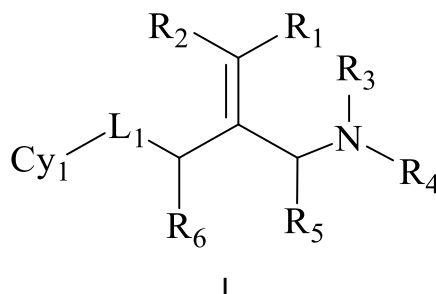


CLAIMS

1. A compound of formula I, or a pharmaceutically acceptable salt, ~~an ester,~~ a stereoisomer or a tautomer thereof,



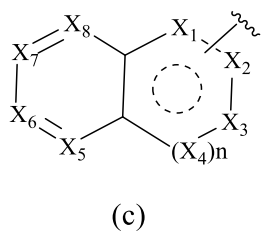
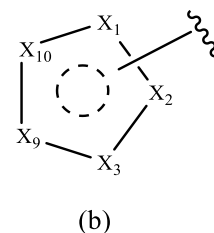
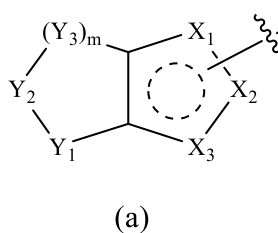
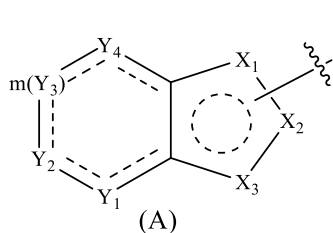
wherein R_1 and R_2 are each independently selected from hydrogen and halogen, and R_1 and R_2 are not both hydrogen;

R_3 and R_4 are each independently selected from hydrogen and C_{1-6} alkyl, ~~or form a 5-10 membered nitrogen containing heterocycle optionally substituted by a substituent along with a N atom connected thereto;~~

R_5 and R_6 are each independently selected from hydrogen and C_{1-6} alkyl;

L_1 is absent, or is $-CR'R''-$, $-N-$, $-O-$, $-S-$, $-SO_2-$, $S(O)$, $-SONR'-$, $-SO_2NR'-$ or $-NR'CONR'-$, and R' and R'' are each independently selected from hydrogen and C_{1-6} alkyl;

Cy_1 is a group that is unsubstituted or substituted by one or more R^a shown in general formula (A), (a), (b) or (c) below:



m is an integer from 0 to 3, and n is an integer from 0 to 2;

Y_1 , Y_2 , Y_3 and Y_4 are each independently selected from CH_2 , CH, NH , O , S and $C=O$;

X_1 , X_2 , X_3 , X_4 , X_9 and X_{10} are each independently selected from CH_2 , CH , N , O , S , NH

and C=O, X₅, X₆, X₇ and X₈ are each independently selected from CH and N, and at least one of X₁, X₂ and X₃ is N;

each R^a is independently selected from hydroxyl, amino, carboxyl, cyano, nitro, halogen, and C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ alkoxy C₁₋₆ alkyl, C₁₋₆ alkoxy C₁₋₆ alkoxy, C₁₋₆ alkylthio, C₁₋₆ alkylthio C₁₋₆ alkyl, C₁₋₆ alkylamino, (C₁₋₆ alkyl)₂ amino, C₁₋₆ alkylamino C₁₋₆ alkyl, C₁₋₆ alkylaminocarbonyl, C₁₋₆ alkylaminocarbonyl C₁₋₆ alkyl, C₁₋₆ alkylcarbonylamino, C₁₋₆ alkylcarbonylamino C₁₋₆ alkyl, (C₁₋₆ alkyl)₂ amino C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkylcarbonyl C₁₋₆ alkyl, C₁₋₆ alkylaminosulfonyl, C₁₋₆ alkylaminosulfonyl C₁₋₆ alkyl, C₁₋₆ alkylsulfonylamino, C₁₋₆ alkylsulfonylamino C₁₋₆ alkyl, C₁₋₆ alkylsulfonyl, C₁₋₆ alkylsulfonyl C₁₋₆ alkyl, Cy₂-, Cy₂-C₁₋₆ alkyl, Cy₂-C₁₋₆ alkoxy, Cy₂-carbonyl and Cy₂-aminocarbonyl unsubstituted or substituted by one or more R^b, Cy₂ is 3-12 membered cycloalkyl, 3-12 membered cycloalkenyl, 3-12 membered heterocyclyl, aryl or 5-14 membered heteroaryl;

each R^b is independently selected from hydroxyl, amino, carboxyl, cyano, nitro, halogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ alkoxy C₁₋₆ alkyl, C₁₋₆ alkoxy C₁₋₆ alkoxy, C₁₋₆ alkylthio, C₁₋₆ alkylamino, (C₁₋₆ alkyl)₂ amino, C₁₋₆ alkylaminocarbonyl, C₁₋₆ alkylcarbonylamino, C₁₋₆ alkylcarbonyl, C₁₋₆ alkylaminosulfonyl, C₁₋₆ alkylsulfonylamino and C₁₋₆ alkylsulfonyl;

