

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
16 October 2003 (16.10.2003)

PCT

(10) International Publication Number
WO 03/084947 A1

(51) International Patent Classification⁷: C07D 333/68, 333/66, 409/12, 409/14, 495/04, 495/14, A61K 31/381, A61P 31/06 // (C07D 495/04, 333:00, 239:00, (C07D 495/04, 335:00, 333:00) (C07D 495/14, 333:00, 249:00, 239:00)

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(21) International Application Number: PCT/EP03/03697

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(22) International Filing Date: 9 April 2003 (09.04.2003)

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data: 02007923.2 9 April 2002 (09.04.2002) EP

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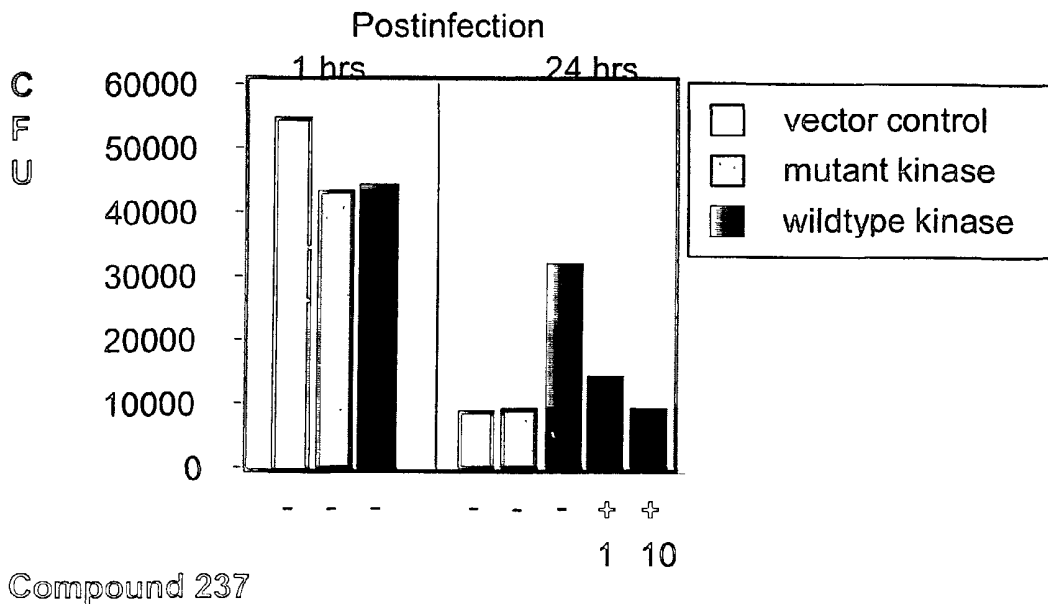
(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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[Continued on next page]

(54) Title: 4,5,6,7-TRETRAHYDROBENZO[B] THIOPHENE DERIVATIVES AND METHODS FOR MEDICAL INTERVENTION AGAINST MYCOBACTERIAL INFECTIONS



(57) Abstract: Described are 4,5,6,7-tetrahydrobenzo[b]thiophene derivatives and pharmaceutically acceptable salts thereof, the use of these derivatives for the prophylaxis and/or treatment of mycobacteria-induced infections and opportunistic infections, as well as compositions containing at least one 4,5,6,7-tetrahydrobenzo[b]thiophene derivative and/or pharmaceutically acceptable salts thereof. Furthermore, the present developing methods for detection and determination of these kinases for recognising and monitoring diseases and for controlling therapy of diseases.



WO 03/084947 A1



Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

5 **4,5,6,7-Tetrahydrobenzo[b]thiophene derivatives and methods for medical
intervention against mycobacterial infections**

Description

10 The present invention relates to 4,5,6,7-tetrahydrobenzo[b]thiophene derivatives and
pharmaceutically acceptable salts thereof, the use of these derivatives for the
prophylaxis and/or treatment of mycobacteria-induced infections and opportunistic
infections, as well as compositions containing at least one 4,5,6,7-
15 tetrahydrobenzo[b]thiophene derivative and/or pharmaceutically acceptable salts
thereof.

Mycobacteria is the cause for a number of severe diseases, among them
tuberculosis, leprosy, and mycobacteria-induced meningitis. Tuberculosis is an
ancient scourge of human beings, caused by *Mycobacterium tuberculosis*. Although
20 more than three billion people have been inoculated with the vaccine BCG, presently
more than 50,000 people die every week of tuberculosis world-wide, and there are
estimations that one third of the world's population is infected by *Mycobacterium
tuberculosis*. According to a recent report of the World Health Organisation (WHO)
on tuberculosis epidemic, distributed via the internet ([http://www.who.int/inf-
fs/en/fact104.html](http://www.who.int/inf-
25 fs/en/fact104.html)), it is estimated that between the years 2000 and 2020, nearly one
billion people will carry tuberculosis bacteria, 200 million people will get sick, and 35
million will die of tuberculosis, if control of the disease and preventive measures are
not strengthened. Moreover, it has been reported that 32% of HIV infected
30 individuals die of tuberculosis. The situation has become even more dramatic since
a number of *Mycobacterium tuberculosis* strains have shown a multidrug resistance,
which cannot be attacked by conventional therapy, e.g. antibiotics. In addition,
immune-suppressed people like AIDS patients are often victims of mycobacterial
infections leading to a poor prognosis.

35 There are several reasons why mycobacteria-induced diseases are difficult to cure:
First of all, mycobacteria can perform a differentiation process called "dormancy" or
"persistence". Dormant mycobacteria are much more resistant against conventional
antibacterial drug treatment. Secondly, many of the mycobacteria species have long
replication times, resulting in a slow growth. One consequence thereof is that

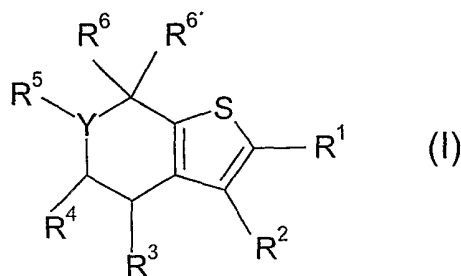
antimycobacterial drugs need longer medication times compared to the medication of faster growing pathogenic bacteria. Both factors cited above are reasons why a medical treatment of mycobacteria-induced diseases has to last at least for several months. A third factor why conventional antibacterial drug treatment is so difficult with regard to mycobacteria-induced diseases is that these bacteria have a relatively thick cell wall, which is not or almost not permeable for many substances.

Taking into account the above-mentioned problems with conventional antimycobacterial treatment, it is the object of the present invention to provide compounds and/or pharmaceutically acceptable salts thereof which can be used as pharmaceutically active substances, especially for the prophylaxis and/or treatment of mycobacteria-induced infections, a method to treat mycobacteria-induced diseases by means of those compounds, as well as compositions comprising at least one of those compounds and/or pharmaceutically acceptable salts thereof as pharmaceutically active ingredients.

This object is solved by the 4,5,6,7-tetrahydrobenzo[b]thiophene compounds and/or their pharmaceutically acceptable salts of independent claim 1, the use of at least one of the those compounds and/or the pharmaceutically acceptable salts thereof as pharmaceutically active agents according to independent claim 8, the use of the compounds as an inhibitor for a protein kinase according to independent claim 14, the use of at least one compound and/or a pharmaceutically active salt thereof for the preparation of a pharmaceutical composition according to independent claim 18, and the use of protein kinases according to independent claim 23. Further advantageous features, aspects and details of the invention are evident from the dependent claims, the description, the examples and the drawings.

The 4,5,6,7-tetrahydrobenzo[b]thiophene compounds according to the present invention have the following general formula (I)

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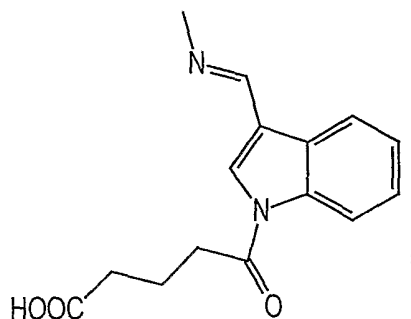
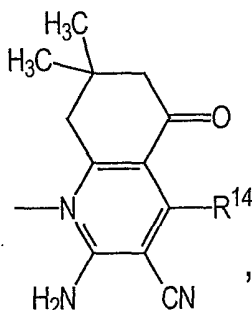
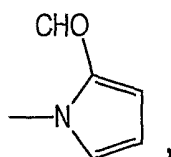
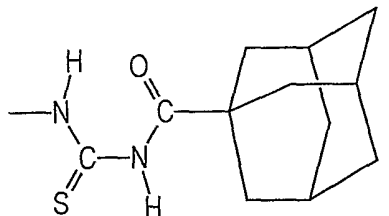
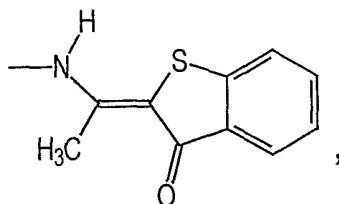
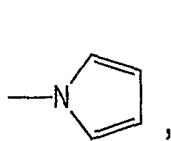
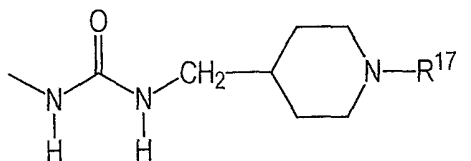
wherein

Y represents C or S;

R^1 represents R^2 , $-\text{NH}-\text{CO}-R^{16}$, $-\text{NH}_2$, $-\text{N}=\text{CH}-R^{15}$, $-\text{N}=\text{CH}-R^{16}$,
 $-\text{NH}-\text{CH}_2-R^{14}$, $-\text{NH}-\text{CH}_2-R^{16}$, $-\text{NH}-\text{SO}_2-R^{14}$, $-\text{NH}-\text{CO}-\text{NH}-R^{14}$,
 $-\text{NH}-\text{CS}-\text{NH}-\text{CH}(\text{CCl}_3)-\text{NH}-\text{CO}-R^{16}$,

$-\text{NH}-\text{CH}(\text{CCl}_3)-\text{NH}-\text{CO}-R^{12}$,

$-\text{NH}-\text{CS}-\text{NH}-R^{12}$, $\text{N}=\text{CH}-R^{12}$,



5

R^2 represents $-\text{COOR}^{12}$, $-\text{CONR}^{12}R^{12'}$, $-\text{CONR}^{12}R^{14}$, $-\text{C}\equiv\text{N}$, $-\text{COCOOR}^{12}$,
 $-\text{COCH}_2\text{Cl}$, $-\text{COCONHNH}_2$;

10

R^3 , R^4 , R^5 represent independently of each other $-\text{R}^{11}$, $-\text{R}^{12}$, $-\text{R}^{12'}$,
 $-\text{OR}^{12}$, $-\text{SR}^{12}$, $-\text{NO}_2$, $-\text{CO}-\text{R}^{12}$, $-\text{NO}$, $-\text{N}_3$, $-\text{CN}$, $-\text{OCN}$, $-\text{NCO}$,
 $-\text{SCN}$, $-\text{NCS}$, $-\text{COOR}^{12}$, $-\text{COCN}$, $-\text{CONR}^{12}R^{12'}$, $-\text{NR}^{12}R^{12'}$, $-\text{SOR}^{12}$,
 $-\text{SO}_2R^{12}$, $-\text{SO}_3R^{12}$, $-\text{CH}_2\text{OR}^{12}$;

15

in one case R^6 represents $-\text{R}^{11}$, $-\text{R}^{12}$, $-\text{R}^{12'}$, $-\text{OR}^{12}$, $-\text{SR}^{12}$, $-\text{NO}_2$,
 $-\text{CO}-\text{R}^{12}$, $-\text{NO}$, $-\text{N}_3$, $-\text{CN}$, $-\text{OCN}$, $-\text{NCO}$, $-\text{SCN}$, $-\text{NCS}$,
 $-\text{COOR}^{12}$, $-\text{COCN}$, $-\text{CONR}^{12}R^{12'}$, $-\text{NR}^{12}R^{12'}$, $-\text{SOR}^{12}$, $-\text{SO}_2R^{12}$,
 $-\text{SO}_3R^{12}$, and R^6 is hydrogen;

in the other case R^6 and R^6 together represent a carbonyl oxygen or a
oximo residue $=\text{N}-\text{OH}$ or $=\text{N}-\text{O}(\text{O})\text{C}-\text{R}^{12}$;

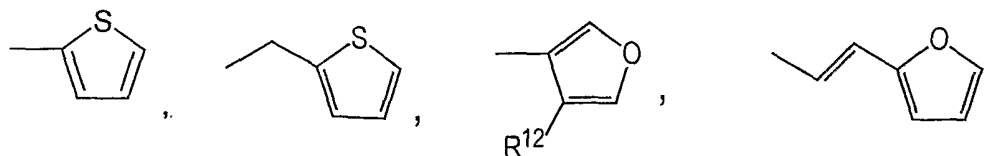
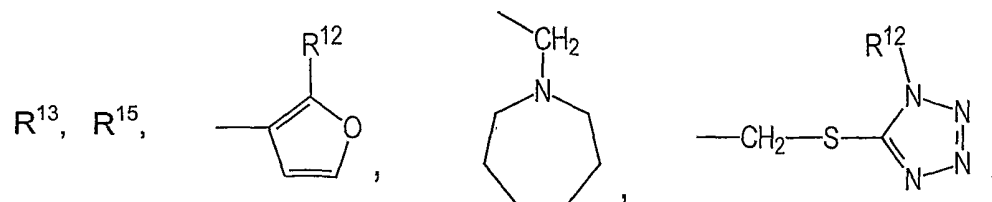
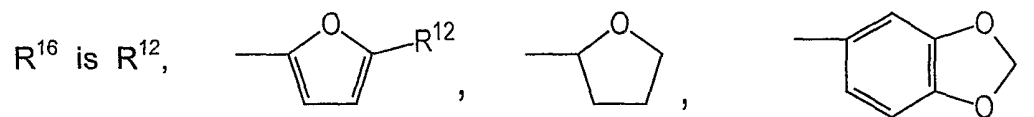
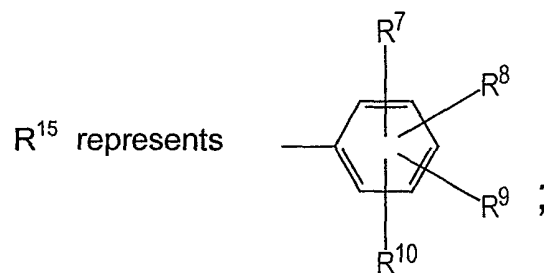
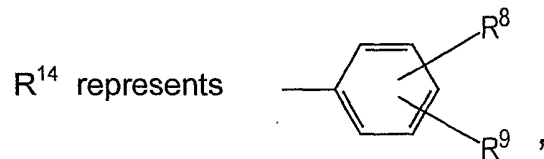
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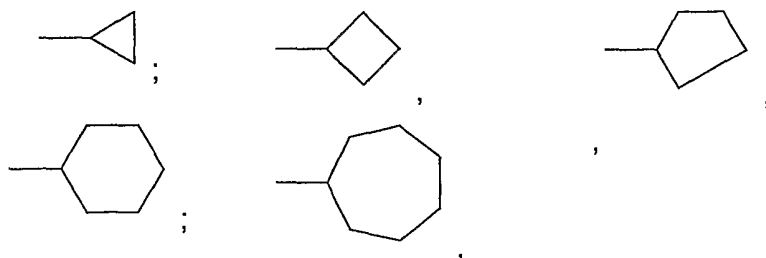
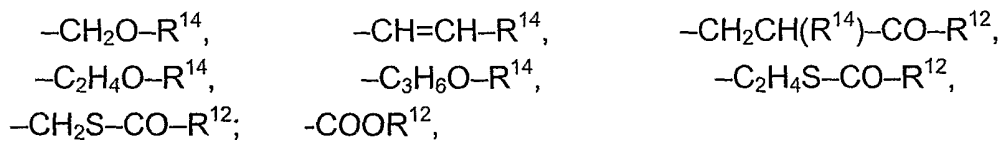
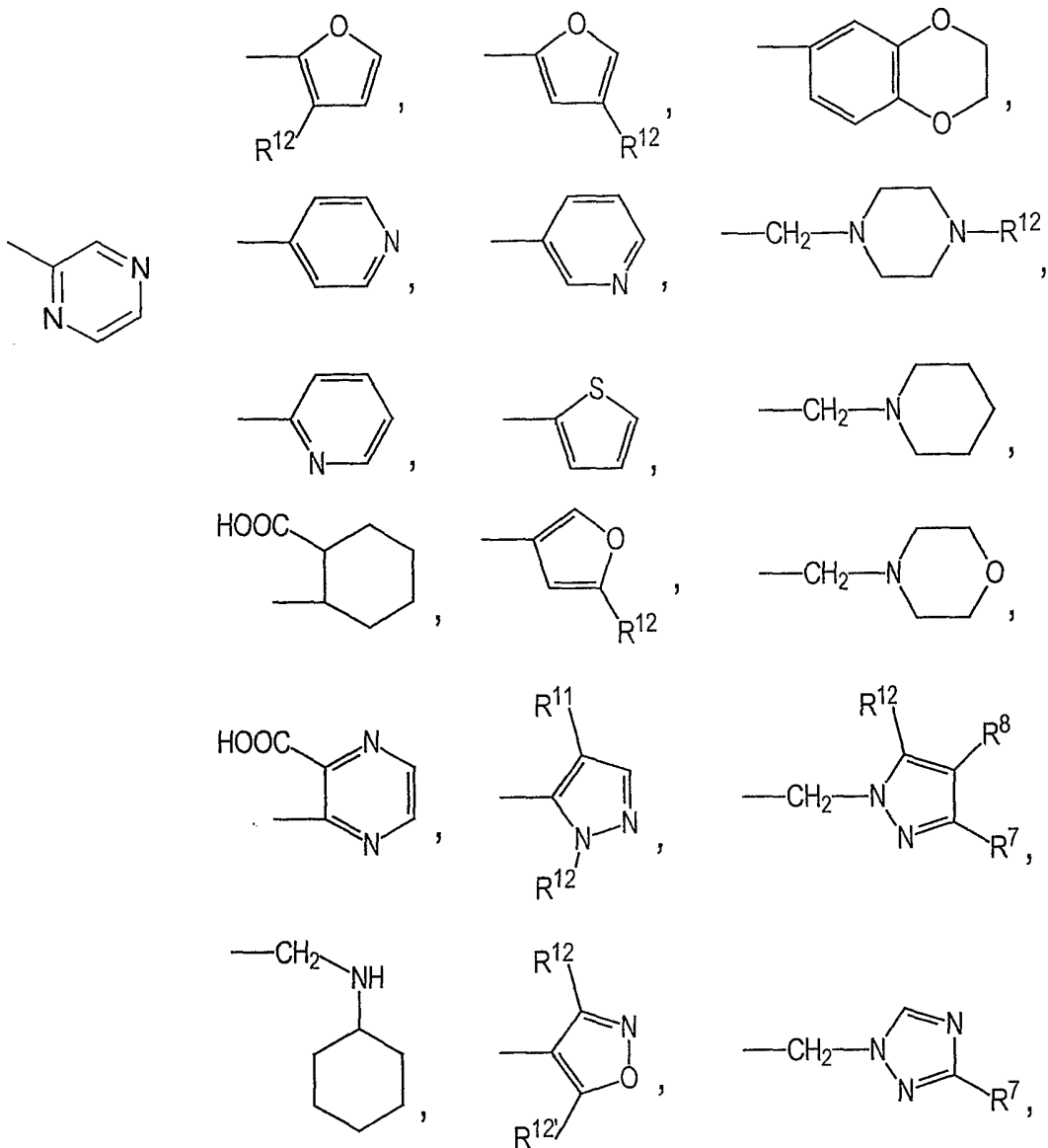
R^7 , R^8 , R^9 , R^{10} represent independently of each other $-\text{R}^{11}$, $-\text{R}^{12}$, $-\text{OR}^{12}$,
 $-\text{SR}^{12}$, $-\text{NO}_2$, $-\text{CO}-\text{R}^{12}$, $-\text{COOR}^{12}$, $-\text{OOCR}^{16}$;

R¹¹ represents -F, -Cl, -Br, -I;

R¹², R^{12'} represent independently of each other -H, -CH₃, -C(R¹¹)₃,
 -C₂H₅, -C₃H₇, -CH(CH₃)₂, -CH₂-CH=CH₂, -CCH₃=CH₂, -CH=C(CH₃)₂,
 5 -CH=CH-CH₃, -CH=CHC₂H₅, -CH(CH₃)C₂H₅, -(CH₂)_n-C≡C-R⁵, -C₄H₉,
 -C(CH₃)₃, -Ph, -CH₂-R¹⁵, -C₂H₄OH with n being an integer from 0-2;

R¹³ represents -CF₂CHF₂, -C₅H₁₁, -C₆H₁₁, -C₆H₁₃, -C₇H₁₅, -C₈H₁₇,
 -C₉H₁₉, -C₁₀H₂₁, -C₁₁H₂₃, -C₁₂H₂₅, -C₁₃H₂₇, -CH₂SPh, -CH₂R¹¹,
 10 -C₂H₄R¹¹, -C₃H₆R¹¹, -C₄H₈R¹¹, -C₂H₄Ph, -CH=CH-COOR¹²,
 -CH₂COOR¹², -C₂H₄COOR¹², -C₃H₆COOR¹², -CH(Ph)-SPh, -C₃H₅,
 -CH₂CH(Ph)₂, -C₄H₇, -C₅H₉, -C(CH₃)₂CH₂R¹¹, -CH₂CH(CH₃)₂,
 -CH(R¹¹)Ph, -CH₂CH(CH₃)CH₂C(CH₃)₃, -CH(C₂H₅)-C₄H₉, -CH(R¹¹)₂,
 15 -CH(Ph)-C₂H₅, -CH₂C(CH₃)₃,

