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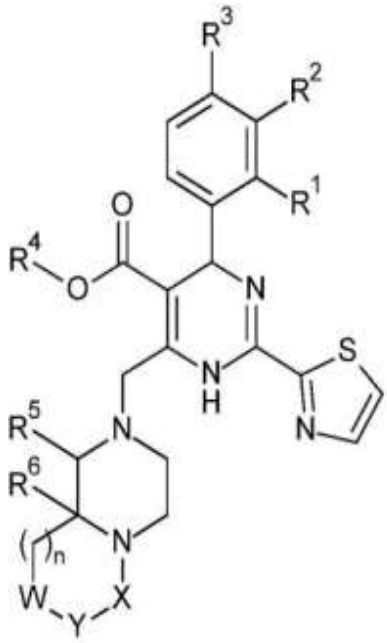
(54) Title **NOVEL 6-FUSED HETEROARYLDIHYDROPYRIMIDINES FOR THE TREATMENT AND PROPHYLAXIS OF HEPATITIS B VIRUS INFECTION**

(56) References Cited:

WO-A1-2014/029193
WO-A1-2014/184328
DE-A1- 10 013 126

PATENTKRAV

1. Forbindelse med formel (I)



(I)

hvori

R^1 er hydrogen, halogen eller C_{1-6}alkyl;

R^2 er hydrogen eller halogen;

R^3 er hydrogen eller halogen;

R^4 er C_{1-6}alkyl;

R^5 er hydrogen, hydroksyC_{1-6}alkyl, aminokarbonyl, C_{1-6}alkoksykarbonyl eller karboksy;

R^6 er hydrogen, C_{1-6}alkoksykarbonyl eller karboksy$-C_mH_{2m}-$;

X er karbonyl eller sulfonyl;

Y er $-CH_2-$, $-O-$ eller $-N(R^7)-$,

hvori R^7 er hydrogen, C_{1-6}alkyl, haloC_{1-6}alkyl, C_{3-7}sykloalkyl$-C_mH_{2m}-$, C_{1-6}alkoksykarbonyl$-C_mH_{2m}-$, $-C_tH_{2t}-$COOH, $-$haloC_{1-6}alkyl$-$COOH, $-(C_{1-6}$alkoksy$)C_{1-6}$alkyl$-$COOH, $-C_{1-6}$alkyl$-O-C_{1-6}$alkyl$-$COOH, $-C_{3-7}$sykloalkyl$-C_mH_{2m}-$COOH, $-C_mH_{2m}-C_{3-7}$sykloalkyl$-$COOH, hydroksy$-C_tH_{2t}-$, karboksyspiro[3.3]heptyl eller karboksyfenyl$-C_mH_{2m}-$, karboksypyridinyl$-C_mH_{2m}-$;

W er $-CH_2-$, $-C(C_{1-6}$alkyl$)_2-$, $-O-$ eller karbonyl;

n er 0 eller 1;

m er 0-7;

t er 1-7;

eller farmasøytisk akseptable salter eller enantiomerer eller diastereomerer derav.

2. Forbindelse ifølge krav 1, hvori

R^1 er hydrogen, klor, brom eller metyl;

R^2 er hydrogen eller fluor;

R^3 er hydrogen, klor eller fluor;

R^4 er metyl, etyl eller propyl;

R^5 er hydrogen, hydroksymetyl, aminokarbonyl, metoksykarbonyl eller karboksy;

R^6 er hydrogen, metyl–O-karbonyl eller karboksymetyl;

X er karbonyl eller sulfonyl;

Y er $-CH_2-$, $-O-$, $-N(R^7)-$,

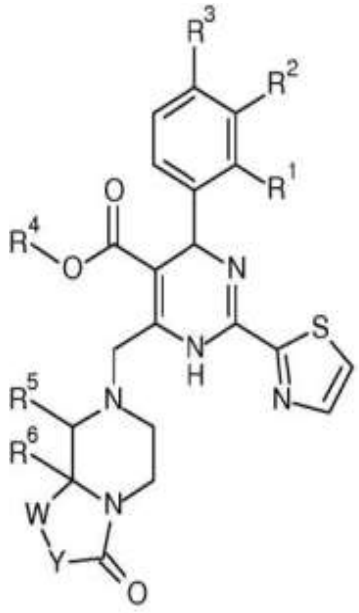
hvori R^7 er hydrogen, metyl, difluoretyl, isopropyl, isobutyl, t-butyl, syklopropyl, syklopropylmetyl, metyl–O-karbonylisopropyl, karboksyetyl, karboksydifluoretyl, karboksypropyl, karboksybutyl, karboksy(gemdimetyl)metyl, karboksy(gemdimetyl)etyl, karboksy(gemdimetyl)propyl, karboksy(gemdimetyl)butyl, karboksy(metyl)etyl, karboksy(etyl)etyl, karboksy(metoksy)etyl, karboksysyklobutyl, karboksysyklobutylmetyl, karboksysyklopentyl, karboksysykloheksyl, karboksymetylsyklopropyl, karboksysyklopropylmetyl, karboksysyklobutylmetyl, karboksyspiro[3.3]heptyl, karboksymetoksyetyl, karboksymetoksypropyl, hydroksyetyl, hydroksymetyl(gemdimetyl)butyl, hydroksy(gemdimetyl)etyl, karboksyfenyl, karboksypyridinyl eller karboksyfenylmetyl;

W er $-CH_2-$, $-C(CH_3)_2-$, $-O-$ eller karbonyl;

n er 0 eller 1;

eller farmasøytisk akseptable salter eller enantiomerer eller diastereomerer derav.

