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(54) Title **PYRIDINE-2-AMIDES USEFUL AS CB2 AGONISTS**

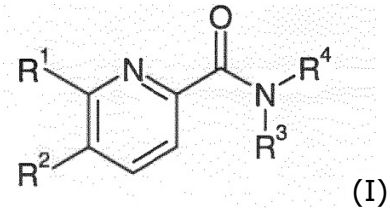
(56) References Cited:

WO-A1-2012/032018 WO-A1-2012/168350 WO-A2-2008/040649
DUBOIS K J ET AL: "A New Pathway to Substituted 6-Chloro-2-pyridinecarboxylic Acid Derivatives from the Reaction of 4,6-Dichloro-2-oxa-5-azabicyclo[2.2.2]oct- 5-en-3-ones with Nucleophiles", TETRAHEDRON, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 52, no. 20, 13 May 1996 (1996-05-13), pages 6997-7002, XP004103942, ISSN: 0040-4020, DOI: 10.1016/0040-4020(96)00304-3

Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of the application/patent granted at the EPO. In matters concerning the validity of the patent, language of the application/patent granted at the EPO will be used as the basis for the decision. The patent documents published by the EPO are available through Espacenet (http://worldwide.espacenet.com) or via the search engine on our website here: https://search.patentstyret.no/

PATENTKRAV

1. Forbindelse med formel (I):



(I)

hvori

R^1 er sykloalkylalkoksy, halofenyl, tetrahydrofuranylalkoksy, halofenylalkyl, haloalkyloksy, alkylsulfonyl, tetrahydropyranylalkoksy eller halogen;

R^2 er alkyl, pyrrolidinyl, sykloalkyl, haloazetidinyl, haloalkyl, sykloalkylalkoksy, haloalkyloksy, halosykloalkyl, hydroksysykloalkyl eller halooksetanyl;

én av R^3 og R^4 er alkyl, sykloalkyl, haloalkyl eller hydroksyalkyl, og den andre er alkyl, alkyloksyalkyl, (haloazetidinyl)(sykloalkyloksy)pyridinylkarbonyloksyalkyl, haloalkylsykloalkyl, hydroksyalkyl, fenylalkyl, alkoksykarbonylalkyl, karboksyalkyl, alkylaminokarbonylalkyl, (alkyloksadiazolyl)(sykloalkylalkyl)alkyl, (alkyloksadiazolyl)(sykloalkyl)alkyl, pyridazinylalkyl, aminokarbonylalkyl, alkyloksadiazolylalkyl, alkyltetrazolylalkyl, formyl, fenyl, dialkylpyrazolyl, alkylkarbonylpiperidinyl eller sykloalkylalkyl;

eller R^3 og R^4 sammen med nitrogenatomet som de er bundet til, danner heterosyklyl eller substituert heterosyklyl;

hvori heterosyklyl er 6-oksa-1-aza-spiro[3.3]heptyl, oksazolidinyl, morfolinyl, pyrrolidinyl, piperazinyl, 2-oksa-5-aza-spiro[3.4]oktyl, piperidinyl, 6-aza-bisyklo[3.2.1.]oktyl, imidazolidinyl, 4-aza-spiro[2.4]heptyl, 2-aza-bisyklo[2.2.1]heptyl, 2-tia-5-aza-bisyklo[2.2.1]heptyl, 2,5-diazabisyklo[2.2.1]heptyl, 2-oksa-5-aza-bisyklo[2.2.1]heptyl, heksahydro-furo[2,3-c]pyrrolyl, 2-tia-6-aza-spiro[3.3]heptyl, 1,8-diaza-spiro[4.5]decyl, 1-oksa-7-aza-spiro[4.4)nonyl, 5-oksa-2-aza-spiro[3.4]oktyl, 8-oksa-3-aza-bisyklo[3.2.1]oktyl, 3-oksa-8-aza-bisyklo[3.2.1]oktyl, tiomorfolinyl, tiazolidinyl, 5-aza-spiro[3.4]oktyl, azetidinyl, 5-aza-spiro[2.4]heptyl, 3-aza-bisyklo[3.1.0]heksyl eller 5-aza-spiro[2.4]heptyl, 1,3,3a,4,6,6a-heksahydrofuro[3,4-c]pyrrolyl; og

