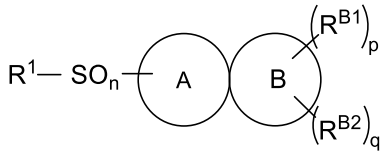
20) Najjar, M., Suebsuwong, C., Ray, S. S., Thapa, R. J., Maki, J. L., Nogusa, S., Shah, S., Saleh, D., Gough, P. J., Bertin, J., Yuan, J., Balachandran, S., Cuny, G. D. and Degterev, A. (2015) Structure Guided Design of Potent and Selective Ponatinib-Based Hybrid Inhibitors for RIPK1. Cell Rep.

21) International Patent Publication No. WO 2014/125444.

22) International Patent Publication No. WO 2017/004500.

SUMMARY

Provided herein are compounds of formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, CH_2-(C_3-C_6 cycloalkyl), C_1-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, C_1-C_6 alkyl-$N(R^N)_2$, phenyl, benzyl, 4 to 8 membered heterocyclyl and 5 to 6 membered heteroaryl; and wherein R^1 is optionally substituted by one or two substituents selected from the group consisting of halogen, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, C_1-C_6 alkyl-$N(R^N)_2$, hydroxyl, C_1-C_6 hydroxyalkyl, cyano, C_1-C_6cyanoalkyl, $C(O)C_1$-C_6 alkyl, phenyl, benzyl, CH_2-(C_3-C_6 cycloalkyl), 5 to 6 membered heteroaryl, and CH_2-(5 to 6 membered heteroaryl);

n is 0, 1 or 2;

each R^2 is independently selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, and C_1-C_6 haloalkyl; or two R^2 together with the nitrogen atom to which they are both attached form a 4-6 membered heterocyclic ring;

the A ring and the B ring are fused to form a polycyclic ring system, wherein

the A ring is a 5 membered heteroaromatic ring having as its only heteroatoms, either (i) two or three nitrogen atoms, (ii) one nitrogen atom and one oxygen atom, or (iii) one nitrogen atom and one sulfur atom; wherein the A ring is optionally substituted at a carbon atom by one substituent selected from the group consisting of fluoro, chloro, methyl, and trifluoromethyl; and

the B ring is a 4 to 8 membered carbocyclic ring, or a 4 to 8 membered heterocyclic ring having 1 to 3 heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur;

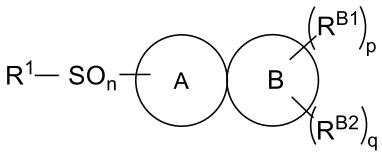
p is 1 or 2, and q is 0 or 1; or p is 0, and q is 1;

wherein when p is 1, R^{B1} is R^{3a} and when p is 2, R^{B1} is independently R^{3a} and R^{3b} and each R^{3a} and R^{3b},when present, is/areindependently selected from the group consisting of halogen, deutero, hydroxyl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_1-C_6 thioalkyl, C_1-C_6 alkyl-$N(R^2)_2$, and cyano; wherein two C_1-C_6 alkyl substituents may together form a bridged or spirocyclic ring; and wherein if a nitrogen atom in the B ring is substituted, the substituent is not halogen, cyano, or a C_1-C_6 alkoxy, C_1-C_6 haloalkoxy or C_1-C_6 thioalkyl having an oxygen or sulfur atom directly bonded to the nitrogen atom; and

wherein when q is 1, R^{B2} is R^4 and R^4 is selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_1-C_6 thioalkyl, C_1-C_6 alkyl-$N(R^2)_2$, phenyl, benzyl, CH_2-(C_3-C_6 cycloalkyl), CH_2CH_2-(C_3-C_6 cycloalkyl), CH_2-(4 to 6 membered heterocyclyl), CH_2CH_2-(4 to 6 membered heterocyclyl), 5 to 6 membered heteroaryl, and CH_2-(5 to 6 membered heteroaryl);

wherein when R^4 is phenyl, heteroaryl or benzyl the phenyl or heteroaryl ring is optionally substituted by 1 to 3 substituents selected from the group consisting of halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, and cyano.

In one aspect, provided herein is a compound of formula I:



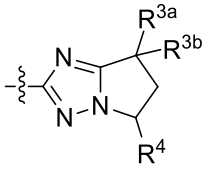
(I),

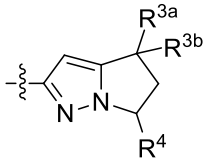
or a pharmaceutically acceptable salt thereof, wherein:

the A ring and the B ring are fused to form a polycyclic ring system;

p is 2 and q is 1;

the A ring and the B ring together are selected from the group consisting of:



, and


;