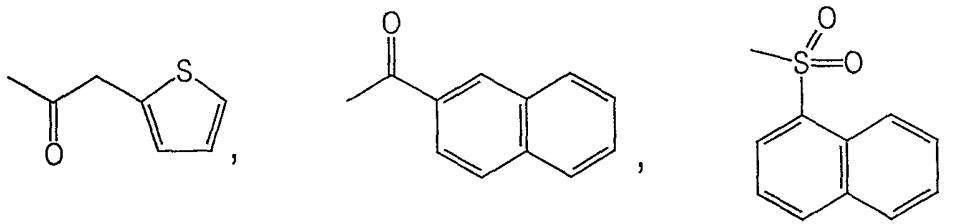




nitrobenzyl, particularly p-nitrobenzyl;

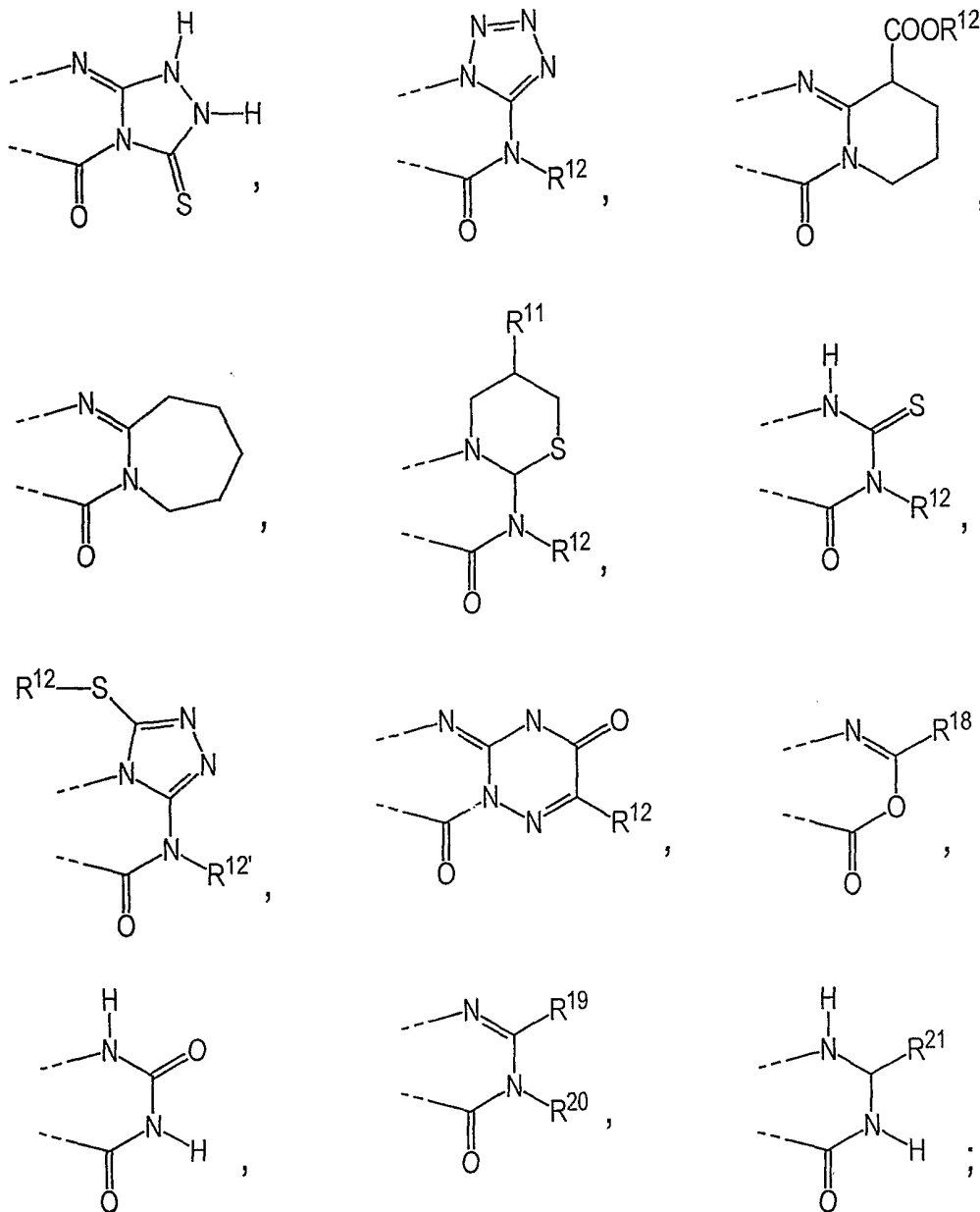
R^{17} represents $-\text{H}$, $-\text{CO}-\text{R}^{12}$, $-\text{CO}-\text{R}^{13}$, $-\text{CO}-\text{R}^{14}$, $-\text{CO}-\text{NH}-\text{R}^{12}$,
 $-\text{CO}-\text{NH}-\text{R}^{13}$, $-\text{CO}-\text{NH}-\text{R}^{14}$, $-\text{SO}_2-\text{R}^{14}$, $-\text{CO}-\text{NH}-\text{CH}_2-\text{COO}-\text{R}^{12}$,
 $-\text{CO}-\text{CH}_2-\text{O}-\text{R}^{14}$, $-\text{CO}-\text{CH}=\text{CH}-\text{R}^{14}$,

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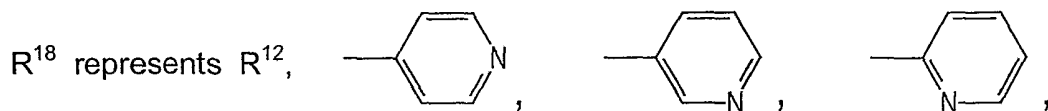


or R¹ and R² together represent a heterocyclic ring system having the following formula

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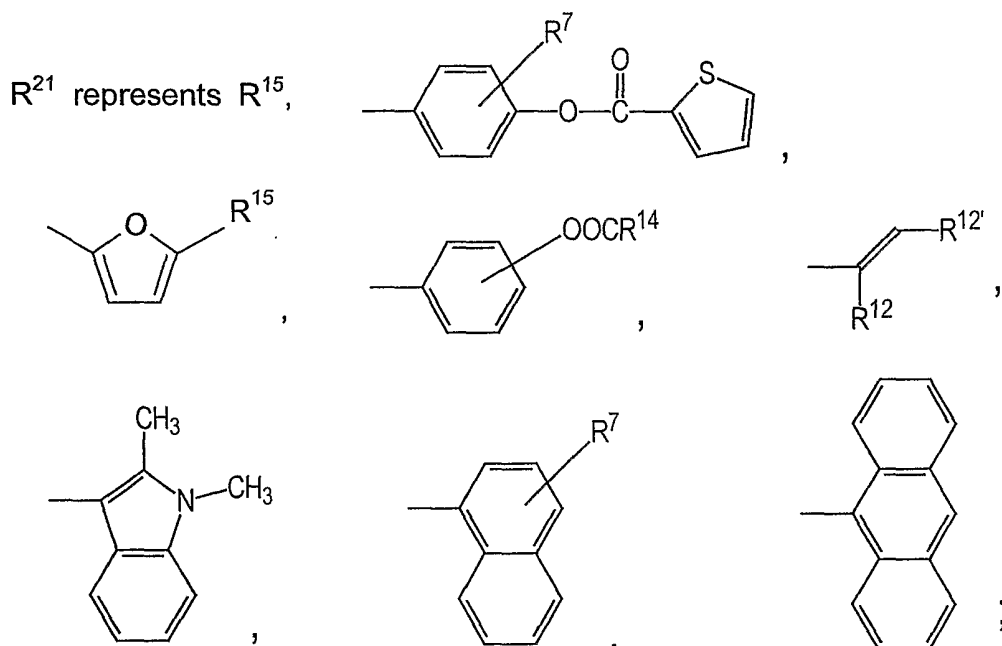
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R¹⁹ represents R³, R¹⁴, -SCH₂-R³, -SCH₂-CO-R¹⁴, -SCH₂-CO-NH-R¹⁴,
-SCH₂-CO-NH-CH₂-R¹², -NH-CO-CH₂-OR¹⁴, -CO-NH-N=CHR¹²(R¹⁴),



5 R²⁰ represents R¹², -NH-CO-R¹², -N=CH-R¹⁵;



10 The present invention also comprises pharmaceutically active salts of these 4,5,6,7-tetrahydrobenzo[b]thiophene compounds.

The inventive compounds of the general formula (I) can be synthesized according to the procedures given in WO 99/46267 and WO 01/98290. One synthetic route, for instance, starts from cyclohexanone or cyclohexanone substituted with R³ to R⁶ as defined above which is reacted with alkyl cyanoacetate to the corresponding cyclohexylidene cyano acetic acid alkyl ester. Said ester is converted to the corresponding 4,5,6,7-tetrahydrobenzo[b]thiophene derivative by the reaction with equimolar amounts of sulphur, preferably at temperatures between 40 and 80°C.

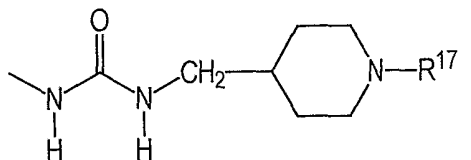
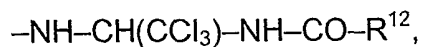
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20 After having set up the bicyclic tetrahydrobenzo[b]thiophene ring system, the amino

and/or carboxyl residues on the thiophene ring may be further modified by esterification or amid bond formation according to standard procedures. Said synthesis may also be accomplished in a combinatorial chemistry fashion with or without the use of solid support to which one reaction component could be attached.

5

Preferred are the compounds wherein R^1 is R^2 , $-NH-CO-R^{16}$, $-NH-CO-NH-R^{14}$, $-N=CH-R^{15}$, $-NH-CH_2-R^{14}$, $-NH-SO_2-R^{14}$, $-NH-CS-NH-CH(CCl_3)-NH-CO-R^{16}$,



and wherein R^2 , R^{12} , R^{14} , R^{15} , R^{16} , and R^{17} have the meanings as defined above in the general formula (I).

10

Preferred are also compounds wherein R^3 , R^4 , R^5 and R^6 represent independently of each other $-R^{11}$, $-R^{12}$, $-R^{12'}$, $-OR^{12}$, $-SR^{12}$, $-NO_2$, $-CO-R^{12}$, $-COOR^{12}$, $-CONR^{12}R^{12'}$, $-NR^{12}R^{12'}$, $-SO_2R^{12}$, $-SO_3R^{12}$, $-CH_2OR^{12}$, and wherein R^{11} , R^{12} , and $R^{12'}$ have the meanings as defined above in the general

15

Another preferred subgroup of compounds of the general formula (I) is the group wherein R^7 , R^8 , R^9 , R^{10} represent independently of each other $-R^{11}$, $-R^{12}$, $-OR^{12}$, $-SR^{12}$, $-NO_2$, $-CO-R^{12}$, $-COOR^{12}$, $-OOCR^{16}$, and wherein R^{11} and R^{12} have the

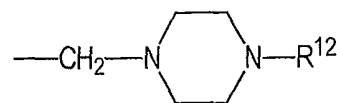
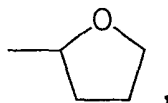
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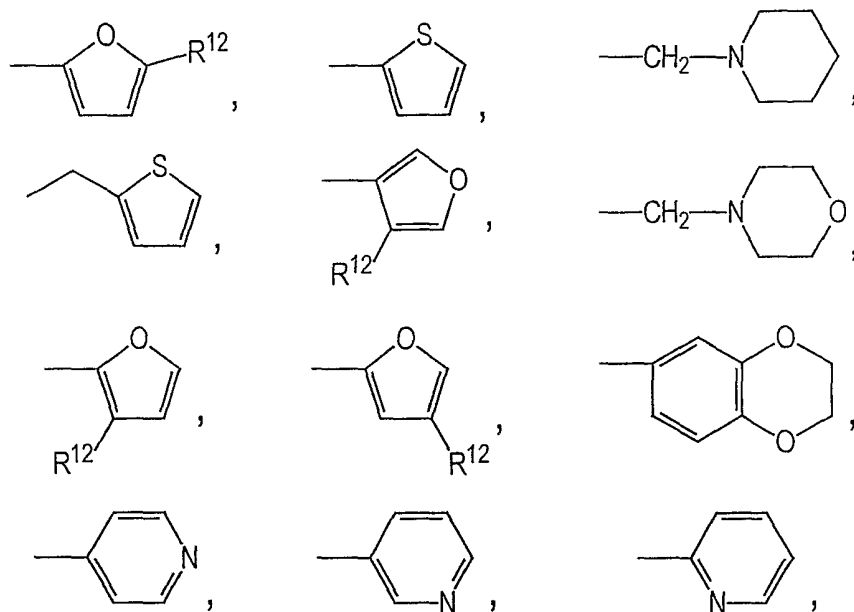
Furthermore, compounds of the general formula (I) are preferred wherein R^{13} represents $-CF_2CHF_2$, $-C_5H_{11}$, $-C_6H_{11}$, $-C_6H_{13}$, $-C_7H_{15}$, $-C_8H_{17}$, $-C_9H_{19}$, $-C_{10}H_{21}$, $-C_{11}H_{23}$, $-C_{12}H_{25}$, $-C_{13}H_{27}$, $-CH_2SPh$, $-CH_2R^{11}$, $-C_2H_4R^{11}$, $-C_3H_6R^{11}$, $-C_4H_8R^{11}$, $-C_2H_4Ph$, $-CH=CH-COOR^{12}$, $-CH(R^{11})_2$, $-CH_2COOR^{12}$, $-C_2H_4COOR^{12}$, $-C_3H_6COOR^{12}$, $-CH(Ph)-SPh$, $-C_3H_5$, $-CH_2CH(Ph)_2$, $-C_4H_7$, $-C_5H_9$, $-C(CH_3)_2CH_2R^{11}$, $-CH_2CH(CH_3)_2$, $-CH(R^{11})Ph$, $-CH_2CH(CH_3)_2CH_2C(CH_3)_3$, $-CH(C_2H_5)-C_4H_9$, $-CH(Ph)-C_2H_5$, $-CH_2C(CH_3)_3$, and wherein R^{11} and R^{12} have the meanings as defined above in the general formula (I).

30

The following compounds are also advantageous wherein

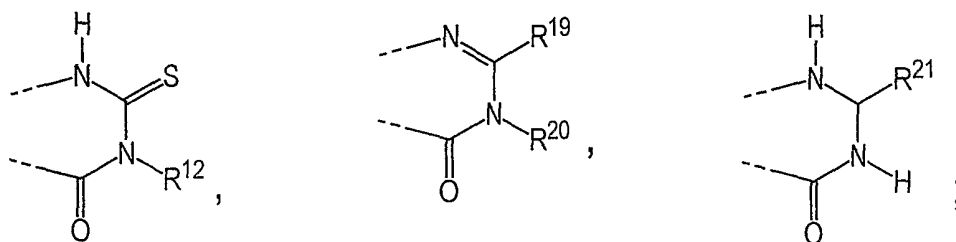
R^{16} represents R^{12} , R^{13} , R^{15} ,





and wherein R^{12} , R^{13} , and R^{15} have the meanings as defined above in the general formula (I).

5 Preferred is also the group of compounds wherein R^1 and R^2 form a heterocyclic ring system having the following formulas



and wherein R^{12} , R^{19} , R^{20} , and R^{21} have the meanings as defined above in the general formula (I).

Particularly preferred are the compounds selected from the group comprising:

- 10 (Compound 1) 2-{3-[1-(2-Chloro-acetyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 2) 2-[3-(1-Butyryl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 3) 2-[3-(1-Propanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 4) 2-[3-(1-Benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 5) 2-{3-[1-(2-Chloro-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

- (Compound 6) 2-[3-(1-Isobutyryl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 7) 2-{3-[1-(4-Methyl-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 8) 2-[3-(1-Cyclohexanecarbonyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 9) 2-[3-(1-Cyclopropanecarbonyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 10) 2-[3-(1-Hexanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 11) 2-{3-[1-(2-Methyl-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 12) 2-{3-[1-(3-Chloro-2,2-dimethyl-propionyl)-piperidin-4-ylmethyl]-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 13) 2-{3-[1-(3,5,5-Trimethyl-hexanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 14) 2-{3-[1-(2-Ethyl-hexanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 15) 2-{3-[1-(2-Phenyl-butyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 25 (Compound 16) 2-[3-(1-Cyclopentylcarbonyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 17) 2-{3-[1-(2-Chloro-2-phenyl-acetyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 30 (Compound 18) 2-{3-[1-(4-Butyl-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 19) 2-[3-(1-Decanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 20) 2-[3-(1-Heptanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 35 (Compound 21) 2-[3-(1-Nonanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 22) 2-[3-(1-Dodecanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

- (Compound 23) 2-{3-[1-(3-Methy-butyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 24) 2-[3-(1-Tetradecanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 25) 2-[3-(1-Cyclohexylcarbamoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 26) 2-[3-(1-Phenylcarbamoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 27) 2-[3-(1-Benzylcarbamoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 28) 2-{3-[1-(4-Ethoxycarbonyl-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 29) 2-{3-[1-(3-Bromo-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 30) 2-{3-[1-(2-Methoxy-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 31) 2-{3-[1-(2-Methyl-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 32) 2-{3-[1-(4-Chloro-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 25 (Compound 33) 2-{3-[1-(4-Fluoro-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 30 (Compound 34) 2-{3-[1-(4-Methyl-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 35) 2-{3-[1-Naphtalene-1-sulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 35 (Compound 36) 2-{3-[1-(4-Chloro-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

- (Compound 37) 2-{3-[1-(2,5-Dichloro-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 38) 2-{3-[1-(2,2-Dichloro-acetyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 39) 2-{3-[1-(3,3-Dimethyl-butyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 40) 2-{3-[1-(Ethoxycarbonylmethyl-carbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 41) 2-{3-[1-(3-Methoxy-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 42) 2-{3-[1-(3,5-Bis-trifluoromethyl-benzoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 43) 2-[3-(1-Phenylacetyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 44) 2-{3-[1-(3,4-Dichloro-benzoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 45) 2-{3-[1-(2,4,6-Trimethyl-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 25 (Compound 46) 2-{3-[1-(4-Methoxy-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 47) 2-{3-[1-(Naphthalene-2-sulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 30 (Compound 48) 2-(3-Piperidin-4-ylmethyl-ureido)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 49) 2-(3-{1-[2-(4-Chloro-phenoxy)-acetyl]-piperidin-4-ylmethyl}-ureido)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 35 (Compound 50) 2-(3-{1-[3-(4-Nitro-phenoyl)-acryloyl]-piperidin-4-ylmethyl}-ureido)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

- (Compound 51) 2-[3-(1-Octanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 52) 2-[3-(1-Benzenesulfonyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 53) 2-[3-(1-Ethylcarbonyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 54) 2-[3-[1-(3-Fluoro-benzoyl-piperidin-4-ylmethyl)]-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 55) 2-[3-[1-(4-Chloro-phenylcarbonyl)-piperidin-4-ylmethyl]-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 56) 4-[3-(3-ethoxycarbonyl-4,5,6,7-tetrahydro-benzo [b] thiophene-2-yl)-ureidomethyl]-piperidine-1-carboxylic acid phenyl ester;
- (Compound 57) 2-[3-[1-(3-Trifluoromethyl-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 58) 2-[3-[1-(3-Bromo-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 59) 2-[3-[1-(2,4-Dichloro-phenylcarbonyl)-piperidin-4-ylmethyl]-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 60) 2-[3-[1-(2-Trifluoromethyl-phenylcarbonyl)-piperidin-4-ylmethyl]-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 25 (Compound 61) 2-[3-[1-(4-*tert*-Butyl-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 62) 2-[3-[1-(3-Nitro-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 63) 2-[3-(1-Cyclobutanecarbonyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 30 (Compound 64) 2-[3-[1-(2-Thiophen-2-ylacetyl)-piperidin-4-ylmethyl]-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 35 (Compound 65) 2-[3-[1-(Naphthalene-2-carbonyl)-piperidin-4-ylmethyl]-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 66) 5,6,7,8-Tetrahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidine-2,4-dione;

- (Compound 67) 4-Oxo-3,4,5,6,7,8-hexahydro-benzo[4,5]thieno[2,3-*d*]pyrimidine-2-carboxylic acid ethyl ester;
- (Compound 68) 2-Acetylamino-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 69) 2-Amino-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 70) 2-Amino-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid amide;
- (Compound 71) 2-Acetylamino-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid;
- 10 (Compound 72) 2-(Toluene-4-sulfonylamino)-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid amide;
- (Compound 73) 7-Methyl-1,3,4,9-tetrahydro-2*H*-11-thia-5a,6,9,10-tetraaza-benzo[*b*]fluorene-5,8-dione;
- 15 (Compound 74) 7-Phenyl-1,3,4,9-tetrahydro-2*H*-11-thia-5a,6,9,10-tetraaza-benzo[*b*]fluorene-5,8-dione;
- (Compound 75) 2-(5-Nitro-furan-2-yl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 76) 2-[(5-Bromo-2-hydroxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid amide;
- 20 (Compound 77) 2-[(4,5-Dibromo-2-hydroxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 78) 2-[(2-Chloro-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid amide;
- 25 (Compound 79) 2-[1-(3-Oxo-3*H*-benzo[*b*]thiophen-2-ylidene)-ethylamino]-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 80) 2-Heptanoylamino-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 81) 2-(3-Bromo-benzoylamino)-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- 30 (Compound 82) 2-Ethyl-5,6,7,8-tetrahydro-3-oxa-9-thia-1-aza-fluoren-4-one;
- (Compound 83) Furan-2-carboxylic acid [3-(4-methoxy-phenylcarbonyl)-4,5,6,7-tetrahydro-benzo[*b*]thiophen-2-yl]-amide;
- (Compound 84) 2-Pyridin-3-yl-5,6,7,8-tetrahydro-3-oxa-9-thia-1-aza-fluoren-4-one;
- 35 (Compound 85) 2-Propionylamino-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid phenylamide;
- (Compound 86) 1-Allylsulfanyl-4-phenyl-6,7,8,9-tetrahydro-4*H*-10-thia-2,3,4,10*b*-tetraaza-cyclopenta[*a*]fluoren-5-one;