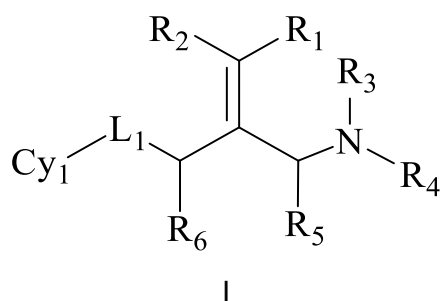
with the *proviso* that when Cy₁ is formula (c), formula (c) is substituted by one or more R^a;

with the *proviso* that when Cy₁ is formula (b), X₁, X₂, X₃, X₉ and X₁₀ are not C=O;

== represents a single bond or a double bond; and

○ represents a double bond optionally present in the ring structure.

2. The compound, or the pharmaceutically acceptable salt, ~~the ester~~, the stereoisomer or the tautomer thereof according to claim 1,



wherein R₁ and R₂ are each independently selected from hydrogen and halogen, and R₁ and R₂ are not both hydrogen;

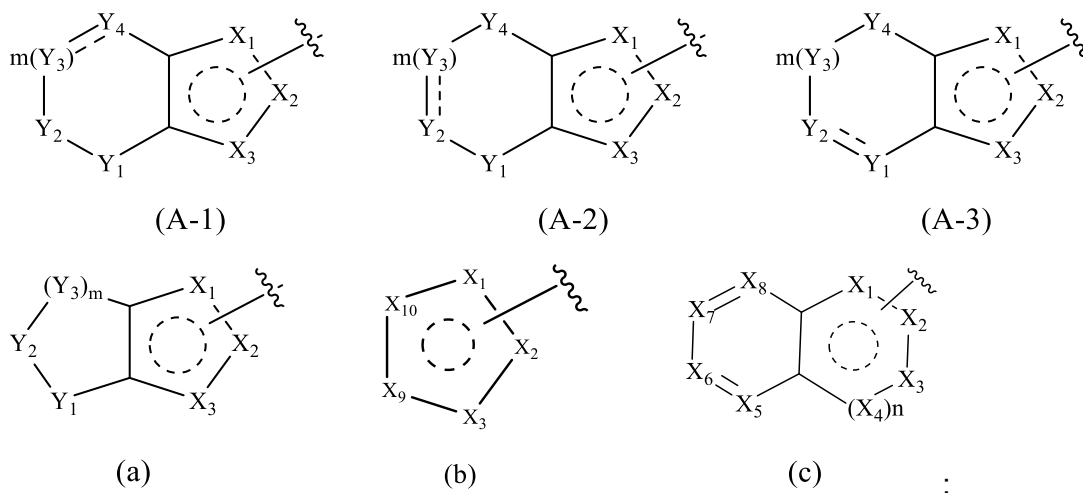
R₃ and R₄ are each independently selected from hydrogen and C₁₋₆ alkyl, ~~or form a 5-10 membered nitrogen containing heterocycle optionally substituted by a substituent~~

along with a N atom connected thereto;

R₅ and R₆ are each independently selected from hydrogen and C₁₋₆ alkyl;

L₁ is absent, or is -CR'R"-, -N-, -O-, -S-, -SO₂-, S(O), -SONR'-, -SO₂NR'- or -NR'CONR'-, and R' and R" are each independently selected from hydrogen and C₁₋₆ alkyl;

Cy₁ is a group that is unsubstituted or substituted by one or more R^a shown in general formula (A-1), (A-2), (A-3), (a), (b) or (c) below:



m is an integer from 0 to 3, and n is an integer from 0 to 2;

