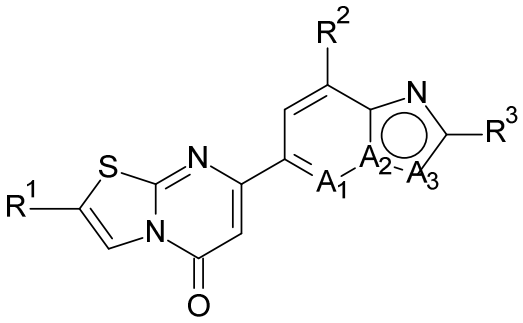
Claims

1. A compound of formula (I)



(I)

wherein

R^1 is hydrogen, alkyl, cycloalkyl, aryl, heteroaryl or heterocycloalkyl, wherein each instance of cycloalkyl, aryl, heteroaryl and heterocycloalkyl is optionally substituted with one, two, three or four substituents independently selected from R^4;

R^2 is hydrogen, cycloalkyl, alkenyl, cyano, amino, hydroxy, halogen, alkyl, haloalkyl, haloalkoxy or alkoxy;

R^3 is alkyl, hydrogen, halogen or haloalkyl;

R^4 is halogen, alkyl, heterocycloalkyl, heterocycloalkylalkyl, alkylheterocycloalkyl, haloheterocycloalkyl, cycloalkyl, cycloalkylalkyl, alkylcycloalkyl, halocycloalkyl, cycloalkylamino, aryl, arylalkyl, alkylaryl, haloaryl, cyano, hydroxy, oxo, haloalkyl, alkylcarbonyl, alkoxy, haloalkoxy, alkoxyalkyl, alkoxycarbonyl, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, aminoalkylamino, alkoxyalkylamino, alkylcarbonylamino, alkoxycarbonylamino, hydroxyalkyl, hydroxyalkoxyalkyl or hydroxyalkylamino; and

(i) A_1 is -N-, A^2 is -N- and A_3 is -CH-;

(ii) A_1 is -N-, A_2 is -C- and A_3 is -O-; or

(iii) A_1 is -CH-, A_2 is -C- and A_3 is -O-;

or a pharmaceutically acceptable salt thereof;

provided that

2-(4,7-diazaspiro[2.5]octan-7-yl)-7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)thiazolo[3,2-a]pyrimidin-5-one;

is excluded.

2. A compound according to claim 1, wherein R^1 is heterocylcoalkyl optionally substituted with one or two substituents independently selected from R^4.

3. A compound according to claim 1 or 2, wherein R^1 is piperazin-1-yl, 1,2,3,6-tetrahydropyridin-4-yl, 4,7-diazaspiro[2.5]octan-7-yl, (8aS)-3,4,6,7,8,8a-hexahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl, 3,8-diazabicyclo[3.2.1]octan-8-yl, (8aR)-3,4,6,7,8,8a-hexahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl, (1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl, , 2,3,3a,4,6,6a-hexahydro-1H-pyrrolo[3,4-c]pyrrol-5-yl, pyrrolidin-1-yl, 2,8-diazaspiro[4.5]decan-2-yl, (7R)-4-azaspiro[2.5]octan-7-yl, (7S)-4-azaspiro[2.5]octan-7-yl, 4-piperidyl, [rac-(1R,5S)-9-oxa-3-azabicyclo[3.3.1]nonan-7-yl], [rac-(1S,5R)-9-oxa-3-azabicyclo[3.3.1]nonan-7-yl or [rac-(1S,5R)-3-azabicyclo[3.1.0]hexan-6-yl], and wherein R^1 is optionally substituted with one or two substituents independently selected from R^4.

4. A compound according to any one of claims 1 to 3, wherein R^1 is piperazin-1-yl, 4-piperidyl, pyrrolidin-1-yl, 1,2,3,6-tetrahydropyridin-4-yl, (7S)-4-azaspiro[2.5]octan-7-yl, (7R)-4-azaspiro[2.5]octan-7-yl or (8aR)-3,4,6,7,8,8a-hexahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl, and wherein R^1 is optionally substituted with one or two substituents independently selected from R^4.

5. A compound according to any one of claims 1 to 4, wherein R^2 is hydrogen, cycloalkyl, alkenyl, halogen, alkyl, haloalkyl, haloalkoxy or alkoxy.

6. A compound according to any one of claims 1 to 5, wherein R^2 is hydrogen, cyclopropyl, isopropenyl, fluoro, methyl, ethyl, isopropyl, trifluoromethyl, difluoromethoxy or methoxy.