- (Compound 87) 2-[2-(1-Phenyl-1*H*-tetrazol-5-ylsulfanyl)-acetylamino]-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 88) 2-[3-(4-Methoxy-phenyl)-3-(2,2,2-trifluoro-acetylamino)-propionyl-amino]-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid amide;
- 5 (Compound 89) 2-(3-Chloro-benzylamino)-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 90) 2-[[1-(4-Carboxy-butyryl)-1*H*-indol-3-ylmethylene]-amino]-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 91) 2-(7-Ethyl-4-oxo-3-phenyl-3,4,5,6,7,8-hexahydro-benzo[4,5]thieno [2,3-*d*]pyrimidin-2-ylsulfanyl)-*N*-(2-isopropoxy-phenyl)-acetamide;
- (Compound 92) *N,N*-Diethyl-2-(7-ethyl-4-oxo-3-phenyl-3,4,5,6,7,8-hexahydro-benzo[4,5]thieno[2,3-*d*]pyrimidin-2-ylsulfanyl)-acetamide;
- 15 (Compound 93) 3-[(4-Hydroxy-3-methoxy-benzylidene)-amino]-2-methyl-5,6,7,8-tetrahydro-3*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 94) 6-Ethyl-2-(3-phenyl-thioureido)-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 95) 2-[3-(Adamantane-1-carbonyl)-thioureido]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 96) 2-[(3,5-Dibromo-2,4-dihydroxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 97) Benzoic acid 2-ethoxy-4-(4-oxo-1,2,3,4,4a,5,6,7,8,9a-decahydro-benzo [4,5]thieno[2,3-*d*]pyrimidin-2-yl)-phenylester;
- 25 (Compound 98) 2-(1-Acetylamino-2,2,2-trichloro-ethylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 99) 2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- 30 (Compound 100) 4-Oxo-3,4,5,6,7,8-hexahydro-benzo[4,5]thieno[2,3-*d*]pyrimidine-2-carboxylic acid [1-(3-nitro-phenyl)-ethylidene]-hydrazide;
- (Compound 101) 2-[(Pyridine-4-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 102) 2-(2,2,3,3-Tetrafluoro-propionylamino)-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid amide;
- 35 (Compound 103) 2-[3-(1-Acetylamino-2,2,2-trichloro-ethyl)-thioureido]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 104) 2-[3-(2,2,2-Trichloro-1-propionylamino-ethyl)-thioureido]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid amide;

- (Compound 105) 2-(3-Chloro-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 106) 2-(2-Chloro-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- 5 (Compound 107) 2-Anthracene-9-yl-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 108) 2-(3,5-Dibromo-2-methoxy-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 109) 2-[5-(4-Bromo-phenyl)-furan-2-yl]-2,3,4a,5,6,7,8,9a-octahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- 10 (Compound 110) 2-(2,4-Dichlorophenoxy)-*N*-(4-oxo-2-propyl-5,6,7,8-tetrahydro-4*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-3-yl)-acetamide;
- (Compound 111) 2-(3,4-Dimethoxy-benzoylamino)-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 112) 2-[3-(2-Chloro-phenyl)-acryloylamino]-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 113) 3-(3-Ethoxycarbonyl-4,5,6,7-tetrahydro-benzo[*b*]thiophene-2-ylcarb-amoyl)-pyrazine-2-carboxylic acid;
- (Compound 114) 2-(3-{2,2,2-Trichloro-1-[(furan-2-carbonyl)-amino]-ethyl}-thioureido)-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 115) 2-(1-Methyl-2-phenyl-vinyl)-2,3,4a,5,6,7,8,9a-octahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 116) 2-(2-Methoxy-naphtalen-1-yl)-2,3,4a,5,6,7,8,9a-octahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- 25 (Compound 117) 2-(1,2-Dimethyl-1*H*-indol-3-yl)-2,3,4a,5,6,7,8,9a-octahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 118) 2-(Cyclohexanecarbonyl-amino)-6-methyl-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- 30 (Compound 119) 3-Bromo-benzoic acid 3-(4-oxo-1,2,3,4,5,6,7,8-octahydro-benzo[4,5]thieno[2,3-*d*]pyrimidin-2-yl)-phenyl ester;
- (Compound 120) 3-Thioxo-2,3,5,6,7,8-hexahydro-1*H*-9-thia-1,2,3a,10-tetraaza-cyclopenta[*b*]fluorene-4-one;
- (Compound 121) 2-(2,3-Dibromo-5-ethoxy-4-hydroxy-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- 35 (Compound 122) 2-[2-(4-Chloro-phenoxy)-acetylamino]-6-methyl-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 123) 4-Phenyl-5a,6,7,8,9,10a-hexahydro-4*H*-10-thia-1,2,3,4,10b-pentaaza-cyclopenta[*a*]fluorene-5-one;

- (Compound 124) 6-Methyl-2-[(thiophene-2-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid amide;
- (Compound 125) 3-Allyl-2-(2-oxo-2-thiophen-2-yl-ethylsulfanyl)-5,6,7,8-tetrahydro-3*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- 5 (Compound 126) 2-[(2-Chloro-4-nitro-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 127) 2-(2-Methyl-3,5-dinitro-benzoylamino)-4,5,6,7-tetrahydro-benzo[*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 128) 2-(4-Acetyl-benzoylamino)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 129) 2-Benzoylamino-7-hydroxyimino-4,5,6,7-tetrahydro-benzo [b] thio-phene-3-carboxylic acid ethyl ester;
- (Compound 130) 2-Formylamino-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 131) 5-Oxo-1,2,3,4,6,7,8,9-octahydro-5*H*-11-thia-5a,10-diazabenzo[*b*]fluorene-9-carboxylic acid ethyl ester;
- (Compound 132) 2-Benzoylamino-7-oxo-4,5,6,7-tetrahydro-benzo [b] thio-phene-3-carboxylic acid ethyl ester;
- (Compound 133) 2-(2-Phenylsulfanyl-acetylamino)-4,5,6,7-tetrahydro-benzo [b] thio-phene-3-carboxylic acid ethyl ester;
- 20 (Compound 134) 2-(4-Nitro-benzylamino)-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 135) 2-[2-(4-Ethyl-piperazin-1-yl)-acetylamino]-7-oxo-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 25 (Compound 136) 2-Phenylsulfanyl-3,4,7,8,9,10-hexahydro-2*H*,6*H*-12-thia-5,11-diazacyclohepta[*b*]fluorene-1,5-dione;
- (Compound 137) 7-Hydroxy-2-(4-nitro-benzoylamino)-4,5,6,7-tetrahydro-benzo[*b*] thio-phene-3-carboxylic acid ethyl ester;
- (Compound 138) 2-(2-Cyclohexylamino-acetylamino)-7-oxo-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 30 (Compound 139) 2-(2-Azepan-1-yl-acetylamino)-7-oxo-4,5,6,7-tetrahydro-benzo[*b*] thio-phene-3-carboxylic acid ethyl ester;
- (Compound 140) 7-Hydroxyimino-2-pentanoylamino-4,5,6,7-tetrahydro-benzo[*b*] thio-phene-3-carboxylic acid ethyl ester;
- 35 (Compound 141) 2-(2-Morpholin-4-yl-acetylamino)-7-oxo-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 142) 2-Benzoyloxyimino-4,5,7,8,9,10,11-heptahydro-3*H*-1-thia-6a,12-diazacyclohepta[*b*]fluorene-6-one;

- (Compound 143) 2-(3-Acetylsulfanyl-propionylamino)-4,5,6,7-tetrahydro-benzo[*b*]thio-phene-3-carboxylic acid ethyl ester;
- (Compound 144) 2-[3-(3,4-Dichloro-phenyl-ureido)]-4,5,6,7-tetrahydro-benzo [*b*]thio- phene-3-carboxylic acid amide;
- 5 (Compound 145) 2-(2-Chloro-5-iodo-benzoylamino)-4,5,6,7-tetrahydro-benzo [*b*]thio-phene-3-carboxylic acid ethyl ester;
- (Compound 146) 2-[(5-Benzyl-2-hydroxy-3-nitro-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 147) 2-[(Pyridine-3-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo[*b*]thiophene -3-carboxylic acid ethyl ester;
- 10 (Compound 148) 2-(3-Thiophen-2-yl-propionylamino)-4,5,6,7-tetrahydro-benzo [*b*]thio- phene-3-carboxylic acid ethyl ester;
- (Compound 149) 6-Methyl-2-(3-methyl-4-nitro-benzoylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 150) 2-Isopropyl-5,6,7,8-tetrahydro-3-oxa-9-thia-1-aza-fluor-4-one;
- (Compound 151) 2-(2-Piperidin-1-yl-acetylamino)-4,5,6,7-tetrahydro-benzo [*b*] thio-phene-3-carboxylic acid amide;
- (Compound 152) 3-Allyl-2-prop-2-ynylsulfanyl-5,6,7,8-tetrahydro-3*H*-benzo [4,5]thieno [2,3-*d*]pyrimidin-4-one;
- 20 (Compound 153) 2-(Trifluoromethyl)-5,6,7,8-tetrahydro-3*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 154) 2-[2-(4-Methyl-piperazin-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid amide;
- (Compound 155) Furan-2-carboxylic acid-(3-phenylcarbamoyl-4,5,6,7-tetrahydro-benzo[*b*]thiophen-2-yl)-amide;
- 25 (Compound 156) 3-Phenyl-5,6,7,8-tetrahydro-3*H*-benzo [4,5] thieno [2,3-*d*]pyrimidin-4-one;
- (Compound 157) 2-(4-Oxo-3-phenyl-3,4,5,6,7,8-hexahydro-benzo[4,5]thieno[2,3-*d*]pyrimidin-2-ylsulfanyl)-*N*-phenethyl-acetamide;
- 30 (Compound 158) 2-(3-Benzoylsulfanyl-acetylamino)-4,5,6,7-tetrahydro-benzo[*b*] -thiophene-3-carboxylic acid ethyl ester;
- (Compound 159) 2-(5-Hydroxy-2-nitro-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5] thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 160) 2-[2-(2-Benzoylamino-2-carboxy-ethylsulfanyl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 35 (Compound 161) 2-[(5-Bromo-2-hydroxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;

- (Compound 162) 3-[(2,4-Dihydroxy-benzylidene)-amino]-2-methyl-5,6,7,8-tetrahydro-3*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 163) *N*-(4-Oxo-2-pentyl-5-pentyl-5,6,7,8-tetrahydro-4*H*-benzo[4,5]thieno [2,3-*d*]pyrimidin-3-yl)-2-phenyl-acetamide;
- 5 (Compound 164) 2-[(2,3-Dihydro-benzo[1,4]dioxine-5-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 165) 2-[(3,5-Dichloro-4-methoxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 166) 2-Iodo-5-phenyl-2,3,4*a*,5,6,7,8,9,10-octahydro-1*H*-4,11-dithia-
10 5,11*b*-diazabenzofluoren-6-one;
- (Compound 167) 2-Benzoylamino-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid;
- (Compound 168) 2-(2,2,2-Trichloro-1-phenylacetyl-amino-ethyl-amino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 169) 2-(3-Furan-2-yl-acryloylamino)-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid amide;
- (Compound 170) 3-[(3-Bromo-4-hydroxy-5-methoxy-benzylidene)-amino]-2-methyl-5,6,7,8-tetrahydro-3*H*-benzo[4,5] thieno [2,3-*d*]pyrimidin-4-one;
- (Compound 171) 3-[(3-Chloro-4-hydroxy-5-methoxy-benzylidene)-amino]-2-methyl-
20 5,6,7,8-tetrahydro-3*H*-benzo[4,5] thieno [2,3-*d*]pyrimidin-4-one;
- (Compound 172) 2-[3-(4-Chloro-2-methyl-phenoxy)-propionyl-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 173) 2-Amino-6-methyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid isopropyl ester;
- 25 (Compound 174) 7-Benzoyloxyimino-2-pyrrol-1-yl-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 175) 2-(2-Formyl-pyrrol-1-yl)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid;
- (Compound 176) 2-(5-Chloro-pentanoylamino)-4,5,6,7-tetrahydro-benzo [*b*]
30 thiophene-3-carboxylic acid ethyl ester;
- (Compound 177) 3-Allyl-6-methyl-2-thioxo-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno [2,3-*d*]pyrimidin-4-one;
- (Compound 178) (3-Allyl-6-methyl-4-oxo-3,4,5,6,7,8-hexahydro-benzo[4,5]thieno[2,3-*d*]pyrimidin-2-ylsulfanyl)-acetic acid;
- 35 (Compound 179) 2-[2-(4-Bromo-phenyl-2-oxo-ethylsulfanyl)]-6-methyl-3-phenyl-5,6,7,8-tetrahydro-3*H*-benzo [4,5] thieno [2,3-*d*]pyrimidin-4-one;
- (Compound 180) 2-Amino-5-methyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;

- (Compound 181) 2-(2-Bromo-benzoylamino)-7-oxo-4,5,6,7-tetrahydro-benzo[*b*]thio- phene-3-carboxylic acid ethyl ester;
- (Compound 182) 2-(3-Methyl-benzoylamino)- 4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 183) 2-(4-Benzoyl-benzoylamino)- 4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 184) 2-[(2-Ethoxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo[*b*]thio- phene-3-carboxylic acid amide;
- (Compound 185) 2-[2-Amino-3-cyano-7,7-dimethyl-4-(3-nitro-phenyl)-5-oxo-
10 4a,5,6,7,8,8a-hexahydro-4*H*-quinolin-1-yl]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 186) 2-[2-Amino-3-cyano-7,7-dimethyl-4-(4-chloro-phenyl)-5-oxo-4a,5,6,7,8,8a-hexahydro-4*H*-quinolin-1-yl]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 187) 2-[2-Amino-3-cyano-7,7-dimethyl-4-(4-ethyl-phenyl)-5-oxo-4a,5,6,7,8,8a-hexahydro-4*H*-quinolin-1-yl]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 188) 2-[2-Amino-3-cyano-7,7-dimethyl-4-(4-nitro-phenyl)-5-oxo-
20 4a,5,6,7,8,8a-hexahydro-4*H*-quinolin-1-yl]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 189) (3-Allyl--4-oxo-3,4,5,6,7,8-hexahydro-benzo[4,5]thieno [2,3-*d*]pyrimidin-2-ylsulfanyl)-acetic acid methyl ester;
- (Compound 190) 2-(2-Hydroxy-ethylsulfanyl)-5,6,7,8-tetrahydro-3*H*-benzo[4,5]thieno [2,3-*d*]pyrimidin-4-one;
- 25 (Compound 191) Thiophene-2-carboxylic acid 2-ethoxy-4-(4-oxo-3,4,5,6,7,8-hexahydro-benzo-[4,5]thieno-[2,3-*d*]pyrimidin-2-ylsulfanyl)-phenyl ester;
- (Compound 192) 2-(2-Fluoro-benzoylamino)-6-methyl-4,5,6,7-tetrahydro-benzo[*b*] thiophene-3-carboxylic acid isopropyl ester;
- 30 (Compound 193) 3a,7a-Dihydro-benzo[1,3]dioxole-5-carboxylic acid (3-carbamoyl-5-methyl-4,5,6,7-tetrahydro-benzo[*b*]thiophen-2-yl)-amide;
- (Compound 194) 2-[(3a,7a-Dihydro-benzo[1,3]dioxole-5-carbonyl)-amino]-6-methyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid isopropyl ester;
- 35 (Compound 195) 2-[(3a,7a-Dihydro-benzo[1,3]dioxole-5-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 196) 6-Methyl-2-(3-phenyl-propionylamino)-4,5,6,7-tetrahydro-benzo[*b*] thiophene-3-carboxylic acid amide;

- (Compound 197) 2-(2,4-Dichloro-benzoylamino)-6-Methyl-4,5,6,7-tetrahydro-benzo[*b*] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 198) 2-(4-Methoxy-benzoylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- 5 (Compound 199) Tetrahydro-furan-2-carboxylic acid (3-carbamoyl-6-methyl-4,5,6,7-tetrahydro-benzo[*b*]thiophen-2-yl)-amide;
- (Compound 200) 2-[2-(5-Methyl-3-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 201) 2-(4-Fluoro-benzenesulfonylamino)-4,5,6,7-tetrahydro-10 benzo[*b*]thio- phene-3-carboxylic acid amide;
- (Compound 202) 6-*tert*-Butyl-2-(3-phenyl-3-phenylsulfanyl-propionylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 203) 2-[2-(3,5-Dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-6-methyl-15 4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 204) 2-[2-(3,5-Dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 205) 6-Methyl-2-(3,3-diphenyl-propionylamino)-4,5,6,7-tetrahydro-20 benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 206) 2-(3,5-Dimethoxy-benzoylamino)-6-(1,1-dimethyl-propyl)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 207) 6-*tert*-Butyl-2-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl-25 amino]-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid amide;
- (Compound 208) 6-*tert*-Butyl-2-(3-phenyl-3-phenylsulfanyl-propionylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 209) 2-[2-(5-Methyl-3-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-30 tetrahydro-benzo [*b*] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 210) 6-*tert*-Butyl-2-[2-(3-nitro-[1,2,4]triazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 211) 6-*tert*-Butyl-2-[2-(3,5-dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester; 35
- (Compound 212) 6-Methyl-2-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;

- (Compound 213) 6-Methyl-2-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid methyl ester;
- 5 (Compound 214) 6-*tert*-Butyl-2-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 215) 6-*tert*-Butyl-2-[2-(3,5-dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid amide;
- 10 (Compound 216) 6-*tert*-Butyl-2-(3-carboxy-acryloylamino)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid methyl ester;
- (Compound 217) 6-*tert*-Butyl-2-(4-carboxy-butyrylamino)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid methyl ester;
- (Compound 218) 2-[(4-Iodo-2-methyl-2*H*-pyrazole-3-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 219) 2-[4-(4-Chloro-2-methyl-phenoxy)-butyrylamino]-6-methyl-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 220) 2-(2-Phenyl-2-phenylsulfanyl-acetylamino)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 221) 2-[(5-Methyl-3-phenyl-isoxazole-4-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 222) 6-Methyl-2-[2-(3-nitro-[1,2,4]triazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid methyl ester;
- 25 (Compound 223) 6-Methyl-2-[2-(3-nitro-[1,2,4]triazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 224) 2-Amino-6-*tert*-butyl-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid methyl ester;
- (Compound 225) 2-Amino-6-*tert*-butyl-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid amide;
- 30 (Compound 226) 6-Methyl-2-[2-(5-methyl-3-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid methyl ester;
- (Compound 227) 2-[2-(3,5-Dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid methyl ester;
- 35 (Compound 228) 2-[2-(3,5-Dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid amide;
- (Compound 229) 2-[2-(5-Methyl-3-trifluoromethyl-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid methyl ester;

- (Compound 230) 6-Methyl-2-[2-(3-nitro-[1,2,4]triazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 231) 2-[(2-Carboxy-cyclohexanecarbonyl)-amino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid isopropyl ester;
- 5 (Compound 232) 2-(3-Carboxy-acryloylamino)-6-(1,1-dimethyl-propyl)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid amide;
- (Compound 233) 6-(1,1-Dimethyl-propyl)-2-[(5-methyl-furan-2-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid amide;
- (Compound 234) 6-Methyl-2-[(2-methyl-furan-3-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid isopropyl ester;
- 10 (Compound 235) 2-(4-Chloro-benzoylamino)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 236) 2-Benzoylamino-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 237) 2-(Cyclopropanecarbonyl-amino)-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- (Compound 238) 2-[2-(4-Nitrophenyl)-acetylamino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- (Compound 239) 6-Methyl-2-[2-(3-nitro-[1,2,4]triazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- 20 (Compound 240) Furan-2-carboxylic acid [3-(2-hydroxy-ethylcarbamoyl)-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl]-amide;
- (Compound 241) Cyclopropanecarboxylic acid (3-ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-amide;
- 25 (Compound 242) *N*-(3-Ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-acetamide;
- (Compound 243) *N*-(3-Ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-propionamide;
- (Compound 244) *N*-(3-Ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-2-methylacrylamide;
- 30 (Compound 245) 3-Methyl-but-2-enoic acid (3-ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-amide;
- (Compound 246) But-2-enoic acid (3-ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-amide;
- 35 (Compound 247) *N*-(3-ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-2,2-dimethyl-propionamide;
- (Compound 248) Thiophene-2-carboxylic acid (3-ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-amide;

- (Compound 249) Furan-2-carboxylic acid (3-ethoxy-4,5,6,7-tetrahydrobenzo[*b*]thiophen-2-yl)-amide;
- (Compound 250) 2-Acetylamino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylic acid amide;
- 5 (Compound 251) 2-(2,2-Dimethyl-propionylamino)-4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid amide;
- (Compound 252) 2-(Cyclopropanecarbonyl-amino)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylic acid;
- (Compound 253) Cyclopropanecarboxylic acid (3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thiophen-2-yl) amide;
- 10 (Compound 254) 2-Amino-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carbonitrile;
- (Compound 255) 2-Isobutyrylamino-4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid amide;
- (Compound 256) 2-Isobutyrylamino-4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 257) 2-(Ethoxyoxalyl-amino)-4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid ethyl ester;
- (Compound 258) 2-Amino-4-methyl-4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 259) 2-(Cyclopropanecarbonyl amino)-4-methyl-4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid ethyl ester;
- (Compound 260) Oxo-(4,5,6,7-tetrahydrobenzo-[*b*]-thiophen-2-yl)-acetic acid;
- (Compound 261) 2-Chloro-1-(4,5,6,7-tetrahydrobenzo-[*b*]-thiophen-2-yl)-ethanone;
- (Compound 262) 2-Hydrazino-1-(4,5,6,7-tetrahydrobenzo-[*b*]-thiophen-2-yl)-ethanone;
- 25 (Compound 263) 2-(2-Methyl-acryloylamino)-4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid amide;
- (Compound 264) 2-[(Thiophene-2-carbonyl)-amino]- 4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid amide;
- 30 (Compound 265) Furan-2-carboxylic acid (3-carbamoyl-4,5,6,7-tetrahydrobenzo[*b*]-thiophen-2-yl)-amide;
- (Compound 266) 2-(Cyclobutanecarbonyl-amino)-4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid amide;
- (Compound 267) 2-(2-Methyl-butyrylamino)- 4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid amide;
- 35 (Compound 268) 2-(Cyclopropanecarbonyl-amino)-4-methyl-4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid amide;
- (Compound 269) 6-*tert*-Butyl 2-(cyclopropanecarbonyl-amino)- -4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid amide;

- (Compound 270) 2-(Cyclopropanecarbonyl-amino)-6-methyl-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid amide;
- (Compound 271) 2-(Cyclopropylmethyl-amino)- 4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid amide;
- 5 (Compound 272) *N*-(3-Cyano-4,5,6,7-tetrahydrobenzo-[b]-thiophen-2-yl)-acetamide;
- (Compound 273) *N*-(3-Cyano-4,5,6,7-tetrahydrobenzo-[b]-thiophen-2-yl)-benzamide;
- (Compound 274) 5-Bromo-furan-2-carboxylic acid (3-cyano-4,5,6,7-tetrahydrobenzo-[b]-thiophen-2-yl)- amide;
- 10 (Compound 275) *N*-(3-Cyano-4,5,6,7-tetrahydrobenzo-[b]-thiophen-2-yl)-2,2,2,-trifluoro-acetamide;
- (Compound 276) 2-[(Furan-2-ylmethylene)-amino]-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carbonitrile;
- 15 (Compound 277) *N*-(3-Cyano-6-methyl-4,5,6,7-tetrahydrobenzo-[b]-thiophen-2-yl)-acetamide;
- (Compound 278) 2-[(Pyrazine-2-carbonyl)-amino]-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid methyl ester;
- (Compound 279) 2-Isobutyrylamino- 4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid methyl ester;
- 20 (Compound 280) 6-Methyl-2-[(thiophene-2-carbonyl)-amino]- 4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid;
- (Compound 281) 2-[(Thiophene-2-carbonyl)-amino]- 4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid;
- 25 (Compound 282) 2-(Cyclopropanecarbonyl-amino) 4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid;
- (Compound 283) 2-(Cyclohexanecarbonyl-amino) 4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid amide;
- (Compound 284) 2-Acetylamino-6-methyl- 4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid amide;
- 30 (Compound 285) 2-Amino-4,7-dihydro-5*H*-thieno[2,3-*c*]-thiopyran-3-carboxylic acid amide;
- (Compound 286) 2-(Cyclopropanecarbonyl-amino)-4,7-dihydro-5*H*-thieno[2,3-*c*]-thiopyran-3-carboxylic acid amide;
- 35 (Compound 287) 2-(Cyclopropanecarbonyl-amino)-6 λ^4 -oxo-4,5,6,7-tetrahydro-thieno[2,3-*c*]thiopyran-3-carboxylic acid amide.