hvori substituert heterosyklyl er heterosyklyl substituert med én til fire

substituenter uavhengig valgt blant alkyl, okso, hydroksyl, karboksyl, alkylkarbonylamino, alkyloksyalkyl, hydroksyalkyl, aminokarbonyl, halogen, fenylalkyl, fenyl, alkoksykarbonyl, sykloalkylalkyl, fenylalkoksykarbonyl, sykloalkyl, halohydroksyalkyl og haloalkyl;

forutsatt at R^3 og R^4 sammen med nitrogenatomet som de er bundet til, ikke danner usubstituert piperidinyl, usubstituert tiomorfolinyl eller hydroksyalkylpyrrolidinyl;

eller et farmasøytisk akseptabelt salt eller ester derav.

2. Forbindelse ifølge krav 1, hvori R^1 er sykloalkylalkoksy, tetrahydrofuranylalkoksy, alkylsulfonyl eller halofenylalkyl.

3. Forbindelse ifølge krav 1 eller 2, hvori R^1 er syklopropylmetoksy, tetrahydrofuranylmetoksy, isobutylsulfonyl eller fluorfenylmetyl.

4. Forbindelse ifølge et hvilket som helst av kravene 1 til 3, hvori R^2 er haloazetidinyl, sykloalkyl eller halosykloalkyl.

5. Forbindelse ifølge et hvilket som helst av kravene 1 til 4, hvori R^2 er difluorazetidinyl, syklopropyl eller fluorsyklobutyl.

6. Forbindelse ifølge et hvilket som helst av kravene 1 til 5, hvori én av R^3 og R^4 er alkyl og den andre er alkyl eller haloalkylsykloalkyl.

7. Forbindelse ifølge et hvilket som helst av kravene 1 til 6, hvori én av R^3 og R^4 er metyl og den andre er tert-butyl eller trifluormetylsyklopropyl.

8. Forbindelse ifølge et hvilket som helst av kravene 1 til 7, hvori R^3 og R^4 sammen med nitrogenatomet som de er bundet til, danner heterosyklyl eller substituert heterosyklyl, hvori heterosyklyl er oksazolidinyl, morfolinyl, pyrrolidinyl, 6-aza-bisyklo[3.2.1.]oktyl, 4-aza-spiro[2.4]heptyl, 2-tia-5-aza-bisyklo[2.2.1]heptyl, 5-aza-spiro[3.4]oktyl, 5-aza-spiro|2.4]heptyl, 1,8-diaza-spiro[4.5]decyl, tiazolidinyl eller 5-aza-spiro[2.4]heptyl, og hvori substituert

heterosyklyl er heterosyklyl substituert med en til tre substituenter uavhengig valgt blant alkyl, hydroksyalkyl, halogen, aminokarbonyl, alkoksykarbonyl, okso eller hydroksyl.

9. Forbindelse ifølge et hvilket som helst av kravene 1 til 8, hvori R^3 og R^4 sammen med nitrogenatomet som de er bundet til, danner heterosyklyl eller substituert heterosyklyl, hvori heterosyklyl er oksazolidinyl, morfolinyl, pyrrolidinyl, 6-aza-bisyklo[3.2.1.]oktyl, 4-aza-spiro[2.4]heptyl, 2-tia-5-aza-bisyklo[2.2.1]heptyl, 5-aza-spiro[3.4]oktyl, 5-aza-spiro|2.4]heptyl, 1,8-diaza-spiro[4.5]decyl, tiazolidinyl eller 5-aza-spiro[2.4]heptyl, og hvori substituert heterosyklyl er heterosyklyl substituert med én til tre substituenter uavhengig valgt blant metyl, hydroksymetyl, fluor, aminokarbonyl, tert-butoksykarbonyl, okso eller hydroksyl.