R^1 is selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, C_1-C_6 hydroxyalkyl, C_1-C_6 cyanoalkyl, C_3-C_6 cycloalkyl-C_1-C_3 alkyl, C_1-C_6 alkyl-$N(R^2)_2$, C_1-C_6 alkoxy-C_1-C_6 alkyl, C_1-C_6 haloalkoxy-C_1-C_6 alkyl , phenyl, benzyl, difluoro(phenyl)methyl, 4 to 6 membered heterocyclyl, 5 to 6 membered heteroaryl, and CH_2-(5 to 6 membered heteroaryl); wherein:

when R^1 is haloalkyl, the haloalkyl is optionally substituted by hydroxyl;

when R^1 is phenyl, benzyl, difluoro(phenyl)methyl, 5 to 6 membered heteroaryl or CH_2-(5 to 6 membered heteroaryl), the phenyl or heteroaryl moiety of R^1 is optionally substituted by one or two substituents independently selected from the group consisting of halogen, C_1-C_6 alkyl, hydroxyl, hydroxymethyl, methoxymethyl, cyano, trifluoromethyl, difluoromethoxy and trifluoromethoxy; and

when R^1 is cycloalkyl, the cycloalkyl is optionally substituted by by one, two or three substituents independently selected from the group consisting of fluoro, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, hydroxyl, C_1-C_6 hydroxyalkyl, and cyano;

n is 1 or 2;

each R^2 is independently selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, and C_1-C_6 haloalkyl; or two R^2 together with the nitrogen atom to which they are both attached form a 4-6 membered heterocyclic ring;

R^{B1} is independently R^{3a} and R^{3b} and each R^{3a} and R^{3b} is independently selected from the group consisting of hydrogen, halogen, deutero, hydroxyl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_1-C_6 thioalkyl, C_1-C_6 alkyl-$N(R^2)_2$, and cyano; and

R^{B2} is R^4 and R^4 is selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_1-C_6 thioalkyl, C_1-C_6 alkyl-$N(R^2)_2$, phenyl, benzyl, CH_2-(C_3-C_6 cycloalkyl), CH_2CH_2-(C_3-C_6 cycloalkyl), CH_2-(4 to 6 membered heterocyclyl), CH_2CH_2-(4 to 6 membered heterocyclyl), 5 to 6 membered heteroaryl, and CH_2-(5 to 6 membered heteroaryl);

wherein when R^4 is phenyl, heteroaryl or benzyl, the phenyl or heteroaryl ring is optionally substituted by 1 to 3 substituents selected from the group consisting of halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, and cyano.

Also provided herein are pharmaceutical compositions comprising a compound of formula I, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable carriers or excipients. Provided herein, in another aspect, is a pharmaceutical composition comprising a compound as defined herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier. Specific embodiments include pharmaceutical compositions suitable for oral delivery.

Also provided herein are oral formulations of a compound of formula I, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable carriers or excipients suitable for oral delivery.

Also provided herein are methods of treatment of diseases and disorders associated with inflammation, cell death, and others related to RIP1 kinase, as described further below.

Also provided herein are compounds or pharmaceutical compositons for use as therapeutically active substances. Provided herein, in another aspect, is a compound as defined herein, or a pharmaceutically acceptable salt thereof, or pharmaceutical composition as defined herein, for use as a therapeutically active substance.

Provided herein, in another aspect, is a compound as defined herein, or a pharmaceutically acceptable salt thereof, or pharmaceutical composition as defined herein, for use in the treatment of a disease or disorder selected from the group consisting of Parkinson's Disease, Lewy body dementia, multiple system atrophy, Parkinson-plus syndrome, tauopathy, Alzheimer's Disease, frontotemporal dementia, amyotrophic lateral sclerosis, spinal muscular atrophy, primary lateral sclerosis, Huntington's disease, ischemia, stroke, intracranial hemorrhage, cerebral hemorrhage, muscular dystrophy, progressive muscular atrophy, pseudobulbar palsy, progressive bulbar palsy, spinal muscular atrophy, inherited muscular atrophy, peripheral neuropathy, progressive supranuclear palsy, corticobasal degeneration, and demyelinating disease.

Also provided herein are uses of compounds or pharmaceutical compositons for use in the treatment of diseases and disorders associated with inflammation, cell death, and others related to RIP1 kinase, as described further below.

Also provided herein are uses of compounds or pharmaceutical compositions for the preparation of a medicament for the treatment of diseases and disorders associated with inflammation, cell death, and others related to RIP1 kinase, as described further below.