Y₁, Y₂, Y₃ and Y₄ are each independently selected from CH₂, CH, NH, O, S and C=O; X₁, X₂, X₃, X₄, X₉ and X₁₀ are each independently selected from CH₂, CH, N, O, S, NH and C=O, X₅, X₆, X₇ and X₈ are each independently selected from CH and N, and at least one of X₁, X₂ and X₃ is N;

each R^a is independently selected from hydroxyl, amino, carboxyl, cyano, nitro, halogen, and C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ alkoxy C₁₋₆ alkyl, C₁₋₆ alkoxy C₁₋₆ alkoxy, C₁₋₆ alkylthio, C₁₋₆ alkylthio C₁₋₆ alkyl, C₁₋₆ alkylamino, (C₁₋₆ alkyl)₂ amino, C₁₋₆ alkylamino C₁₋₆ alkyl, C₁₋₆ alkylaminocarbonyl, C₁₋₆ alkylaminocarbonyl C₁₋₆ alkyl, C₁₋₆ alkylcarbonylamino, C₁₋₆ alkylcarbonylamino C₁₋₆ alkyl, (C₁₋₆ alkyl)₂ amino C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkylcarbonyl C₁₋₆ alkyl, C₁₋₆ alkylaminosulfonyl, C₁₋₆ alkylaminosulfonyl C₁₋₆ alkyl, C₁₋₆ alkylsulfonylamino, C₁₋₆ alkylsulfonylamino C₁₋₆ alkyl, C₁₋₆ alkylsulfonyl, C₁₋₆ alkylsulfonyl C₁₋₆ alkyl, Cy₂-, Cy₂-C₁₋₆ alkyl, Cy₂-C₁₋₆ alkoxy, Cy₂-carbonyl and Cy₂-aminocarbonyl unsubstituted or substituted by one or more R^b,

Cy₂ is 3-12 membered cycloalkyl, 3-12 membered cycloalkenyl, 3-12 membered heterocyclyl, aryl or 5-14 membered heteroaryl;

each R^b is independently selected from hydroxyl, amino, carboxyl, cyano, nitro, halogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ alkoxy C₁₋₆ alkyl, C₁₋₆ alkoxy C₁₋₆ alkoxy, C₁₋₆ alkylthio, C₁₋₆ alkylamino, (C₁₋₆ alkyl)₂ amino, C₁₋₆ alkylaminocarbonyl, C₁₋₆ alkylcarbonylamino, C₁₋₆ alkylcarbonyl, C₁₋₆

alkylaminosulfonyl, C₁₋₆ alkylsulfonylamino and C₁₋₆ alkylsulfonyl;

with the *proviso* that when Cy₁ is formula (c), formula (c) is substituted by one or more R^a;

with the *proviso* that when Cy₁ is formula (b), X₁, X₂, X₃, X₉ and X₁₀ are not C=O;

== represents a single bond or a double bond; and

○ represents a double bond optionally present in the ring structure.

3. The compound, or the pharmaceutically acceptable salt, ~~the ester~~, the stereoisomer or the tautomer thereof according to claim 2,

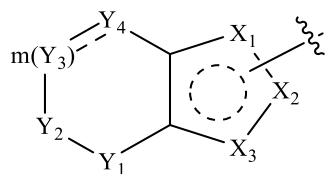
wherein R₁ and R₂ are each independently selected from hydrogen and halogen, and R₁ and R₂ are not both hydrogen;

R₃ and R₄ are each independently selected from hydrogen and C₁₋₆ alkyl;

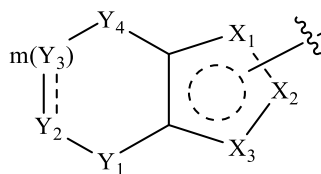
R₅ and R₆ are each independently selected from hydrogen and C₁₋₆ alkyl;

L₁ is absent, or is -CR'R"-, -N-, -O- or -S-, and R' and R" are each independently selected from hydrogen and C₁₋₆ alkyl;

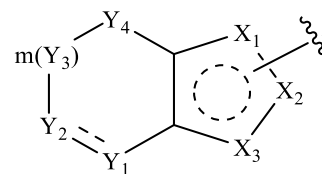
Cy₁ is a group that is unsubstituted or substituted by one or more R^a shown in general formula (A-1), (A-2), (A-3), (a), (b) or (c) below:



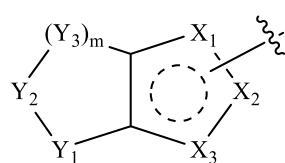
(A-1)



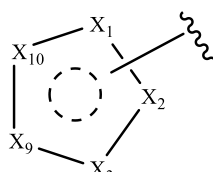
(A-2)



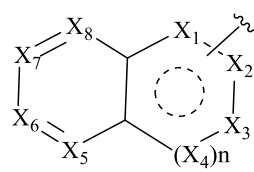
(A-3)



(a)



(b)



(c)

;

m is an integer from 0 to 3, and n is an integer from 0 to 2;

