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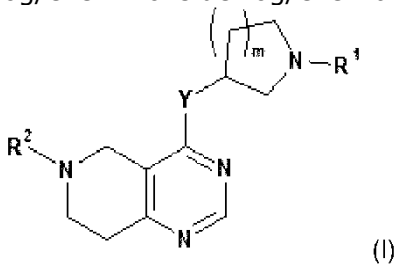
(54) Title **USE OF INHIBITORS OF THE ACTIVITY OR FUNCTION OF PI3K**

(56) References Cited: WO-A1-2008/012326, WO-A1-2009/058361, WO-A1-2010/036908, WO-A2-2010/129816, WO-A1-2012/004299, WO-A2-2005/086814, WO-A2-2008/157191, WO-A1-2010/120991

Patentkrav

1. PI3K-inhibitor, hvori inhibitoren har en inhiberende virkning på PI3K isoform delta, for anvendelse i behandling av en immunpatologi hos et individ som lider av en sykdom eller en lidelse valgt fra akutt og cerebral malaria, via funksjonell inhibering av TLR9 hos det infiserte individet, hvori PI3K-inhibitoren er valgt fra tetrahydro-pyrido-pyrimidin-forbindelser med formel (I) og/eller tautomerer og/eller N-oksider og/eller farmasøytisk akseptable salter derav,



(I)

hvori

Y er valgt fra O eller NR^3;

R^1 er valgt fra fenyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, 1,2,3-triazinyl, 1,2,4-triazinyl, 1,3,5-triazinyl,

eller

-C(O)-R^4

hvori

R^4 er valgt fra C_1-C_8-alkyl, halo-C_1-C_8-alkyl, hydroksy-C_1-C_8-alkyl, C_1-C_8-alkoksy-C_1-C_8-alkyl, C_1-C_8-alkyl-sulfonyl-C_1-C_8-alkyl, heterosyklyl, heterosyklyl-oksy, heterosyklyl-C_1-C_8-alkyl, C_3-C_{12}-sykloalkyl, C_3-C_{12}-sykloalkyl-C_1-C_8-alkyl, heteroaryl, heteroaryl-oksy, heteroaryl-C_1-C_8-alkyl, hydroksy, C_1-C_8-alkoksy, amino, N-C_1-C_8-alkylamino eller N,N-di-C_1-C_8-alkyl-amino,

hvori 'C_1-C_8-alkyl' i N-C_1-C_8-alkyl-amino og N,N-di-C_1-C_8-alkyl-amino kan være usubstituert eller substituert med halogen, hydroksy eller C_1-C_4-alkoksy;

hvori 'C_3-C_{12}-sykloalkyl' i C_3-C_{12}-sykloalkyl og C_3-C_{12}-sykloalkyl-C_1-C_8-alkyl kan være usubstituert eller substituert med 1-5 substituenter uavhengig valgt fra okso, halogen, C_1-C_8-alkyl, halo-C_1-C_8-alkyl, hydroksy-C_1-C_8-alkyl, hydroksyl, C_1-C_8-alkoksy, C_1-C_8-alkoksy-C_1-C_8-alkyl, amino, N-C_1-C_8-alkyl-amino, N,N-di-C_1-C_8-alkylamino, C_1-C_8-alkyl-karbonyl, halo-C_1-C_8-alkyl-karbonyl, hydroksy-C_1-C_8-alkyl-karbonyl eller C_1-C_8-alkoksy-C_1-C_8-alkyl-karbonyl;

hvori 'heterosyklyl' er valgt fra oksiranyl, aziridinyl, oksetanyl, tietanyl, acetitinyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydrotiofenyl, 2,3-dihydrofuranyl,