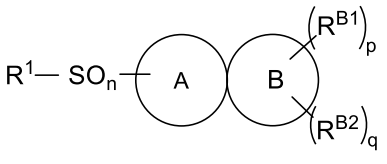
Provided herein, in another aspect, is use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, or pharmaceutical composition as defined herein, in the preparation of a medicament for the treatment of a disease or disorder selected from the group consisting of Parkinson's Disease, Lewy body dementia, multiple system atrophy, Parkinson-plus syndrome, tauopathy, Alzheimer's Disease, frontotemporal dementia, amyotrophic lateral sclerosis, spinal muscular atrophy, primary lateral sclerosis, Huntington's disease, ischemia, stroke, intracranial hemorrhage, cerebral hemorrhage, muscular dystrophy, progressive muscular atrophy, pseudobulbar palsy, progressive bulbar palsy, spinal muscular atrophy, inherited muscular atrophy, peripheral neuropathy, progressive supranuclear palsy, corticobasal degeneration, and demyelinating disease.

Also provided herein are compounds or pharmaceutical compositons for use in the treatment of diseases and disorders associated with inflammation, cell death, and others related to RIP1 kinase, as described further below.

CLAIMS

WE CLAIM:

1. A compound of formula I:



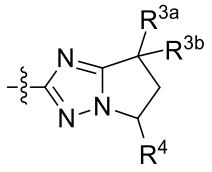
(I),

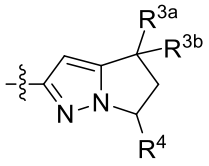
or a pharmaceutically acceptable salt thereof, wherein:

the A ring and the B ring are fused to form a polycyclic ring system;

p is 2 and q is 1;

the A ring and the B ring together are selected from the group consisting of:



, and


;

R^1 is selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, C_1-C_6 hydroxyalkyl, C_1-C_6 cyanoalkyl, C_3-C_6 cycloalkyl-C_1-C_3 alkyl, C_1-C_6 alkyl-$N(R^2)_2$, C_1-C_6 alkoxy-C_1-C_6 alkyl, C_1-C_6 haloalkoxy-C_1-C_6 alkyl , phenyl, benzyl, difluoro(phenyl)methyl, 4 to 6 membered heterocyclyl, 5 to 6 membered heteroaryl, and CH_2-(5 to 6 membered heteroaryl); wherein:

when R^1 is haloalkyl, the haloalkyl is optionally substituted by hydroxyl;

when R^1 is phenyl, benzyl, difluoro(phenyl)methyl, 5 to 6 membered heteroaryl or CH_2-(5 to 6 membered heteroaryl), the phenyl or heteroaryl moiety of R^1 is optionally substituted by one or two substituents independently selected from the group consisting of halogen, C_1-C_6 alkyl, hydroxyl, hydroxymethyl, methoxymethyl, cyano, trifluoromethyl, difluoromethoxy and trifluoromethoxy; and

when R^1 is cycloalkyl, the cycloalkyl is optionally substituted by by one, two or three substituents independently selected from the group consisting of fluoro, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, hydroxyl, C_1-C_6 hydroxyalkyl, and cyano;

n is 1 or 2;

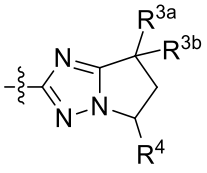
each R^2 is independently selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, and C_1-C_6 haloalkyl; or two R^2 together with the nitrogen atom to which they are both attached form a 4-6 membered heterocyclic ring;

R^{B1} is independently R^{3a} and R^{3b} and each R^{3a} and R^{3b} is independently selected from the group consisting of hydrogen, halogen, deutero, hydroxyl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_1-C_6 thioalkyl, C_1-C_6 alkyl-$N(R^2)_2$, and cyano; and

R^{B2} is R^4 and R^4 is selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_1-C_6 thioalkyl, C_1-C_6 alkyl-$N(R^2)_2$, phenyl, benzyl, CH_2-(C_3-C_6 cycloalkyl), CH_2CH_2-(C_3-C_6 cycloalkyl), CH_2-(4 to 6 membered heterocyclyl), CH_2CH_2-(4 to 6 membered heterocyclyl), 5 to 6 membered heteroaryl, and CH_2-(5 to 6 membered heteroaryl);

wherein when R^4 is phenyl, heteroaryl or benzyl, the phenyl or heteroaryl ring is optionally substituted by 1 to 3 substituents selected from the group consisting of halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, and cyano.

2. A compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the A ring and the B ring together are:



.

3. A compound according to claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein:

R^{3a} and R^{3b} are selected as follows:

one of R^{3a} and R^{3b} is H, and the other is selected from the group consisting of hydrogen, deutero, fluoro, chloro, hydroxyl, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl, cyclopropyl, C_1-C_4 alkoxy and C_1-C_4 haloalkoxy; or

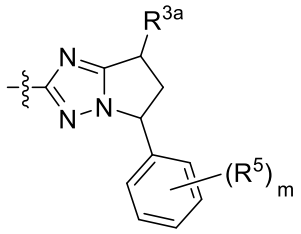
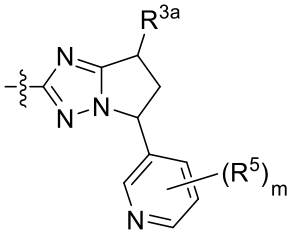
each of R^{3a} and R^{3b} is independently selected from the group consisting of deutero, fluoro, chloro, hydroxyl, cyano, and methyl, provided that R^{3a} and R^{3b} cannot both be OH or CN; and

R^4 is selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, phenyl, and pyridinyl wherein the phenyl ring or pyridinyl ring is optionally substituted by 1 to 3 substituents selected from the group consisting of halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, and cyano.

