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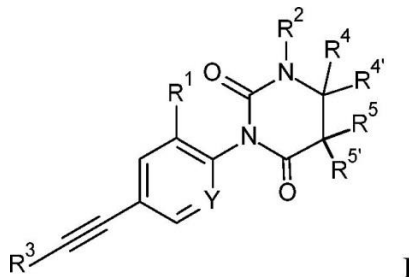
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(54)	Title	ETHYNYL DERIVATIVES
(56)	References Cited:	WO-A1-2011/128279, WO-A1-2015/044075, WO-A1-2011/029104, US-A1- 2011 124 663

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

hvor

Y er N eller C-R¹';

R¹' er hydrogen eller F;

R¹ er hydrogen, halogen eller C₁-₇-alkyl substituert med halogen;

R² er hydrogen eller C₁-₇-alkyl;

eller R² danner sammen med R⁴ en 6-leddet heterosyklisk ring inneholdende
 -CH₂-CH₂-O-CH₂- eller -CH₂-CH₂-NR-C(O)-;

R er hydrogen, C₁-₇-alkyl, fenyl eller benzyl;

R³ er fenyl eller pyridinyl, hvor N-atomet i pyridinylgruppen kan være i
 forskjellige posisjoner;

R⁴' er hydrogen, C₁-₇-alkyl eller C₁-₇-alkoksyalkyl;

R⁴ er hydrogen, C₁-₇-alkyl, fenyl eventuelt substituert med halogen
 eller C₁-₇-alkoksy, eller er sykloalkyl, eller er pyridinyl eventuelt substituert med
 halogen, C₁-₇-alkyl, C₁-₇-alkoksy eller =O, eller er pyrimidinyl eventuelt
 substituert med C₁-₇-alkyl, C₁-₇-alkoksy eller =O, eller er 1-C₁-₇-alkylpyridinyl,
 eller er

pyrazinyl, eller er pyridazinyl eventuelt substituert med C₁-₇-alkyl,
 C₁-₇-alkoksy eller =O,

eller er

1-metylpyrrolo[2,3-b]pyridin-5-yl, eller er 6-imidazo[1,2-
 b]pyridazin-6-yl;

eller R⁴ danner sammen med R⁴ en 4-, 5- eller 6-leddet heterosyklisk ring
 inneholdende

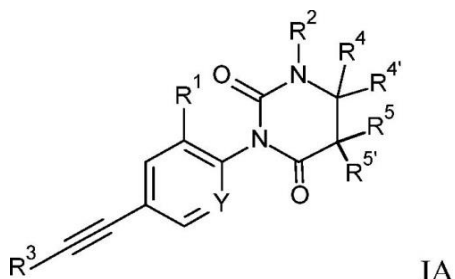
$-(CH_2)_5-$, $-CH_2-CH_2-O-CH_2-CH_2-$, $CH_2-CH_2-CH_2-$, $-CH_2-CH_2-CH_2-CH_2-$,
 $-CH_2-O-CH_2-CH_2-$ eller $CH_2-CH_2-CH_2-O-CH_2$;

R^5 og $R^{5'}$ er hydrogen eller C_{1-7} -alkyl;

eller R^4 danner sammen med R^5 en mettet 5-leddet ring inneholdende
 $-CH_2-CH_2-CH_2-$;

eller et farmasøytisk aksepterbart salt eller syreaddisjonssalt, en rasemisk blanding eller den tilsvarende enantiomeren og/eller optiske isomeren og/eller stereoisomeren av den.

2. Forbindelse med formel IA ifølge krav 1,



IA

hvor

Y er N eller $C-R^{1'}$;

$R^{1'}$ er hydrogen eller F;

R^1 er hydrogen, halogen eller C_{1-7} -alkyl substituert med halogen;

R^2 er hydrogen eller C_{1-7} -alkyl;

R^3 er fenyl eller pyridinyl, hvori N-atomet i pyridinylgruppen kan være i forskjellige posisjoner;

$R^{4'}$ er hydrogen, C_{1-7} -alkyl eller C_{1-7} -alkoksyalkyl;