3. Forbindelse med formel (IA) ifølge krav 1,



(IA)

hvori

R^1 er halogen eller C_{1-6}alkyl;

R^2 er hydrogen eller halogen;

R^3 er hydrogen eller halogen;

R^4 er C_{1-6}alkyl;

R^5 er hydrogen, hydroksyC_{1-6}alkyl, aminokarbonyl, C_{1-6}alkoksykarbonyl eller karboksy;

R^6 er hydrogen, C_{1-6}alkoksykarbonyl eller karboksy$-C_mH_{2m}-$;

Y er $-N(R^7)-$,

hvori R^7 er hydrogen, C_{1-6}alkyl, haloC_{1-6}alkyl, C_{3-7}sykloalkyl$-C_mH_{2m}-$, C_{1-6}alkoksykarbonyl$-C_mH_{2m}-$, $-C_tH_{2t}-$COOH, $-$haloC_{1-6}alkyl$-$COOH, $-(C_{1-6}$alkoksy$)C_{1-6}$alkyl$-$COOH, $-C_{1-6}$alkyl$-O-C_{1-6}$alkyl$-$COOH, $-C_{3-7}$sykloalkyl$-C_mH_{2m}-$COOH, $-C_mH_{2m}-C_{3-7}$sykloalkyl$-$COOH, hydroksy$-C_tH_{2t}-$, karboksyspiro[3.3]heptyl eller karboksyfenyl$-C_mH_{2m}-$, karboksypyridinyl$-C_mH_{2m}-$;

W er $-CH_2-$ eller karbonyl;

m er 0-7;

t er 1-7;

eller farmasøytisk akseptable salter eller enantiomerer eller diastereomerer derav.

4. Forbindelse ifølge krav 1 eller 3 eller farmasøytisk akseptable salter, eller enantiomerer eller diastereomerer derav, hvori

R^1 er klor, brom eller metyl;

R^2 er hydrogen eller fluor;

R^3 er hydrogen, klor eller fluor;

R^4 er metyl, etyl eller propyl;

R^5 er hydrogen, hydroksymetyl, aminokarbonyl, metoksykarbonyl eller karboksy;

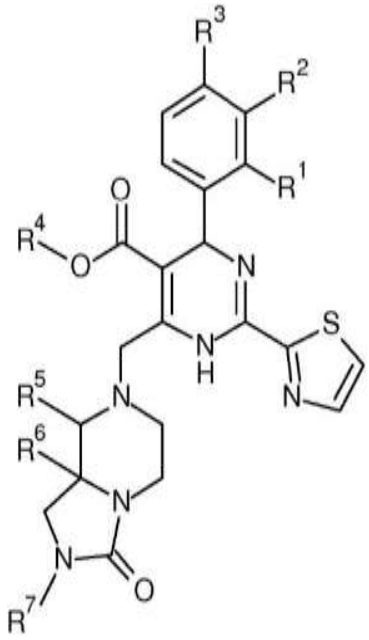
R^6 er hydrogen, metyl–O-karbonyl eller karboksymetyl;

Y er $-N(R^7)-$,

hvori R^7 er hydrogen, metyl, difluoretyl, isopropyl, isobutyl, t-butyl, syklopropyl, syklopropylmetyl, metyl–O-karbonylisopropyl, karboksyetyl, karboksydifluoretyl, karboksypropyl, karboksybutyl, karboksy(gemdimetyl)metyl, karboksy(gemdimetyl)etyl, karboksy(gemdimetyl)propyl, karboksy(gemdimetyl)butyl, karboksy(metyl)etyl, karboksy(etyl)etyl, karboksy(metoksy)etyl, karboksysyklobutyl, karboksysyklobutylmetyl, karboksysyklopentyl, karboksysykloheksyl, karboksymetylsyklopropyl, karboksysyklopropylmetyl, karboksysyklobutylmetyl, karboksyspiro[3.3]heptyl, karboksymetoksyetyl, karboksymetoksypropyl, hydroksyetyl, hydroksymetyl(gemdimetyl)butyl, hydroksy(gemdimetyl)etyl, karboksyfenyl, karboksypyridinyl eller karboksyfenylmetyl;

W er $-CH_2-$ eller karbonyl.

5. Forbindelse med formel (IAA) ifølge krav 1 eller 3,



(IAA)

hvori

R^1 er halogen eller C_{1-6}alkyl;

R^2 er hydrogen eller halogen;

R^3 er hydrogen eller halogen;

R^4 er C_{1-6}alkyl;

R^5 er hydrogen, aminokarbonyl eller karboksy;

R^6 er hydrogen;

R^7 er C_{1-6}alkyl, haloC_{1-6}alkyl, C_{3-7}sykloalkyl, C_{3-7}sykloalkyl$-C_mH_{2m}-$, $-C_tH_{2t}-$COOH, $-C_mH_{2m}-C_{3-7}$sykloalkyl$-$COOH eller karboksyfenyl;

m er 0-7;

t er 1-7;

eller farmasøytisk akseptable salter eller enantiomerer eller diastereomerer derav.