Other aspects of the present invention relate to 4,5,6,7-tetrahydrobenzo[b]thiophene derivatives of the general formula (I) as shown above as new pharmaceutically active agents, particularly for the prophylaxis and/or treatment of mycobacteria-induced infections (including opportunistic infections) and diseases, pharmaceutical compositions comprising these 4,5,6,7-tetrahydrobenzo[b]thiophene derivatives as active ingredients and a method for treating virally and/or bacterially induced diseases, particularly mycobacteria-induced infections, in mammals, including humans.

10 Surprisingly, it was found that 4,5,6,7-tetrahydrobenzo[b]thiophene derivatives of the general formula I as well as pharmaceutically acceptable salts of these derivatives are effective against mycobacteria-induced infections and diseases at pharmaceutically acceptable concentrations.

15 Additionally, the present invention relates to the use of 4,5,6,7-tetrahydrobenzo[b]thiophene derivatives of the general formula I as well as pharmaceutically acceptable salts thereof for the manufacturing of a pharmaceutical composition for the prophylaxis and/or treatment of virally and/or bacterially induced diseases, particularly mycobacteria-induced infections, including opportunistic infections, and diseases.

The 4,5,6,7-tetrahydrobenzo[b]thiophene derivatives as well as pharmaceutically acceptable salts thereof according to the present invention are effective against mycobacteria induced infections, particularly tuberculosis, but also e.g. leprosy and mycobacteria-induced meningitis. Mycobacteria which induce or cause these infectious diseases are members of the group comprising the tuberculous bacteria *Mycobacterium tuberculosis*, *M. bovis*, *M. africanum* and *M. leprae* as well as the non-tuberculous bacteria *M. abscessus*, *M. avium*, *M. celatum*, *M. chelonae*, *M. fortuitum*, *M. genavense*, *M. gordonae*, *M. haemophilum*, *M. intracellulare*, *M. kansasii*, *M. malmoense*, *M. marinum*, *M. scrofulaceum*, *M. simiae*, *M. szulgai*, *M. ulcerans* and *M. xenopi*. Because of the outstanding clinical importance of tuberculosis, microbiologists have distinguished the so-called "Mycobacterium tuberculosis complex" consisting of *Mycobacterium tuberculosis*, *M. bovis*, and *M. africanum* from all other mycobacteria which form the group of the so-called "atypical mycobacteria" or "non-tuberculous mycobacteria (NTM)".

The present invention also provides a method for treating mycobacteria-induced infections (including opportunistic infections) in mammals (including humans), which method comprises administering to the mammal an amount of at least one 4,5,6,7-

tetrahydrobenzo[b]thiophene derivative and/or a pharmaceutically acceptable salts thereof effective to treat a mycobacteria-induced infection. Especially, the method is used for the treatment of tuberculosis, but also for other mycobacteria-induced infections like leprosy or mycobacteria-induced meningitis.

5

According to a still further aspect, the present invention refers to pharmaceutical compositions comprising at least one 4,5,6,7-tetrahydrobenzo[b]thiophene compound as active ingredient together with at least one pharmaceutically acceptable (i.e. non-toxic) carrier, excipient and/or diluent. The pharmaceutical compositions of the present invention can be prepared in a conventional solid or liquid carrier or diluent and a conventional pharmaceutically-made adjuvant at suitable dosage level in a known way. The preferred preparations are adapted for oral application. These administration forms include, for example, pills, tablets, film tablets, coated tablets, capsules, powders and deposits.

15

Furthermore, the present invention also includes pharmaceutical preparations for parenteral application, including dermal, intradermal, intragastral, intracutan, intravasal, intravenous, intramuscular, intraperitoneal, intranasal, intravaginal, intrabuccal, percutan, rectal, subcutaneous, sublingual, topical, or transdermal application, which preparations in addition to typical vehicles and/or diluents contain at least one 4,5,6,7-tetrahydrobenzo[b]thiophene derivative and/or a pharmaceutical acceptable salt thereof as active ingredient.

25

The pharmaceutical compositions according to the present invention containing at least one 4,5,6,7-tetrahydrobenzo[b]thiophene derivative and/or a pharmaceutical acceptable salt thereof as active ingredient will typically be administered together with suitable carrier materials selected with respect to the intended form of administration, i.e. for oral administration in the form of tablets, capsules (either solid filled, semi-solid filled or liquid filled), powders for constitution, gels, elixirs, dispersable granules, syrups, suspensions, and the like, and consistent with conventional pharmaceutical practices. For example, for oral administration in the form of tablets or capsules, the active drug component may be combined with any oral non-toxic pharmaceutically acceptable carrier, preferably with an inert carrier like lactose, starch, sucrose, cellulose, magnesium stearate, dicalcium phosphate, calcium sulfate, talc, mannitol, ethyl alcohol (liquid filled capsules) and the like. Moreover, suitable binders, lubricants, disintegrating agents and coloring agents may also be incorporated into the tablet or capsule. Powders and tablets may contain about 5 to about 95 weight % of the 4,5,6,7-tetrahydrobenzo[b]thiophene compound or the respective pharmaceutically active salt as active ingredient.

35

Suitable binders include starch, gelatin, natural sugars, corn sweeteners, natural and synthetic gums such as acacia, sodium alginate, carboxymethylcellulose, polyethylene glycol and waxes. Among suitable lubricants there may be mentioned boric acid, sodium benzoate, sodium acetate, sodium chloride, and the like. Suitable disintegrants include starch, methylcellulose, guar gum, and the like. Sweetening and flavoring agents as well as preservatives may also be included, where appropriate. The disintegrants, diluents, lubricants, binders etc. are discussed in more detail below.

Moreover, the pharmaceutical compositions of the present invention may be formulated in sustained release form to provide the rate controlled release of any one or more of the components or active ingredients to optimise the therapeutic effect(s), e.g. antihistaminic activity and the like. Suitable dosage forms for sustained release include tablets having layers of varying disintegration rates or controlled release polymeric matrices impregnated with the active components and shaped in tablet form or capsules containing such impregnated or encapsulated porous polymeric matrices.

Liquid form preparations include solutions, suspensions, and emulsions. As an example, there may be mentioned water or water/propylene glycol solutions for parenteral injections or addition of sweeteners and opacifiers for oral solutions, suspensions, and emulsions. Liquid form preparations may also include solutions for intranasal administration.

Aerosol preparations suitable for inhalation may include solutions and solids in powder form, which may be present in combination with a pharmaceutically acceptable carrier such as an inert, compressed gas, e.g. nitrogen.

For preparing suppositories, a low melting wax, such as a mixture of fatty acid glycerides like cocoa butter is melted first, and the active ingredient is then dispersed homogeneously therein e.g. by stirring. The molten, homogeneous mixture is then poured into conveniently sized moulds, allowed to cool, and thereby solidified.

Also included are solid form preparations which are intended to be converted, shortly before use, to liquid form preparations for either oral or parenteral administration. Such liquid forms include solutions, suspensions, and emulsions.

The 4,5,6,7-tetrahydrobenzo[b]thiophene compounds as well as pharmaceutically acceptable salts thereof according to the present invention may also be delivered transdermally. The transdermal compositions may have the form of a cream, a lotion, an aerosol and/or an emulsion and may be included in a transdermal patch of the matrix or reservoir type as is known in the art for this purpose.

The term capsule as recited herein refers to a specific container or enclosure made e.g. of methyl cellulose, polyvinyl alcohols, or denatured gelatins or starch for holding or containing compositions comprising the active ingredient(s). Capsules with hard shells are typically made of blended or relatively high gel strength gelatins from bones or pork skin. The capsule itself may contain small amounts of dyes, opaquing agents, plasticisers and/or preservatives.

Under tablet a compressed or moulded solid dosage form is understood which comprises the active ingredients with suitable diluents. The tablet may be prepared by compression of mixtures or granulations obtained by wet granulation, dry granulation, or by compaction well known to a person of ordinary skill in the art.

Oral gels refer to the active ingredients dispersed or solubilised in a hydrophilic semi-solid matrix.

Powders for constitution refers to powder blends containing the active ingredients and suitable diluents which can be suspended e.g. in water or in juice.

Suitable diluents are substances that usually make up the major portion of the composition or dosage form. Suitable diluents include sugars such as lactose, sucrose, mannitol, and sorbitol, starches derived from wheat, corn rice, and potato, and celluloses such as microcrystalline cellulose. The amount of diluent in the composition can range from about 5 to about 95 % by weight of the total composition, preferably from about 25 to about 75 weight %, and more preferably from about 30 to about 60 weight %.

The term disintegrants refers to materials added to the composition to support break apart (disintegrate) and release the pharmaceutically active ingredients of a medicament. Suitable disintegrants include starches, "cold water soluble" modified starches such as sodium carboxymethyl starch, natural and synthetic gums such as locust bean, karaya, guar, tragacanth and agar, cellulose derivatives such as methylcellulose and sodium carboxymethylcellulose, microcrystalline celluloses, and cross-linked microcrystalline celluloses such as sodium croscarmellose, alginates

such as alginic acid and sodium alginate, clays such as bentonites, and effervescent mixtures. The amount of disintegrant in the composition may range from about 2 to about 20 weight % of the composition, more preferably from about 5 to about 10 weight %.

5

Binders are substances which bind or "glue" together powder particles and make them cohesive by forming granules, thus serving as the "adhesive" in the formulation. Binders add cohesive strength already available in the diluent or bulking agent. Suitable binders include sugars such as sucrose, starches derived from wheat corn
10 rice and potato, natural gums such as acacia, gelatin and tragacanth, derivatives of seaweed such as alginic acid, sodium alginate and ammonium calcium alginate, cellulose materials such as methylcellulose, sodium carboxymethylcellulose and hydroxypropylmethylcellulose, polyvinylpyrrolidone, and inorganic compounds such as magnesium aluminum silicate. The amount of binder in the composition may
15 range from about 2 to about 20 weight % of the composition, preferably from about 3 to about 10 weight %, and more preferably from about 3 to about 6 weight %.

Lubricants refer to a class of substances which are added to the dosage form to enable the tablet granules etc. after being compressed to release from the mould or
20 die by reducing friction or wear. Suitable lubricants include metallic stearates such as magnesium stearate, calcium stearate, or potassium stearate, stearic acid, high melting point waxes, and other water soluble lubricants such as sodium chloride, sodium benzoate, sodium acetate, sodium oleate, polyethylene glycols and D,L-leucine. Lubricants are usually added at the very last step before compression, since
25 they must be present at the surface of the granules. The amount of lubricant in the composition may range from about 0.2 to about 5 weight % of the composition, preferably from about 0.5 to about 2 weight %, and more preferably from about 0.3 to about 1.5 weight % of the composition.

30 Glidants are materials that prevent caking of the components of the pharmaceutical composition and improve the flow characteristics of granulate so that flow is smooth and uniform. Suitable glidants include silicon dioxide and talc. The amount of glident in the composition may range from about 0.1 to about 5 weight % of the final composition, preferably from about 0.5 to about 2 weight %.

35

Coloring agents are excipients that provide coloration to the composition or the dosage form. Such excipients can include food grade dyes adsorbed onto a suitable adsorbent such as clay or aluminum oxide. The amount of the coloring agent may

vary from about 0.1 to about 5 weight % of the composition, preferably from about 0.1 to about 1 weight %.

To identify substances for drug development against mycobacteria-induced diseases,
5 it was searched for inhibitors of signal transduction components present in mycobacteria. As already mentioned above, the elimination of mycobacteria from the human body is presently achieved by inhibiting the growth of respective bacteria by means of antibiotics. According to the present invention, a novel strategy has been used to fight against mycobacteria, namely to attack mycobacterial signal
10 transduction components which are involved in the persistence of the bacteria within the host cell. Previously, it had been shown that mycobacteria penetrate cells via the endocytotic pathway. Endosomes containing non-pathogenic mycobacteria fuse to lysosomes and subsequently the bacteria are degraded by lysosomal enzymes. However, pathogenic mycobacteria, like *Mycobacterium tuberculosis*, contain
15 additional "virulence genes" which prevent fusion of endosomes and lysosomes and thus circumvent the degradation within a host cell.

Mycobacterial protein serine/threonine kinases, particularly protein kinase G (PknG), have been identified as an essential component involved in the persistence and
20 enhanced survival of pathogenic mycobacteria within a macrophage cell line. Furthermore, it could be demonstrated that the activity of PknG is an essential factor for virulence of mycobacteria. In accordance with the present invention, compounds have been found which are blocking the activity of PknG in a submicromolar range thus showing that PknG is a suitable target for recognising diseases, monitoring
25 diseases, and controlling therapy of diseases related to mycobacterial infections. These compounds (inhibitors) were able to induce efficient degradation of mycobacteria within host cells so that the present invention provides a novel mode for elimination of mycobacteria.

30 It has been found that certain disease inducing factors can be secreted by a cellular organism to the environment of the organism. Specifically, in the present case it has been found that mycobacterial proteins are secreted from the bacterium *Mycobacterium tuberculosis* to the environment of such a bacterium. A protein, which can be secreted by *Mycobacterium tuberculosis* is the protein serine/threonine kinase
35 PknG. The fact that the above-mentioned inventive compounds are particularly effective against PknG may be due to the fact that this protein kinase can be attacked by these compounds without the need to penetrate the (thick) cell wall of *Mycobacterium tuberculosis*.

Consequently, the present invention also refers to the use of at least one protein serine/threonine kinase for developing methods for detection and/or determination of these kinases for recognising diseases, for monitoring diseases, and/or for controlling therapy of diseases. Preferably, the methods are immunochemical methods.

5 According to a preferred embodiment of the present invention, the protein serine/threonine kinase is a mycobacterial protein kinase, particularly the mycobacterial protein serine/threonine kinase G (PknG), which is from *Mycobacterium tuberculosis*.

10

Examples

In the following documents, background information is given with regard to the methods, microorganisms and enzymes used according to the present invention:

15 Peirs et al., *A serine/threonine protein kinase from Mycobacterium tuberculosis*, Eur. J. Biochem., Mar 1, 244(2), 604-612 (1997); Arruda et al., *Cloning of an M. tuberculosis DNA fragment associated with entry and survival inside cells*, Science 261, 1454-1457 (1993); Wieles et al., *Increased intracellular survival of Mycobacterium smegmatis containing the Mycobacterium leprae thioredoxin-thioredoxin reductase gene*, Infect Immun. 65(7), 2537-2541 (1997); Zahrt, *Mycobacterium tuberculosis signal transduction system required for persistent infections*, Proc. Natl. Acad. Sci. 98 (22), 12706-12711 (2001); and Mundayoor et al., *Identification of genes involved in the resistance of mycobacteria to killing by macrophages*, Ann. N. Y. Acad. Sci. 730, 26-36 (1994).

25

Bacterial strains and culture conditions

Mycobacterium smegmatis was grown in Middlebrook 7H9 medium (supplier: Difco), supplemented with 10% ADC (Difco), 0.05% Tween-80 and 0.5% glycerol. *E. coli* was cultivated in LB- or TB-broth without any additional ingredients. Cloning, mutagenesis and expression of PknG and other mycobacterial kinases was done as described by Koul et. al. (Serine/threonine kinases, PknG and PknF of *Mycobacterium tuberculosis*: characterisation and localisation. Microbiology, 147, 2001).

35

GST-fusion protein purification

Purification of GST-fusion proteins was done as described previously by Koul et. al. (Serine/threonine kinases, PknG and PknF of *Mycobacterium tuberculosis*:

characterisation. and localisation. Microbiology, 147, 2001). *E. coli* BL21 cultures containing the respective plasmids were grown overnight in TB-broth. After IPTG induction, the suspensions were incubated for another 16 hours at room temperature. The bacteria were harvested by centrifugation, resuspended in 1x PBS and lysed by sonification. After addition of Triton X-100 (1% final concentration) and subsequent clarifying of the lysates the GST-fusion proteins were purified by addition of GST-sepharose following PBS washes. The proteins were eluted with a buffer containing 50 mM glutathion, 20 mM Tris (pH 8.0), 0.1 M NaCl, 0.1 M Triton X-100 and 1 mM DTT. Thereafter, the eluates were dialysed in 20 mM HEPES (pH 7.5) and 30 % glycerol.

Determination of protein kinase activity

The activity of all protein serine threonine kinases from *Mycobacterium tuberculosis* was determined by addition of myelin basic protein as a substrate in an *in vitro* kinase assay. The buffer conditions were as follows: 20 mM HEPES (pH 7.5), 20 mM MgCl₂, and 5 mM MnCl₂, for all kinases except PknG, PknI, PknJ, and PknL. These protein kinases required lower salt concentrations, namely 1 mM MgCl₂, and 1 mM MnCl₂. The optimum ATP concentration for each kinase was determined by titration of ATP in a range between 0.0033 μM and 100 μM. The inhibitor studies were performed with ATP concentrations similar to the Michaelis constant (K_m) for ATP. We further analysed the role of PknG in pathogenesis of mycobacteria in cellular infection model.

Infection of macrophage cells with recombinant *Mycobacterium smegmatis*

Mycobacterium smegmatis, electroporated with either vector alone or mycobacterial expression vector containing PknG (wild type) or PknG-K181M (Mutant), was cultured for 2 days in Middlebrook 7H9 medium containing 0.05% Tween-80 and 0.5% glycerol. Bacteria were pelleted at 1500 x g for 3 minutes by centrifugation and resuspended by vigorous agitating (Vortex) in Dulbecco's modified Eagle's medium (DMEM, GIBCO-BRL, Gaithersburg, USA) containing 5 % fetal bovine serum (FBS) for infecting murine macrophage cell line RAW (American Type Culture Collection No. 91B-71). This yielded a bacterial supernatant consisting mostly of single mycobacterial cells as observed by acid fast staining. Under the assumption that an optical density (O.D.) of 0.1 at 650 nm equals to 10⁸ CFU/ml (see in this respect Wei et al., "Identification of a *Mycobacterium tuberculosis* Gene that enhances survival of *M. smegmatis* in Macrophages", J. Bacteriol. 182, 377-384 (2000)), the O.D. of *Mycobacterium smegmatis* cell suspension was measured and diluted to 5 x 10⁶

CFU/ml in DMEM containing 5 % FBS. Viable counts were performed on Middlebrook 7H10 medium.

The RAW cell line was maintained in DMEM medium supplemented with 10 % FBS.

5 The survival assay for recombinant *Mycobacterium smegmatis* was performed as described by Wei et al., cited above. RAW cells were plated in a 24 well tissue culture plate (4×10^5 cells/well) and incubated overnight in 5 % CO₂ at 37°C. The inoculum (1 ml) containing 5×10^6 recombinant *Mycobacterium smegmatis* was added to achieve multiplicities of infection (moi) of 10. The plate was incubated for 2

10 hours at 37°C in 5 % CO₂. The infected monolayers were washed twice with warm DMEM and treated with 2 % FCS containing 200 µg of amikacin/ml for 1 hour at 37°C to kill extracellular *M. smegmatis*. The cells were again washed twice with warm DMEM and further incubated in DMEM containing 20 µg of amikacin. This time point was considered 0 hours of infection. The 24 hours infected monolayer was incubated

15 with 20 µg of amikacin/ml to prevent extracellular growth of any bacteria released by premature lysis of infected RAW cells. Cells were washed twice with warm DMEM before lysis was effected by addition of a 0.1 % SDS solution and vigorously pipeting several times to ensure lysis of cells and release of surviving bacteria. The lysates were diluted in 7H9 broth and plated onto 7H10 agar plates and CFU were counted

20 after incubation at 37°C for 4 to 5 days.