2,5-dihydrofuranyl, 2,3-dihydrotiofenyl, 1-pyrrolinyl, 2-pyrrolinyl, 3-pyrrolinyl, tetrahydropyranyl, piperidinyl, tetrahydrotiopyranyl, morfolinyl, tiomorfolinyl, piperazinyl, azepanyl, tiepanyl eller oksepanyl; der hver av disse er usubstituert eller substituert med 1-5 substituenter uavhengig valgt fra okso, halogen, C_1-C_8-alkyl, halo-C_1-C_8-alkyl, hydroksy-C_1-C_8-alkyl, hydroksyl, C_1-C_8-alkoksy, C_1-C_8-alkoksy-C_1-C_8-alkyl, amino, N-C_1-C_8-alkyl-amino, N,N-di-C_1-C_8-alkyl-amino, C_1-C_8-alkylkarbonyl, halo-C_1-C_8-alkyl-karbonyl, hydroksy-C_1-C_8-alkyl-karbonyl eller C_1-C_8-alkoksy-C_1-C_8-alkyl-karbonyl;

hvori 'heterosyklyl' kan være festet til et heteroatom eller et karbonatom, og hvor N- og/eller S-heteroatomene eventuelt også kan være oksidert til ulike oksidasjonstilstander;

hvori 'heteroaryl' er valgt fra

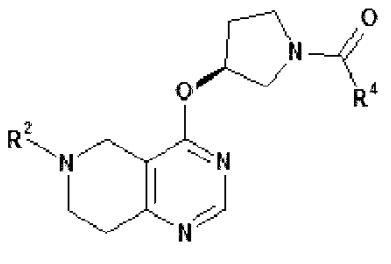
furanyl, tiofenyl, pyrrolyl, imidazolyl, pyrazolyl, tiazolyl, isotiazolyl, oksazolyl, isoksazolyl, 1,2,5-oksadiazolyl, 1,2,4-oksadiazolyl, 1,2,3-oksadiazolyl,1,3,4-oksadiazolyl, 1,2,5-tiadiazolyl, 1,2,4-tiadiazolyl, 1,2,3-tiadiazolyl,1,3,4-tiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, 1,2,3-triazinyl, 1,2,4-triazinyl eller 1,3,5-triazinyl; der hver av disse er usubstituert eller substituert med 1-5 substituenter uavhengig valgt fra halogen, C_1-C_8-alkyl, halo-C_1-C_8-alkyl, hydroksy-C_1-C_8-alkyl, hydroksyl, C_1-C_8-alkoksy, C_1-C_8-alkoksy-C_1-C_8-alkyl, amino, N-C_1-C_8-alkyl-amino, N,N-di-C_1-C_8-alkyl-amino, C_1-C_8-alkyl-karbonyl, halo-C_1-C_8-alkyl-karbonyl, hydroksy-C_1-C_8-alkyl-karbonyl eller C_1-C_8-alkoksy-C_1-C_8-alkyl-karbonyl; hvori 'heteroaryl' kan være festet til et heteroatom eller et karbonatom, og hvor N- og/eller S-heteroatomene eventuelt også kan være oksidert til ulike oksidasjonstilstander;

R^2 er valgt fra fenyl, naftyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, kinolinyl eller isokinolinyl, der hver av disse er usubstituert eller substituert med 1-5 substituenter uavhengig valgt fra halogen, cyano, nitro, C_1-C_8-alkyl, halo-C_1-C_8-alkyl, hydroksy-C_1-C_8-alkyl, hydroksyl, C_1-C_8-alkoksy, C_1-C_8-alkoksy-C_1-C_8-alkyl, amino, N-C_1-C_8-alkyl-amino, N,N-di-C_1-C_8-alkyl-amino, C_1-C_8-alkyl-karbonyl, halo-C_1-C_8-alkyl-karbonyl, hydroksy-C_1-C_8-alkylkarbonyl eller C_1-C_8-alkoksy-C_1-C_8-alkyl-karbonyl;

R^3 er valgt fra H, C_1-C_4-alkyl eller halo-C_1-C_4-alkyl; og

m er valgt fra 0 eller 1.

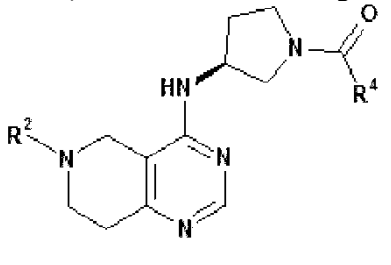
2. PI3K-inhibitor, hvori inhibitoren har en inhiberende virkning på PI3K isoform delta, for anvendelse ifølge krav 1 med formel (Id')



(Id'),

og/eller tautomerer og/eller N-oksider og/eller farmasøytisk akseptable salter derav.