10. Forbindelse ifølge et hvilket som helst av kravene 1 til 9, hvori R^3 og R^4 sammen med nitrogenatomet som de er bundet til, danner dimetyloksazolidinyl, dimetylmorfolinyl, dimetylpyrrolidinyl, trimetyl-6-aza-bisyklo[3.2.1.]oktyl, (hydroksymetyl)(difluor)pyrrolidinyl, 4-aza-spiro[2.4]heptyl, (aminokarbonyl)(difluor)pyrrolidinyl, 2-tia-5-aza-bisyklo[2.2.1]heptyl, (aminokarbonyl)(dimetyl)pyrrolidinyl, 5-aza-spiro[3.4]oktyl, difluor-5-aza-spiro[2.4]heptyl, 5-aza-spiro[2.4]heptyl, tert-butoksykarbonyl-1,8-diaza-spiro[4.5]decyl, aminokarbonyl-1,1-diokso-1λ6-tiazolidinyl, aminokarbonyl-1,1-diokso-1,3-tiazolidinyl, (aminokarbonyl)(metyl)(hydroksyl)pyrrolidinyl eller (aminokarbonyl)-5-aza-spiro[2.4]heptyl.

11. Forbindelse ifølge et hvilket som helst av kravene 1 til 10, valgt blant
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-tert-butyl-metylamid;
6-syklopropylmetoksy-5 (3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyredimetylamid;
5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karboksylsyre-tert-butyl-metyl-amid;

5-syklopropyl-6-(tetrahydro-furan-2-ylmetoksy)-pyridin-2-karboksylsyre-tert-butyl-metyl-amid;
5-syklopropyl-6-(4-fluor-benzyl)-pyridin-2-karboksylsyre-tert-butyl-metyl-amid;
5-syklopropyl-6-(2-metyl-propan-1-sulfonyl)-pyridin-2-karboksylsyre-tert-butyl-metyl-amid;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-tert-butyl-etyl-amid;
6-syklopropylmetoksy-5-(3,3-difluorazetidin-1-yl)-pyridin-2-karboksylsyre-diisopropylamid;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-(2-metoksy-1,1-dimetyl-etyl)-metyl-amid;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(6-oksa-1-aza-spiro[3.3]hept-1-yl)-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(2-oksa-6-aza-spiro[3.3]hept-6-yl)-metanon;
5-syklopropyl-6-(2,2,2-trifluor-1-metyl-etoksy)-pyridin-2-karboksylsyre-tert-butyl-metyl-amid;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(4,4-dimetyl-oksazolidin-3-yl)metanon;
6-(tetrahydro-furan-2-ylmetoksy)-5-trifluormetyl-pyridin-2-karboksylsyre-tert-butyl-metyl-amid;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-metyl-(1-trifluormetyl-syklopropyl)-amid;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(3,3-dimetyl-morfolin-4-yl)-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(2,2-dimetyl-pyrrolidin-1-yl)-metanon;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-(2-hydroksy-1,1-dimetyl-etyl)-(2-metoksy-etyl)-amid;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-tert-butyl-(2-metoksy-etyl)-amid;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-etyl-