R^4 er hydrogen, C_{1-7} -alkyl, fenyl eventuelt substituert med halogen eller C_{1-7} -alkoksy, eller er sykloalkyl, eller er pyridinyl eventuelt substituert med halogen, C_{1-7} -alkyl, C_{1-7} -alkoksy eller =O, eller er pyrimidinyl eventuelt substituert med C_{1-7} -alkyl, C_{1-7} -alkoksy eller =O, eller er 1- C_{1-7} -alkylpyridinyl, eller er pyrazinyl, eller er

pyridazinyl eventuelt substituert med C_{1-7} -alkyl, C_{1-7} -alkoksy eller =O, eller er 1-metylpyrrolo[2,3-b]pyridin-5-yl, eller er 6-imidazo[1,2-b]pyridazin-6-yl;

R⁵ og R^{5'} er hydrogen eller C₁₋₇-alkyl;
 eller et farmasøytisk aksepterbart salt eller syreaddisjonssalt, en rasemisk blanding, eller den tilsvarende enantiomeren og/eller optiske isomeren og/eller stereoisomeren av den.

3. Forbindelse med formel IA ifølge krav 2, hvori forbindelsene er

3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6,6-trimetyl-heksahydropyrimidin-2,4-dion

3-[2-klor-4-(2-fenyletynyl)fenyl]-1,6,6-trimetyl-heksahydropyrimidin-2,4-dion
 (5RS)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,5,6,6-tetrametyl-heksahydropyrimidin-2,4-dion

3-[2-klor-6-fluor-4-[2-(3-pyridyl)etynyl]fenyl]-1,6,6-trimetyl-heksahydropyrimidin-2,4-dion

3-[2-klor-6-fluor-4-[2-(3-pyridyl)etynyl]fenyl]-1-etyl-6,6-dimetyl-heksahydropyrimidin-2,4-dion

(6RS)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-fenyl-heksahydropyrimidin-2,4-dion

(6RS)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-fenyl-heksahydropyrimidin-2,4-dion

(6RS)-3-[2,6-difluor-4-[2-(3-pyridyl)etynyl]fenyl]-1-etyl-6-metyl-6-fenyl-heksahydropyrimidin-2,4-dion

(6RS)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-6-etyl-1,6-dimetyl-heksahydropyrimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-fenyl-heksahydropyrimidin-2,4-dion

(6R)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-fenyl-heksahydropyrimidin-2,4-dion

3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-6,6-dietyl-heksahydropyrimidine-2,4-dion

3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-6,6-dietyl-1-metyl-heksahydropyrimidin-2,4-dion

(6RS)-1,6-dimetyl-6-fenyl-3-[5-(2-fenyletynyl)-2-pyridyl]heksahydropyrimidin-2,4-dion

(6RS)-1,6-dimetyl-6-fenyl-3-[4-(2-fenyletynyl)fenyl]heksahidropirimidin-2,4-dion

(6RS)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-6-isopropyl-1,6-dimetyl-heksahidropirimidin-2,4-dion

(6RS)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-(2-pyridyl)heksahidropirimidin-2,4-dion

(6RS)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-(4-pyridyl)heksahidropirimidin-2,4-dion

(6RS)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-(3-pyridyl)heksahidropirimidin-2,4-dion

(6RS)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-6-(metoksümetyl)-1,6-dimetyl-heksahidropirimidin-2,4-dion

(6RS)-6-sikloheksyl-3-[2,6-difluor-4-[2-(3-pyridyl)etynyl]fenyl]-1,6-dimetyl-heksahidropirimidin-2,4-dion

(6RS)-3-[3-klor-5-(2-fenyletynyl)-2-pyridyl]-1,6-dimetyl-6-fenyl-heksahidropirimidin-2,4-dion

(6RS)-3-[2-klor-6-fluor-4-[2-(3-pyridyl)etynyl]fenyl]-1,6-dimetyl-6-(3-pyridyl)heksahidropirimidin-2,4-dion

(6RS)-3-[2-klor-6-fluor-4-[2-(3-pyridyl)etynyl]fenyl]-1,6-dimetyl-6-fenyl-heksahidropirimidin-2,4-dion

(6RS)-6-(3-klorfenyl)-3-[2,6-difluor-4-[2-(3-pyridyl)etynyl]fenyl]-1,6-dimetyl-heksahidropirimidin-2,4-dion

(6RS)-6-(2-klorfenyl)-3-[2,6-difluor-4-[2-(3-pyridyl)etynyl]fenyl]-1,6-dimetyl-heksahidropirimidin-2,4-dion

(6RS)-6-(4-klorfenyl)-3-[2,6-difluor-4-[2-(3-pyridyl)etynyl]fenyl]-1,6-dimetyl-heksahidropirimidin-2,4-dion