4. A compound any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein R^{3a} and R^{3b} are independently hydrogen or fluorine; and R^4 is selected from the group consisting of

ethyl, isopropyl n-propyl, trifluoromethyl, 1,1-difluoroethyl, 1,1-difluoropropyl, optionally substituted phenyl, and optionally substituted pyridine-2-yl.

5. A compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein the A ring and the B ring together are selected from the group consisting of:

 and  ;

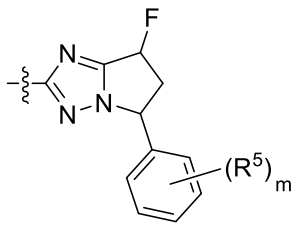
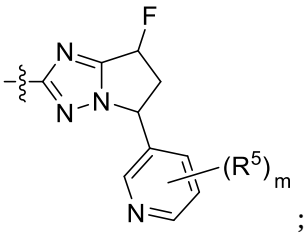
wherein:

R^{3a} is hydrogen or fluorine

each R^5 is selected from the group consisting of hydrogen, fluoro, chloro, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkoxy; and

m is 1, 2 or 3.

6. A compound of any of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein the A ring and the B ring together are:

 or  ;

wherein:

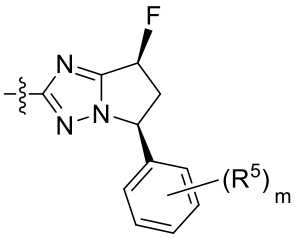
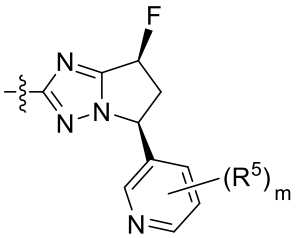
each R^5 is selected from the group consisting of hydrogen, fluoro, chloro, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkoxy; and

m is 1, 2 or 3.

7. A compound of any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein R^5 is selected from the group consisting of H, F, Cl, CH_3, CH_2CH_3, OCH_3, CF_3, OCF_3, CF_2H, and OCF_2H.

8. A compound of any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein R^5 is halo.

9. A compound of any one of claims 1 to 8 or a pharmaceutically acceptable salt thereof, wherein the A ring and the B ring together are:

10. A compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from the group consisting of C_1-C_6 alkyl, optionally substituted C_3-C_6 cycloalkyl, C_3-C_6 spirocycloalkyl. C_1-C_6 haloalkyl, C_1-C_6 alkoxy-C_1-C_6 alkyl, C_1-C_6 cyanoalkyl, C_1-C_6 hydroxyalkyl, phenyl, benzyl, and difluoro(phenyl)methyl.

11. A compound of any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from the group consisting of methyl, ethyl, *tert*-butyl, difluoromethyl, trifluoromethyl, cyclopropyl, fluorocyclopropyl, difluorocyclopropyl, phenyl, benzyl, and difluoro(phenyl)methyl.

12. A compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from the group consisting of ethyl, difluoromethyl, trifluoromethyl,. cyclopropyl, fluorocyclopropyl or difluorocyclopropyl.

13. A compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the group consisting of:

2-(difluoromethylsulfinyl)-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

2-ethylsulfonyl-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S)-2-[(S)-ethylsulfinyl]-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

2-[difluoro(phenyl)methyl]sulfonyl-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

2-[difluoro(phenyl)methyl]sulfinyl-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

2-(difluoromethylsulfonyl)-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(S)-5-(2-fluorophenyl)-2-methylsulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(S)-2-ethylsulfonyl-5-(2-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

2-methylsulfonyl-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

5-phenyl-2-(trifluoromethylsulfinyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S)-2-[(R)-difluoromethylsulfinyl]-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S)-2-[(S)-difluoromethylsulfinyl]-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

rac-(5S,7S)-2-(difluoromethylsulfinyl)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5R,7R)-2-cyclopropylsulfonyl-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5R)-5-(2-chlorophenyl)-2-(difluoromethylsulfonyl)-6,7-dihydro-5H-pyrrolo[1,2- b][1,2,4]triazole ;