(1-trifluormetyl-syklopropyl)-amid;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-benzyl-(1-trifluormetyl-syklopropyl)-amid;
{tert-butyl-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-amino}-eddiksyreetylester;
{tert-butyl-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-amino}-eddiksyre;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-benzyl-tert-butyl-amid;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-tert-butyl-metylkarbamoylmetyl-amid;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-tert-butyl-dimetylkarbamoylmetyl-amid;
4-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-3,3-dimetyl-piperazin-2-on;
4-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-3,3-dietyl-piperazin-2-on;
[5-syklopropyl-6-(2-metyl-propan-1-sulfonyl)-pyridin-2-yl]-(2,2-dimetyl-pyrrolidin-1-yl)-metanon;
[5-syklopropyl-6-(2-metyl-propan-1-sulfonyl)-pyridin-2-yl]-(4,4-dimetyl-oksazolidin-3-yl)-metanon;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-[(S)-2-syklopropyl-1-(5-metyl-[1,2,4]oksadiazol-3-yl)-etyl]-metyl-amid;
5-syklopropyl-6-(tetrahydro-pyran-4-ylmetoksy)-pyridin-2-karbokylsyre-[syklopropyl-(5-metyl-[1,2,4]oksadiazol-3-yl)-metyl]-metyl-amid;
(+)-6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-metyl-(3-metyl-1-pyridazin-3-yl-butyl)-amid;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-tert-butyl-karbamoylmetyl-amid;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-tert-butyl-(5-metyl-[1,3,4]oksadiazol-2-ylmetyl)-amid;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(3-hydroksy-3-

metyl-pyrrolidin-1-yl)-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(2-oksa-5-aza-spiro[3.4]okt-5-yl)-metanon;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-etyl-(2-metoksy-etyl)-amid;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-tert-butyl-(1-metyl-1H-tetrazol-5-ylmetyl)-amid;
N-{1-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-pyrrolidin-3-yl}-acetamid;
[5-syklopropyl-6-(4-fluor-benzyl)-pyridin-2-yl]-(4,4-dimetyl-piperidin-1-yl)-metanon;
[5-syklopropyl-6-(tetrahydro-furan-2-ylmetoksy)-pyridin-2-yl]-(4,4-dimetyl-piperidin-1-yl)-metanon;
[5-syklopropyl-6-(4-fluor-benzyl)-pyridin-2-yl]-(4,4-dimetyl-oksazolidin-3-yl)-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-((1S,5R)-1,3,3-trimetyl-6-aza-bisyklo[3.2.1]okt-6-yl)-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-((R)-2-metoksymetyl-pyrrolidin-1-yl)-metanon;
(6-klor-5-syklopropylmetoksy-pyridin-2-yl)-(2,2-dimetyl-pyrrolidin-1-yl)-metanon;
(6-syklopropylmetoksy-5-trifluormetoksy-pyridin-2-yl)-(4,4-dimetyl-oksazolidin-3-yl)-metanon;
(6-klor-5-syklopropylmetoksy-pyridin-2-yl)-(4,4-dimetyl-oksazolidin-3-yl)-metanon;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-(1-acetyl-piperidin-4-yl)-syklopropyl-amid;
6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)-N-formyl-N-metylpyridin-2-karboksamid;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-metyl-fenyl-amid;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-((S)-4,4-

difluor-2-hydroksymetyl-pyrrolidin-1-yl)-metanon;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-(1,4-dimetyl-1H-pyrazol-3-yl)-metyl-amid;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(2,2-dimetyl-morfolin-4-yl)-metanon;
(R)-2-tert-butyl-1-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-3-metyl-imidazolidin-4-on;
(4-aza-spiro[2.4]hept-4-yl)-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-metanon;
3-{1-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-piperidin-4-yl}-5,5-dimetyl-pyrrolidin-2-on;
(1S,4R)-2-aza-bisyklo[2.2.1]hept-2-yl-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-metanon;
(S)-1-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-4,4-difluor-pyrrolidin-2-karboksylsyreamid;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(4-hydroksy-4-metyl-piperidin-1-yl)-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(1S,4S)-2-tia-5-aza-bisyklo[2.2.1]hept-5-yl-metanon;
((1S,4S)-5-benzyl-2,5-diaza-bisyklo[2.2.1]hept-2-yl)-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(2-metyl-3-fenyl-piperidin-1-yl)-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(1S,4S)-2-oksa-5-aza-bisyklo[2.2.1]hept-5-yl-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(4-hydroksy-2,2-dimetyl-piperidin-1-yl)-metanon;
1-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-2-fenyl-piperidin-3-karboksylsyreetylester;
(S)-1-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-4,4-difluor-pyrrolidin-2-karboksylsyreamid;
(2S,4S)-1-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-4-fluor-