Validation of mycobacterial kinase as a mycobacterial virulence gene

Mycobacterium smegmatis was electroporated either with wildtype or mutant kinase

25 (which exerts no kinase activity) or vector control. Mouse macrophage cell line (RAW) was infected with the various recombinant *M. smegmatis* expressing either pknG wild type or PknG K/M mutant or vector alone. After infection, the cells were lysed at different time points and the amount of intracellular bacteria was analysed. As can be seen from Fig. 1, after one hour postinfection the amount of bacteria

30 recovered from macrophages infected with *M. smegmatis* expressing PknG wild type or K/M mutant or vector alone was the same. This shows that the recombinant *M. smegmatis* strains were internalised with equal efficiency. However, after 24 hour postinfection the amount of *M. smegmatis* transformed with the vector control or the mutant kinase was substantially decreased within macrophages. This shows an

35 efficient clearance or degradation of the the *M. smegmatis* expressing vector alone or PknG K/M mutant by the lysosomal degradation pathway with in the macrophages.

But in contrast, after 24 hrs an approximately tenfold increased amount of *M. smegmatis* survived within the cells expressing wildtype PknG compared to the mutant. This clearly demonstrates that the kinase activity of PknG increases the intracellular survival of *M. smegmatis* within macrophages and as such makes PknG an important virulence factor of mycobacteria. Consequently, the kinase is a promising target for recognising, monitoring, and controlling therapy of various diseases.

10 Screening for inhibitors of PknG

A search was conducted for specific molecules inhibiting the target kinase (PknG) of *Mycobacterium tuberculosis*. In a kinase platform a suitable substrate was identified and an *in vitro* assay was adapted to high throughput screening. Subsequently, a library comprising 55.000 compounds using the established *in vitro* kinase assay was screened. Table I shows the half-maximal inhibition constant (IC₅₀) values of small synthetic molecules (compound 237 (2-(Cyclopropanecarbonyl-amino)-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide), compound 238 (2-[2-(4-Nitrophenyl)-acetylamino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide), compound 239 (6-Methyl-2-[2-(3-nitro-[1,2,4]triazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide), compound 240 (Furan-2-carboxylic acid [3-(2-hydroxy-ethylcarbamoyl)-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl]-amide), compound 250 (2-Acetyl-amino-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylic acid amide), compound 252 (2-(Cyclopropanecarbonyl-amino)-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid), compound 255 (2-Isobutyrylamino-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid amide), compound 256 (2-Isobutyrylamino-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid ethyl ester), compound 266 (2-Cyclobutanecarbonyl-amino)-4,5,6,7-tetrahydro-benzo-[b]-thiophene-3-carboxylic acid amide), compound 267 (2-(2-Methyl-butyrylamino)-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid amide), compound 270 (2-(Cyclopropanecarbonyl-amino)-6-methyl-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid amide), compound 284 (2-Acetylamino-6-methyl-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid amide) and compound 286 (2-(Cyclopropanecarbonyl-amino)-4,7-dihydro-5H-thieno[2,3-c]-thiopyran-3-carboxylic acid amide)) for inhibiting mycobacterial PknG .

35 As is evident from Table I, compound 237 and compound 270 are the most effective ones among of those tested in inhibiting the activity of protein serine/threonine kinase

G of *M. tuberculosis*, compound 270 having an IC₅₀ value of only 900 nm and compound 237 having an IC₅₀-value of even only 200 nM. With compounds 238, 239, 240, 250, 252, 255, 256, 266, 267, 284 and 286 also satisfactory results were obtained, the compounds having IC₅₀-values, between 2 μm and more than 30 μm.

5

Table I

Small synthetic molecules which inhibit mycobacterial protein kinase G (PknG)

Compound No.	Inhibition of PknG (IC ₅₀ , [μM])
Compound 237	0.2
Compound 238	~ 5
Compound 239	> 30
Compound 240	16
Compound 250	> 30
Compound 252	~ 19
Compound 255	~ 3
Compound 256	> 30
Compound 266	~ 3
Compound 267	~15
Compound 270	0.9
Compound 284	~12
Compound 286	~ 2

10

Survival of *Mycobacterium smegmatis* transformed with wildtype PknG within cells in the presence or absence of Compound 237

15 *M. smegmatis* was electroporated with either wildtype or mutant PknG construct or with vector control. RAW cells were infected with recombinant *M. smegmatis* expressing wildtype PknG in the presence of different concentrations of compound A. After infection, the cells were lysed at different time points and the amount of intracellular bacteria was analysed. At one hour postinfection equal amounts of

bacteria were recovered from the macrophages expressing either PknG wild type or mutant or vector alone (see Fig. 2). However 24 h postinfection, as shown in Fig. 1, bacteria transformed with mutant or vector control was cleared or degraded in macrophages up to 85%. In contrast, *M. smegmatis* expressing wild type pknG was cleared only 25%, showing an increased resistance towards intracellular degradation within macrophage cell line. In the presence of 10 μ M compound 237 the clearance of PknG expressing *M. smegmatis* was as efficient as observed with the mutant or vector control transformants (Fig. 2). This shows that PknG kinase activity was essential for the increased intracellular survival of *M. smegmatis* within macrophages. Furthermore, this demonstrates that compound 237 affected survival of *M. smegmatis* expressing PknG wildtype within macrophages.

Secretion of PknG outside the bacterial cell

In the following it is demonstrated that PknG is secreted outside the cell into the culture supernatant by mycobacterial cells.

1) PknG and ESAT (a secretory protein that acts as a positive control) are cloned in BamH1 site of pYUB 2401. This vector contains the promoter for hsp60. A in-frame fusion with the start of hsp60 and phoA at the C-terminus by cloning into the BamH1 site. The vector is kanamycin resistant. After cloning PknG and ESAT in pYUB2401 they were electroporated in *M. smegmatis* and the colonies were grown on LB plates with 40 μ g of 5-bromo-4-chloro-3-indoylphosphate (BCIP) and with 20 μ g of kanamycin used for screening.

PhoA fusion proteins that are exported beyond cytoplasm are enzymatic ally active and capable of hydrolysing the BCIP, the chromogenic substrate of PhoA to produce the blue colonies.

2) *M. smegmatis* strains containing either

- 1) ESAT-PhoA
- 2) PknG-PhoA or
- 3) PhoA alone

were grown in 7H9 medium with kanamycin to saturation for 5-6 days and then diluted to the final optical density (O.D.) of 0.005 at 600 nm.

3) These cultures were then grown for 40 hours at 37 $^{\circ}$ C. The OD₆₀₀ of each strain was measured at the start of the experiment.

- 4) A 0.5 ml portion of the cell culture was pelleted and resuspended in equal volume 1 M Tris (pH. 8.0).
- 5) Then 0.1 ml of cells was added to 1.0 ml of 2 mM p-nitrophenyl phosphate plus sodium salt in 1 M Tris (pH 8.0).
- 6) The reaction was incubated in dark at 37 °C until a yellow reaction product was formed.
- 7) Next , 0.1 ml of 1 M K₂HP0₄ was added to terminate the reaction.
- 8) The bacteria were pelleted and the OD₄₂₀ of 1.0 ml of the supernatant was measured.
- 9) Alkaline phosphatase activity units were determined by the following formula:

$$\frac{1000 \times OD_{420}}{OD_{600} \times 0.1 \text{ ml volume of cells}}$$

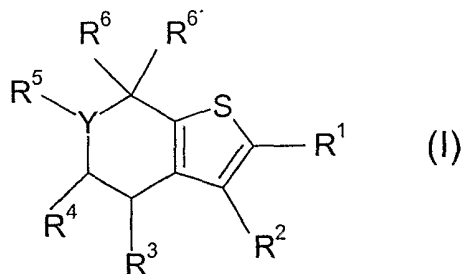
The negative control will be the *M. smegmatis* cells alone and PhoA transfected *M. smegmatis*.

The above method is described in Braunstein M, Griffin TJ IV, Kriakov JI, Friedman ST, Grindley ND, Jacobs WR Jr., „*Mycobacterium tuberculosis* proteins using a *Tn552'*phoA *in vitro* transposition system”, J Bacteriol. 2000 May;182(10):2732-40.

- 30 The result of the above-mentioned experiment shows that PknG is a secretory protein that is secreted outside the mycobacterial cells. Fig. 3 shows the alkaline phosphatase secretions assay for PknG for different PhoA fusion constructs. The secreted PknG can phosphorylate host cell proteins that might be critical in survival of mycobacterium in host cells.

Claims

1. Compounds having the general formula (I)



5

wherein

Y represents C or S;

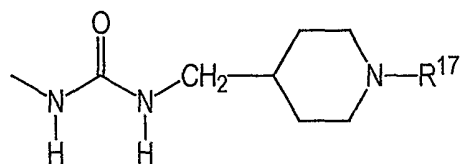
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wherein

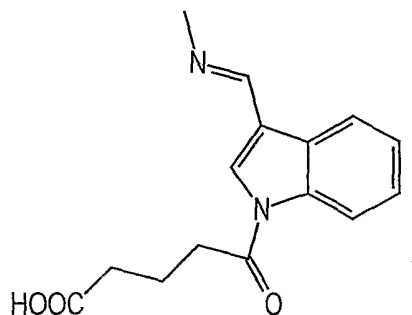
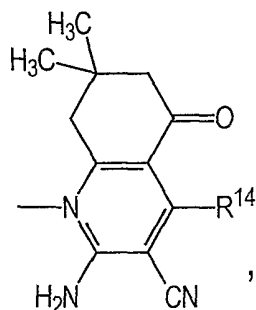
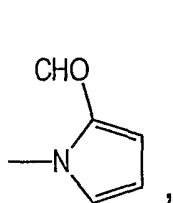
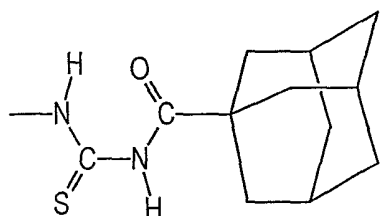
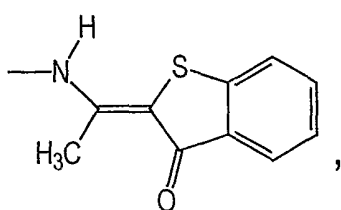
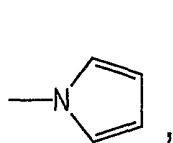
R¹ represents R², -NH-CO-R¹⁶, -NH₂, -N=CH-R¹⁵, -N=CH-R¹⁶,
 -NH-CH₂-R¹⁴, -NH-CH₂-R¹⁶, -NH-SO₂-R¹⁴, -NH-CO-NH-R¹⁴,
 -NH-CS-NH-CH(CCl₃)-NH-CO-R¹⁶,

-NH-CH(CCl₃)-NH-CO-R¹²,

-NH-CS-NH-R¹², -N=CH-R¹²,



15



R² represents -COOR¹², -CONR¹²R¹², -CONR¹²R¹⁴, -C≡N, -COCOOR¹²,
 -COCH₂Cl, -COCONHNH₂,

R^3, R^4, R^5 represent independently of each other $-R^{11}, -R^{12}, -R^{12'}, -OR^{12}, -SR^{12}, -NO_2, -CO-R^{12}, -NO, -N_3, -CN, -OCN, -NCO, -SCN, -NCS, -COOR^{12}, -COCN, -CONR^{12}R^{12'}, -NR^{12}R^{12'}, -SOR^{12}, -SO_2R^{12}, -SO_3R^{12}, -CH_2OR^{12}$;

5

in one case R^6 represents $-R^{11}, -R^{12}, -R^{12'}, -OR^{12}, -SR^{12}, -NO_2, -CO-R^{12}, -NO, -N_3, -CN, -OCN, -NCO, -SCN, -NCS, -COOR^{12}, -COCN, -CONR^{12}R^{12'}, -NR^{12}R^{12'}, -SOR^{12}, -SO_2R^{12}, -SO_3R^{12}$, and R^6 is hydrogen;

10

in the other case R^6 and $R^{6'}$ together represent a carbonyl oxygen or a oximo residue $=N-OH$ or $=N-OOC-R^{12}$;

R^7, R^8, R^9, R^{10} represent independently of each other $-R^{11}, -R^{12}, -OR^{12}, -SR^{12}, -NO_2, -CO-R^{12}, -COOR^{12}, -OOCR^{16}$;

15

R^{11} represents $-F, -Cl, -Br, -I$;

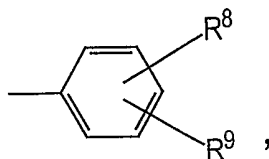
$R^{12}, R^{12'}$ represent independently of each other $-H, -CH_3, -C(R^{11})_3, -C_2H_5, -C_3H_7, -CH(CH_3)_2, -CH_2-CH=CH_2, -CCH_3=CH_2, -CH=C(CH_3)_2, -CH=CH-CH_3, -CH=CHC_2H_5, -CH(CH_3)C_2H_5, -(CH_2)_n-C\equiv C-R^5, -C_4H_9, -C(CH_3)_3, -Ph, -CH_2-R^{15}; -C_2H_4OH$ with n being an integer from 0-2

20

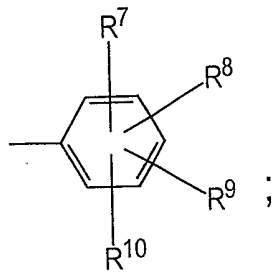
R^{13} represents $-CF_2CHF_2, -C_5H_{11}, -C_6H_{11}, -C_6H_{13}, -C_7H_{15}, -C_8H_{17}, -C_9H_{19}, -C_{10}H_{21}, -C_{11}H_{23}, -C_{12}H_{25}, -C_{13}H_{27}, -CH_2SPh, -CH_2R^{11}, -C_2H_4R^{11}, -C_3H_6R^{11}, -C_4H_8R^{11}, -C_2H_4Ph, -CH=CH-COOR^{12}, -CH_2COOR^{12}, -C_2H_4COOR^{12}, -C_3H_6COOR^{12}, -CH(Ph)-SPh, -C_3H_5, -CH_2CH(Ph)_2, -C_4H_7, -C_5H_9, -C(CH_3)_2CH_2R^{11}, -CH_2CH(CH_3)_2, -CH(R^{11})Ph, -CH_2CH(CH_3)CH_2C(CH_3)_3, -CH(C_2H_5)-C_4H_9, -CH(R^{11})_2, -CH(Ph)-C_2H_5, -CH_2C(CH_3)_3$,

30

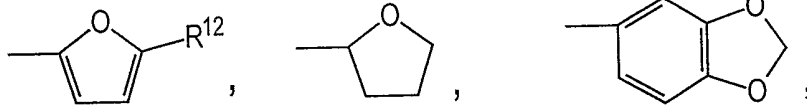
R^{14} represents



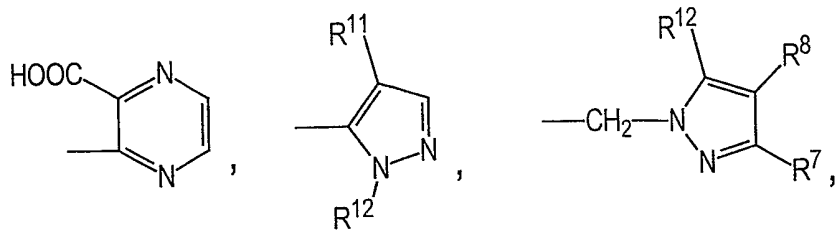
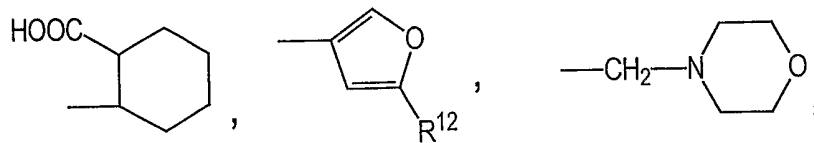
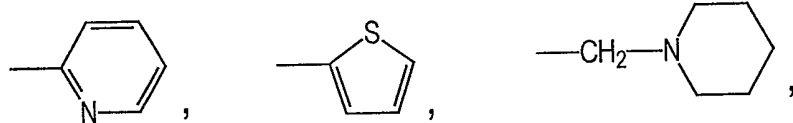
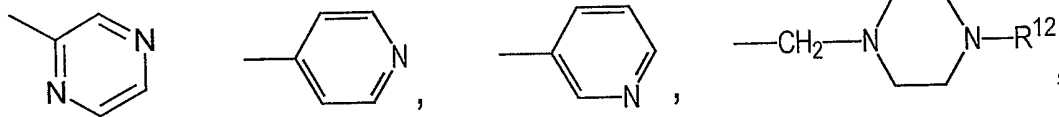
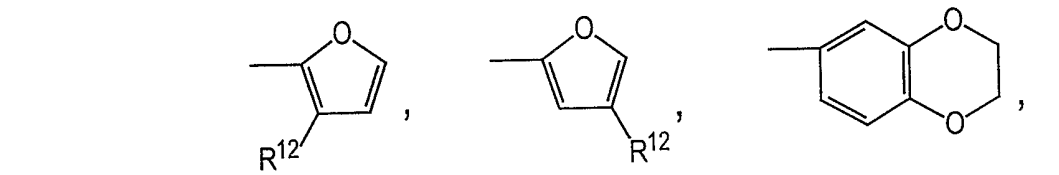
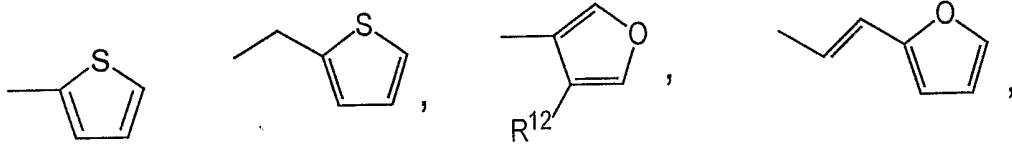
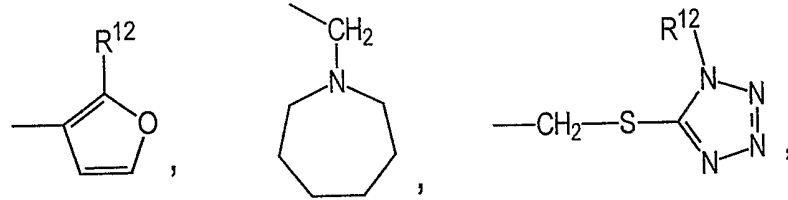
R¹⁵ represents

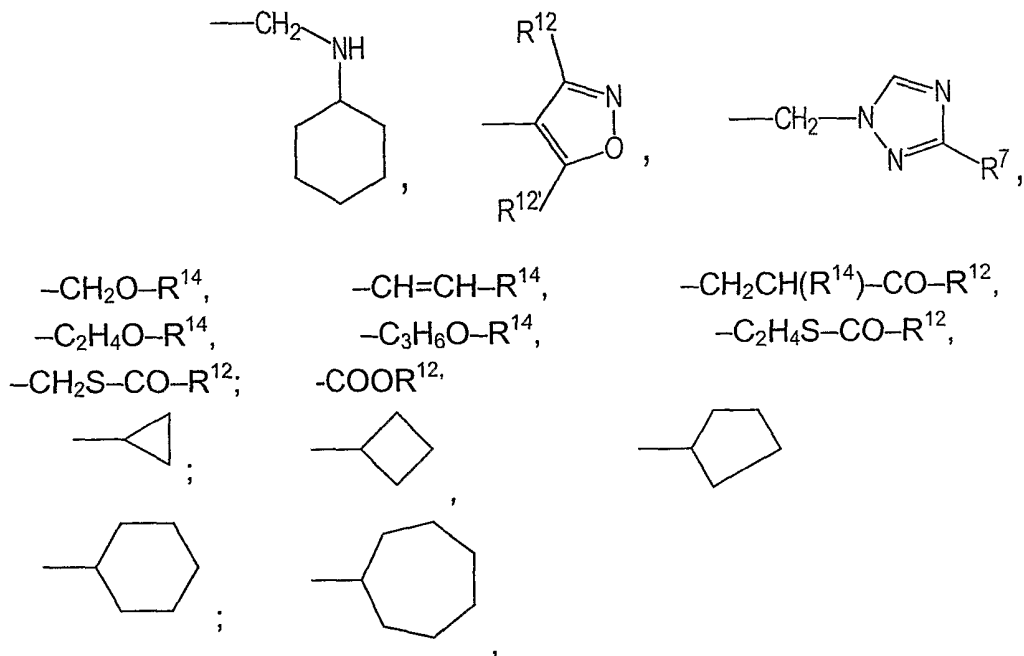


R¹⁶ is R¹²,



R¹³, R¹⁵,

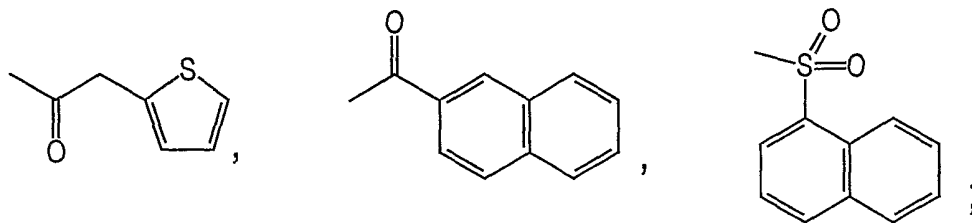




nitrobenzyl, particularly p-nitrobenzyl;