7. A compound according to any one of claims 1 to 5, wherein R^2 is alkyl, haloalkyl or alkoxy.

8. A compound according to any one of claims 1 to 7, wherein R^2 is methyl, ethyl, trifluoromethyl or methoxy.

9. A compound according to any one of claims 1 to 8, wherein R^3 is alkyl or halogen.

10. A compound according to any one of claims 1 to 9, wherein R^3 is methyl or chloro.

11. A compound according to any one of claims 1 to 10, wherein R^4 is halogen, alkyl or heterocycloalkyl.

12. A compound according to any one of claims 1 to 11, wherein R^4 is fluoro, methyl or pyrrolidinyl.

13. A compound according to any one of claims 1 to 12, wherein A_1 is -N-, A^2 is -N- and A_3 is -CH-.

14. A compound according to any one of claims 1 to 13, wherein A_1 is -N-, A_2 is -C- and A_3 is -O-.

15. A compound according to any one of claims 1 to 14, wherein A_1 is -CH-, A_2 is -C- and A_3 is -O-.

16. A compound according to any one of claims 1 to 15 selected from

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-(3,3-dimethylpiperazin-1-yl)thiazolo[3,2-a]pyrimidin-5-one;

7-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(3S)-3-methylpiperazin-1-yl]thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(3R)-3-methylpiperazin-1-yl]thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-(3,5-dimethylpiperazin-1-yl)thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(8aS)-3,4,6,7,8,8a-hexahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl]thiazolo[3,2-a]pyrimidin-5-one;

7-(2-methylimidazo[1,2-b]pyridazin-6-yl)-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

7-[2-methyl-8-(trifluoromethyl)imidazo[1,2-b]pyridazin-6-yl]-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

7-(8-ethyl-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

2-(3,8-diazabicyclo[3.2.1]octan-8-yl)-7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(8aR)-3,4,6,7,8,8a-hexahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl]thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]thiazolo[3,2-a]pyrimidin-5-one;

2-(2,3,3a,4,6,6a-hexahydro-1H-pyrrolo[3,4-c]pyrrol-5-yl)-7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)thiazolo[3,2-a]pyrimidin-5-one;

7-(8-cyclopropyl-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

7-(8-isopropenyl-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

7-(2,7-dimethyloxazolo[5,4-b]pyridin-5-yl)-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(3S)-3-pyrrolidin-1-ylpyrrolidin-1-yl]thiazolo[3,2-a]pyrimidin-5-one;

2-(2,8-diazaspiro[4.5]decan-2-yl)-7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)thiazolo[3,2-a]pyrimidin-5-one;

7-(8-isopropyl-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-(4-piperidyl)thiazolo[3,2-a]pyrimidin-5-one;

7-[2-methyl-8-(trifluoromethyl)imidazo[1,2-b]pyridazin-6-yl]-2-[(8aR)-3,4,6,7,8,8a-hexahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl]thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-(4-fluoro-4-piperidyl)thiazolo[3,2-a]pyrimidin-5-one;

7-[8-(difluoromethoxy)-2-methyl-imidazo[1,2-b]pyridazin-6-yl]-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

7-[2-methyl-7-(trifluoromethyl)oxazolo[5,4-b]pyridin-5-yl]-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-(4-piperidyl)thiazolo[3,2-a]pyrimidin-5-one;

7-(2,7-dimethyloxazolo[5,4-b]pyridin-5-yl)-2-(4-piperidyl)thiazolo[3,2-a]pyrimidin-5-one;

7-(2-chloro-8-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-(4-piperidyl)thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(3R,4R)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(3S,4S)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one;

7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-[(3R,4R)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one;

7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-[(3S,4S)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(7S)-4-azaspiro[2.5]octan-7-yl]thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(7R)-4-azaspiro[2.5]octan-7-yl]thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(3S,4R)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(3R,4S)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one;

7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-[(7S)-4-azaspiro[2.5]octan-7-yl]thiazolo[3,2-a]pyrimidin-5-one;

7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-[(7R)-4-azaspiro[2.5]octan-7-yl]thiazolo[3,2-a]pyrimidin-5-one;

2-(4-fluoro-4-piperidyl)-7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)thiazolo[3,2-a]pyrimidin-5-one;

7-(2-chloro-8-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-[(3R,4R)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one or 7-(2,7-dimethyloxazolo[5,4-b]pyridin-5-yl)-2-[(3S,4S)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one;

7-(2,7-dimethyloxazolo[5,4-b]pyridin-5-yl)-2-[(3R,4R)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one or 7-(2,7-dimethyloxazolo[5,4-b]pyridin-5-yl)-2-[(3S,4S)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one;

7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-[(3S,4R)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one; and

7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-[(3R,4S)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one;

or a pharmaceutically acceptable salt thereof.