pyrrolidin-2-karboksylsyreamid;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(heksahydro-furo[2,3-c]pyrrol-5-yl)-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(2,2-diokso-2λ6-tia-6-aza-spiro[3.3]hept-6-yl)-metanon;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-tert-butyl-(2-karbamoyl-etyl)-amid;
(S)-1-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-pyrrolidin-2-karboksylsyreamid;
1-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-1,8-diaza-spiro[4.5]dekan-8-karboksylsyre-tert-butylester;
(S)-1-{5-syklopropyl-6-[(R,S)-1-(tetrahydro-furan-2-yl)metoksy]-pyridin-2-karbonyl}-4,4-difluor-pyrrolidin-2-karboksylsyreamid;
(S)-1-[5-syklopropyl-6-(4-fluor-benzyl)-pyridin-2-karbonyl]-4,4-difluor-pyrrolidin-2-karboksylsyreamid;
(+)-1-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-4,4-dimetyl-pyrrolidin-2-karboksylsyreamid;
(-)-1-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-4,4-dimetyl-pyrrolidin-2-karboksylsyreamid;
(2S,4S)-1-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-4-hydroksy-pyrrolidin-2-karboksylsyreamid;
(2S,4S)-1-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-4-fluor-pyrrolidin-2-karboksylsyreamid;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyresyklopropyl-(5-metyl-[1,3,4]oksadiazol-2-ylmetyl)-amid;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(3-hydroksy-1-oksa-7-aza-spiro[4.4]non-7-yl)-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(7-hydroksy-5-oksa-2-aza-spiro[3.4]okt-2-yl)-metanon;
[5-syklopropyl-6-(2,2,3,3,3-pentafluor-propoksy)-pyridin-2-yl]-(2,2-dimetyl-pyrrolidin-1-yl)-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(1S,5R)-8-

oksa-3-aza-bisyklo[3.2.1]okt-3-yl-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(1R,5S)-3-oksa-8-aza-bisyklo[3.2.1]okt-8-yl-metanon;
(R)-1-[5-syklopropyl-6-(2,2,3,3,3-pentafluor-propoksy)-pyridin-2-karbonyl]-4,4-difluor-pyrrolidin-2-karboksylsyreamid;
1-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-piperidin-2-karboksylsyreamid;
4-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-tiomorfolin-3-karboksylsyreamid;
1-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-4,4-dimetyl-pyrrolidin-2-karboksylsyreamid;
(+)-1-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-piperidin-2-karboksylsyreamid;
(-)-1-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-piperidin-2-karboksylsyreamid;
(-)-4-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-tiomorfolin-3-karboksylsyreamid;
(+)-1-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-4,4-dimetyl-pyrrolidin-2-karboksylsyreamid;
(-)-1-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-4,4-dimetyl-pyrrolidin-2-karboksylsyreamid;
3-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-tiazolidin-4-karboksylsyreamid;
(-)-3-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-tiazolidin-4-karboksylsyreamid;
1-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-4,4-dimetyl-pyrrolidin-2-karboksylsyreamid;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(5-oksa-2-aza-spiro [3.4]okt-2-yl)-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(1-oksa-7-aza-spiro[4.4]non-7-yl)-metanon;
(5-aza-spiro[3.4]okt-5-yl)-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-