3. PI3K-inhibitor, hvori inhibitoren har en inhiberende virkning på PI3K isoform delta, for anvendelse ifølge krav 1 med formel (Ie')



(Ie'),

og/eller tautomerer og/eller N-oksider og/eller farmasøytisk akseptable salter derav.

4. PI3K-inhibitor, hvori inhibitoren har en inhiberende virkning på PI3K isoform delta, for anvendelse ifølge et hvilket som helst av kravene 1 til 3, hvori

R^2 er valgt fra naftyl, pyridyl eller pyrimidinyl; der hver av disse er usubstituert eller substituert med 1–3 substituenter uavhengig valgt fra halogen, cyano, nitro, C_1-C_8-alkyl, halo-C_1-C_8-alkyl, hydroksy-C_1-C_8-alkyl, hydroksyl, C_1-C_8-alkoksy, C_1-C_8-alkoksy-C_1-C_8-alkyl, amino, N-C_1-C_8-alkyl-amino, N,N-di-C_1-C_8-alkyl-amino, C_1-C_8-alkyl-karbonyl, halo-C_1-C_8-alkyl-karbonyl, hydroksy-C_1-C_8-alkyl-karbonyl eller C_1-C_8-alkoksy-C_1-C_8-alkyl-karbonyl.

5. PI3K-inhibitor, hvori inhibitoren har en inhiberende virkning på PI3K isoform delta, for anvendelse ifølge et hvilket som helst av kravene 1 til 4, hvori

R^1, hvis den er til stede, er -C(O)-R^4, hvori

R^4 er valgt fra heterosyklyl, C_4-C_8-sykloalkyl eller heteroaryl;

hvori 'C_3-C_{12}-sykloalkyl' kan være usubstituert eller substituert med 1–3 substituenter uavhengig valgt fra fluor, C_1-C_4-alkyl, hydroksyl, C_1-C_4-alkoksy;

hvori 'heterosyklyl' er valgt fra pyrrolidinyl, tetrahydropyranyl, piperidinyl, tetrahydrotiopyranyl, morfolinyl eller piperazinyl; der hver av disse er usubstituert eller substituert med 1–3 substituenter uavhengig valgt fra okso, halogen, C_1-C_4-alkyl, hydroksyl, C_1-C_4-alkyl-karbonyl;

hvori 'heterosyklyl' kan være festet til et heteroatom eller et karbonatom, og hvor N- og/eller S-heteroatomene eventuelt også kan være oksidert til ulike oksidasjonstilstander;

hvori 'heteroaryl' er valgt fra

furanyl, imidazolyl, pyrazolyl, tiazolyl, oksazolyl, isoksazolyl, 1,3,4-oksadiazyolyl, pyridyl, pyrazinyl; der hver av disse er usubstituert eller substituert med 1–3 substituenter uavhengig valgt fra C_1-C_4-alkyl, hydroksyl;

hvori 'heteroaryl' kan være festet til et heteroatom eller et karbonatom, og hvor N- og/eller S-heteroatomene eventuelt også kan være oksidert til forskjellige oksideringstilstander.

6. PI3K-inhibitor, hvori inhibitoren har en inhiberende virkning på PI3K isoform delta, for anvendelse ifølge et hvilket som helst av kravene 1 til 4, hvori

R^1, hvis den er til stede, er -C(O)-R^4, og

R^4 er valgt fra C_1-C_8-alkyl, C_1-C_8-alkoksy-C_1-C_8-alkyl, C_1-C_8-alkoksy eller N,N-di-C_1-C_8-alkyl-amino,

hvori 'C_1-C_8-alkyl' i N,N-di-C_1-C_8-alkyl-amino kan være usubstituert eller substituert med halogen, hydroksy eller C_1-C_4-alkoksy.