Y₁, Y₂, Y₃ and Y₄ are each independently selected from CH₂, CH, NH and C=O;

X₁, X₂, X₃, X₄, X₉ and X₁₀ are each independently selected from CH₂, CH, N, NH and C=O, X₅, X₆, X₇ and X₈ are each independently selected from CH and N, and at least one of X₁, X₂ and X₃ is N;

each R^a is independently selected from hydroxyl, amino, carboxyl, cyano, nitro, halogen, and C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ alkoxy C₁₋₆ alkyl, C₁₋₆ alkoxy C₁₋₆ alkoxy, C₁₋₆ alkylthio, C₁₋₆ alkylthio C₁₋₆ alkyl, C₁₋₆ alkylamino, C₁₋₆ alkylamino C₁₋₆ alkyl, C₁₋₆ alkylaminocarbonyl, C₁₋₆ alkylaminocarbonyl C₁₋₆ alkyl, C₁₋₆ alkylcarbonylamino, C₁₋₆

alkylcarbonylamino C₁₋₆ alkyl, C₁₋₆ alkylcarbonyl, C₁₋₆ alkylcarbonyl C₁₋₆ alkyl, Cy₂, Cy₂-C₁₋₆ alkyl, Cy₂-C₁₋₆ alkoxy, Cy₂-carbonyl and Cy₂-aminocarbonyl unsubstituted or substituted by one or more substituents R^b,

Cy₂ is 3-8 membered cycloalkyl, 5-10 membered heterocyclyl, phenyl or 5-10 membered heteroaryl;

each R^b is independently selected from hydroxyl, amino, carboxyl, cyano, nitro, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ alkoxy C₁₋₆ alkyl, C₁₋₆ alkoxy C₁₋₆ alkoxy, C₁₋₆ alkylthio, C₁₋₆ alkylamino, C₁₋₆ alkylaminocarbonyl, C₁₋₆ alkylcarbonylamino and C₁₋₆ alkylcarbonyl;

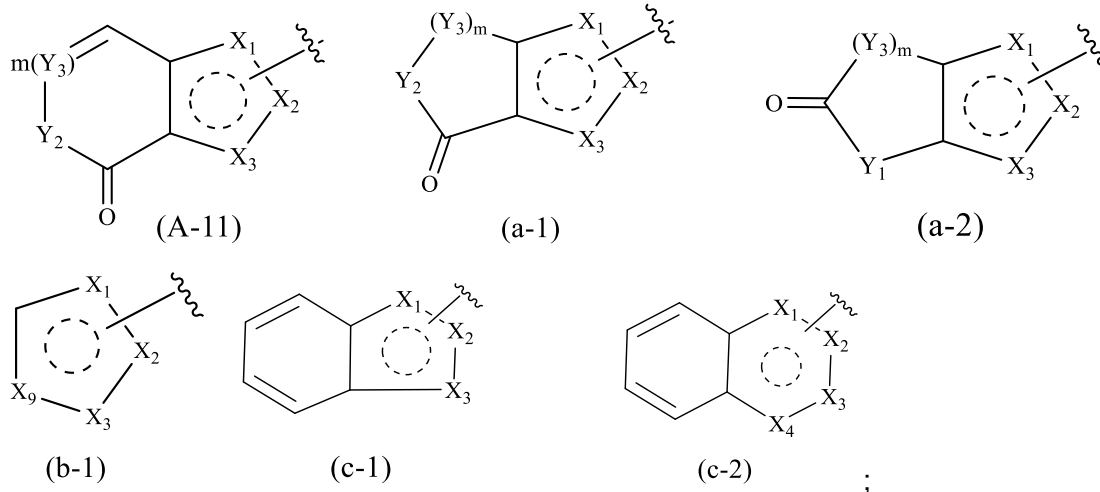
with the *proviso* that when Cy₁ is formula (c), formula (c) is substituted by one or more R^a;

with the *proviso* that when Cy₁ is formula (b), X₁, X₂, X₃, X₉ and X₁₀ are not C=O; and

○ represents a double bond optionally present in the ring structure.