17. A compound according to any one of claims 1 to 16 selected from

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(3R)-3-methylpiperazin-1-yl]thiazolo[3,2-a]pyrimidin-5-one;

7-[2-methyl-8-(trifluoromethyl)imidazo[1,2-b]pyridazin-6-yl]-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

7-(8-ethyl-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(8aR)-3,4,6,7,8,8a-hexahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl]thiazolo[3,2-a]pyrimidin-5-one;

7-(2,7-dimethyloxazolo[5,4-b]pyridin-5-yl)-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-(4-piperidyl)thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-(4-fluoro-4-piperidyl)thiazolo[3,2-a]pyrimidin-5-one;

7-[8-(difluoromethoxy)-2-methyl-imidazo[1,2-b]pyridazin-6-yl]-2-piperazin-1-yl-thiazolo[3,2-a]pyrimidin-5-one;

7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-(4-piperidyl)thiazolo[3,2-a]pyrimidin-5-one;

7-(2,7-dimethyloxazolo[5,4-b]pyridin-5-yl)-2-(4-piperidyl)thiazolo[3,2-a]pyrimidin-5-one;

7-(2-chloro-8-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-(4-piperidyl)thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(3R,4R)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(3S,4S)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one;

7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-[(3R,4R)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one ;

7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-[(3S,4S)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(7S)-4-azaspiro[2.5]octan-7-yl]thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(7R)-4-azaspiro[2.5]octan-7-yl]thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(3S,4R)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one;

7-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-[(3R,4S)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one;

7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-[(7S)-4-azaspiro[2.5]octan-7-yl]thiazolo[3,2-a]pyrimidin-5-one;

7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-[(7R)-4-azaspiro[2.5]octan-7-yl]thiazolo[3,2-a]pyrimidin-5-one;

2-(4-fluoro-4-piperidyl)-7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)thiazolo[3,2-a]pyrimidin-5-one;

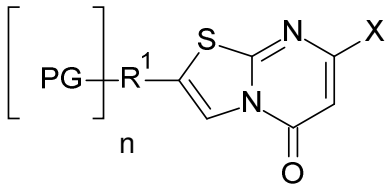
7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-[(3S,4R)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one; and

7-(8-methoxy-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-2-[(3R,4S)-3-fluoro-4-piperidyl]thiazolo[3,2-a]pyrimidin-5-one;

or a pharmaceutically acceptable salt thereof.

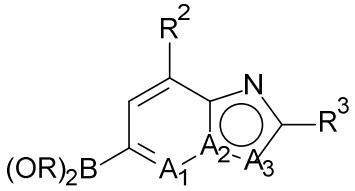
18. A process for the preparation of a compound according to any one of claims 1 to 17, comprising at least one of the following steps:

(a) the reaction of a compound of formula (B1)



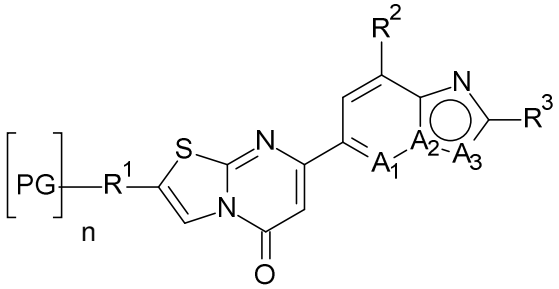
(B1)

with a compound of formula (B2)



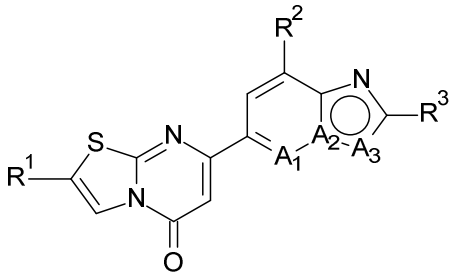
(B2)

in a suitable solvent in the presence of a base and a suitable palladium catalyst, wherein n is 0 or 1, X is O-tosylate, O-triflate, O-mesylate or halogen, and wherein in $-B(OR)_2$ each R is independently selected from hydrogen and alkyl, or $-B(OR)_2$ is optionally substituted dioxaborolanyl, to arrive at a compound of fomula (B3)



(B3)

(b) the reaction of the compound of formula (B3), wherein n is 1, in a suitable solvent and in presence of an acid to yield the compound of formula (I)



(I)

wherein in the process R^1, R^2, R^3, R^4, A_1, A_2 and A_3 are as defined in any one of claims 1 to 13, and PG is a protecting group.

19. A compound according to any one of claims 1 to 17, when manufactured according to a process of claim 18.

20. A compound according to any one of claims 1 to 17 for use as therapeutically active substance.

21. A pharmaceutical composition comprising a compound according to any one of claims 1 to 17 and a therapeutically inert carrier.

22. A compound according to any one of claims 1 to 17 for use in the treatment or prophylaxis of a neurodegenerative disease, in particular Huntington's disease.

23. The use of a compound according to any one of claims 1 to 17 for the treatment or prophylaxis of a neurodegenerative disease, in particular Huntington's disease;

24. The use of a compound according to any one of claims 1 to 17 for the preparation of a medicament for the treatment or prophylaxis of a neurodegenerative disease, in particular Huntington's disease.

25. A method for the treatment or prophylaxis of a neurodegenerative disease, in particular Huntington's disease, which method comprises administering an effective amount of a compound according to any one of claims 1 to 17 to a patient in need thereof.