7. PI3K-inhibitor, hvori inhibitoren har en inhiberende virkning på PI3K isoform delta, for anvendelse ifølge krav 1, hvori PI3K-inhibitoren er valgt fra gruppen bestående av

{(S)-3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(tetrahydro-pyran-4-yl)-metanon;

{3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(tetrahydro-pyran-4-yl)-metanon;

{(S)-3-[6-(2,4-Dimetoksy-pyrimidin-5-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(tetrahydro-pyran-4-yl)-metanon;

{3-[6-(2,4-Dimetoksy-pyrimidin-5-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(tetrahydro-pyran-4-yl)-metanon;

2-Metoksy-5-{4-[(S)-1-(tetrahydro-pyran-4-karbonyl)-pyrrolidin-3-yloksy]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-nikotinonitril;

2-Metoksy-5-{4-[1-(tetrahydro-pyran-4-karbonyl)-pyrrolidin-3-yloksy]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-nikotinonitril;

1-{(S)-3-[6-(5,6-Dimetoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-propan-1-on;

1-{3-[6-(5,6-Dimetoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-propan-1-on;

{(S)-3-[6-(5,6-Dimetoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(tetrahydro-pyran-4-yl)-metanon;

{3-[6-(5,6-Dimetoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(tetrahydro-pyran-4-yl)-metanon;

2-Amino-5-{4-[(S)-1-(tetrahydro-pyran-4-karbonyl)-pyrrolidin-3-yloksy]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-nikotinonitril;

2-Amino-5-{4-[1-(tetrahydro-pyran-4-karbonyl)-pyrrolidin-3-yloksy]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-nikotinonitril;

(S)-(3-(6-(5-Fluor-6-metoksypyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(tetrahydro-2H-pyran-4-yl)metanon;

(3-(6-(5-Fluor-6-metoksypyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(tetrahydro-2H-pyran-4-yl)metanon;

(S)-2-Metoksy-5-(4-(1-(2-metoksyacetyl)pyrrolidin-3-yloksy)-7,8-dihydropyrido[4,3-d]pyrimidin-6(5H)-yl)nikotinonitril;

2-Metoksy-5-(4-(1-(2-metoksyacetyl)pyrrolidin-3-yloksy)-7,8-dihydropyrido[4,3-d]pyrimidin-6(5H)-yl)nikotinonitril;

(S)-5-(4-(1-(Syklopentankarbonyl)pyrrolidin-3-yloksy)-7,8-dihydropyrido[4,3-d]pyrimidin-6(5H)-yl)-2-metoksynikotinonitril;

5-(4-(1-(Syklopentankarbonyl)pyrrolidin-3-yloksy)-7,8-dihydropyrido[4,3-d]pyrimidin-6(5H)-yl)-2-metoksynikotinonitril;

(2,4-Dimetyl-oksazol-5-yl)-{(S)-3-[6-(6-metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;

(2,4-Dimetyl-oksazol-5-yl)-{3-[6-(6-metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;

Furan-3-yl-{(S)-3-[6-(6-metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;

Furan-3-yl-{3-[6-(6-metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;

Furan-3-yl-{(S)-3-[6-(6-metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;

Furan-3-yl-{3-[6-(6-metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;

{(S)-3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(3-metyl-3H-imidazol-4-yl)-metanon;

{3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(3-metyl-3H-imidazol-4-yl)-metanon;

{(S)-3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(2-metyl-oksazol-4-yl)-metanon;

{3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(2-metyl-oksazol-4-yl)-metanon;

(3-Metoksy-syklobutyl)-{(S)-3-[6-(6-metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;

(3-Metoksy-syklobutyl)-{3-[6-(6-metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;

({(S)-3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-oksazol-4-yl-metanon;

({3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-oksazol-4-yl-metanon;

1-(4-{(S)-3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-karbonyl}-piperidin-1-yl)-etanon;

1-(4-{3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-karbonyl}-piperidin-1-yl)-etanon;

{(S)-3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(4-metyl-oksazol-5-yl)-metanon;

{3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(4-metyl-oksazol-5-yl)-metanon;

5-{(S)-3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-karbonyl}-1H-pyridin-2-on;

5-{3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-karbonyl}-1H-pyridin-2-on;

{(S)-3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(1-metyl-1H-imidazol-4-yl)-metanon;

{3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(1-metyl-1H-imidazol-4-yl)-metanon;

