to claim 13, wherein the flavivirus infection is an infection with a Dengue virus or a yellow fever virus.

15. A pharmaceutical composition comprising a pharmaceutically acceptable carrier, and as active ingredient an effective amount of the compound according to any one of claims 1-10 or a pharmaceutically acceptable salt thereof.

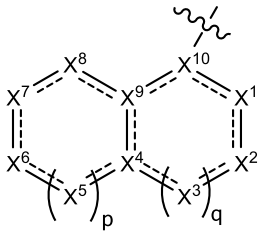
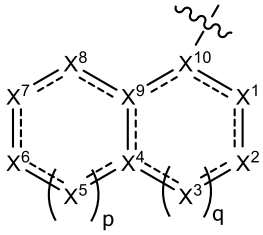
16. A method for the preparation of the compound according to any one of claims 1-10

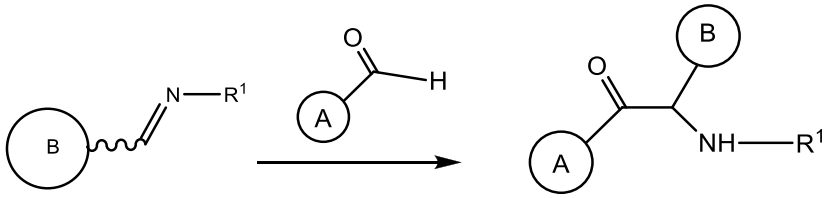
comprising the step of

– reacting compound of formula (X1) with the amine R^1R^2NH in a suitable solvent, wherein cycle A corresponds to moiety  of formula (B) as defined in claims 1-10, cycle B, R^1, and R^2 have the meaning according to any one of claims 1-10, and LG is a leaving group, preferably selected from chlorine, bromine, and iodine; or



(X1)

– reacting the imine of formula (X2) with an aldehyde of formula (X3) in the presence of a catalyst and a suitable solvent to obtain compound of formula (A1), wherein cycle A of formula  corresponds to moiety  of formula (B) as defined in claims 1-10, cycle B, and R^1, have the meaning according to any one of claims 1-10, and provided that in cycle A of formulae (X3) and (A1), a carbon atom is binding to the carbonyl.



(X2) (X3) (A1)

17. Use of an effective amount of a compound according to any one of claims 1-10 or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for treatment or prevention of Flaviviral infections in humans, wherein the medicament is to be optionally administered in combination with one or more other medicines, to a patient in need thereof, substantially as described in the specification.

18. The use according to claim 17, wherein the Flaviviral infection is an infection by the Dengue virus or yellow fever virus.

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