(5S)-5-(2-chlorophenyl)-2-(difluoromethylsulfonyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S)-5-(2-chlorophenyl)-2-[(S)-difluoromethylsulfinyl]-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S)-5-(2-chlorophenyl)-2-[(R)-difluoromethylsulfinyl]-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-benzylsulfonyl-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-benzylsulfinyl-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-[(S)-difluoromethylsulfinyl]-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-[(R)-difluoromethylsulfinyl]-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-(difluoromethylsulfonyl)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-tert-butylsulfinyl-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-tert-butylsulfonyl-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-cyclopropylsulfinyl-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-[(R)-cyclopropylsulfinyl]-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-[(S)-cyclopropylsulfinyl]-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-cyclopropylsulfonyl-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(4S,6S)-2-cyclopropylsulfonyl-4-fluoro-6-phenyl-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazole;

(5S,7S)-5-(2-chlorophenyl)-2-cyclopropylsulfonyl-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-cyclopropylsulfonyl-7-fluoro-5-(2-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-cyclopropylsulfonyl-7-fluoro-5-(4-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-cyclopropylsulfonyl-5-(2,6-difluorophenyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5R,7R)-2-cyclopropylsulfonyl-5-(2,3-difluorophenyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-cyclopropylsulfonyl-5-(2,5-difluorophenyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-cyclopropylsulfonyl-7-fluoro-5-(2,3,6-trifluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

rac-(5S,7S)-2-cyclopropylsulfonyl-7-fluoro-5-(2,3,5-trifluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-cyclopropylsulfonyl-5-(2,3-difluorophenyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-cyclopropylsulfonyl-7-deuterio-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-cyclopropylsulfonyl-5-(3,5-difluorophenyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-5-(3-chlorophenyl)-2-cyclopropylsulfonyl-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-cyclopropylsulfonyl-5-(3,4-difluorophenyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-5-(2-chloro-3-fluoro-phenyl)-2-cyclopropylsulfonyl-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(3-chloro-2-fluoro-phenyl)-2-cyclopropylsulfonyl-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(5-chloro-2-fluoro-phenyl)-2-cyclopropylsulfonyl-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-cyclopropylsulfonyl-7-fluoro-5-(3-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-(3,3-difluorocyclobutyl)sulfinyl-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-(3,3-difluorocyclobutyl)sulfonyl-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-[(S)-difluoromethylsulfinyl]-7-fluoro-5-(2-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-[(R)-difluoromethylsulfinyl]-7-fluoro-5-(2-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-(difluoromethylsulfonyl)-7-fluoro-5-(2-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-(difluoromethylsulfinyl)-7-fluoro-5-(3-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-(difluoromethylsulfinyl)-7-fluoro-5-(4-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-(difluoromethylsulfonyl)-7-fluoro-5-(4-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(4R,6R)-2-(difluoromethylsulfonyl)-4-fluoro-6-phenyl-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazole;

(5S,7S)-2-(difluoromethylsulfonyl)-5-(2,6-difluorophenyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-(difluoromethylsulfonyl)-7-fluoro-5-(2,3,6-trifluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-(difluoromethylsulfonyl)-7-fluoro-5-(2,3,5-trifluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(3-chlorophenyl)-2-(difluoromethylsulfonyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

2-[(5S,7S)-2-(difluoromethylsulfonyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-5-yl]benzonitrile;

(5S,7S)-2-(difluoromethylsulfonyl)-5-(3,4-difluorophenyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2-chloro-3-fluoro-phenyl)-2-(difluoromethylsulfonyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(3-chloro-2-fluoro-phenyl)-2-(difluoromethylsulfonyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(5-chloro-2-fluoro-phenyl)-2-(difluoromethylsulfonyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-(difluoromethylsulfonyl)-5-(2,5-difluorophenyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-(difluoromethylsulfonyl)-5-(2,3-difluorophenyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-(difluoromethylsulfonyl)-5-(3,5-difluorophenyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-(difluoromethylsulfonyl)-7-fluoro-5-(3-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-[(S)-fluoromethylsulfinyl]-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-(fluoromethylsulfonyl)-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-[(R)-fluoromethylsulfinyl]-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-[(R)-fluoromethylsulfinyl]-5-(2-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-[(S)-fluoromethylsulfinyl]-5-(2-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-5-(2,3-difluorophenyl)-7-fluoro-2-[(R)-fluoromethylsulfinyl]-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2,3-difluorophenyl)-7-fluoro-2-[(S)-fluoromethylsulfinyl]-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2,5-difluorophenyl)-7-fluoro-2-[(R)-fluoromethylsulfinyl]-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2,5-difluorophenyl)-7-fluoro-2-[(S)-fluoromethylsulfinyl]-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2,6-difluorophenyl)-7-fluoro-2-[(R)-fluoromethylsulfinyl]-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2,6-difluorophenyl)-7-fluoro-2-[(S)-fluoromethylsulfinyl]-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-[(R)-fluoromethylsulfinyl]-5-(3-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-[(S)-fluoromethylsulfinyl]-5-(3-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(3,5-difluorophenyl)-7-fluoro-2-[(R)-fluoromethylsulfinyl]-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(3,5-difluorophenyl)-7-fluoro-2-[(S)-fluoromethylsulfinyl]-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2-chlorophenyl)-7-fluoro-2-[(R)-fluoromethylsulfinyl]-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-5-(2-chlorophenyl)-7-fluoro-2-[(S)-fluoromethylsulfinyl]-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