{(S)-3-[6-(5,6-Dimetoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-oksazol-4-yl-metanon;

{3-[6-(5,6-Dimetoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-oksazol-4-yl-metanon;

{(S)-3-[6-(5,6-Dimetoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-oksazol-5-yl-metanon;

{3-[6-(5,6-Dimetoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-oksazol-5-yl-metanon;
{(S)-3-[6-(5,6-Dimetoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(2-metyl-oksazol-4-yl)-metanon;
{3-[6-(5,6-Dimetoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(2-metyl-oksazol-4-yl)-metanon;
{(S)-3-[6-(5,6-Dimetoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(2,2-dimetyl-tetrahydro-pyran-4-yl)-metanon;
{3-[6-(5,6-Dimetoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(2,2-dimetyl-tetrahydro-pyran-4-yl)-metanon;
{(S)-3-[6-(5,6-Dimetoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(2,4-dimetyl-oksazol-5-yl)-metanon;
{3-[6-(5,6-Dimetoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(2,4-dimetyl-oksazol-5-yl)-metanon;
(4,4-Difluor-sykloheksyl)-{(S)-3-[6-(5,6-dimetoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;
(4,4-Difluor-sykloheksyl)-{3-[6-(5,6-dimetoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;
2-Metoksy-5-{4-[(S)-1-(2-tetrahydro-pyran-4-yl-acetyl)-pyrrolidin-3-yloksy]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-nikotinonitril;
2-Metoksy-5-{4-[1-(2-tetrahydro-pyran-4-yl-acetyl)-pyrrolidin-3-yloksy]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-nikotinonitril;
5-{4-[(S)-1-(2,4-Dimetyl-oksazol-5-karbonyl)-pyrrolidin-3-yloksy]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-2-metoksy-nikotinonitril;
5-{4-[1-(2,4-Dimetyl-oksazol-5-karbonyl)-pyrrolidin-3-yloksy]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-2-metoksy-nikotinonitril;
5-{4-[(S)-1-(2,2-Dimetyl-tetrahydro-pyran-4-karbonyl)-pyrrolidin-3-yloksy]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-2-metoksy-nikotinonitril;
5-{4-[1-(2,2-Dimetyl-tetrahydro-pyran-4-karbonyl)-pyrrolidin-3-yloksy]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-2-metoksy-nikotinonitril;
{(S)-3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(5-metyl-oksazol-4-yl)-metanon;
{3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(5-metyl-oksazol-4-yl)-metanon;
{(S)-3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(5-metyl-isoksazol-4-yl)-metanon;

{3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(5-metyl-isoksazol-4-yl)-metanon;
{(S)-3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(3-metyl-isoksazol-4-yl)-metanon;
{3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(3-metyl-isoksazol-4-yl)-metanon;
{(S)-3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(3-metyl-isoksazol-4-yl)-metanon;
{3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(3-metyl-isoksazol-4-yl)-metanon;
Isoksazol-3-yl-{(S)-3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;
Isoksazol-3-yl-{3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;
Isoksazol-5-yl-{(S)-3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;
Isoksazol-5-yl-{3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;
2-Metoksy-5-{4-[(S)-1-(tiazol-4-karbonyl)-pyrrolidin-3-yloksy]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-nikotinonitril;
2-Metoksy-5-{4-[1-(tiazol-4-karbonyl)-pyrrolidin-3-yloksy]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-nikotinonitril;
2-Metoksy-5-{4-[(S)-1-(1-metyl-1H-pyrazol-4-karbonyl)-pyrrolidin-3-yloksy]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-nikotinonitril;
2-Metoksy-5-{4-[1-(1-metyl-1H-pyrazol-4-karbonyl)-pyrrolidin-3-yloksy]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-nikotinonitril;
2-Metoksy-5-{4-[(S)-1-(1-metyl-1H-pyrazol-3-karbonyl)-pyrrolidin-3-yloksy]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-nikotinonitril;
2-Metoksy-5-{4-[1-(1-metyl-1H-pyrazol-3-karbonyl)-pyrrolidin-3-yloksy]-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl}-nikotinonitril;
(2,2-Dimetyl-tetrahydro-pyran-4yl)-{(S)-3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;
(2,2-Dimetyl-tetrahydro-pyran-4yl)-{3-[6-(6-Metoksy-5-metyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;
(1,1-Diokso-heksahydro-1lambda*6*-tiopyran-4-yl)-{(S)-3-[6-(6-metoksy-5-trifluormetyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;