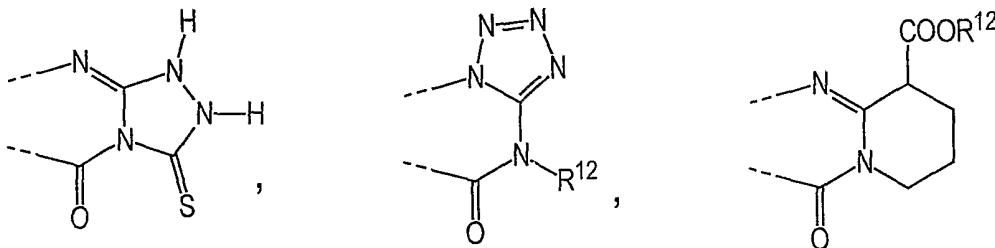
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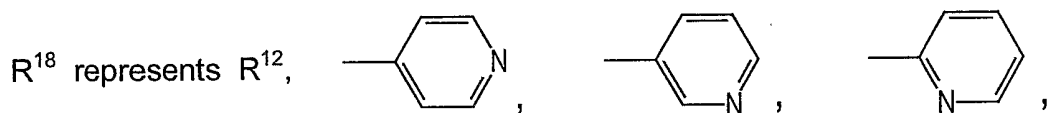
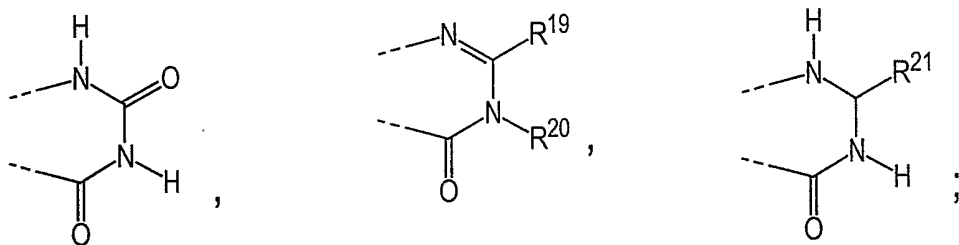
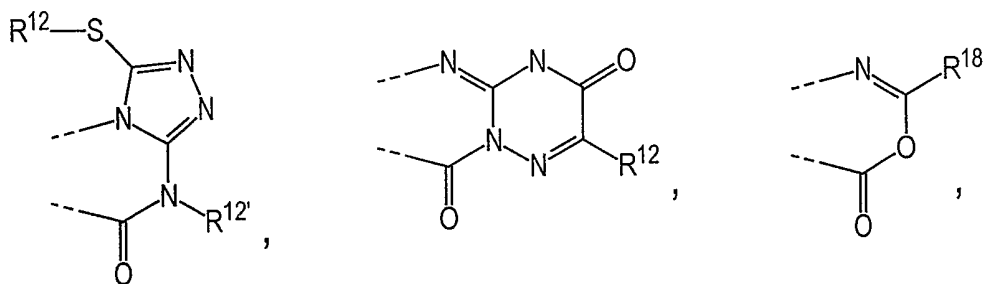
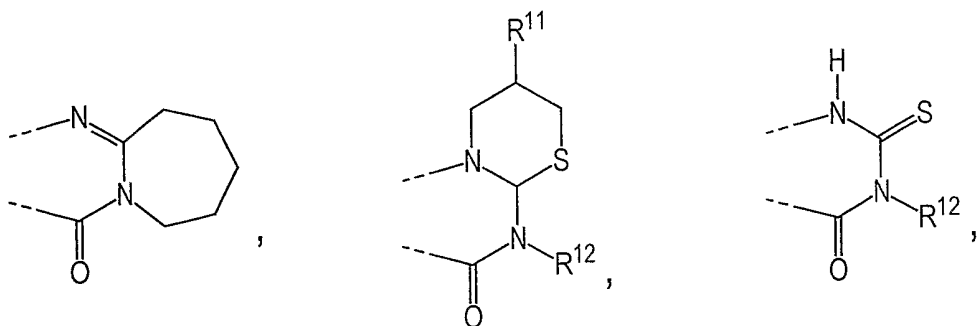
R^{17} represents ---H , ---CO---R^{12} , ---CO---R^{13} , ---CO---R^{14} , $\text{---CO---NH---R}^{12}$,
 $\text{---CO---NH---R}^{13}$, $\text{---CO---NH---R}^{14}$, $\text{---SO}_2\text{---R}^{14}$, $\text{---CO---NH---CH}_2\text{---COO---R}^{12}$,
 $\text{---CO---CH}_2\text{---O---R}^{14}$, $\text{---CO---CH=CH---R}^{14}$,



10

or R^1 and R^2 together represent a heterocyclic ring system having the following formula

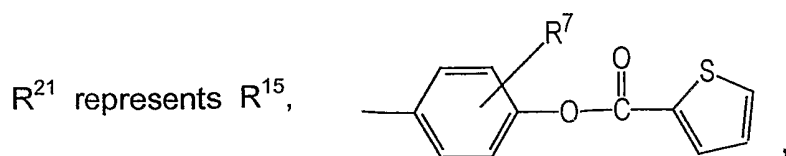


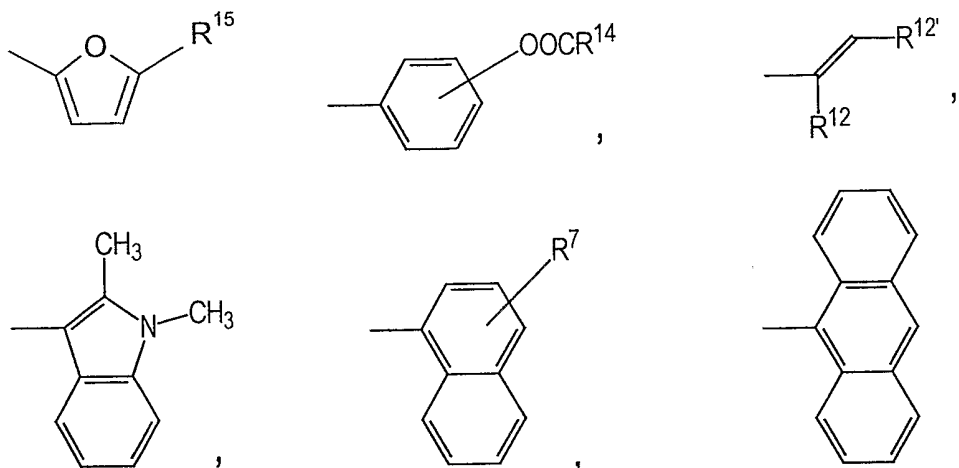


5 R¹⁹ represents R³, R¹⁴, -SCH₂-R³, -SCH₂-CO-R¹⁴, -SCH₂-CO-NH-R¹⁴, -SCH₂-CO-NH-CH₂-R¹², -NH-CO-CH₂-OR¹⁴, -CO-NH-N=CHR¹²(R¹⁴),



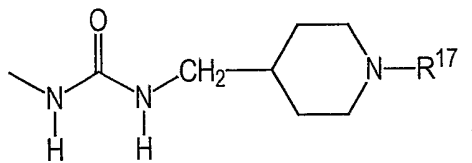
R²⁰ represents R¹², -NH-CO-R¹², -N=CH-R¹⁵;





and pharmaceutically acceptable salts of these compounds.

- 5 2. Compounds according to claim 1, wherein
 R^1 represents R^2 , $-\text{NH}-\text{CO}-R^{16}$, $-\text{N}=\text{CH}-R^{15}$, $-\text{NH}-\text{CH}_2-R^{14}$,
 $-\text{NH}-\text{SO}_2-R^{14}$, $-\text{NH}-\text{CO}-\text{NH}-R^{14}$, $-\text{NH}-\text{CS}-\text{NH}-\text{CH}(\text{CCl}_3)-\text{NH}-\text{CO}-R^{16}$,
 $-\text{NH}-\text{CH}(\text{CCl}_3)-\text{NH}-\text{CO}-R^{12}$,
 $-\text{NH}-\text{CS}-\text{NH}-R^{12}$,



and wherein R^2 , R^{12} , R^{14} , R^{15} , R^{16} , and R^{17} have the meanings as defined in claim 1.

- 10 3. Compounds according to any previous claim, wherein
 R^3 , R^4 , R^5 and R^6 represent independently of each other $-\text{R}^{11}$, $-\text{R}^{12}$,
 $-\text{R}^{12'}$, $-\text{OR}^{12}$, $-\text{SR}^{12}$, $-\text{NO}_2$, $-\text{CO}-\text{R}^{12}$, $-\text{COOR}^{12}$, $-\text{CONR}^{12}\text{R}^{12'}$,
 $-\text{NR}^{12}\text{R}^{12'}$, $-\text{SO}_2\text{R}^{12}$, $-\text{SO}_3\text{R}^{12}$, $-\text{CH}_2\text{OR}^{12}$,
15 and wherein R^{11} , R^{12} , and $R^{12'}$ have the meanings as defined in claim 1.

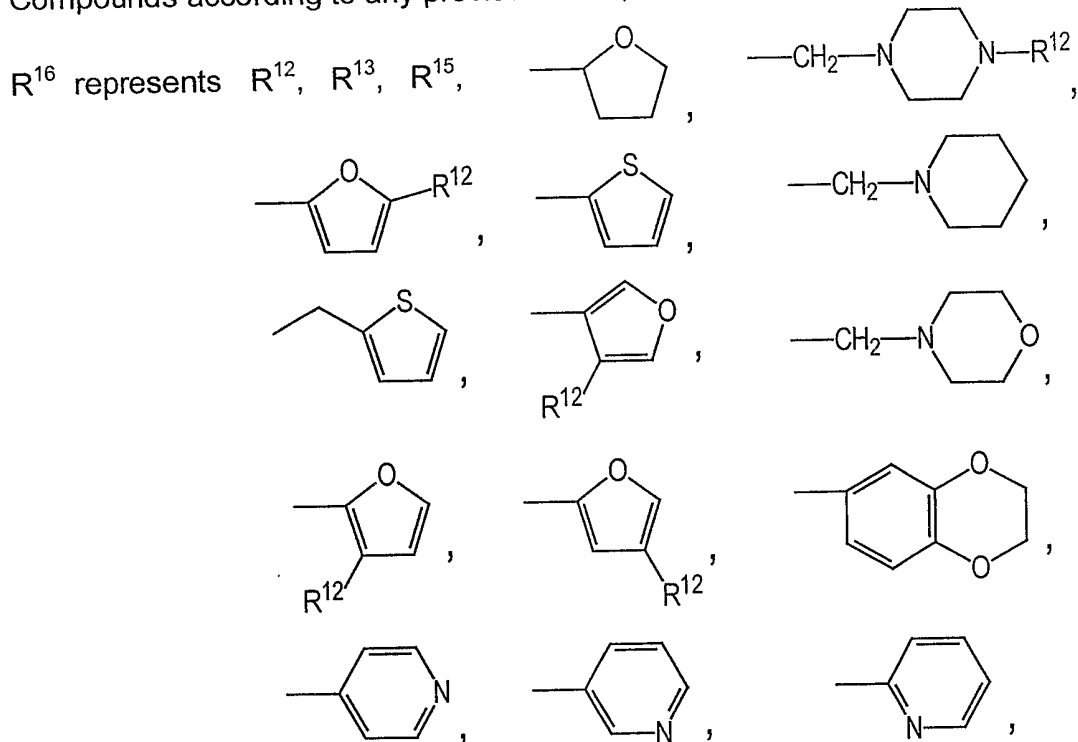
4. Compounds according to any previous claim, wherein
 R^7 , R^8 , R^9 , R^{10} represent independently of each other $-\text{R}^{11}$, $-\text{R}^{12}$, $-\text{OR}^{12}$,
 $-\text{SR}^{12}$, $-\text{NO}_2$, $-\text{CO}-\text{R}^{12}$, $-\text{COOR}^{12}$, $-\text{OOCR}^{12}$,
20 and wherein R^{11} and R^{12} have the meanings as defined in claim 1.

5. Compounds according to any previous claim, wherein
 R^{13} represents $-\text{CF}_2\text{CHF}_2$, $-\text{C}_5\text{H}_{11}$, $-\text{C}_6\text{H}_{11}$, $-\text{C}_6\text{H}_{13}$, $-\text{C}_7\text{H}_{15}$, $-\text{C}_8\text{H}_{17}$,
 $-\text{C}_9\text{H}_{19}$, $-\text{C}_{10}\text{H}_{21}$, $-\text{C}_{11}\text{H}_{23}$, $-\text{C}_{12}\text{H}_{25}$, $-\text{C}_{13}\text{H}_{27}$, $-\text{CH}_2\text{SPh}$, $-\text{CH}_2\text{R}^{11}$,
25 $-\text{C}_2\text{H}_4\text{R}^{11}$, $-\text{C}_3\text{H}_6\text{R}^{11}$, $-\text{C}_4\text{H}_8\text{R}^{11}$, $-\text{C}_2\text{H}_4\text{Ph}$, $-\text{CH}=\text{CH}-\text{COOR}^{12}$,
 $-\text{CH}_2\text{COOR}^{12}$, $-\text{C}_2\text{H}_4\text{COOR}^{12}$, $-\text{C}_3\text{H}_6\text{COOR}^{12}$, $-\text{CH}(\text{Ph})-\text{SPh}$, $-\text{C}_3\text{H}_5$,

$-\text{CH}_2\text{CH}(\text{Ph})_2$, $-\text{C}_4\text{H}_7$, $-\text{C}_5\text{H}_9$, $-\text{C}(\text{CH}_3)_2\text{CH}_2\text{R}^{11}$, $-\text{CH}_2\text{CH}(\text{CH}_3)_2$,
 $-\text{CH}(\text{R}^{11})\text{Ph}$, $-\text{CH}_2\text{CH}(\text{CH}_3)\text{CH}_2\text{C}(\text{CH}_3)_3$, $-\text{CH}(\text{C}_2\text{H}_5)-\text{C}_4\text{H}_9$, $-\text{CH}(\text{R}^{11})_2$,
 $-\text{CH}(\text{Ph})-\text{C}_2\text{H}_5$, $-\text{CH}_2\text{C}(\text{CH}_3)_3$,
 and wherein R^{11} and R^{12} have the meanings as defined in claim 1.

5

6. Compounds according to any previous claim, wherein

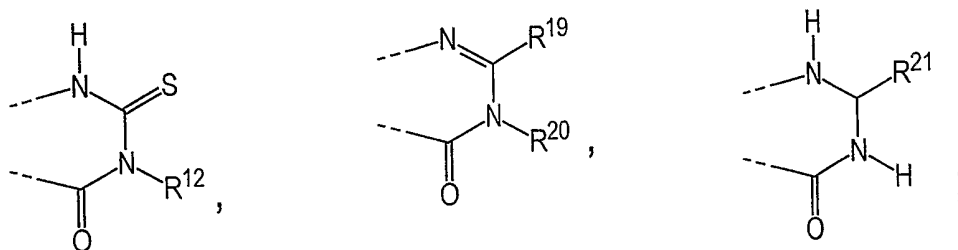


and wherein R^{12} , R^{13} , and R^{15} have the meanings as defined in claim 1.

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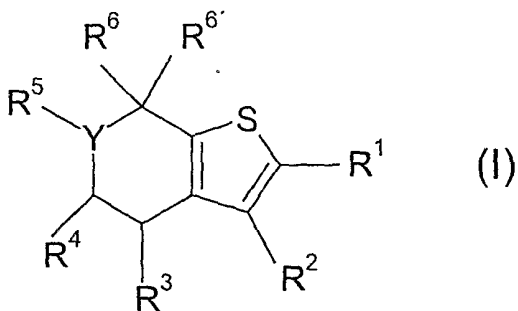
7. Compounds according to any previous claim, wherein

R^1 and R^2 form a heterocyclic ring system having the following formula



and wherein R^{12} , R^{19} , R^{20} , and R^{21} have the meanings as defined in claim 1.

8. Use of at least one compound of the general formula (I)



5

wherein

Y represents C or S;

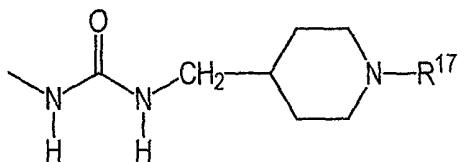
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wherein

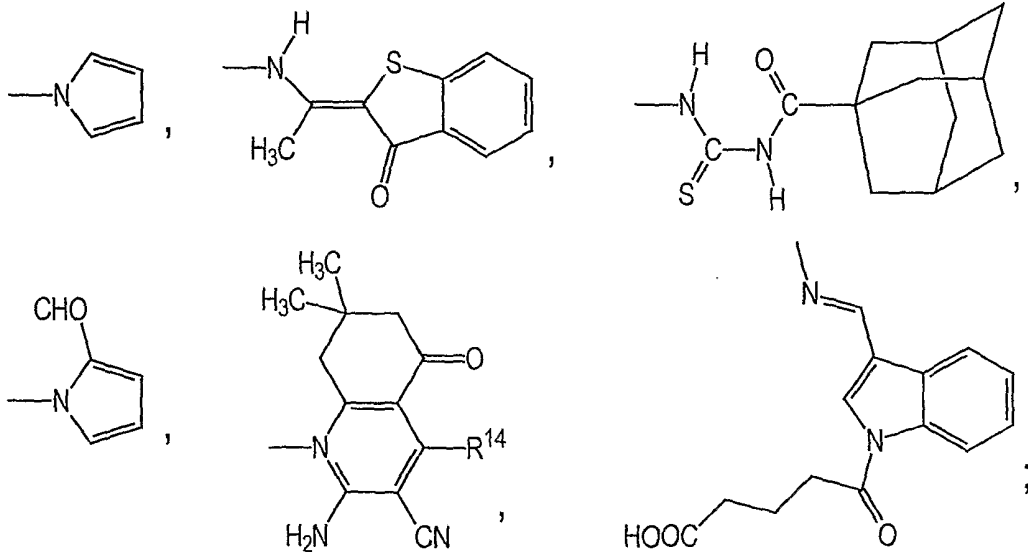
R^1 represents R^2 , $-NH-CO-R^{16}$, $-NH_2$, $-N=CH-R^{15}$, $-N=CH-R^{16}$,
 $-NH-CH_2-R^{14}$, $-NH-CH_2-R^{16}$, $-NH-SO_2-R^{14}$, $-NH-CO-NH-R^{14}$,
 $-NH-CS-NH-CH(CCl_3)-NH-CO-R^{16}$,

$-NH-CH(CCl_3)-NH-CO-R^{12}$,

$-NH-CS-NH-R^{12}$,



15



R^2 represents $-COOR^{12}$, $-CONR^{12}R^{12'}$, $-CONR^{12}R^{14}$,

R^3, R^4, R^5 represent independently of each other $-R^{11}, -R^{12}, -R^{12'}$,
 $-OR^{12}, -SR^{12}, -NO_2, -CO-R^{12}, -NO, -N_3, -CN, -OCN, -NCO,$
 $-SCN, -NCS, -COOR^{12}, -COCN, -CONR^{12}R^{12'}, -NR^{12}R^{12'}, -SOR^{12},$
 $-SO_2R^{12}, -SO_3R^{12}, -CH_2OR^{12};$

5

in one case R^6 represents $-R^{11}, -R^{12}, -R^{12'}, -OR^{12}, -SR^{12}, -NO_2,$
 $-CO-R^{12}, -NO, -N_3, -CN, -OCN, -NCO, -SCN, -NCS,$
 $-COOR^{12}, -COCN, -CONR^{12}R^{12'}, -NR^{12}R^{12'}, -SOR^{12}, -SO_2R^{12},$
 $-SO_3R^{12},$ and R^6 is hydrogen;

10

in the other case R^6 and $R^{6'}$ together represent a carbonyl oxygen or a
oximo residue $=N-OH$ or $=N-OOC-R^{12};$

R^7, R^8, R^9, R^{10} represent independently of each other $-R^{11}, -R^{12}, -OR^{12},$
 $-SR^{12}, -NO_2, -CO-R^{12}, -COOR^{12}, -OOCR^{16};$

15

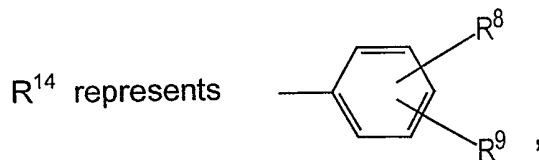
R^{11} represents $-F, -Cl, -Br, -I;$

$R^{12}, R^{12'}$ represent independently of each other $-H, -CH_3, -C(R^{11})_3,$
 $-C_2H_5, -C_3H_7, -CH(CH_3)_2, -CH_2-CH=CH_2, -CCH_3=CH_2, -CH=C(CH_3)_2, -$
 $CH=CH-CH_3, -CH=CHC_2H_5, -CH(CH_3)C_2H_5, -(CH_2)_n-C\equiv C-R^5, -C_4H_9,$
 $-C(CH_3)_3, -Ph, -CH_2R^{15}; -C_2H_4OH$ with n being an integer from 0-2

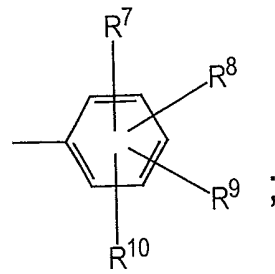
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R^{13} represents $-CF_2CHF_2, -C_5H_{11}, -C_6H_{11}, -C_6H_{13}, -C_7H_{15}, -C_8H_{17},$
 $-C_9H_{19}, -C_{10}H_{21}, -C_{11}H_{23}, -C_{12}H_{25}, -C_{13}H_{27}, -CH_2SPh, -CH_2R^{11},$
 $-C_2H_4R^{11}, -C_3H_6R^{11}, -C_4H_8R^{11}, -C_2H_4Ph, -CH=CH-COOR^{12},$
 $-CH_2COOR^{12}, -C_2H_4COOR^{12}, -C_3H_6COOR^{12}, -CH(Ph)-SPh, -C_3H_5,$
 $-CH_2CH(Ph)_2, -C_4H_7, -C_5H_9, -C(CH_3)_2CH_2R^{11}, -CH_2CH(CH_3)_2,$
 $-CH(R^{11})Ph, -CH_2CH(CH_3)_2CH_2C(CH_3)_3, -CH(C_2H_5)-C_4H_9, -CH(R^{11})_2,$
 $-CH(Ph)-C_2H_5, -CH_2C(CH_3)_3,$