(6RS)-3-[2,6-difluor-4-[2-(3-pyridyl)etynyl]fenyl]-6-(3-metoksifenyl)-1,6-dimetyl-heksahidropirimidin-2,4-dion

(6RS)-6-tert-butyl-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-6-metyl-heksahidropirimidin-2,4-dion

(6RS)-6-tert-butyl-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-heksahidropirimidin-2,4-dion

(6RS)-3-[3-fluor-5-(2-fenyletynyl)-2-pyridyl]-1,6-dimetyl-6-fenyl-heksahidropirimidin-2,4-dion

(6RS)-1,6-dimetyl-6-fenyl-3-[5-(2-fenyletynyl)-3-(trifluormetyl)-2-pyridyl]heksahidropirimidin-2,4-dion

(6RS)-3-[2-klor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-(3-pyridyl)heksahidropirimidin-2,4-dion

(6RS)-3-[2,6-difluor-4-[2-(3-pyridyl)etynyl]fenyl]-6-etyl-1-metyl-6-fenyl-heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-(3-pyridyl)heksahidropirimidin-2,4-dion

(6S)-3-[3-fluor-5-(2-fenyletynyl)-2-pyridyl]-1,6-dimetyl-6-(3-pyridyl)heksahidropirimidin-2,4-dion

(6RS)-6-(6-klor-3-pyridyl)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1-etyl-6-metyl-6-(3-pyridyl)heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-[2-(3-pyridyl)etynyl]fenyl]-1,6-dimetyl-6-(3-pyridyl)heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-(6-metyl-3-pyridyl)heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-pirimidin-4-yl-heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-pirimidin-5-yl-heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-pyrazin-2-yl-heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-pyridazin-3-yl-heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-6-(5-fluor-3-pyridyl)-1,6-dimetyl-heksahidropirimidin-2,4-dion

(6S)-6-(2-klor-4-pyridyl)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-pyridazin-4-yl-heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-(2-metyl-4-pyridyl)heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-6-(6-metoksy-3-pyridyl)-1,6-dimetyl-heksahidropirimidin-2,4-dion

(6S)-6-(2-klor-4-pyridyl)-3-[2,6-difluor-4-[2-(3-pyridyl)etynyl]fenyl]-1,6-dimetyl-heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-(6-okso-1H-pyridin-3-yl)heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-(1-metyl-6-okso-3-pyridyl)heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-6-(1-etyl-6-okso-3-pyridyl)-1,6-dimetyl-heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-6-(1-isopropyl-6-okso-3-pyridyl)-1,6-dimetyl-heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-6-(6-isopropoksy-3-pyridyl)-1,6-dimetyl-heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1-isopropyl-6-metyl-6-(3-pyridyl)heksahidropirimidin-2,4-dion

(6S)-3-[2-klor-6-fluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-(3-pyridyl)heksahidropirimidin-2,4-dion

(6RS)-3-[2,6-difluor-4-[2-(3-pyridyl)etynyl]fenyl]-1-metyl-6-fenyl-6-(trifluormetyl)heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-6-(2-metoksy-4-pyridyl)-1,6-dimetyl-heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-(2-okso-1H-pyridin-4-yl)heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-(1-metyl-2-okso-4-pyridyl)heksahidropirimidin-2,4-dion

(6S)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,6-dimetyl-6-(2-metylpyrimidin-4-yl)heksahidropirimidin-2,4-dion

R³ er fenyl eller pyridinyl, hvori N-atomet i pyridinylgruppen kan være i forskjellige posisjoner;

R^{4'} er hydrogen, C₁₋₇-alkyl eller C₁₋₇-alkoksyalkyl;

R⁵ og R^{5'} er hydrogen eller C₁₋₇-alkyl;

eller et farmasøytisk aksepterbart salt eller syreaddisjonssalt, en rasemisk blanding eller den tilsvarende enantiomeren og/eller optiske isomeren og/eller stereoisomeren av den.