pyridin-2-yl]-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(3,3-difluor-azetidin-1-yl)-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(1,1-difluor-5-aza-spiro[2.4]hept-5-yl)-metanon;
(5-aza-spiro[2.4|hept-5-yl)-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-metanon;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyresyklopropylmetyl-metyl-amid;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(4-syklopropylmetyl-piperazin-1-yl)-metanon;
3-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)pyridin-2-karbonyl]-3-aza-bisyklo[3.1.0]heksan-6-karboksylsyreetylester;
1-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-pyrrolidin-2-karboksylsyremetylester;
4-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-piperazin-1-karboksylsyrebenzylester;
3-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-3-aza-bisyklo[3.1.0]heksan-6-karboksylsyre;
1-[5-syklopropyl-6-(4-fluor-benzyl)-pyridin-2-karbonyl]-1,8-diaza-spiro[4.5]dekan-8-karboksylsyre-tert-butylester;
(-)-3-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-tiazolidin-4-karboksylsyreamid;
[5-syklopropyl-6-(4-fluor-benzyl)-pyridin-2-yl]-(1,8-diaza-spiro[4.5]dek-1-yl)-metanon;
1-(6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-pyrrolidin-2-karboksylsyreamid;
(-)-3-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-1,1-diokso-1λ6-tiazolidin-4-karboksylsyreamid;
(1S,4R)-3-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-1-okso-1λ4-tiazolidin-4-karboksylsyreamid;
(1R,4S)-3-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-1-okso-1λ4-

tiazolidin-4-karboksylsyreamid;
(+)-3-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-1,1-diokso-1λ6-tiazolidin-4-karboksylsyreamid;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(3,3,4,4-tetrafluor-pyrrolidin-1-yl)-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(2,6-dimetyl-morfolin-4-yl)-metanon;
(R)-3-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-5,5-dimetyl-tiazolidin-4-karboksylsyreamid;
(S)-1-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-5,5-dimetyl-pyrrolidin-2-karboksylsyreamid;
3-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-tiazolidin-4-karboksylsyreamid;
(2S,4R)-1-[5-syklopropyl-6-(syklopropylmetoksy)pyridin-2-karbonyl]-4-fluorpyrrolidin-2-karboksamid;
3-[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-karbonyl]-1-okso-1,3-tiazolidin-4-karboksamid;
3-[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-karbonyl]-1,1-diokso-1,3-tiazolidin-4-karboksamid;
(2S,4R)-1-[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-karbonyl]-4-fluorpyrrolidin-2-karboksamid;
(-)-3-[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-karbonyl]-1,1-diokso-1,3-tiazolidin-4-karboksamid;
3-[6-(syklopropylmetoksy)-5-(3-metoksyazetidin-1-yl)pyridin-2-karbonyl]-1,1-diokso-1,3-tiazolidin-4-karboksamid;
(2S)-1-[6-(syklopropylmetoksy)-5-(1-hydroksysyklobutyl)pyridin-2-karbonyl]-4,4-difluorpyrrolidin-2-karboksamid;
(2S)-1-[6-(syklopropylmetoksy)-5-(1-fluorsyklobutyl)pyridin-2-karbonyl]-4,4-difluorpyrrolidin-2-karboksamid;
3-[6-(syklopropylmetoksy)-5-(1-hydroksysyklobutyl)pyridin-2-karbonyl]-1,1-diokso-1,3-tiazolidin-4-karboksamid;
(2S)-1-[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-karbonyl]-