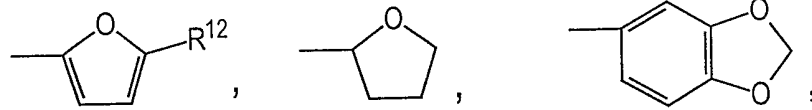
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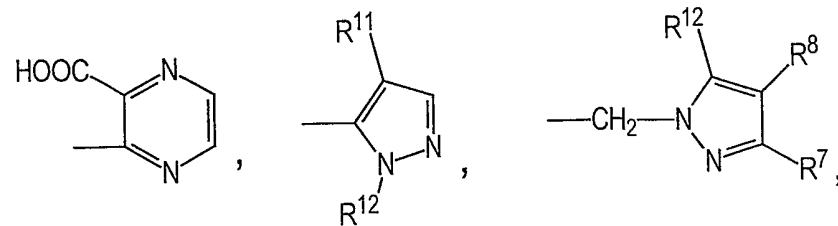
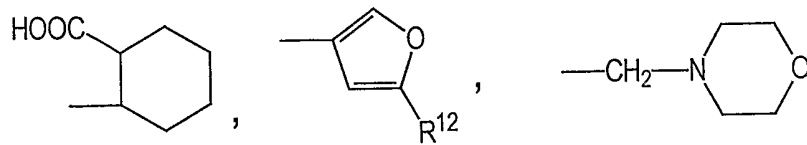
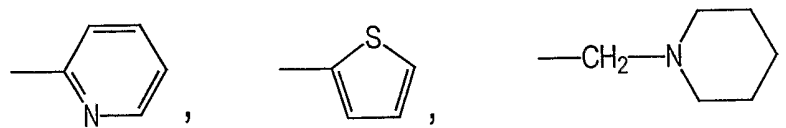
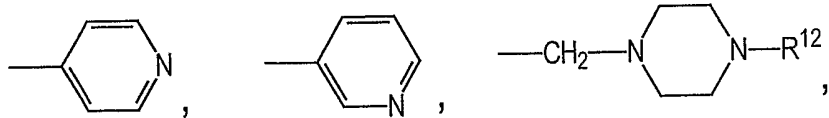
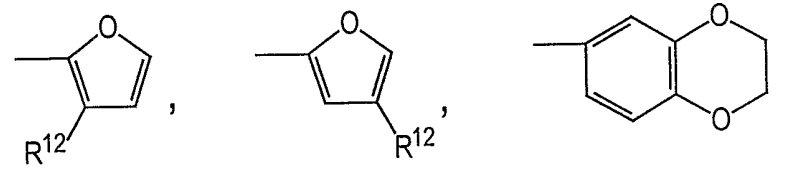
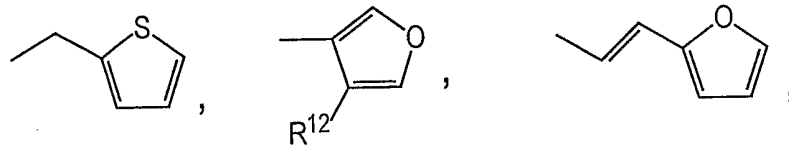
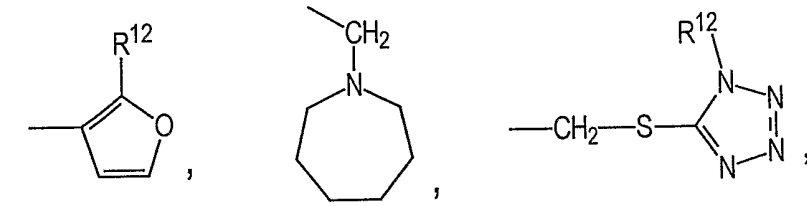
R¹⁵ represents

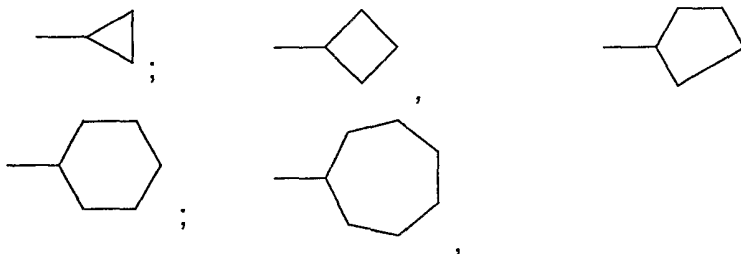
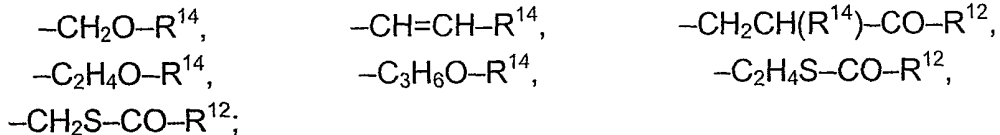
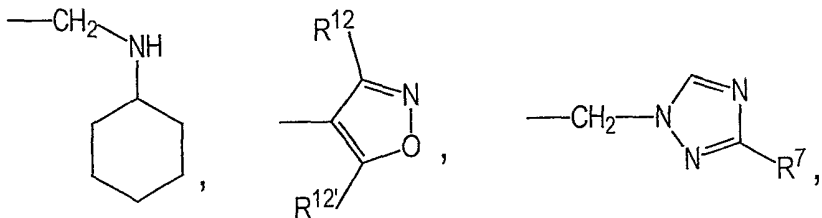


R¹⁶ is R¹²,



R¹³, R¹⁵,

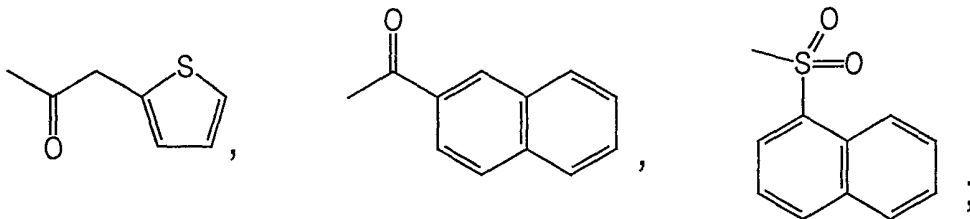




nitrobenzyl, particularly p-nitrobenzyl;

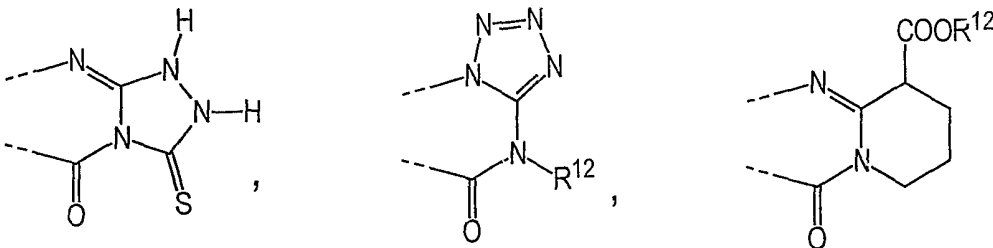
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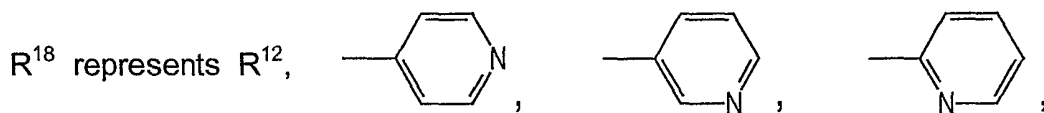
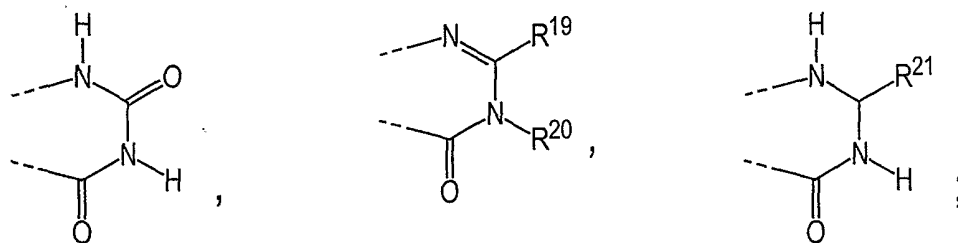
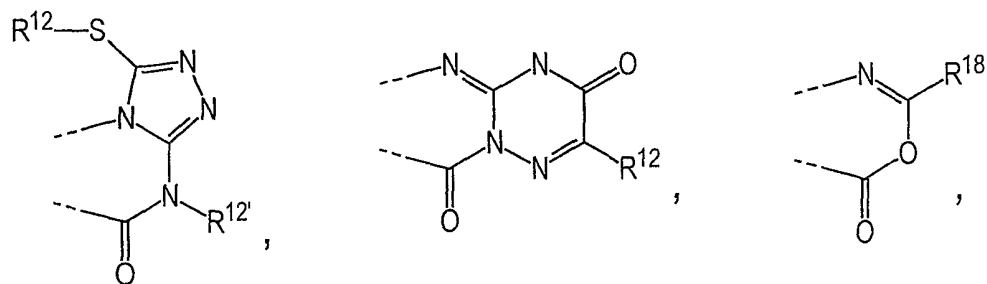
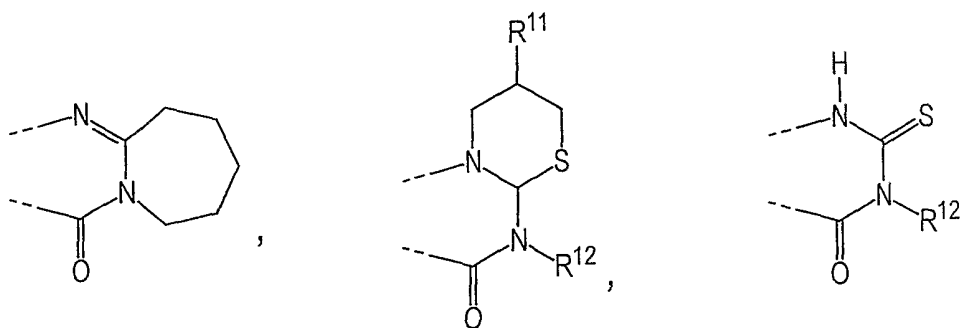
R^{17} represents $-\text{H}$, $-\text{CO}-\text{R}^{12}$, $-\text{CO}-\text{R}^{13}$, $-\text{CO}-\text{R}^{14}$, $-\text{CO}-\text{NH}-\text{R}^{12}$,
 $-\text{CO}-\text{NH}-\text{R}^{13}$, $-\text{CO}-\text{NH}-\text{R}^{14}$, $-\text{SO}_2-\text{R}^{14}$, $-\text{CO}-\text{NH}-\text{CH}_2-\text{COO}-\text{R}^{12}$,
 $-\text{CO}-\text{CH}_2-\text{O}-\text{R}^{14}$, $-\text{CO}-\text{CH}=\text{CH}-\text{R}^{14}$,



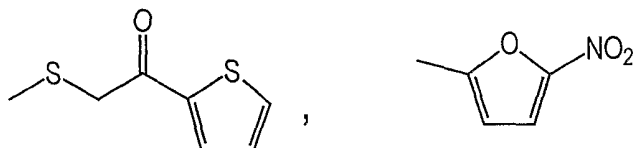
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or R^1 and R^2 together represent a heterocyclic ring system having the following formula

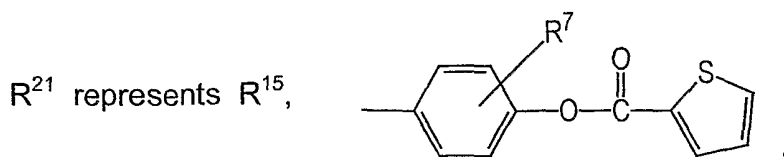


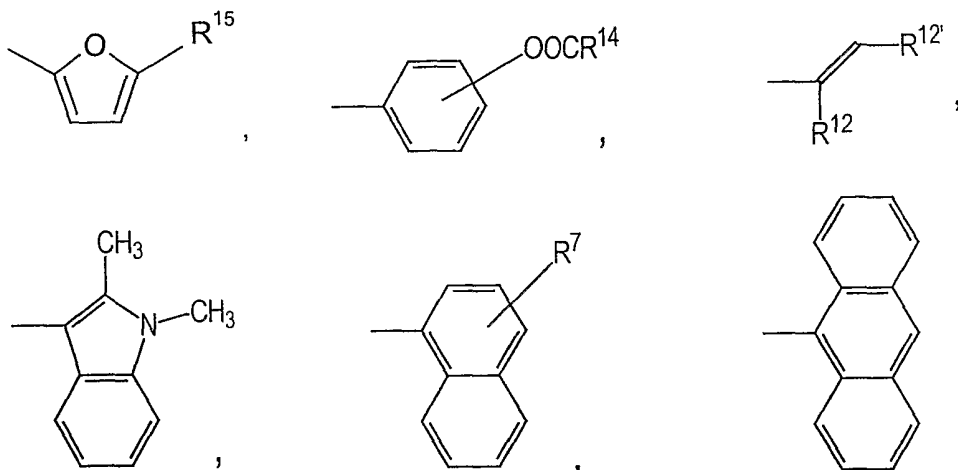


5 R¹⁹ represents R³, R¹⁴, -SCH₂-R³, -SCH₂-CO-R¹⁴, -SCH₂-CO-NH-R¹⁴, -SCH₂-CO-NH-CH₂-R¹², -NH-CO-CH₂-OR¹⁴, -CO-NH-N=CHR¹²(R¹⁴),



R²⁰ represents R¹², -NH-CO-R¹², -N=CH-R¹⁵;





and/or pharmaceutically acceptable salts of these compounds as
pharmaceutically active agents.

5

9. Use according to claim 8 of a compound and/or a pharmaceutically acceptable salt of this compound selected from the group comprising:

(Compound 1) 2-{3-[1-(2-Chloro-acetyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

10 (Compound 2) 2-[3-(1-Butyryl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

(Compound 3) 2-[3-(1-Propanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

15 (Compound 4) 2-[3-(1-Benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

(Compound 5) 2-{3-[1-(2-Chloro-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

(Compound 6) 2-[3-(1-Isobutyryl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

20 (Compound 7) 2-{3-[1-(4-Methyl-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

(Compound 8) 2-[3-(1-Cyclohexanecarbonyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

25 (Compound 9) 2-[3-(1-Cyclopropanecarbonyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

(Compound 10) 2-[3-(1-Hexanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

(Compound 11) 2-{3-[1-(2-Methyl-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

- (Compound 12) 2-{3-[1-(3-Chloro-2,2-dimethyl-propionyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 13) 2-{3-[1-(3,5,5-Trimethyl-hexanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 14) 2-{3-[1-(2-Ethyl-hexanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 15) 2-{3-[1-(2-Phenyl-butyryl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 16) 2-[3-(1-Cyclopentylcarbonyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 17) 2-{3-[1-(2-Chloro-2-phenyl-acetyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 18) 2-{3-[1-(4-Butyl-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 19) 2-[3-(1-Decanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 20) 2-[3-(1-Heptanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 21) 2-[3-(1-Nonanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 22) 2-[3-(1-Dodecanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 23) 2-{3-[1-(3-Methy-butyryl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 25 (Compound 24) 2-[3-(1-Tetradecanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 25) 2-[3-(1-Cyclohexylcarbamoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 30 (Compound 26) 2-[3-(1-Phenylcarbamoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 27) 2-[3-(1-Benzylcarbamoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 28) 2-{3-[1-(4-Ethoxycarbonyl-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 35 (Compound 29) 2-{3-[1-(3-Bromo-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

- (Compound 30) 2-{3-[1-(2-Methoxy-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 31) 2-{3-[1-(2-Methyl-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 32) 2-{3-[1-(4-Chloro-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 33) 2-{3-[1-(4-Fluoro-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 34) 2-{3-[1-(4-Methyl-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 35) 2-{3-[1-Naphtalene-1-sulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 36) 2-{3-[1-(4-Chloro-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 37) 2-{3-[1-(2,5-Dichloro-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 38) 2-{3-[1-(2,2-Dichloro-acetyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 39) 2-{3-[1-(3,3-Dimethyl-butyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 40) 2-{3-[1-(Ethoxycarbonylmethyl-carbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 25 (Compound 41) 2-{3-[1-(3-Methoxy-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 42) 2-{3-[1-(3,5-Bis-trifluoromethyl-benzoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 30 (Compound 43) 2-{3-[1-(1-Phenylacetyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 44) 2-{3-[1-(3,4-Dichloro-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 35 (Compound 45) 2-{3-[1-(2,4,6-Trimethyl-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

- (Compound 46) 2-{3-[1-(4-Methoxy-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 47) 2-{3-[1-(Naphthalene-2-sulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 48) 2-(3-Piperidin-4-ylmethyl-ureido)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 49) 2-(3-{1-[2-(4-Chloro-phenoxy)-acetyl]-piperidin-4-ylmethyl}-ureido)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 50) 2-(3-{1-[3-(4-Nitro-phenoyl)-acryloyl]-piperidin-4-ylmethyl}-ureido)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 51) 2-[3-(1-Octanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 52) 2-[3-(1-Benzenesulfonyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 53) 2-[3-(1-Ethyllylcarbonyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 54) 2-[3-[1-(3-Fluoro-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 55) 2-[3-[1-(4-Chloro-phenylcarbonyl)-piperidin-4-ylmethyl]-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 56) 4-[3-(3-ethoxycarbonyl-4,5,6,7-tetrahydro-benzo [b] thiophene-2-yl)-ureidomethyl]-piperidine-1-carboxylic acid phenyl ester;
- (Compound 57) 2-[3-[1-(3-Trifluoromethyl-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 25 (Compound 58) 2-[3-[1-(3-Bromo-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 59) 2-[3-[1-(2,4-Dichloro-phenylcarbonyl)-piperidin-4-ylmethyl]-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 30 (Compound 60) 2-[3-[1-(2-Trifluoromethyl-phenylcarbonyl)-piperidin-4-ylmethyl]-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 61) 2-[3-[1-(4-*tert*-Butyl-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 35 (Compound 62) 2-[3-[1-(3-Nitro-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 63) 2-[3-(1-Cyclobutanecarbonyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

- (Compound 64) 2-{3-[1-(2-Thiophen-2-ylacetyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 65) 2-{3-[1-(Naphthalene-2-carbonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 66) 5,6,7,8-Tetrahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidine-2,4-dione;
- (Compound 67) 4-Oxo-3,4,5,6,7,8-hexahydro-benzo[4,5]thieno[2,3-*d*]pyrimidine-2-carboxylic acid ethyl ester;
- (Compound 68) 2-Acetylamino-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 69) 2-Amino-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester;
- (Compound 70) 2-Amino-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- 15 (Compound 71) 2-Acetylamino-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid;
- (Compound 72) 2-(Toluene-4-sulfonylamino)-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- (Compound 73) 7-Methyl-1,3,4,9-tetrahydro-2*H*-11-thia-5a,6,9,10-tetraaza-benzo [b]fluorene-5,8-dione;
- 20 (Compound 74) 7-Phenyl-1,3,4,9-tetrahydro-2*H*-11-thia-5a,6,9,10-tetraaza-benzo [b]fluorene-5,8-dione;
- (Compound 75) 2-(5-Nitro-furan-2-yl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- 25 (Compound 76) 2-[(5-Bromo-2-hydroxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- (Compound 77) 2-[(4,5-Dibromo-2-hydroxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester;
- (Compound 78) 2-[(2-Chloro-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- 30 (Compound 79) 2-[1-(3-Oxo-3*H*-benzo[b]thiophen-2-ylidene)-ethylamino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic ethyl ester;
- (Compound 80) 2-Heptanoylamino-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester;
- 35 (Compound 81) 2-(3-Bromo-benzoylamino)-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester;
- (Compound 82) 2-Ethyl-5,6,7,8-tetrahydro-3-oxa-9-thia-1-aza-fluoren-4-one;

- (Compound 83) Furan-2-carboxylic acid [3-(4-methoxy-phenylcarbamoyl)-4,5,6,7-tetra hydro-benzo[*b*]thiophen-2-yl]-amide;
- (Compound 84) 2-Pyridin-3-yl-5,6,7,8-tetrahydro-3-oxa-9-thia-1-aza-fluoren-4-one;
- 5 (Compound 85) 2-Propionylamino-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic phenylamide;
- (Compound 86) 1-Allylsulfanyl-4-phenyl-6,7,8,9-tetrahydro-4*H*-10-thia-2,3,4,10*b*-tetraaza-cyclopenta[*a*]fluoren-5-one;
- (Compound 87) 2-[2-(1-Phenyl-1*H*-tetrazol-5-ylsulfanyl)-acetylamino]-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 88) 2-[3-(4-Methoxy-phenyl)-3-(2,2,2-trifluoro-acetylamino)-propionyl-amino]-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid amide;
- (Compound 89) 2-(3-Chloro-benzylamino)-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 90) 2-[[1-(4-Carboxy-butyryl)-1*H*-indol-3-ylmethylene]-amino]-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 91) 2-(7-Ethyl-4-oxo-3-phenyl-3,4,5,6,7,8-hexahydro-benzo)[4,5]thieno [2,3-*d*]pyrimidin-2-ylsulfanyl)-*N*-(2-isopropoxy-phenyl)-acetamide;
- 20 (Compound 92) *N,N*-Diethyl-2-(7-ethyl-4-oxo-3-phenyl-3,4,5,6,7,8-hexahydro-benzo)[4,5]thieno[2,3-*d*]pyrimidin-2-ylsulfanyl)-acetamide;
- (Compound 93) 3-[(4-Hydroxy-3-methoxy-benzylidene)-amino]-2-methyl-5,6,7,8-tetrahydro-3*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- 25 (Compound 94) 6-Ethyl-2-(3-phenyl-thioureido)-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 95) 2-[3-(Adamantane-1-carbonyl)-thioureido]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 96) 2-[(3,5-Dibromo-2,4-dihydroxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 30 (Compound 97) Benzoic acid 2-ethoxy-4-(4-oxo-1,2,3,4,4*a*,5,6,7,8,9*a*-decahydro-benzo [4,5]thieno[2,3-*d*]pyrimidin-2-yl)-phenylester;
- (Compound 98) 2-(1-Acetylamino-2,2,2-trichloro-ethylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 35 (Compound 99) 2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 100) 4-Oxo-3,4,5,6,7,8-hexahydro-benzo[4,5]thieno[2,3-*d*]pyrimidine-2-carboxylic acid [1-(3-nitro-phenyl)-ethylidene]-hydrazide;