4. The compound, or the pharmaceutically acceptable salt, ~~the ester~~, the stereoisomer or the tautomer thereof according to claims 2 or 3,

wherein Cy₁ is a group that is unsubstituted or substituted by one or more R^a shown in general formula (A-11), (a-1), (a-2), (b-1), (c-1) or (c-2) below:



m is an integer that is 1 or 2;

Y₁, Y₂ and Y₃ are each independently selected from CH₂, CH and NH;

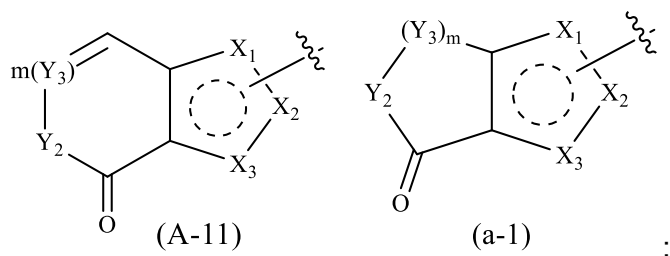
X₁, X₂, X₃, X₄ and X₉ are each independently selected from CH₂, CH, N, NH and C=O, and at least one of X₁, X₂ and X₃ is N;

with the *proviso* that when Cy₁ is formula (c-1) or (c-2), formula (c-1) or (c-2) is substituted by one or more R^a;

with the *proviso* that when Cy₁ is formula (b-1), X₁, X₂, X₃ and X₉ are not C=O; and

○ represents a double bond optionally present in the ring structure.

5. The compound, or the pharmaceutically acceptable salt, the ester, the stereoisomer or the tautomer thereof according to claim 4.



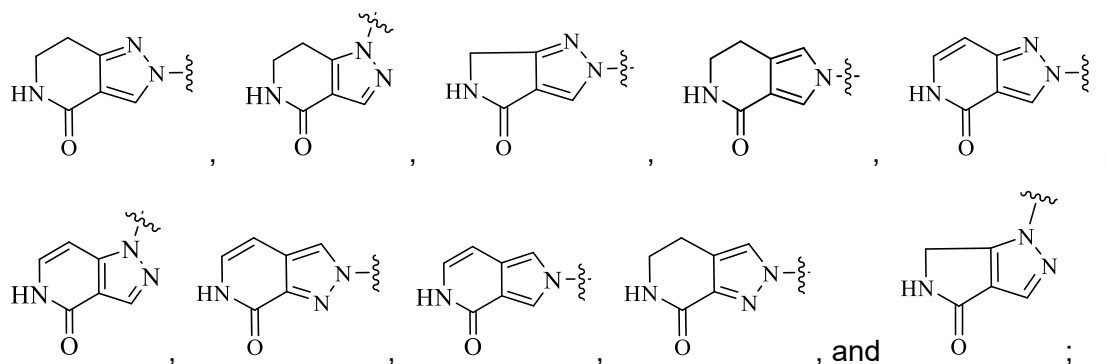
Y₂ and Y₃ are each independently selected from CH₂, CH and NH;

 represents a double bond optionally present in the ring structure.

wherein R₁ and R₂ are each independently selected from hydrogen and halogen, and R₁ and R₂ are not both hydrogen;

R₅ and R₆ are each independently selected from hydrogen and C₁₋₆ alkyl;

Cy₁ is one of the following groups unsubstituted or substituted by one or more R^a:



alkylcarbonyl, C₁₋₆ alkylcarbonyl C₁₋₆ alkyl, Cy₂, Cy₂-C₁₋₆ alkyl, Cy₂-C₁₋₆ alkoxy, Cy₂-carbonyl and Cy₂-aminocarbonyl unsubstituted or substituted by one or more substituents R^b,

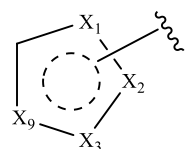
Cy₂ is 3-8 membered cycloalkyl, 5-10 membered heterocyclyl, phenyl or 5-10 membered heteroaryl;

each R^b is independently selected from hydroxyl, amino, carboxyl, cyano, nitro, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ alkoxy C₁₋₆ alkyl, C₁₋₆ alkoxy C₁₋₆ alkoxy, C₁₋₆ alkylthio, C₁₋₆ alkylamino, C₁₋₆ alkylaminocarbonyl, C₁₋₆ alkylcarbonylamino and C₁₋₆ alkylcarbonyl;

 represents a double bond optionally present in the ring structure; and preferably, Cy₂ is 3-6 membered cycloalkyl, 5-6 membered heterocyclyl, phenyl or 5-6 membered heteroaryl.

7. The compound, or the pharmaceutically acceptable salt, ~~the ester~~, the stereoisomer or the tautomer thereof according to claim 4,

wherein Cy₁ is a group that is unsubstituted or substituted by one or more R^a shown in general formula (b-1) below:



(b-1) ;

X₁, X₂, X₃ and X₉ are each independently selected from CH₂, CH, N and NH, and at least one of X₁, X₂ and X₃ is N; and

 represents a double bond optionally present in the ring structure; with the *proviso* that in general formula (b-1), X₁, X₂, X₃ and X₉ are not C=O.