4-hydroksy-4-metylpyrrolidin-2-karboksamid;
3-[6-(syklopropylmetoksy)-5-(1-fluorsyklobutyl)pyridin-2-karbonyl]-1,1-diokso-1,3-tiazolidin-4-karboksamid;
(2S)-1-[6-(syklopropylmetoksy)-5-(3-fluoroksetan-3-yl)pyridin-2-karbonyl]-4,4-difluorpyrrolidin-2-karboksamid;
5-[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-karbonyl]-5-azaspiro[2.4]heptan-6-karboksamid;
[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-yl]-[3-(2,2,2-trifluor-1-hydroksyetyl)pyrrolidin-1-yl]metanon;
[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-yl]-[3-(hydroksymetyl)-3-(trifluormetyl)pyrrolidin-1-yl]metanon;
[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-yl]-[3-hydroksy-3-(trifluormetyl)pyrrolidin-1-yl]metanon;
[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-yl]-[3-hydroksy-3-(trifluormetyl)azetidin-1-yl]metanon;
(+)-(2S)-1-[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-karbonyl]-4-hydroksy-4-metylpyrrolidin-2-karboksamid;
[5-syklopropyl-6-(syklopropylmetoksy)pyridin-2-yl]-[3-(2,2,2-trifluor-1-hydroksyetyl)pyrrolidin-1-yl]metanon;
[5-syklopropyl-6-(syklopropylmetoksy)pyridin-2-yl]-[3-(hydroksymetyl)-3-(trifluormetyl)pyrrolidin-1-yl]metanon;
[5-syklopropyl-6-(syklopropylmetoksy)pyridin-2-yl]-[3-hydroksy-3-(trifluormetyl)pyrrolidin-1-yl)metanon;
[5-syklopropyl-6-(syklopropylmetoksy)pyridin-2-yl]-[3-hydroksy-3-(trifluormetyl)azetidin-1-yl]metanon;
(6S)-5-[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-karbonyl]-5-azaspiro[2.4]heptan-6-karboksamid;
[(3aR,6aS)-1,3,3a,4,6,6a-heksahydrofuro[3,4-c]pyrrol-5-yl]-[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-yl]metanon;
(2S)-1-[5-(3,3-difluorazetidin-1-yl)-6-(2-fluoretoksy)pyridin-2-karbonyl]-4,4-difluor-pyrrolidin-2-karboksamid;
[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)-2-pyridyl]-[3-fluor-3-

(hydroksymetyl)azetidin-1-yl]metanon;
[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)-2-pyridyl]-(3-fluor-3-metyl-azetidin-1-yl)metanon;
(3-syklopropyl-3-fluorazetidin-1-yl)-[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-yl]metanon;
(-)-5-[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-karbonyl]-5-azaspiro[2.4]heptan-4-karboksamid; og
(+)-5-[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-karbonyl]-5-azaspiro[2.4]heptan-4-karboksamid.

12. Forbindelse ifølge et hvilket som helst av kravene 1 til 11, valgt blant
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-tert-butyl-metyl-amid;
5-syklopropyl-6-(tetrahydro-furan-2-ylmetoksy)-pyridin-2-karboksylsyre-tert-butyl-metyl-amid;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(4,4-dimetyl-oksazolidin-3-yl)-metanon;
6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyremetyl-(1-trifluormetyl-syklopropyl)-amid;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(3,3-dimetyl-morfolin-4-yl)-metanon;
[5-syklopropyl-6-(2-metyl-propan-1-sulfonyl)-pyridin-2-yl]-(2,2-dimetyl-pyrrolidin-1-yl)-metanon;
[5-syklopropyl-6-(4-fluor-benzyl)-pyridin-2-yl]-(4,4-dimetyl-oksazolidin-3-yl)-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-((1S,5R)-1,3,3-trimetyl-6-aza-bisyklo[3.2.1]okt-6-yl)-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-((S)-4,4-difluor-2-hydroksymetyl-pyrrolidin-1-yl)-metanon;
(4-aza-spiro[2.4]hept-4-yl)-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(1S,4S)-2-tia-