(1,1-Diokso-heksahydro-1lambda*6*-tiopyran-4-yl)-{3-[6-(6-metoksy-5-trifluormetyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-metanon;

(S)-(2,4-Dimetyloksazol-5-yl)(3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)metanon;

(2,4-Dimetyloksazol-5-yl)(3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)metanon;

(S)-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(tiazol-5-yl)metanon;

(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(tiazol-5-yl)metanon;

(S)-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(1-metyl-1H-pyrazol-5-yl)metanon;

(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(1-metyl-1H-pyrazol-5-yl)metanon;

4-((S)-3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-karbonyl)pyrrolidin-2-on;

4-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-karbonyl)pyrrolidin-2-on;

(S)-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(pyridin-3-yl)metanon;

(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(pyridin-3-yl)metanon;

(S)-(1H-Imidazol-4-yl)(3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)metanon;

(1H-Imidazol-4-yl)(3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)metanon;

5-((S)-3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-karbonyl)pyrrolidin-2-on;

5-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-karbonyl)pyrrolidin-2-on;

(S)-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(pyridin-4-yl)metanon;

(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(pyridin-4-yl)metanon;
(S)-(1,3-Dimetyl-1H-pyrazol-4-yl)(3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)metanon;
(1,3-Dimetyl-1H-pyrazol-4-yl)(3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)metanon;
(S)-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(1H-pyrazol-4-yl)metanon;
(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(1H-pyrazol-4-yl)metanon;
(S)-(3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(5-metyl-1,3,4-oksadiazol-2-yl)metanon;
(3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(5-metyl-1,3,4-oksadiazol-2-yl)metanon;
(S)-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(pyrazin-2-yl)metanon;
(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(pyrazin-2-yl)metanon;
(S)-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(1-metyl-1H-imidazol-4-yl)metanon;
(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(1-metyl-1H-imidazol-4-yl)metanon;
{(S)-3-[6-(6-Metoksy-5-trifluormetyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(1-metyl-1H-pyrazol-4-yl)-metanon;
{3-[6-(6-Metoksy-5-trifluormetyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(1-metyl-1H-pyrazol-4-yl)-metanon;
{(S)-3-[6-(6-Metoksy-5-trifluormetyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-tiazol-4-yl-metanon;
{3-[6-(6-Metoksy-5-trifluormetyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-tiazol-4-yl-metanon;
{(S)-3-[6-(5-Klor-6-metoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(tetrahydro-pyran-4-yl)-metanon;

{3-[6-(5-Klor-6-metoksy-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(tetrahydro-pyran-4-yl)-metanon;

(S)-(3-(6-(6-Amino-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(tetrahydro-2H-pyran-4-yl)metanon;

(3-(6-(6-Amino-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(tetrahydro-2H-pyran-4-yl)metanon;

(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)azetidin-1-yl)(tetrahydro-2H-pyran-4-yl)metanon;

{(S)-3-[6-(2-Metoksy-pyrimidin-5-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(tetrahydro-pyran-4-yl)-metanon;

{3-[6-(2-Metoksy-pyrimidin-5-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(tetrahydro-pyran-4-yl)-metanon;

[(S)-3-(6-Kinolin-3-yl-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy)-pyrrolidin-1-yl]-(tetrahydro-pyran-4-yl)-metanon;

[3-(6-Kinolin-3-yl-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy)-pyrrolidin-1-yl]-(tetrahydro-pyran-4-yl)-metanon;

(S)-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(tetrahydro-2H-pyran-4-yl)metanon;

(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(tetrahydro-2H-pyran-4-yl)metanon;

(S)-1-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)-3,3-dimetylbutan-1-on;

1-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)-3,3-dimetylbutan-1-on;

1-{(S)-3-[6-(6-Metoksy-5-trifluormetyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-propan-1-on;

1-{3-[6-(6-Metoksy-5-trifluormetyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-propan-1-on;