6. Forbindelse ifølge et hvilket som helst av kravene 1, 3 eller 5 eller farmasøytisk akseptable salter, eller enantiomerer eller diastereomerer derav, hvori

R^1 er klor eller metyl;

R^2 er hydrogen eller fluor;

R^3 er hydrogen eller fluor;

R^4 er metyl eller etyl;

R^5 er hydrogen, aminokarbonyl eller karboksy;

R^6 er hydrogen;

R^7 er metyl, isopropyl, isobutyl, t-butyl, difluoretyl, syklopropyl, syklopropylmetyl, karboksy(gemdimetyl)etyl, karboksy(gemdimetyl)propyl, karboksysyklopropylmetyl, karboksysyklobutylmetyl eller karboksyfenyl.

7. Forbindelse ifølge krav 5 eller farmasøytisk akseptable salter, eller enantiomerer eller diastereomerer derav, hvori

R^1 er klor eller metyl;

R^2 er hydrogen eller fluor;

R^3 er hydrogen eller fluor;

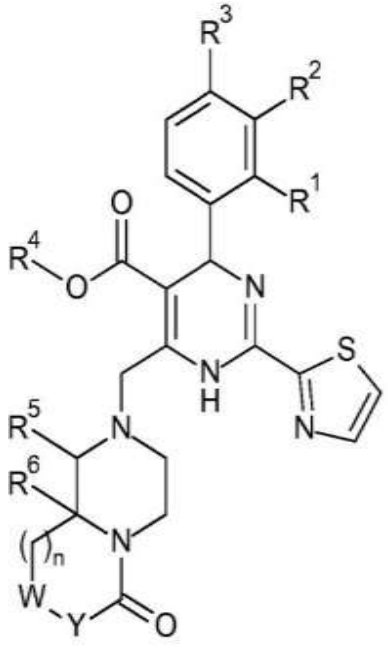
R^4 er metyl eller etyl;

R^5 er hydrogen eller karboksy;

R^6 er hydrogen;

R^7 er metyl, isopropyl, t-butyl, syklopropyl, karboksy(gemdimetyl)etyl, karboksy(gemdimetyl)propyl, karboksysyklopropylmetyl, karboksysyklobutylmetyl eller karboksyfenyl.

8. Forbindelse med formel (IB) ifølge krav 1,



(IB)

hvori

R^1 er hydrogen eller halogen;

R^2 er hydrogen eller halogen;

R^3 er hydrogen eller halogen;

R^4 er C_{1-6}alkyl;

R^5 er hydrogen;

R^6 er hydrogen eller karboksymetyl;

Y er $-CH_2-$ eller $-O-$;

W er $-CH_2-$, $-C(C_{1-6}alkyl)_2-$ eller $-O-$;

n er 0 eller 1;

eller farmasøytisk akseptable salter eller enantiomerer eller diastereomerer derav.

9. Forbindelse ifølge krav 1 eller 7 eller farmasøytisk akseptable salter, eller enantiomerer eller diastereomerer derav, hvori

R^1 er hydrogen, klor eller brom;

R^2 er hydrogen eller fluor;

R^3 er hydrogen eller fluor;

R^4 er metyl eller etyl;

R^5 er hydrogen;

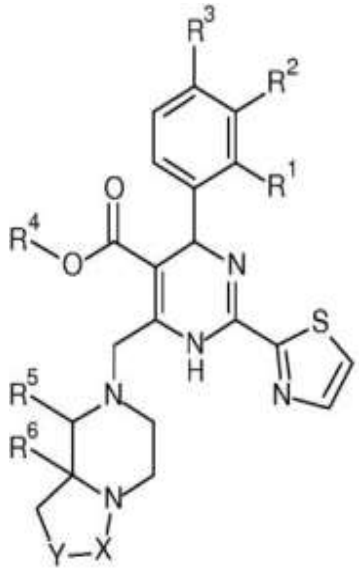
R^6 er hydrogen eller karboksymetyl;

Y er $-CH_2-$ eller $-O-$;

W er $-CH_2-$, $-C(CH_3)_2-$ eller $-O-$;

n er 0 eller 1.

10. Forbindelse med formel (ID) ifølge krav 1,



(ID)

hvori

R^1 er halogen eller C_{1-6}alkyl;

R^2 er hydrogen eller halogen;

R^3 er hydrogen eller halogen;

R^4 er C_{1-6}alkyl;

R^5 er hydrogen, aminokarbonyl eller karboksy;

R^6 er hydrogen eller C_{1-6}alkoksykarbonyl

X er karbonyl;

Y er –O– eller –N(R^7)– eller –CH_2–,

hvori R^7 er hydrogen, C_{1-6}alkyl, haloC_{1-6}alkyl, C_{3-7}sykloalkyl, C_{3-7}sykloalkyl–C_mH_{2m}–, –C_tH_{2t}–COOH-C_mH_{2m}-C_{3-7}sykloalkyl–COOH, hydroksy–C_tH_{2t}–, karboksyspiro[3.3]heptyl eller karboksyfenyl–C_mH_{2m}–;

m er 0-7;

t er 1-7;

eller farmasøytisk akseptable salter eller enantiomerer eller diastereomerer derav.