8. The compound, or the pharmaceutically acceptable salt, ~~the ester~~, the stereoisomer or the tautomer thereof according to claim 7,

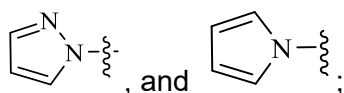
wherein R₁ and R₂ are each independently selected from hydrogen and halogen, and R₁ and R₂ are not both hydrogen;

R₃ and R₄ are each independently selected from hydrogen and C₁₋₆ alkyl;

R₅ and R₆ are each independently selected from hydrogen and C₁₋₆ alkyl;

L₁ is absent;

Cy₁ is one of the following groups unsubstituted or substituted by one or more R^a:



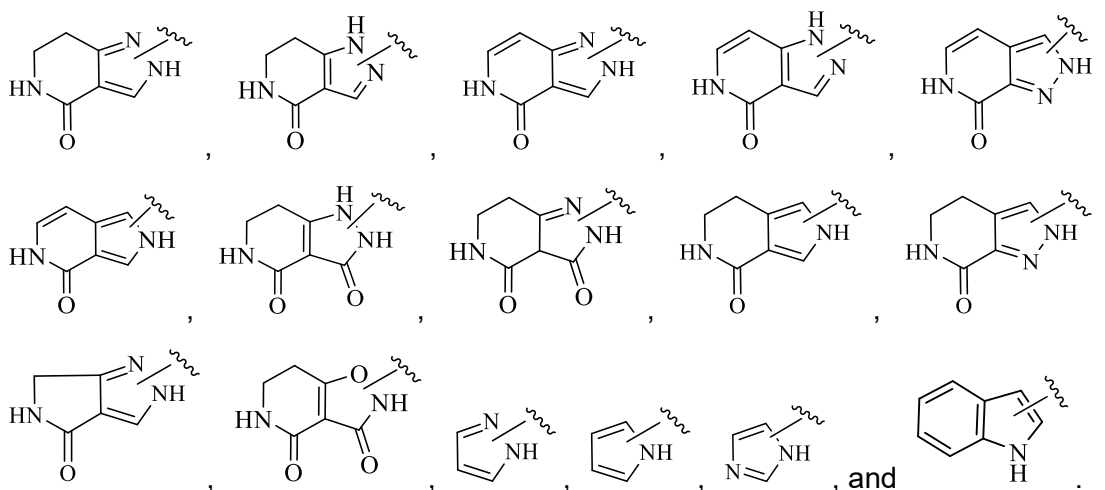
each R^a is independently selected from hydroxyl, amino, carboxyl, cyano, nitro, halogen, and C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy C_{1-6} alkyl, C_{1-6} alkoxy C_{1-6} alkoxy, C_{1-6} alkylamino, C_{1-6} alkylamino C_{1-6} alkyl, C_{1-6} alkylaminocarbonyl, C_{1-6} alkylaminocarbonyl C_{1-6} alkyl, C_{1-6} alkylcarbonylamino, C_{1-6} alkylcarbonylamino C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarbonyl C_{1-6} alkyl, Cy_2 , Cy_2 - C_{1-6} alkyl, Cy_2 - C_{1-6} alkoxy, Cy_2 -carbonyl and Cy_2 -aminocarbonyl unsubstituted or substituted by one or more substituents R^b ,

Cy_2 is 3-8 membered cycloalkyl, 5-10 membered heterocyclyl, phenyl or 5-10 membered heteroaryl; and

each R^b is independently selected from hydroxyl, amino, carboxyl, cyano, nitro, halogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy C_{1-6} alkyl, C_{1-6} alkoxy C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} alkylamino, C_{1-6} alkylaminocarbonyl, C_{1-6} alkylcarbonylamino and C_{1-6} alkylcarbonyl.