2-Metoksy-5-[4-((S)-1-propionyl-pyrrolidin-3-yloksy)-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl]-nikotinonitril;

2-Metoksy-5-[4-(1-propionyl-pyrrolidin-3-yloksy)-7,8-dihydro-5H-pyrido[4,3-d]pyrimidin-6-yl]-nikotinonitril;

(S)-6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-4-(1-(pyridin-2-yl)pyrrolidin-3-yloksy)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidine;

6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-4-(1-(pyridin-2-yl)pyrrolidin-3-yloksy)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidine;
(S)-6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-4-(1-(pyrimidin-2-yl)pyrrolidin-3-yloksy)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidine;
6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-4-(1-(pyrimidin-2-yl)pyrrolidin-3-yloksy)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidine;
(S)-1-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)propan-1-on;
1-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)propan-1-on;
(S)-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)(tetrahydro-2H-pyran-4-yl)metanon;
(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)(tetrahydro-2H-pyran-4-yl)metanon;
(S)-2-Metoksy-5-(4-(1-(tetrahydro-2H-pyran-4-karbonyl)pyrrolidin-3-ylamino)-7,8-dihydropyrido[4,3-d]pyrimidin-6(5H)-yl)nikotinonitril;
2-Metoksy-5-(4-(1-(tetrahydro-2H-pyran-4-karbonyl)pyrrolidin-3-ylamino)-7,8-dihydropyrido[4,3-d]pyrimidin-6(5H)-yl)nikotinonitril;
(S)-1-(4-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-karbonyl)piperidin-1-yl)etanon;
1-(4-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-karbonyl)piperidin-1-yl)etanon;
(2,2-Dimetyltetrahydro-2H-pyran-4-yl)((S)-3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)metanon;
(2,2-Dimetyltetrahydro-2H-pyran-4-yl)(3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)metanon;
(S)-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)(oksazol-5-yl)metanon;
(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)(oksazol-5-yl)metanon;

((S)-3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)((1s,4R)-4-metoksysykloheksyl)metanon;

(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)((1s,4R)-4-metoksysykloheksyl)metanon;

((S)-3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)((1r,4S)-4-metoksysykloheksyl)metanon;

(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)((1r,4S)-4-metoksysykloheksyl)metanon;

((1s,4R)-4-Hydroksysykloheksyl)((S)-3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)metanon;

((1s,4R)-4-Hydroksysykloheksyl)(3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)metanon;

((1r,4S)-4-Hydroksysykloheksyl)((S)-3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)metanon;

((1r,4S)-4-Hydroksysykloheksyl)(3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)metanon;

(S)-(3-(6-(6-Metoksy-5-metylpyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)(1-metyl-1H-imidazol-4-yl)metanon;

(3-(6-(6-Metoksy-5-metylpyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)(1-metyl-1H-imidazol-4-yl)metanon;

(S)-(3-(6-(6-Metoksy-5-metylpyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)(oksazol-5-yl)metanon;

(3-(6-(6-Metoksy-5-metylpyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)(oksazol-5-yl)metanon;

(S)-(3-(6-(6-Metoksy-5-metylpyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)(oksazol-4-yl)metanon;

(3-(6-(6-Metoksy-5-metylpyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)(oksazol-4-yl)metanon;

(2,2-Dimetyltetrahydro-2H-pyran-4-yl)((S)-3-(6-(6-metoksy-5-metylpyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)metanon;

(2,2-Dimetyltetrahydro-2H-pyran-4-yl)(3-(6-(6-metoksy-5-metylpyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)metanon;