11. Forbindelse ifølge krav 1 eller 9 eller farmasøytisk akseptable salter, eller enantiomerer eller diastereomerer derav, hvori

R^1 er klor, brom eller metyl;

R^2 er hydrogen eller fluor;

R^3 er hydrogen eller fluor;

R^4 er metyl, etyl eller propyl;

R^5 er hydrogen, aminokarbonyl eller karboksy;

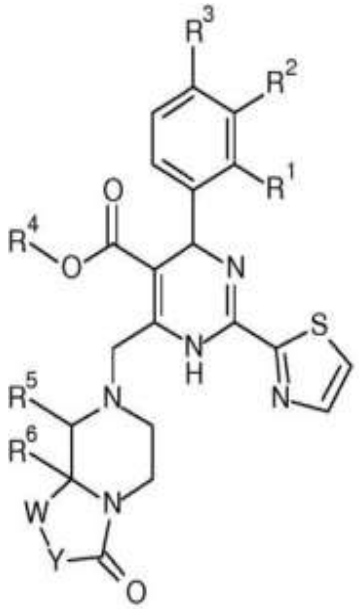
R^6 er hydrogen eller metyl−O-karbonyl;

X er karbonyl;

Y er −O−, −N(R^7)− eller −CH_2−,

hvori R^7 er hydrogen, metyl, isopropyl, difluoretyl, isobutyl, t-butyl, syklopropyl, syklopropylmetyl, karboksy(gemdimetyl)etyl, karboksy(metyl)etyl, karboksysyklopropylmetyl, karboksyfenyl, karboksysyklopentyl, karboksysykloheksyl, karboksy(gemdimetyl)propyl, karboksy(gemdimetyl)butyl, karboksysyklobutylmetyl, karboksyspiro[3.3]heptyl, hydroksyetyl, hydroksy(gemdimetyl)etyl eller karboksyfenylmetyl.

12. Forbindelse med formel (IE) ifølge krav 1,



(IE)

hvori

R^1 er halogen eller C_{1-6}alkyl;

R^2 er hydrogen eller halogen;

R^3 er hydrogen eller halogen;

R^4 er C_{1-6}alkyl;

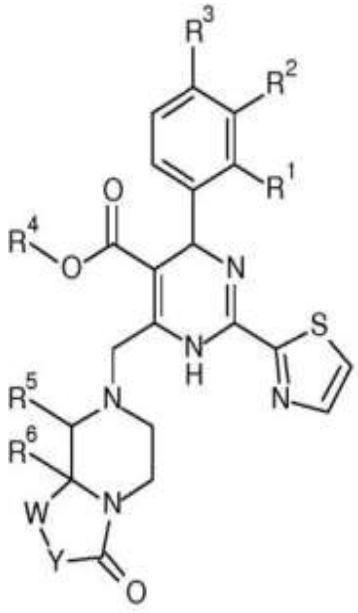
R^5 er hydrogen eller karboksy;

R^6 er hydrogen eller karboksy−C_mH_{2m}−;

Y er $-O-$, $-N(R^7)-$ eller $-CH_2-$,
hvori R^7 er C_{1-6}alkyl, C_{3-7}sykloalkyl, $-C_tH_{2t}-COOH$, $-C_{3-7}$sykloalkyl$-C_mH_{2m}$-COOH, $-C_mH_{2m}-C_{3-7}$sykloalkyl$-COOH$, $-(C_{1-6}$alkoksy$)C_{1-6}$alkyl$-COOH$, $-C_{1-6}$alkyl$-O-C_{1-6}$alkyl$-COOH$, karboksyspiro[3.3]heptyl eller karboksyfenyl$-C_mH_{2m}-$;
W er $-CH_2-$ eller $-C(C_{1-6}alkyl)_2-$;
m er 0-7;
t er 1-7;
eller farmasøytisk akseptable salter eller enantiomerer eller diastereomerer derav.

13. Forbindelse ifølge krav 1 eller 11 eller farmasøytisk akseptable salter, eller enantiomerer eller diastereomerer derav, hvori
R^1 er klor eller metyl;
R^2 er hydrogen eller fluor;
R^3 er hydrogen eller fluor;
R^4 er metyl eller etyl;
R^5 er hydrogen eller karboksy;
R^6 er hydrogen eller karboksymetyl;
Y er $-O-$, $-N(R^7)-$ eller $-CH_2-$,
hvori R^7 er isopropyl, metyl, isobutyl, t-butyl, syklopropyl, karboksyetyl, karboksypropyl, karboksybutyl, karboksy(gemdimetyl)metyl, karboksy(gemdimetyl)etyl, karboksy(metyl)etyl, karboksysyklobutyl, karboksysyklopropylmetyl, karboksysyklopentyl, karboksysykloheksyl, karboksymetylsyklopropyl, karboksy(gemdimetyl)propyl, karboksy(etyl)etyl, karboksy(metoksy)etyl, karboksysyklobutylmetyl, karboksyspiro[3.3]heptyl, karboksymetoksyetyl, karboksymetoksypropyl, karboksyfenylmetyl eller karboksyfenyl;
W er $-CH_2-$ eller $-C(CH_3)_2-$.

14. Forbindelse med formel (IE) ifølge krav 1,



(IE)

hvori

R^1 er halogen eller C_{1-6}alkyl;

R^2 er hydrogen eller halogen;

R^3 er hydrogen eller halogen;

R^4 er C_{1-6}alkyl;

R^5 er hydrogen eller karboksy;

R^6 er hydrogen eller karboksy$-C_mH_{2m}-$;

Y er $-N(R^7)-$,

hvori R^7 er hydrogen, C_{1-6}alkyl, C_{3-7}sykloalkyl, $-C_tH_{2t}-$COOH, $-C_mH_{2m}-C_{3-7}$sykloalkyl$-$COOH eller karboksyfenyl;

W er $-CH_2-$;

m er 0-7;

t er 1-7;

eller farmasøytisk akseptable salter eller enantiomerer eller diastereomerer derav.