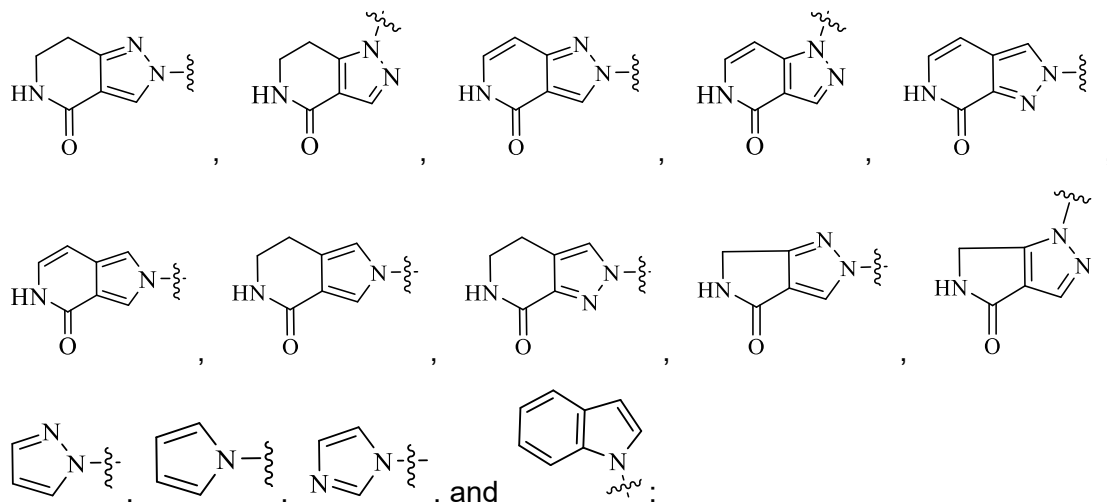
9. The compound, or the pharmaceutically acceptable salt, ~~the ester~~, the stereoisomer or the tautomer thereof according to claim 1,

wherein, Cy_1 is one of the following groups unsubstituted or substituted by one or more R^a :

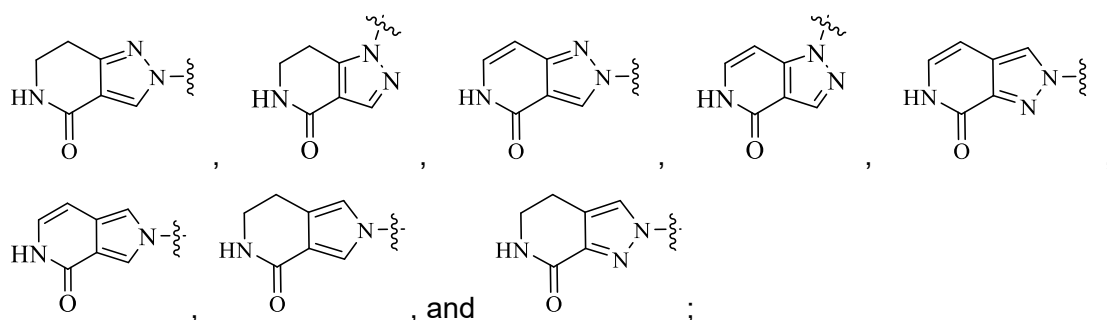


10. The compound, or the pharmaceutically acceptable salt, ~~the ester~~, the stereoisomer or the tautomer thereof according to claim 9,
- wherein R_1 and R_2 are each independently selected from hydrogen and fluorine, and R_1 and R_2 are not both hydrogen;
- R_3 and R_4 are each independently selected from hydrogen and C_{1-6} alkyl;

Cy₁ is one of the following groups unsubstituted or substituted by one or substituent more substituents R^a:



preferably, Cy₁ is one of the following groups substituted by one or more substituents R^a:



preferably, each R^b is independently selected from hydroxyl, amino, cyano, nitro and halogen.