5. Forbindelse med formel IB-1 eller IB-2 ifølge krav 4, hvori forbindelsene er (9aRS)-7-[2,6-difluor-4-(2-fenyletynyl)fenyl]-3,4,9,9a-tetrahydro-1H-pyrimido[6,1-c][1,4]oksazin-6,8-dion

(9aRS)-7-[2,6-difluor-4-(2-fenyletynyl)fenyl]-9a-metyl-2,3,4,9-tetrahydropyrazino[1,2-c]pyrimidin-1,6,8-trion

(9aRS)-7-[2,6-difluor-4-(2-fenyletynyl)fenyl]-2,9a-dimetyl-4,9-dihydro-3H-pyrazino[1,2-c]pyrimidin-1,6,8-trion

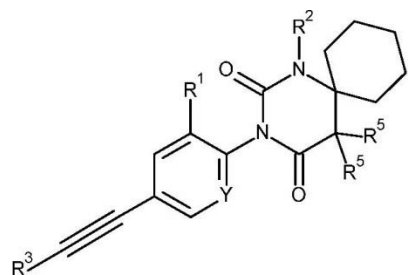
(9aRS)-7-[2,6-difluor-4-(2-fenyletynyl)fenyl]-2-isopropyl-9a-metyl-4,9-dihydro-3H-pyrazino[1,2-c]pyrimidin-1,6,8-trion

(9aRS)-2-benzyl-7-[2,6-difluor-4-(2-fenyletynyl)fenyl]-9a-metyl-4,9-dihydro-3H-pyrazino[1,2-c]pyrimidin-1,6,8-trion

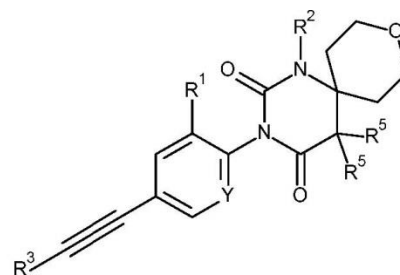
(9aRS)-7-[2,6-difluor-4-(2-fenyletynyl)fenyl]-9a-metyl-2-fenyl-4,9-dihydro-3H-pyrazino[1,2-c]pyrimidin-1,6,8-trion eller

(9aRS)-7-[2-klor-6-fluor-4-(2-fenyletynyl)fenyl]-9a-metyl-2,3,4,9-tetrahydropyrazino[1,2-c]pyrimidin-1,6,8-trion

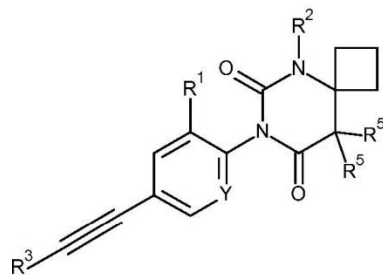
6. Forbindelse med formel IC-1, IC-2, IC-3, IC-4, IC-5 og IC-6 ifølge krav 1



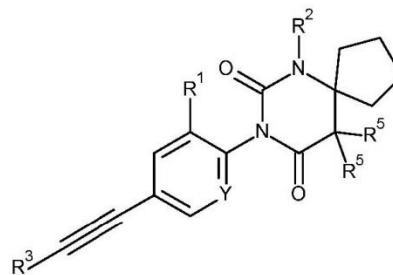
IC-1,



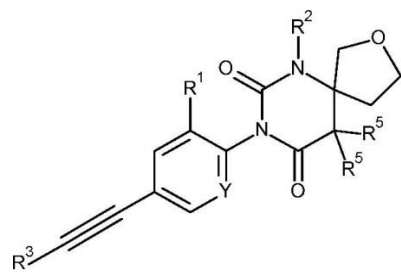
IC-2



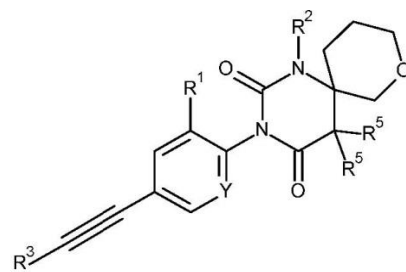
IC-3,



IC-4



IC-5,



IC-6

hvor

Y er N eller C-R^{1'};

R^{1'} er hydrogen eller F;

R¹ er hydrogen, halogen eller C₁₋₇-alkyl substituert med halogen;

R² er hydrogen eller C₁₋₇-alkyl;

R³ er fenyl eller pyridinyl, hvor N-atomet i pyridinylgruppen kan være i forskjellige posisjoner;

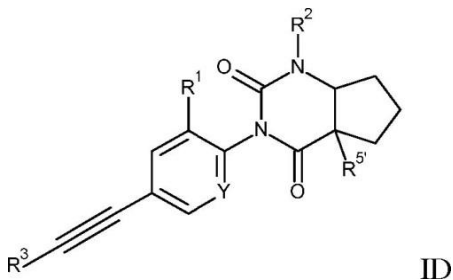
R⁵ og R^{5'} er hydrogen eller C₁₋₇-alkyl;

eller et farmasøytisk aksepterbart salt eller syreaddisjonssalt, en rasemisk blanding eller den tilsvarende enantiomeren og/eller optiske isomeren og/eller stereoisomeren av den.