(S)-1-(3-(6-(6-Metoksy-5-metylpyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)propan-1-on;
1-(3-(6-(6-Metoksy-5-metylpyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)propan-1-on;
(S)-(3-(6-(5-Klor-6-metoksypyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)(tetrahydro-2H-pyran-4-yl)metanon;
(3-(6-(5-Klor-6-metoksypyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)(tetrahydro-2H-pyran-4-yl)metanon;
(S)-(3-(6-(6-Metoksy-5-metylpyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)(tetrahydro-2H-pyran-4-yl)metanon;
(3-(6-(6-Metoksy-5-metylpyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl)(tetrahydro-2H-pyran-4-yl)metanon;
(Tetrahydro-pyran-4-yl)-{(S)-3-{6-(5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl}-metanon;
(Tetrahydro-pyran-4-yl)-{3-{6-(5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylamino)pyrrolidin-1-yl}-metanon;
(S)-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(4-metylpiperazin-1-yl)metanon;
(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(4-metylpiperazin-1-yl)metanon;
(S)-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(morfolino)metanon;
(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(morfolino)metanon;
(S)-(4-Hydroksypiperidin-1-yl)(3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)metanon;
4-Hydroksypiperidin-1-yl)(3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)metanon;
(S)-N-(2-Hydroksyetyl)-3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)-N-metylpyrrolidin-1-karboksamide;
N-(2-Hydroksyetyl)-3-(6-(6-metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)-N-metylpyrrolidin-1-karboksamide;
(S)-1-(4-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-karbonyl)piperazin-1-yl)etanon;

1-(4-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-karbonyl)piperazin-1-yl)etanon;

(S)-2-Metoksy-5-(4-(1-(morfolin-4-karbonyl)pyrrolidin-3-yloksy)-7,8-dihydropyrido[4,3-d]pyrimidin-6(5H)-yl)nikotinonitril;

2-Metoksy-5-(4-(1-(morfolin-4-karbonyl)pyrrolidin-3-yloksy)-7,8-dihydropyrido[4,3-d]pyrimidin-6(5H)-yl)nikotinonitril;

(S)-(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(oksazol-4-yl)metanon;

(3-(6-(6-Metoksy-5-(trifluormetyl)pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl)(oksazol-4-yl)metanon;

1-(4-{(S)-3-[6-(6-Metoksy-5-trifluormetyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-karbonyl}-piperidin-1-yl)-etanon;

1-(4-{3-[6-(6-Metoksy-5-trifluormetyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-karbonyl}-piperidin-1-yl)-etanon;

{(S)-3-[6-(6-Metoksy-5-trifluormetyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(3-metyl-3H-imidazol-4-yl)-metanon;

{3-[6-(6-Metoksy-5-trifluormetyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-(3-metyl-3H-imidazol-4-yl)-metanon;

{(S)-3-[6-(6-Metoksy-5-trifluormetyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-oksazol-5-yl-metanon;

{3-[6-(6-Metoksy-5-trifluormetyl-pyridin-3-yl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yloksy]-pyrrolidin-1-yl}-oksazol-5-yl-metanon;

{(S)-3-[6-(6-Metoksy-pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl}-(tetrahydro-pyran-4-yl)-metanon; og

{3-[6-(6-Metoksy-pyridin-3-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-yloksy)pyrrolidin-1-yl}-(tetrahydro-pyran-4-yl)-metanon.

8. PI3K-inhibitor, hvori inhibitoren har en inhiberende virkning på PI3K isoform delta, for anvendelse ifølge et hvilket som helst av kravene 1 til 7 i form av et salt valgt fra

a) citrat, fumarat eller napadisylat; eller

b) fosfat, hydroklorid eller hippurat.

9. Farmasøytisk sammensetning omfattende en PI3K-inhibitor, hvori inhibitoren har en inhiberende virkning på PI3K isoform delta, eller farmasøytisk akseptable salter eller solvater derav, hvori PI3K-inhibitoren er som definert i hvilke som helst av kravene 1 til 8, for anvendelse i behandling av en immunpatologi hos et individ som lider av en sykdom eller en lidelse valgt fra akutt og cerebral malaria, via funksjonell inhibering av TLR9 hos det infiserte individet.

10. Kombinasjon omfattende en PI3K-inhibitor, hvori inhibitoren har en inhiberende virkning på PI3K isoform delta, eller farmasøytisk akseptable salter eller solvater derav, hvori PI3K-inhibitoren er som definert i hvilke som helst av kravene 1 til 8, for anvendelse i behandling av en immunpatologi hos et individ som lider av en sykdom eller en lidelse valgt fra akutt og cerebral malaria, via funksjonell inhibering av TLR9 hos det infiserte individet, og ett eller flere ytterligere aktive ingredienser.