15. Forbindelse ifølge krav 1 eller 13 eller farmasøytisk akseptable salter, eller enantiomerer eller diastereomerer derav, hvori

R^1 er klor eller metyl;

R^2 er hydrogen eller fluor;

R^3 er hydrogen eller fluor;

R^4 er metyl eller etyl;

R^5 er hydrogen eller karboksy;

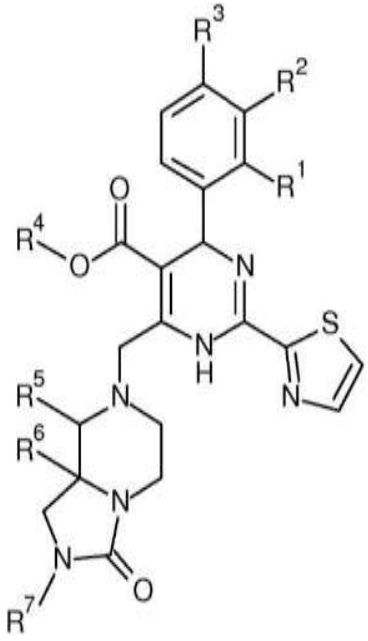
R6 er hydrogen eller karboksymetyl;

Y er $-N(R^7)-$,

hvori R^7 er hydrogen, metyl, t-butyl, syklopropyl, karboksy(gemdimetyl)etyl, karboksy(gemdimetyl)propyl, karboksy(metyl)etyl, karboksysyklopropylmetyl, karboksysyklopentyl, karboksysykloheksyl, karboksysyklobutylmetyl eller karboksyfenyl;

W er $-CH_2-$.

16. Forbindelse med formel (IAA) ifølge krav 1,



(IAA)

hvori

R^1 er halogen eller C_{1-6}alkyl;

R^2 er hydrogen eller halogen;

R^3 er hydrogen eller halogen;

R^4 er C_{1-6}alkyl;

R^5 er hydrogen eller karboksy;

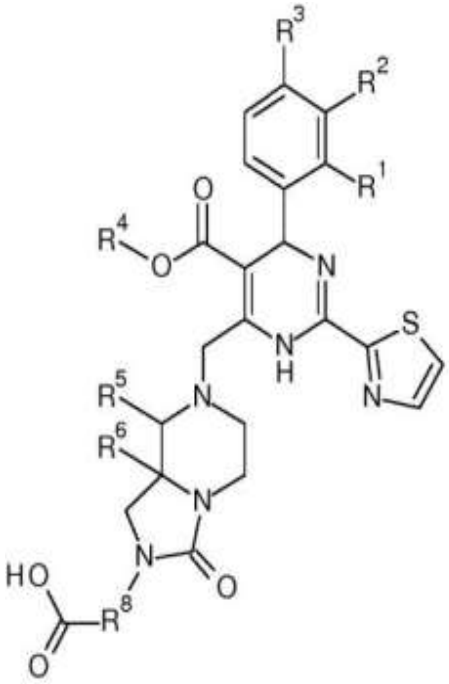
R^6 er hydrogen;

R^7 er C_{1-6}alkyl, haloC_{1-6}alkyl, C_{3-7}sykloalkyl, $-C_mH_{2m}-$COOH, $-C_mH_{2m}-C_{3-7}$sykloalkyl−COOH eller karboksyfenyl;

m er 1-6;

eller farmasøytisk akseptable salter eller enantiomerer eller diastereomerer derav.

17. Forbindelse med formel (IAB) ifølge krav 1,



(IAB)

hvori

R^1 er halogen eller C_{1-6}alkyl;

R^2 er hydrogen eller halogen;

R^3 er hydrogen eller halogen;

R^4 er C_{1-6}alkyl;

R^5 er hydrogen;

R^6 er hydrogen;

R^8 er $-C_mH_{2m}-$, C_{3-7}sykloalkyl$-C_mH_{2m}-$ eller fenyl;

m er 1-6;

eller farmasøytisk akseptable salter eller enantiomerer eller diastereomerer derav.

18. Forbindelse ifølge et hvilket som helst av kravene 1 til 14, valgt fra Metyl-(4R)-4-(2-klor-4-fluor-fenyl)-6-[(6-okso-1,3,4,8,9,9a-heksahydropyrazino[1,2-c][1,3]oksazin-2-yl)metyl]-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

Metyl-(4R)-4-(2-klor-4-fluor-fenyl)-6-[(4-okso-6,7,9,9a-tetrahydro-1H-pyrazino[2,1-c][1,4]oksazin-8-yl)metyl]-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

Metyl-(4R)-6-[[(8aR)-3-okso-5,6,8,8a-tetrahydro-1H-oksazolo[3,4-a]pyrazin-7-yl]metyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

Metyl-(4R)-6-[[(8aS)-3-okso-5,6,8,8a-tetrahydro-1H-oksazolo[3,4-a]pyrazin-7-yl]metyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

Metyl-(4R)-6-[[(8aS)-6-okso-1,3,4,7,8,8a-heksahydropyrrolo[1,2-a]pyrazin-2-yl]metyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

Metyl-(4R)-6-[[(8aR)-6-okso-1,3,4,7,8,8a-heksahydropyrrolo[1,2-a]pyrazin-2-yl]metyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

Metyl-(4R)-6-[[(8aR)-6-okso-1,3,4,7,8,8a-heksahydropyrrolo[1,2-a]pyrazin-2-yl]metyl]-4-(2-brom-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

Etyl-(4R)-6-[[(8aR)-6-okso-1,3,4,7,8,8a-heksahydropyrrolo[1,2-a]pyrazin-2-yl]metyl]-4-(2-brom-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