7. Forbindelse med formel IC-1, IC-2, IC-3, IC-4, IC-5 og IC-6 ifølge krav 6, hvor forbindelsene er

3-[2-klor-4-(2-fenyletynyl)fenyl]-1-metyl-1,3-diazaspiro[5,5]undekan-2,4-dion
 3-[2-klor-4-(2-fenyletynyl)fenyl]-1-metyl-9-oksa-1,3-diazaspiro[5.5]undekan-2,4-dion
 7-[2-klor-4-(2-fenyletynyl)fenyl]-5-metyl-5,7-diazaspiro[3.5]nonan-6,8-dion
 8-[2,6-difluor-4-(2-fenyletynyl)fenyl]-6-metyl-6,8-diazaspiro[4.5]dekan-7,9-dion
 (5RS)-8-[2,6-difluor-4-(2-fenyletynyl)fenyl]-6-metyl-2-oksa-6,8-diazaspiro[4.5]dekan-7,9-dion eller
 (6RS)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1-metyl-8-oksa-1,3-diazaspiro[5.5]undekan-2,4-dion

8. Forbindelse med formel ID ifølge krav 1



hvor

Y er N eller C-R^{1'};

R^{1'} er hydrogen eller F;

R¹ er hydrogen, halogen eller C₁₋₇-alkyl substituert med halogen;

R² er hydrogen eller C₁₋₇-alkyl;

R³ er fenyl eller pyridinyl, hvor N-atomet i pyridinylgruppen kan være i forskjellige posisjoner;

R^{5'} er hydrogen eller C₁₋₇-alkyl;

eller et farmasøytisk aksepterbart salt eller syreaddisjonssalt, en rasemisk blanding eller den tilsvarende enantiomeren og/eller optiske isomeren og/eller stereoisomeren av den.

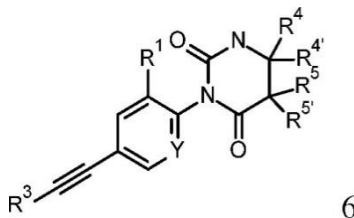
9. Forbindelse med formel ID ifølge krav 8, hvor forbindelsene er

(4aRS,7aSR)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1-metyl-5,6,7,7a-tetrahydro-4aH-syklopenta[d]pyrimidin-2,4-dion eller

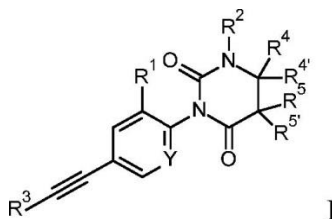
(4aRS,7aRS)-3-[2,6-difluor-4-(2-fenyletynyl)fenyl]-1,7a-dimetyl-4a,5,6,7-tetrahydrocyklopenta[d]pyrimidin-2,4-dion.

10. Framgangsmåte for å framstille en forbindelse med formel I som definert i hvilket som helst av krav 1 - 9, der framgangsmåten omfatter

a) alkylere en forbindelse med formel



med R²-I i nærvær av NaH eller CS₂CO₃ i DMF til en forbindelse med formel



hvor substituentene beskrives i krav 1, eller

hvis det ønskes, å omdanne de framstilte forbindelsene til farmasøytisk aksepterbare syreaddisjonssalter.

11. Forbindelse med formel I ifølge hvilket som helst av krav 1 - 9 til anvendelse som terapeutiske virkestoffer.

12. Forbindelse med formel I ifølge hvilket som helst av krav 1 - 9 til anvendelse ved behandling av Parkinsons sykdom, angst, oppkast, obsessiv-kompulsiv lidelse, autisme, nevroproteksjon, kreft, depresjon og diabetes type 2.

13. Farmasøytisk sammensetning som omfatter en forbindelse med formel ifølge hvilket som helst av krav 1-9 og farmasøytisk aksepterbare hjelpestoffer.

14. Anvendelsen av en forbindelse med formel I ifølge hvilket som helst av

krav 1–9 til fremstilling av et medikament til behandling av Parkinsons sykdom, angst, oppkast, obsessiv-kompulsiv lidelse, autisme, nevroproteksjon, kreft, depresjon og diabetes type 2.