2-[[(5S,7S)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfonyl]acetonitrile;

2-[[(5S,7S)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfanyl]acetonitrile;

2-2-(((4S,6S)-4-fluoro-6-phenyl-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-2-yl)sulfonyl)acetonitrile;

2-2-((R)-((4S,6S)-4-fluoro-6-phenyl-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-2-yl)sulfinyl)acetonitrile;

2-2-((S)-((4S,6S)-4-fluoro-6-phenyl-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-2-yl)sulfinyl)acetonitrile;

2-[(S)-[(5S,7S)-5-(2-chlorophenyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfinyl]acetonitrile;

2-[(R)-[rac-(5S,7S)-5-(2-chlorophenyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfinyl]acetonitrile;

2-[(S)-[(5S,7S)-7-fluoro-5-(2-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfinyl]acetonitrile;

2-[(R)-[(5S,7S)-7-fluoro-5-(2-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfinyl]acetonitrile;

2-[(S)-[(5S,7S)-7-fluoro-5-(3-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfinyl]acetonitrile;

2-[(R)-[(5S,7S)-7-fluoro-5-(3-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfinyl]acetonitrile;

2-[(S)-[(5S,7S)-7-fluoro-5-(4-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfinyl]acetonitrile;

2-[(R)-[(5S,7S)-7-fluoro-5-(4-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfinyl]acetonitrile;;

2-[(S)-[(5R,7R)-5-(2-chlorophenyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfinyl]acetonitrile;

2-[[(5S,7S)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfinyl]acetonitrile;

2-methyl-2-[[(5S,7S)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfinyl]propanenitrile;

2-(((5S,7S)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl)sulfonyl)-2-methylpropanenitrile;

(5S,7S)-7-fluoro-2-methylsulfinyl-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-methylsulfonyl-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-ethylsulfinyl-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-ethylsulfonyl-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-isopropylsulfinyl-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-isopropylsulfonyl-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-(cyclopropylmethylsulfinyl)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-(cyclopropylmethylsulfonyl)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-phenyl-2-(2,2,2-trifluoroethylsulfinyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-phenyl-2-(2,2,2-trifluoroethylsulfonyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-(methoxymethylsulfinyl)-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-(methoxymethylsulfonyl)-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-(2,2-difluorocyclopropyl)sulfinyl-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-((2,2-difluorocyclopropyl)sulfonyl)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-(2-fluorophenyl)-2-[(1S)-2,2-difluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2-chlorophenyl)-7-fluoro-2-[(1S)-2,2-difluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-(2,2-difluorocyclopropyl)sulfonyl-5-(2,3-difluorophenyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-(2,2-difluorocyclopropyl)sulfonyl-5-(2,5-difluorophenyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-(2,2-difluorocyclopropyl)sulfonyl-5-(2,6-difluorophenyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-(2-fluorophenyl)-2-[(1R)-2,2-difluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2-chlorophenyl)-7-fluoro-2-[(1R)-2,2-difluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2,5-difluorophenyl)-7-fluoro-2-[(1S)-2,2-difluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2,5-difluorophenyl)-7-fluoro-2-[(1R)-2,2-difluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2,3-difluorophenyl)-7-fluoro-2-[(1R)-2,2-difluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2,3-difluorophenyl)-7-fluoro-2-[(1S)-2,2-difluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-(((S)-2,2-difluorocyclopropyl)sulfonyl)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-(((R)-2,2-difluorocyclopropyl)sulfonyl)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-phenyl-2-(trifluoromethylsulfinyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-(2-fluorophenyl)-2-(trifluoromethylsulfonyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-5-(2-chlorophenyl)-7-fluoro-2-(trifluoromethylsulfonyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-(3-fluorophenyl)-2-(trifluoromethylsulfonyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-5-(2,3-difluorophenyl)-7-fluoro-2-(trifluoromethylsulfonyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-phenyl-2-(trifluoromethylsulfonyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-5-(2,5-difluorophenyl)-7-fluoro-2-(trifluoromethylsulfonyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-5-(2,6-difluorophenyl)-7-fluoro-2-(trifluoromethylsulfonyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5R,7R)-5-(2,3-difluorophenyl)-7-fluoro-2-(trifluoromethylsulfonyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-(3-fluorophenyl)-2-[(1S,2S)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