Etyl-(4S)-6-[[(8aR)-6-okso-1,3,4,7,8,8a-heksahydropyrrolo[1,2-a]pyrazin-2-yl]metyl]-4-(3,4-difluorfenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

Etyl-(4R)-4-(2-klor-3-fluor-fenyl)-6-[(6-okso-3,4,7,8,9,9a-heksahydro-1H-pyrido[1,2-a]pyrazin-2-yl)metyl]-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

Metyl-(4R)-6-[[(8aR)-3-okso-1,2,5,6,8,8a-heksahydroimidazo[1,5-a]pyrazin-7-yl]metyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

Metyl-(4R)-6-[[(8aS)-3-okso-1,2,5,6,8,8a-heksahydroimidazo[1,5-a]pyrazin-7-yl]metyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

Etyl-(4R)-6-[[(8aS)-3-okso-1,2,5,6,8,8a-heksahydroimidazo[1,5-a]pyrazin-7-yl]metyl]-4-(2-brom-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

Etyl-(4R)-6-[[(8aR)-3-okso-1,2,5,6,8,8a-heksahydroimidazo[1,5-a]pyrazin-7-yl]metyl]-4-(2-brom-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

Metyl-(4R)-6-[[(8aR)-1,3-diokso-5,6,8,8a-tetrahydroimidazo[1,5-a]pyrazin-7-yl]metyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

Metyl-(4R)-6-[[(8aS)-1,3-diokso-5,6,8,8a-tetrahydroimidazo[1,5-a]pyrazin-7-yl]metyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

Metyl-(4R)-6-[[(3aS)-1,1-diokso-2,3,3a,4,6,7-heksahydro-[1,2,5]tiadiazolo[2,3-a]pyrazin-5-yl]metyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

Metyl-(4R)-6-[[(3aR)-1,1-diokso-2,3,3a,4,6,7-heksahydro-[1,2,5]tiadiazolo[2,3-a]pyrazin-5-yl]metyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;

3-[(8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-propansyre;

3-[(8aS)-7-[[(4R)-4-(2-klorfenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2-metyl-propansyre;

3-[(8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2-metyl-propansyre;

3-[(8aS)-7-[[(4S)-4-(3,4-difluor-2-metyl-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-propansyre;

Etyl-(4R)-4-(2-klor-3-fluor-fenyl)-6-[[2-(2-metoksy-1,1-dimetyl-2-okso-etyl)-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-7-yl]metyl]-2-tiazol-2-yl-

1,4-dihydropyrimidin-5-karboksylat;
Metyl-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-2,5,6,8-tetrahydro-1H-imidazo[1,5-a]pyrazin-8a-karboksylat;
(R)-6-[(S)-2-(4-karboksy-fenyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyremetylester;
(R)-6-[(S)-2-(4-karboksy-fenyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyreetylester;
(R)-6-[(S)-2-(3-karboksy-fenyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyreetylester;
(R)-6-[(S)-2-(2-karboksy-fenyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyreetylester;
(R)-6-[(S)-2-(3-karboksy-fenyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyremetylester;
2-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-syklopropyl-3-okso-1,5,6,8-tetrahydroimidazo[1,5-a]pyrazin-8a-yl]eddiksyre;
2-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-isopropyl-3-okso-1,5,6,8-tetrahydroimidazo[1,5-a]pyrazin-8a-yl]eddiksyre;
(R)-6-[(S)-2-(1-karboksy-1-metyl-etyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyreetylester;
3-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-3-metyl-butansyre;
3-[(8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-

dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-3-metyl-butansyre;

1-[[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]metyl]syklopropankarboksylsyre;

1-[[(8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]metyl]syklopropankarboksylsyre;

3-[(8aS)-7-[[(4S)-4-(3,4-difluor-2-metyl-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-3-metyl-butansyre;

1-[[(8aS)-7-[[(4S)-4-(3,4-difluor-2-metyl-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]metyl]syklopropankarboksylsyre;

3-[(2S,8aR)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]syklobutankarboksylsyre;

3-[(8aR)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]syklobutankarboksylsyre;

3-[(8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-propansyre;

3-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-propansyre;

3-[(8aS)-7-[[(4S)-4-(3,4-difluor-2-metyl-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-propansyre;

3-[(8aS)-7-[[(4S)-4-(3-fluor-2-metyl-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-propansyre; og

7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-syklopropyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre.

2-[1-[(8aR)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]syklopropyl]eddiksyre;

2-[1-[(8aR)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]syklopropyl]eddiksyre;

2-[1-[(8aR)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]syklopropyl]eddiksyre;

(1R,2R)-2-[(8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]syklopentankarboksylsyre;

(1S,2R)-2-[(8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]syklopentankarboksylsyre;

(1R,2S)-2-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]syklopentankarboksylsyre;

(1S,2S)-2-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]syklopentankarboksylsyre;

4-[(8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]butansyre;

4-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-butansyre;