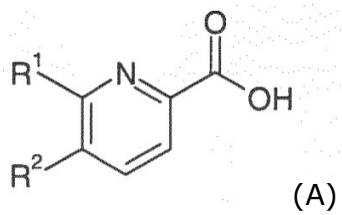
5-aza-bisyklo[2.2.1]hept-5-yl-metanon;
(S)-1-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-4,4-difluor-pyrrolidin-2-karboksylsyreamid;
(-)-1-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karbonyl]-4,4-dimetyl-pyrrolidin-2-karboksylsyreamid;
(5-aza-spiro[3.4]okt-5-yl)-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-metanon;
[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl]-(1,1-difluor-5-aza-spiro[2.4]hept-5-yl)-metanon;
(5-aza-spiro[2.4]hept-5-yl)-[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-yl)-metanon;
1-[5-syklopropyl-6-(4-fluor-benzyl)-pyridin-2-karbonyl]-1,8-diaza-spiro[4.5]dekan-8-karboksylsyre-tert-butylester;
(-)-3-(5-syklopropyl-6-syklopropylmetoksy-pyridin-2-karbonyl)-1,1-diokso-1λ6-tiazolidin-4-karboksylsyreamid;
3-[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-karbonyl]-1,1-diokso-1,3-tiazolidin-4-karboksamid;
(-)-3-[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-karbonyl]-1,1-diokso-1,3-tiazolidin-4-karboksamid;
(2S)-1-[6-(syklopropylmetoksy)-5-(1-hydroksysyklobutyl)pyridin-2-karbonyl]-4,4-difluorpyrrolidin-2-karboksamid;
(2S)-1-[6-(syklopropylmetoksy)-5-(1-fluorsyklobutyl)pyridin-2-karbonyl]-4,4-difluorpyrrolidin-2-karboksamid;
(2S)-1-[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-karbonyl]-4-hydroksy-4-metylpyrrolidin-2-karboksamid;
3-[6-(syklopropylmetoksy)-5-(1-fluorsyklobutyl)pyridin-2-karbonyl] 1,1-diokso-1,3-tiazolidin-4-karboksamid; og
5-[6-(syklopropylmetoksy)-5-(3,3-difluorazetidin-1-yl)pyridin-2-karbonyl]-5-azaspiro[2.4]heptan-6-karboksamid.

13. Forbindelsen 6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-karboksylsyre-2-{[6-syklopropylmetoksy-5-(3,3-difluor-azetidin-1-yl)-pyridin-2-

karbonyl]-metyl-amino}-2-metyl-propylester.

14. Fremgangsmåte for fremstilling av en forbindelse ifølge et hvilket som helst av kravene 1 til 13, som omfatter ett av de følgende trinnene:

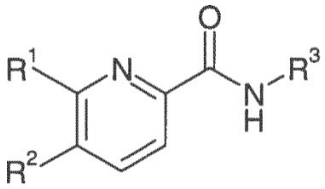
(a) reaksjon av en forbindelse med formel (A)



(A)

i nærværet av NHR^3R^4, et amidbindingsdannende koblingsmiddel og en base; eller

(b) å omsette en forbindelse med formel (B)



(B)

med en forbindelse med formel R^4-X;

hvori R^1 til R^4 er som definert i et hvilket som helst av kravene 1 til 10, og X er en avspaltbar gruppe.

15. Forbindelse ifølge et hvilket som helst av kravene 1 til 13 for anvendelse som terapeutisk aktivt stoff.

16. Farmasøytisk sammensetning som omfatter en forbindelse ifølge et hvilket som helst av kravene 1 til 13, og en terapeutisk inert bærer.

17. Forbindelse ifølge et hvilket som helst av kravene 1 til 13 for anvendelse ved behandling eller profylakse av smerte, aterosklerose, aldersrelatert makuladegenerasjon, diabetisk retinopati, glaukom, retinal veneokklusjon, retinopati hos premature, okulært iskemisk syndrom, geografisk atrofi, diabetes mellitus, betennelse, inflammatorisk tarmsykdom, iskemi-reperfusjonsskade, akutt leversvikt, leverfibrose, lungefibrose, nyrefibrose, systemisk fibrose, akutt

allograftrejeksjon, kronisk allograftnefropati, diabetisk nefropati, glomerulonefropati, kardiomyopati, hjertefeil, myokardiskemi, myokardinfarkt, systemisk sklerose, termisk skade, brenning, hypertrofiske arr, keloider, gingivitt pyreksi, levercirrhose eller svulster, regulering av benmasse, nevrodegenerering, amyotrofisk lateral sklerose, slag, forbigående iskemisk anfall eller uveitt.