rac-(5S,7S)-7-fluoro-5-(3-fluorophenyl)-2-[rac-(1R,2R)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(3,4-difluorophenyl)-7-fluoro-2-[(1S,2S)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(3,4-difluorophenyl)-7-fluoro-2-[(1R,2R)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-phenyl-2-[(1R,2R)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-phenyl-2-[(1S,2S)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-phenyl-2-(2-pyridylmethylsulfinyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-(2,2-difluoroethylsulfinyl)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-(1,1-difluoroethylsulfonyl)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-(1-methylcyclopropyl)sulfonyl-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-phenyl-2-(pyrazol-1-ylmethylsulfonyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-phenyl-2-(pyrazol-1-ylmethylsulfinyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-(1,1,2,2,2-pentafluoroethylsulfonyl)-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-(1,1,2,2,2-pentafluoroethylsulfinyl)-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-2-[1-(difluoromethyl)cyclopropyl]sulfonyl-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

2,2-difluoro-2-[[(5S,7S)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfonyl]ethanol;

1-[[(5S,7S)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfonyl]cyclopropanecarbonitrile;

(5S,7S)-7-fluoro-2-(1-fluoroethylsulfonyl)-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-phenyl-2-[(1S)-1-fluoroethyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-phenyl-2-[(1R)-1-fluoroethyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-phenyl-2-propylsulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-phenyl-2-[rac-(1S,2S)-2-methylcyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-phenyl-2-[rac-(1S,2R)-2-(trifluoromethyl)cyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-(3-fluorocyclobutyl)sulfonyl-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-(1-fluoro-1-methyl-ethyl)sulfonyl-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-phenyl-2-tetrahydrofuran-3-ylsulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-(2,2-difluoro-1-methyl-cyclopropyl)sulfonyl-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

((1R,3S)-3-(((5S,7S)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl)sulfonyl)cyclobutyl)methanol;

((1R,3S)-3-(((5S,7S)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl)sulfonyl)cyclobutyl)methanol;

(5S,7S)-7-fluoro-5-phenyl-2-spiro[2.2]pentan-2-ylsulfonyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-phenyl-2-[(1R)-2,2-difluorocyclobutyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-phenyl-2-[(1S)-2,2-difluorocyclobutyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S)-2-[(R)-difluoromethylsulfinyl]-5-(3,5-difluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

(5S)-2-[(S)-difluoromethylsulfinyl]-5-(3,5-difluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

2-(difluoromethylsulfonyl)-5-(3,5-difluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

2-(difluoromethylsulfinyl)-5-(3,5-difluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

5-phenyl-2-(2,2,2-trifluoroethylsulfinyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-7-fluoro-2-(1-fluorocyclopropyl)sulfonyl-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

rac-(5S,7S)-2-[(S)-difluoromethylsulfinyl]-7-fluoro-5-(3-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

rac-(5S,7S)-7-fluoro-5-phenyl-2-[(S)-trifluoromethylsulfinyl]-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

rac-(5S,7S)-7-fluoro-5-phenyl-2-[(R)-trifluoromethylsulfinyl]-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

rac-(5S,7S)-2-[(R)-difluoromethylsulfinyl]-7-fluoro-5-(3-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

rac-(5S,7S)-7-fluoro-5-phenyl-2-[(S)-2,2,2-trifluoroethylsulfinyl]-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

rac-(5S,7S)-2-[(R)-cyclopropylmethylsulfinyl]-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

rac-(5S,7S)-7-fluoro-5-phenyl-2-[(R)-2,2,2-trifluoroethylsulfinyl]-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

rac-(5S,7S)-2-[(S)-cyclopropylmethylsulfinyl]-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

rac-(5S,7S)-7-fluoro-2-[(R)-isopropylsulfinyl]-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

rac-(5S,7S)-2-[(R)-ethylsulfinyl]-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

rac-(5S,7S)-7-fluoro-2-[(S)-isopropylsulfinyl]-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

rac-(5S,7S)-2-[(S)-ethylsulfinyl]-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

rac-(5S,7S)-2-[(R)-tert-butylsulfinyl]-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

3-[(5S,7S)-2-(difluoromethylsulfonyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-5-yl]benzonitrile;

(5S,7S)-5-(3,5-difluorophenyl)-7-fluoro-2-trans-(3-fluorocyclobutyl)sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

cis-3-[[(5S,7S)-7-fluoro-5-(3-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfonyl]cyclobutanol;