4-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-

a]pyrazin-2-yl]-3,3-dimetyl-butansyre;
(R)-6-[(S)-2-(2-karboksy-etyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyreetylester;
(R)-6-[(S)-2-((R)-2-karboksy-1-metyl-etyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyreetylester;
(R)-6-[(S)-2-((S)-2-karboksy-1-metyl-etyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyreetylester;
(R)-6-[(S)-2-(1-karboksy-syklobutylmetyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyremetylester;
6-[(S)-2-(1-karboksy-syklobutylmetyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-((R)-2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyreetylester;
(R)-6-[(S)-2-((1R,3S)-3-karboksy-syklopentyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyremetylester;
(R)-6-[(S)-2-((R)-(S)-3-karboksy-syklopentyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyreetylester;
(R)-6-[(S)-2-((1R,3R)-3-karboksy-syklopentyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyremetylester;
(R)-6-[(S)-2-((1R,3R)-3-karboksy-syklopentyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyreetylester;
(R)-6-[2-(4-karboksy-benzyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyremetylester;
(R)-6-[2-(4-karboksy-benzyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-

ylmetyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyreetylester;
2-[2-[7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]etoksy]eddiksyre;
2-[3-[7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]propoksy]eddiksyre;
Metyl-(4R)-4-(2-klor-4-fluor-fenyl)-6-[[2-(5-hydroksy-4,4-dimetyl-pentyl)-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-7-yl]metyl]-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;
Etyl-(4R)-4-(2-klor-3-fluor-fenyl)-6-[[2-(2-hydroksyetyl)-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-7-yl]metyl]-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;
Etyl-(4R)-4-(2-klor-3-fluor-fenyl)-6-[[2-(2-hydroksyetyl)-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-7-yl]metyl]-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;
4-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]sykloheksankarboksylsyre;
4-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]sykloheksankarboksylsyre;
3-[(8aS)-7-[[(4R)-4-(2-klorfenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-propansyre;
2-[[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]metyl]butansyre;
3-[(8aS)-7-[[(4S)-5-etoksykarbonyl-4-(3-fluor-2-metyl-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-propansyre;

3-[(8aS)-7-[[4-(4-klorfenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-propansyre;
3-[(8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2-metoksy-propansyre;
2-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]spiro[3.3]heptan-6-karboksylsyre;
5-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]pentansyre;
3-[[(8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]metyl]syklobutankarboksylsyre;
(8R,8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-syklopropyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8S,8aR)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-syklopropyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8R,8aS)-2-syklopropyl-7-[[(4S)-4-(3,4-difluor-2-metyl-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8S,8aR)-2-syklopropyl-7-[[(4S)-4-(3,4-difluor-2-metyl-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8R,8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-isopropyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8S,8aR)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-isopropyl-3-okso-5,6,8,8a-tetrahydro-1H-

imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8R,8aS)-7-[[(4S)-4-(3,4-difluor-2-metyl-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-isopropyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8S,8aR)-7-[[(4S)-4-(3,4-difluor-2-metyl-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-isopropyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8R,8aS)-2-tert-butyl-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8S,8aR)-2-tert-butyl-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8R,8aS)-2-tert-butyl-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8S,8aR)-2-tert-butyl-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8R,8aS)-2-tert-butyl-7-[[(4S)-4-(3,4-difluor-2-metyl-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8S,8aR)-2-tert-butyl-7-[[(4S)-4-(3,4-difluor-2-metyl-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
Metyl-(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-2,5,6,8-tetrahydro-1H-imidazo[1,5-a]pyrazin-8a-karboksylat;
2-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-1,1-dimetyl-3-okso-6,8-dihydro-5H-oksazolo[3,4-a]pyrazin-8a-yl]eddiksyre;
2-[(8aR)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-

dihydropyrimidin-6-yl]metyl]-1,1-dimetyl-3-okso-6,8-dihydro-5H-oksazolo[3,4-a]pyrazin-8a-yl]eddiksyre;
(8S,8aR)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-metyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8R,8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-metyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
Metyl-(4R)-6-[[(8R,8aS)-2-tert-butyl-8-karbamoyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-7-yl]metyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;
Metyl-(4R)-6-[[(8S,8aR)-2-tert-butyl-8-karbamoyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-7-yl]metyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;
3-[(8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-propoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-propansyre;
4-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-butansyre;
5-[7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]pyridin-2-karboksylsyre;
(S)-6-[(S)-2-(2-karboksy-2,2-difluor-etyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(3,4-difluor-2-metyl-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyreetylester;
(8R,8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-(syklopropylmetyl)-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8S,8aR)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-(syklopropylmetyl)-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;

3-[(8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-(4-metyltiazol-2-yl)-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-propansyre;
2-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-6-okso-1,3,4,7,8,8a-heksahydropyrrolo[1,2-a]pyrazin-1-karboksylsyre;
(8R,8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-isobutyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8S,8aR)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-isobutyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8R,8aR)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-oksazolo[3,4-a]pyrazin-8-karboksylsyre;
(8S,8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-oksazolo[3,4-a]pyrazin-8-karboksylsyre;
Etyl-(4R)-6-[[(8R,8aS)-2-tert-butyl-8-(hydroksymetyl)-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-7-yl]metyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;
Etyl-(4R)-6-[[(8S,8aR)-2-tert-butyl-8-(hydroksymetyl)-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-7-yl]metyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;
Etyl-(4R)-6-[[(8aR)-2-isopropyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-7-yl]metyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat; og
Etyl-(4R)-6-[[(8aS)-2-isopropyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-7-yl]metyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;
(8R,8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-(2,2-difluoretyl)-3-okso-5,6,8,8a-tetrahydro-1H-

imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8S,8aR)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-(2,2-difluoretyl)-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
Etyl-(4R)-6-[[(8aR)-2-(2-hydroksy-2-metyl-propyl)-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-7-yl]metyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;
og Etyl-(4R)-6-[[(8aS)-2-(2-hydroksy-2-metyl-propyl)-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-7-yl]metyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;
eller farmasøytisk akseptable salter eller enantiomerer eller diastereomerer derav.