11. The compound, or the pharmaceutically acceptable salt, ~~the ester,~~ the stereoisomer or

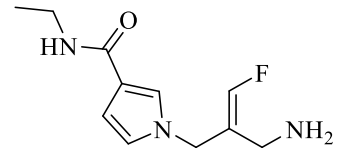
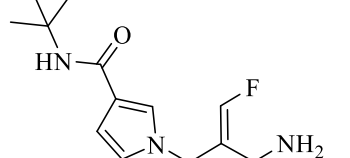
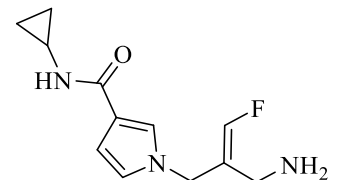
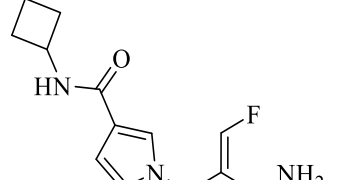
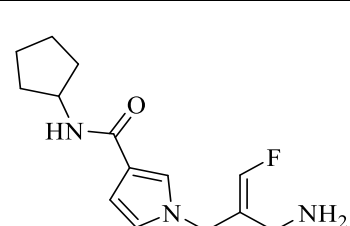
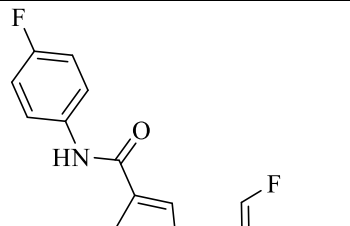
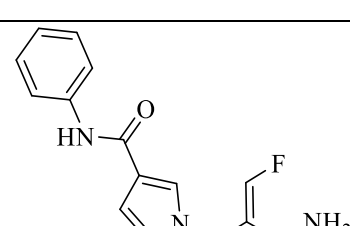
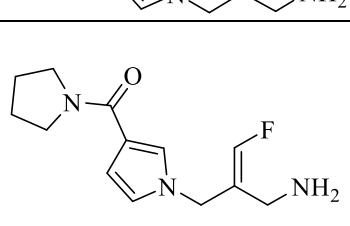
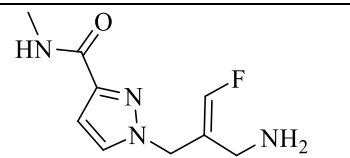
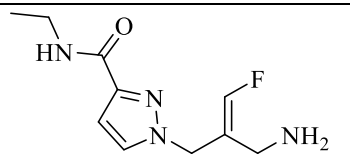
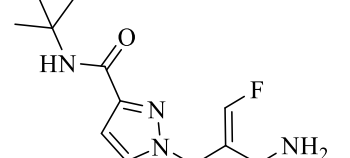
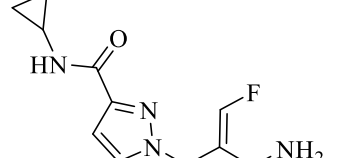
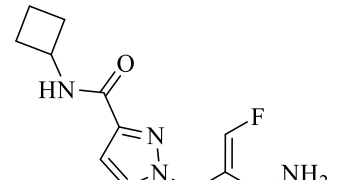
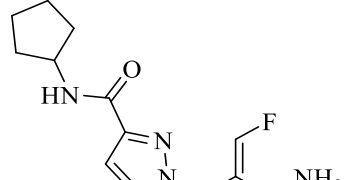
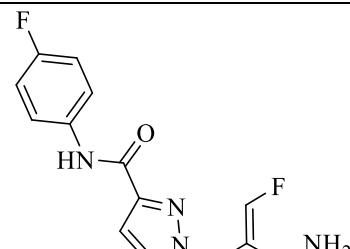
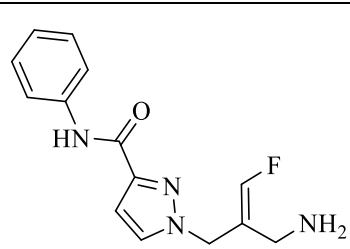
the tautomer thereof according to claim 1, wherein the compound is selected from:

Serial number	Structural formula	Serial number	Structural formula
A1		A2	
A3		A4	
A5		A6	
A7		A8	
A9		A10	
A11		A12	
A13		A14	
A15		A16	

Serial number	Structural formula	Serial number	Structural formula
A17		A18	
A19		A20	
A21		A22	
A23		A24	
A25		A26	
A27		A28	
A29		A30	
A31		A32	

Serial number	Structural formula	Serial number	Structural formula
A33		A34	
A35		A36	
A37		A38	
A39		A40	
A41		A42	
A44		A45	
A46		A47	

Serial number	Structural formula	Serial number	Structural formula
A48		A49	
A50		A51	
A52			
B1		B2	
B3		B4	
B5		B6	
B7		B8	
B9		B10	

Serial number	Structural formula	Serial number	Structural formula
B11		B12	
B13		B14	
B15		B16	
B17		B18	
B19		B20	
B21		B22	
B23		B24	
B25		B26	

Serial number	Structural formula	Serial number	Structural formula
B27		B28	
B29		B30	
~~B34~~			
C1		C2	
C3		C4	
C5		C6	
C7		C8	
C9		C10	

Serial number	Structural formula	Serial number	Structural formula
C11		C12	
C13		C14	
C15			

12. A pharmaceutical composition comprising the compound or the pharmaceutically acceptable salt, ~~the ester~~, the stereoisomer or the tautomer thereof according to any one of claims 1-11, wherein the pharmaceutical composition optionally comprises one or more pharmaceutically acceptable carriers.
13. Use of the compound or the pharmaceutically acceptable salt, ~~the ester~~, the stereoisomer or the tautomer thereof according to any one of claims 1-11, or the pharmaceutical composition according to claim 12 in manufacture of a medicament for preventing and/or treating a disease related to or mediated by the SSAO/VAP-1 protein.