(5S,7S)-7-fluoro-5-(4-fluorophenyl)-2-[(1R,2R)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-(4-fluorophenyl)-2-[(1S,2S)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-2-[2-(difluoromethoxy)ethylsulfonyl]-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(3-chloro-5-fluoro-phenyl)-7-fluoro-2-[(1R,2R)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(3-chloro-5-fluoro-phenyl)-7-fluoro-2-[(1S,2S)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2,5-difluorophenyl)-7-fluoro-2-[(1R,2R)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2,5-difluorophenyl)-7-fluoro-2-[(1S,2S)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(3-chlorophenyl)-2-cyclopropylsulfonyl-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2,3-difluorophenyl)-7-fluoro-2-trans-(3-fluorocyclobutyl)sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-(2-fluorophenyl)-2-[(1R,2R)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-(2-fluorophenyl)-2-[(1S,2S)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(5-chloro-2-fluoro-phenyl)-7-fluoro-2-[(1R,2R)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(3-chloro-2-fluoro-phenyl)-7-fluoro-2-[(1R,2R)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(1R,2S)-2-[[(5S,7S)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfonyl]cyclopropanecarbonitrile;

cis-3-[[(5S,7S)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfonyl]cyclobutanecarbonitrile;

trans-3-[[(5S,7S)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfonyl]cyclobutanecarbonitrile;

(1S,2R)-2-[[(5S,7S)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfonyl]cyclopropanecarbonitrile;

(5S,7S)-2-trans-[3-(difluoromethoxy)cyclobutyl]sulfonyl-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(3-chloro-5-fluoro-phenyl)-2-cyclopropylsulfonyl-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(3-chloro-5-fluoro-phenyl)-2-(difluoromethylsulfonyl)-7-fluoro-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2,3-difluorophenyl)-7-fluoro-2-[(1R,2R)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(2,3-difluorophenyl)-7-fluoro-2-[(1S,2S)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(5-chloro-2-fluoro-phenyl)-7-fluoro-2-[(1S,2S)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-5-(3-chloro-2-fluoro-phenyl)-7-fluoro-2-[(1S,2S)-2-fluorocyclopropyl]sulfonyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

2-(difluoromethylsulfonyl)-7-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(1R,2R)-2-[[(5S,7S)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfonyl]cyclopropanecarbonitrile;

(1S,2S)-2-[[(5S,7S)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfonyl]cyclopropanecarbonitrile;

2-[[(5S,7S)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfonyl]ethanol;

(5S,7S)-7-fluoro-2-(2-methoxyethylsulfonyl)-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole;

cis-(3-[[(5S,7S)-7-fluoro-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-yl]sulfonyl]cyclobutanol;

(5S,7S)-7-fluoro-2-trans-(3-fluorocyclobutyl)sulfonyl-5-(3-fluorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole;

(5S,7S)-7-fluoro-5-(3-fluorophenyl)-2-(oxetan-3-ylsulfonyl)-6,7-dihydro-5H-pyrrolo[1,2b][1,2,4]triazole; and

(5S,7S)-7-fluoro-2-(oxetan-3-ylsulfonyl)-5-phenyl-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazole.

14. A compound of any one of claims 1 to 13 having a RIP1 kinase inhibitory activity K_i of less than 100 nM.

15. A pharmaceutical composition comprising a compound of any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

16. A compound of any one of any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, or pharmaceutical composition of claim 15, for use as a therapeutically active substance.

17. A compound of any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, or pharmaceutical composition of claim 15, for use in the treatment of a disease or disorder selected from the group consisting of Parkinson's Disease, Lewy body dementia, multiple system atrophy, Parkinson-plus syndrome, tauopathy, Alzheimer's Disease, frontotemporal dementia, amyotrophic lateral sclerosis, spinal muscular atrophy, primary lateral sclerosis, Huntington's disease, ischemia, stroke, intracranial hemorrhage, cerebral hemorrhage, muscular dystrophy, progressive muscular atrophy, pseudobulbar palsy, progressive bulbar palsy, spinal muscular atrophy, inherited muscular atrophy, peripheral neuropathy, progressive supranuclear palsy, corticobasal degeneration, and demyelinating disease.

18. The use of a compound of any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, or pharmaceutical composition of claim 15, in the preparation of a medicament for the treatment of a disease or disorder selected from the group consisting of Parkinson's Disease, Lewy body dementia, multiple system atrophy, Parkinson-plus syndrome, tauopathy, Alzheimer's Disease, frontotemporal dementia, amyotrophic lateral sclerosis, spinal muscular atrophy, primary lateral sclerosis, Huntington's disease, ischemia, stroke, intracranial hemorrhage, cerebral hemorrhage, muscular dystrophy, progressive muscular atrophy, pseudobulbar palsy, progressive bulbar palsy, spinal muscular atrophy, inherited muscular atrophy, peripheral neuropathy, progressive supranuclear palsy, corticobasal degeneration, and demyelinating disease.

19. The use of claim 18, wherein the disease or disorder is Alzheimer’s disease.

20. The use of claim 18, wherein the disease or disorder is Parkinson’s disease.

21. The use of claim 18, wherein the disease or disorder is amyotrophic lateral sclerosis.

22. The use of claim 18, wherein the disease or disorder is Huntington’s disease.

23. The use of claim 18, wherein the disease or disorder is spinal muscular atrophy.