19. Forbindelse ifølge et hvilket som helst av kravene 1 til 15 eller 17, valgt fra
3-[(8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-propansyre;
3-[(8aS)-7-[[(4S)-4-(3,4-difluor-2-metyl-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-propansyre;
(R)-6-[(S)-2-(4-karboksy-fenyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyremetylester;
(R)-6-[(S)-2-(4-karboksy-fenyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyreetylester;
(R)-6-[(S)-2-(3-karboksy-fenyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyreetylester;
(R)-6-[(S)-2-(3-karboksy-fenyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyremetylester;
3-[(8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-

dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-3-metyl-butansyre;

1-[[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]metyl]syklopropankarboksylsyre;

1-[[(8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]metyl]syklopropankarboksylsyre;

1-[[(8aS)-7-[[(4S)-4-(3,4-difluor-2-metyl-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]metyl]syklopropankarboksylsyre;

3-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-propansyre; og

3-[(8aS)-7-[[(4S)-4-(3,4-difluor-2-metyl-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-propansyre;

4-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-butansyre;

4-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-3,3-dimetyl-butansyre;

(R)-6-[(S)-2-(1-karboksy-syklobutylmetyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyremetylester;

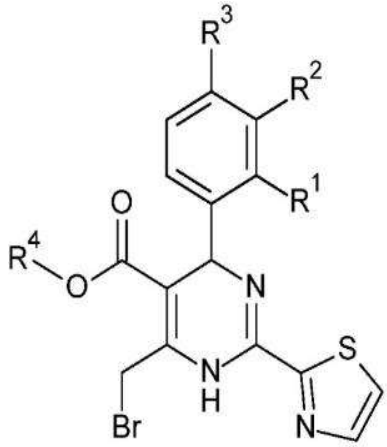
6-[(S)-2-(1-karboksy-syklobutylmetyl)-3-okso-heksahydro-imidazo[1,5-a]pyrazin-7-ylmetyl]-4-((R)-2-klor-3-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydro-pyrimidin-5-karboksylsyreetylester;

3-[(8aS)-7-[[(4S)-5-etoksykarbonyl-4-(3-fluor-2-metyl-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-2-yl]-2,2-dimetyl-propansyre;

(8S,8aR)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-syklopropyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8S,8aR)-2-syklopropyl-7-[[(4S)-4-(3,4-difluor-2-metyl-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8S,8aR)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-isopropyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8S,8aR)-7-[[(4S)-4-(3,4-difluor-2-metyl-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-isopropyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8S,8aR)-2-tert-butyl-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8S,8aR)-2-tert-butyl-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8S,8aR)-2-tert-butyl-7-[[(4S)-4-(3,4-difluor-2-metyl-fenyl)-5-metoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8R,8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-metyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
Metyl-(4R)-6-[[(8R,8aS)-2-tert-butyl-8-karbamoyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-7-yl]metyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;
Metyl-(4R)-6-[[(8S,8aR)-2-tert-butyl-8-karbamoyl-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-7-yl]metyl]-4-(2-klor-4-fluor-fenyl)-2-tiazol-2-yl-1,4-dihydropyrimidin-5-karboksylat;
4-[(8aS)-7-[[(4R)-4-(2-klor-4-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-

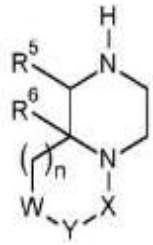
a]pyrazin-2-yl]-2,2-dimetyl-butansyre;
(8R,8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-(syklopropylmetyl)-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
(8S,8aR)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-(syklopropylmetyl)-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
2-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-6-okso-1,3,4,7,8,8a-heksahydropyrrolo[1,2-a]pyrazin-1-karboksylsyre;
(8R,8aR)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-oksazolo[3,4-a]pyrazin-8-karboksylsyre;
(8S,8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-3-okso-5,6,8,8a-tetrahydro-1H-oksazolo[3,4-a]pyrazin-8-karboksylsyre;
(8R,8aS)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-(2,2-difluoretyl)-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre; og
(8S,8aR)-7-[[(4R)-4-(2-klor-3-fluor-fenyl)-5-etoksykarbonyl-2-tiazol-2-yl-1,4-dihydropyrimidin-6-yl]metyl]-2-(2,2-difluoretyl)-3-okso-5,6,8,8a-tetrahydro-1H-imidazo[1,5-a]pyrazin-8-karboksylsyre;
eller farmasøytisk akseptable salter eller enantiomerer eller diastereomerer derav.

20. Prosess for fremstilling av en forbindelse ifølge et hvilket som helst av kravene 1 til 19, som omfatter reaksjonen av en forbindelse med formel (A)



(A)

med



i tilstedeværelse av en base;

hvori R^1 til R^6, X, Y, W og n er definert som i et hvilket som helst av kravene 1 til 18.

21. Forbindelse ifølge et hvilket som helst av kravene 1 til 19 for anvendelse som et terapeutisk aktivt stoff.

22. Farmasøytisk sammensetning som omfatter en forbindelse ifølge et hvilket som helst av kravene 1 til 19 og en terapeutisk inert bærer.

23. Anvendelsen av en forbindelse ifølge et hvilket som helst av kravene 1 til 19 for fremstilling av et medikament for behandling eller profylakse av hepatitt B-virusinfeksjon.

24. Forbindelse ifølge et hvilket som helst av kravene 1 til 19 for anvendelse ved behandling eller profylakse av hepatitt B-virusinfeksjon.