- (Compound 101) 2-[(Pyridine-4-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo[*b*]thio-phene-3-carboxylic acid ethyl ester;
- (Compound 102) 2-(2,2,3,3-Tetrafluoro-propionylamino)-4,5,6,7-tetrahydro-benzo[*b*] thiophene-3-carboxylic acid amide;
- 5 (Compound 103) 2-[3-(1-Acetylamino-2,2,2-trichloro-ethyl)-thioureido]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 104) 2-[3-(2,2,2-Trichloro-1-propionylamino-ethyl)-thioureido]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid amide;
- (Compound 105) 2-(3-Chloro-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- 10 (Compound 106) 2-(2-Chloro-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 107) 2-Anthracene-9-yl-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*] pyrimidin-4-one;
- 15 (Compound 108) 2-(3,5-Dibromo-2-methoxy-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 109) 2-[5-(4-Bromo-phenyl)-furan-2-yl]-2,3,4a,5,6,7,8,9a-octahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 110) 2-(2,4-Dichlorophenoxy)-*N*-(4-oxo-2-propyl-5,6,7,8-tetrahydro-4*H*-benzo[4,5]thieno [2,3-*d*]pyrimidin-3-yl)-acetamide;
- 20 (Compound 111) 2-(3,4-Dimethoxy-benzoylamino)-4,5,6,7-tetrahydro-benzo[*b*]thio- phene-3-carboxylic acid ethyl ester;
- (Compound 112) 2-[3-(2-Chloro-phenyl)-acryloylamino]-4,5,6,7-tetrahydro-benzo[*b*] thiophene-3-carboxylic acid ethyl ester;
- 25 (Compound 113) 3-(3-Ethoxycarbonyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-2-ylcarb-amoyl)-pyrazine-2-carboxylic acid;
- (Compound 114) 2-(3-{2,2,2-Trichloro-1-[(furan-2-carbonyl)-amino]-ethyl}-thioureido)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 30 (Compound 115) 2-(1-Methyl-2-phenyl-vinyl)-2,3,4a,5,6,7,8,9a-octahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 116) 2-(2-Methoxy-naphtalen-1-yl)-2,3,4a,5,6,7,8,9a-octahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 117) 2-(1,2-Dimethyl-1*H*-indol-3-yl)-2,3,4a,5,6,7,8,9a-octahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- 35 (Compound 118) 2-(Cyclohexanecarbonyl-amino)-6-methyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 119) 3-Bromo-benzoic acid 3-(4-oxo-1,2,3,4,5,6,7,8-octahydro-benzo[4,5]thieno[2,3-*d*]pyrimidin-2-yl)-phenyl ester;

- (Compound 120) 3-Thioxo-2,3,5,6,7,8-hexahydro-1*H*-9-thia-1,2,3a,10-tetraaza-cyclopenta[*b*]fluorene-4-one;
- (Compound 121) 2-(2,3-Dibromo-5-ethoxy-4-hydroxy-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- 5 (Compound 122) 2-[2-(4-Chloro-phenoxy)-acetylamino]-6-methyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 123) 4-Phenyl-5a,6,7,8,9,10a-hexahydro-4*H*-10-thia-1,2,3,4,10b-pentaaza-cyclopenta[*a*]fluoren-5-one;
- (Compound 124) 6-Methyl-2-[(thiophene-2-carbonyl)-amino]-4,5,6,7-10 tetrahydro-benzo [*b*] thiophene-3-carboxylic acid amide;
- (Compound 125) 3-Allyl-2-(2-oxo-2-thiophen-2-yl-ethylsulfanyl)-5,6,7,8-tetrahydro-3*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 126) 2-[(2-Chloro-4-nitro-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 127) 2-(2-Methyl-3,5-dinitro-benzoylamino)-4,5,6,7-tetrahydro-benzo[*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 128) 2-(4-Acetyl-benzoylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 129) 2-Benzoylamino-7-hydroxyimino-4,5,6,7-tetrahydro-benzo 20 [*b*] thio-phene-3-carboxylic acid ethyl ester;
- (Compound 130) 2-Formylamino-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 131) 5-Oxo-1,2,3,4,6,7,8,9-octahydro-5*H*-11-thia-5a,10-diaza-benzo[*b*]fluo- rene-9-carboxylic acid ethyl ester;
- 25 (Compound 132) 2-Benzoylamino-7-oxo-4,5,6,7-tetrahydro-benzo [*b*] thio-phene-3-carboxylic acid ethyl ester;
- (Compound 133) 2-(2-Phenylsulfanyl-acetylamino)-4,5,6,7-tetrahydro-benzo [*b*] thio-phene-3-carboxylic acid ethyl ester;
- (Compound 134) 2-(4-Nitro-benzylamino)-4,5,6,7-tetrahydro-30 benzo[*b*]thiophene-3-carb- oxylic acid ethyl ester;
- (Compound 135) 2-[2-(4-Ethyl-piperazin-1-yl)-acetylamino]-7-oxo-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 136) 2-Phenylsulfanyl-3,4,7,8,9,10-hexahydro-2*H*,6*H*-12-thia-5,11-diaza-cyclohepta[*b*]fluorene-1,5-dione;
- 35 (Compound 137) 7-Hydroxy-2-(4-nitro-benzoylamino)-4,5,6,7-tetrahydro-benzo[*b*] thio- phene-3-carboxylic acid ethyl ester;
- (Compound 138) 2-(2-Cyclohexylamino-acetylamino)-7-oxo-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;

- (Compound 139) 2-(2-Azepan-1-yl-acetylamino)-7-oxo-4,5,6,7-tetrahydro-benzo[*b*]thio- phene-3-carboxylic acid ethyl ester;
- (Compound 140) 7-Hydroxyimino-2-pentanoylamino-4,5,6,7-tetrahydro-benzo[*b*]thio- phene-3-carboxylic acid ethyl ester;
- 5 (Compound 141) 2-(2-Morpholin-4-yl-acetylamino)-7-oxo-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 142) 2-Benzoyloxyimion-4,5,7,8,9,10,11-heptahydro-3*H*-1-thia-6a,12-diaza-cyclohepta[*b*]fluorene-6-one;
- (Compound 143) 2-(3-Acetylsulfanyl-propionylamino)-4,5,6,7-tetrahydro-10 benzo[*b*]thio-phene-3-carboxylic acid ethyl ester;
- (Compound 144) 2-[3-(3,4-Dichloro-phenyl-ureido)]-4,5,6,7-tetrahydro-benzo [*b*]thio- phene-3-carboxylic acid amide;
- (Compound 145) 2-(2-Chloro-5-iodo-benzoylamino)-4,5,6,7-tetrahydro-benzo [*b*]thio-phene-3-carboxylic acid ethyl ester;
- 15 (Compound 146) 2-[(5-Benzyl-2-hydroxy-3-nitro-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 147) 2-[(Pyridine-3-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo[*b*] thiophene -3-carboxylic acid ethyl ester;
- (Compound 148) 2-(3-Thiophen-2-yl-propionylamino)-4,5,6,7-tetrahydro-20 benzo [*b*]thio- phene-3-carboxylic acid ethyl ester;
- (Compound 149) 6-Methyl-2-(3-methyl-4-nitro-benzoylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 150) 2-Isopropyl-5,6,7,8-tetrahydro-3-oxa-9-thia-1-aza-fluor-4-one;
- 25 (Compound 151) 2-(2-Piperidin-1-yl-acetylamino)-4,5,6,7-tetrahydro-benzo [*b*]thio-phene-3-carboxylic acid amide;
- (Compound 152) 3-Allyl-2-prop-2-ynylsulfanyl-5,6,7,8-tetrahydro-3*H*-benzo [4,5] thieno [2,3-*d*]pyrimidin-4-one;
- (Compound 153) 2-(Trifluoromethyl)-5,6,7,8-tetrahydro-3*H*-30 benzo[4,5]thieno[2,3-*d*] pyrimidin-4-one;
- (Compound 154) 2-[2-(4-Methyl-piperazin-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid amide;
- (Compound 155) Furan-2-carboxylic acid-(3-phenylcarbamoyl-4,5,6,7-tetrahydro-benzo[*b*]thiophen-2-yl)-amide;
- 35 (Compound 156) 3-Phenyl-5,6,7,8-tetrahydro-3*H*-benzo [4,5] thieno [2,3-*d*]pyrimidin-4-one;
- (Compound 157) 2-(4-Oxo-3-phenyl-3,4,5,6,7,8-hexahydro-benzo[4,5]thieno[2,3-*d*] pyrimidin-2-ylsulfanyl)-*N*-phenethyl-acetamide;

- (Compound 158) 2-(3-Benzoylsulfanyl-acetylamino)-4,5,6,7-tetrahydro-benzo[*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 159) 2-(5-Hydroxy-2-nitro-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5] thieno[2,3-*d*]pyrimidin-4-one;
- 5 (Compound 160) 2-[2-(2-Benzoylamino-2-carboxy-ethylsulfanyl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 161) 2-[(5-Bromo-2-hydroxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 162) 3-[(2,4-Dihydroxy-benzylidene)-amino]-2-methyl-5,6,7,8-tetrahydro-3*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 163) *N*-(4-Oxo-2-pentyl-5-pentyl-5,6,7,8-tetrahydro-4*H*-benzo[4,5]thieno [2,3-*d*]pyrimidin-3-yl)-2-phenyl-acetamide;
- (Compound 164) 2-[(2,3-Dihydro-benzo[1,4]dioxine-5-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 165) 2-[(3,5-Dichloro-4-methoxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 166) 2-Iodo-5-phenyl-2,3,4a,5,6,7,8,9,10-octahydro-1*H*-4,11-dithia-5,11b-diaza-benzo[*a*]fluoren-6-one;
- 20 (Compound 167) 2-Benzoylamino-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid;
- (Compound 168) 2-(2,2,2-Trichloro-1-phenylacetylamino-ethylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 169) 2-(3-Furan-2-yl-acryloylamino)-4,5,6,7-tetrahydro-
- 25 benzo[*b*]thiophene-3-carboxylic acid amide;
- (Compound 170) 3-[(3-Bromo-4-hydroxy-5-methoxy-benzylidene)-amino]-2-methyl-5,6,7,8-tetrahydro-3*H*-benzo[4,5] thieno [2,3-*d*]pyrimidin-4-one;
- (Compound 171) 3-[(3-Chloro-4-hydroxy-5-methoxy-benzylidene)-amino]-2-methyl-5,6,7,8-tetrahydro-3*H*-benzo[4,5] thieno [2,3-*d*]pyrimidin-4-one;
- 30 (Compound 172) 2-[3-(4-Chloro-2-methyl-phenoxy)-propionylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 173) 2-Amino-6-methyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 174) 7-Benzoyloxyimino-2-pyrrol-1-yl-4,5,6,7-tetrahydro-
- 35 benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 175) 2-(2-Formyl-pyrrol-1-yl)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid;
- (Compound 176) 2-(5-Chloro-pentanoylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;

- (Compound 177) 3-Allyl-6-methyl-2-thioxo-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno [2,3-*d*]pyrimidin-4-one;
- (Compound 178) (3-Allyl-6-methyl-4-oxo-3,4,5,6,7,8-hexahydro-benzo[4,5]thieno[2,3-*d*]pyrimidin-2-ylsulfanyl)-acetic acid;
- 5 (Compound 179) 2-[2-(4-Bromo-phenyl-2-oxo-ethylsulfanyl)]-6-methyl-3-phenyl-5,6,7,8-tetrahydro-3*H*-benzo [4,5] thieno [2,3-*d*]pyrimidin-4-one;
- (Compound 180) 2-Amino-5-methyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 181) 2-(2-Bromo-benzoylamino)-7-oxo-4,5,6,7-tetrahydro-benzo[*b*]thio- phene-3-carboxylic acid ethyl ester;
- 10 (Compound 182) 2-(3-Methyl-benzoylamino)- 4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 183) 2-(4-Benzoyl-benzoylamino)- 4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 184) 2-[(2-Ethoxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo[*b*]thio- phene-3-carboxylic acid amide;
- (Compound 185) 2-[2-Amino-3-cyano-7,7-dimethyl-4-(3-nitro-phenyl)-5-oxo-4a,5,6,7,8,8a-hexahydro-4*H*-quinolin-1-yl]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 186) 2-[2-Amino-3-cyano-7,7-dimethyl-4-(4-chloro-phenyl)-5-oxo-4a,5,6,7,8,8a-hexahydro-4*H*-quinolin-1-yl]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 187) 2-[2-Amino-3-cyano-7,7-dimethyl-4-(4-ethyl-phenyl)-5-oxo-4a,5,6,7,8,8a-hexahydro-4*H*-quinolin-1-yl]-4,5,6,7-tetrahydro-benzo [*b*]
- 25 thiophene-3-carboxylic acid ethyl ester;
- (Compound 188) 2-[2-Amino-3-cyano-7,7-dimethyl-4-(4-nitro-phenyl)-5-oxo-4a,5,6,7,8,8a-hexahydro-4*H*-quinolin-1-yl]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 189) (3-Allyl--4-oxo-3,4,5,6,7,8-hexahydro-benzo[4,5]thieno [2,3-*d*]pyrimidin-2-ylsulfanyl)-acetic acid methyl ester;
- 30 (Compound 190) 2-(2-Hydroxy-ethylsulfanyl)-5,6,7,8-tetrahydro-3*H*-benzo[4,5]thieno [2,3-*d*]pyrimidin-4-one;
- (Compound 191) Thiophene-2-carboxylic acid 2-ethoxy-4-(4-oxo-3,4,5,6,7,8-hexahydro-benzo-[4,5]thieno-[2,3-*d*]pyrimidin-2-ylsulfanyl)-phenyl ester;
- 35 (Compound 192) 2-(2-Fluoro-benzoylamino)-6-methyl-4,5,6,7-tetrahydro-benzo[*b*] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 193) 3a,7a-Dihydro-benzo[1,3]dioxole-5-carboxylic acid (3-carbamoyl-5-methyl-4,5,6,7-tetrahydro-benzo[*b*]thiophen-2-yl)-amide;

- (Compound 194) 2-[(3a,7a-Dihydro-benzo[1,3]dioxole-5-carbonyl)-amino]-6-methyl-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid isopropyl ester;
- 5 (Compound 195) 2-[(3a,7a-Dihydro-benzo[1,3]dioxole-5-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 196) 6-Methyl-2-(3-phenyl-propionylamino)-4,5,6,7-tetrahydro-benzo[b] thiophene-3-carboxylic acid amide;
- (Compound 197) 2-(2,4-Dichloro-benzoylamino)-6-Methyl-4,5,6,7-tetrahydro-benzo[b] thiophene-3-carboxylic acid isopropyl ester;
- 10 (Compound 198) 2-(4-Methoxy-benzoylamino)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid methyl ester;
- (Compound 199) Tetrahydro-fruan-2-carboxylic acid (3-carbamoyl-6-methyl-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-amide;
- (Compound 200) 2-[2-(5-Methyl-3-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid methyl ester;
- 15 (Compound 201) 2-(4-Fluoro-benzenesulfonylamino)-4,5,6,7-tetrahydro-benzo[b]thio- phene-3-carboxylic acid amide;
- (Compound 202) 6-*tert*-Butyl-2-(3-phenyl-3-phenylsulfanyl-propionylamino)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid methyl ester;
- 20 (Compound 203) 2-[2-(3,5-Dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-6-methyl-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 204) 2-[2-(3,5-Dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 205) 6-Methyl-2-(3,3-diphenyl-propionylamino)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 25 (Compound 206) 2-(3,5-Dimethoxy-benzoylamino)-6-(1,1-dimethyl-propyl)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid methyl ester;
- (Compound 207) 6-*tert*-Butyl-2-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl-amino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- 30 (Compound 208) 6-*tert*-Butyl-2-(3-phenyl-3-phenylsulfanyl-propionylamino)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 209) 2-[2-(5-Methyl-3-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 210) 6-*tert*-Butyl-2-[2-(3-nitro-[1,2,4]triazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid methyl ester;
- 35 (Compound 211) 6-*tert*-Butyl-2-[2-(3,5-dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid methyl ester;

- (Compound 212) 6-Methyl-2-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 213) 6-Methyl-2-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 214) 6-*tert*-Butyl-2-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl- amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 215) 6-*tert*-Butyl-2-[2-(3,5-dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid amide;
- (Compound 216) 6-*tert*-Butyl-2-(3-carboxy-acryloylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 217) 6-*tert*-Butyl-2-(4-carboxy-butyrylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- 15 (Compound 218) 2-[(4-Iodo-2-methyl-2*H*-pyrazole-3-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 219) 2-[4-(4-Chloro-2-methyl-phenoxy)-butyrylamino]-6-methyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid isopropyl ester;
- 20 (Compound 220) 2-(2-Phenyl-2-phenylsulfanyl-acetylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 221) 2-[(5-Methyl-3-phenyl-isoxazole-4-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 222) 6-Methyl-2-[2-(3-nitro-[1,2,4]triazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- 25 (Compound 223) 6-Methyl-2-[2-(3-nitro-[1,2,4]triazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 224) 2-Amino-6-*tert*-butyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carbox- ylic acid methyl ester;
- 30 (Compound 225) 2-Amino-6-*tert*-butyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carbox- ylic acid amide;
- (Compound 226) 6-Methyl-2-[2-(5-methyl-3-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 227) 2-[2-(3,5-Dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- 35 (Compound 228) 2-[2-(3,5-Dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid amide;
- (Compound 229) 2-[2-(5-Methyl-3-trifluoromethyl-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;

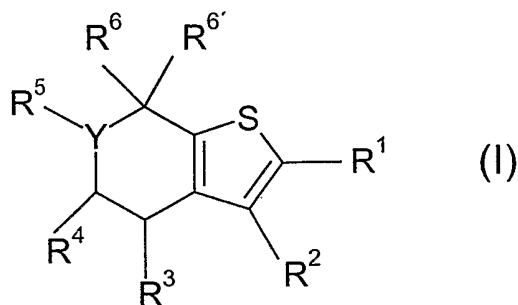
- (Compound 230) 6-Methyl-2-[2-(3-nitro-[1,2,4]triazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 231) 2-[(2-Carboxy-cyclohexanecarbonyl)-amino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid isopropyl ester;
- 5 (Compound 232) 2-(3-Carboxy-acryloylamino)-6-(1,1-dimethyl-propyl)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid amide;
- (Compound 233) 6-(1,1-Dimethyl-propyl)-2-[(5-methyl-furan-2-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid amide;
- (Compound 234) 6-Methyl-2-[(2-methyl-furan-3-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid isopropyl ester;
- 10 (Compound 235) 2-(4-Chloro-benzoylamino)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 236) 2-Benzoylamino-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 237) 2-(Cyclopropanecarbonyl-amino)-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- (Compound 238) 2-[2-(4-Nitrophenyl)-acetylamino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- (Compound 239) 6-Methyl-2-[2-(3-nitro-[1,2,4]triazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- 20 (Compound 240) Furan-2-carboxylic acid [3-(2-hydroxy-ethylcarbonyl)-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl]-amide;
- (Compound 241) Cyclopropanecarboxylic acid (3-ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-amide;
- 25 (Compound 242) *N*-(3-Ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-acet-amide;
- (Compound 243) *N*-(3-Ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-propion-amide;
- (Compound 244) *N*-(3-Ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-2-
- 30 methyl-acrylamide;
- (Compound 245) 3-Methyl-but-2-enoic acid (3-ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-amide;
- (Compound 246) But-2-enoic acid (3-ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-amide;
- 35 (Compound 247) *N*-(3-ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-2,2-dimethyl-propionamide;
- (Compound 248) Thiophene-2-carboxylic acid (3-ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-amide;

- (Compound 249) Furan-2-carboxylic acid (3-ethoxy-4,5,6,7-tetrahydrobenzo[*b*]thiophen-2-yl)-amide;
- (Compound 250) 2-Acetyl-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylic acid amide;
- 5 (Compound 251) 2-(2,2,-Dimethyl-propionylamino)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylic acid amide;
- (Compound 252) 2-(Cyclopropanecarbonyl-amino)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylic acid;
- (Compound 253) Cyclopropanecarboxylic acid (3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thiophen-2-yl) amide;
- 10 (Compound 254) 2-Amino-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carbonitrile;
- (Compound 255) 2-Isobutyrylamino-4,5,6,7-tetrahydrobenzo-*[b]*-thiophene-3-carboxylic acid amide;
- 15 (Compound 256) 2-Isobutyrylamino-4,5,6,7-tetrahydrobenzo-*[b]*-thiophene-3-carboxylic acid ethyl ester;
- (Compound 257) 2-(Ethoxyoxalyl-amino)-4,5,6,7-tetrahydrobenzo-*[b]*-thiophene-3-carboxylic acid ethyl ester;
- (Compound 258) 2-Amino-4-methyl-4,5,6,7-tetrahydrobenzo-*[b]*-thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 259) 2-(Cyclopropanecarbonyl amino)-4-methyl-4,5,6,7-tetrahydro-benzo-*[b]*-thiophene-3-carboxylic acid ethyl ester;
- (Compound 260) Oxo-(4,5,6,7-tetrahydrobenzo-*[b]*-thiophen-2-yl)-acetic acid;
- 25 (Compound 261) 2-Chloro-1-(4,5,6,7-tetrahydrobenzo-*[b]*-thiophen-2-yl)-ethanone;
- (Compound 262) 2-Hydrazino-1-(4,5,6,7-tetrahydrobenzo-*[b]*-thiophen-2-yl)-ethanone;
- 30 (Compound 263) 2-(2-Methyl-acryloylamino)-4,5,6,7-tetrahydrobenzo-*[b]*-thiophene-3-carboxylic acid amide;
- (Compound 264) 2-[(Thiophene-2-carbonyl)-amino]- 4,5,6,7-tetrahydrobenzo-*[b]*-thiophene-3-carboxylic acid amide;
- (Compound 265) Furan-2-carboxylic acid (3-carbamoyl-4,5,6,7-tetrahydrobenzo[*b*]thiophen-2-yl)-amide;
- 35 (Compound 266) 2-(Cyclobutanecarbonyl-amino)-4,5,6,7-tetrahydrobenzo-*[b]*-thiophene-3-carboxylic acid amide;
- (Compound 267) 2-(2-Methyl-butyrylamino)- 4,5,6,7-tetrahydrobenzo-*[b]*-thiophene-3-carboxylic acid amide;

- (Compound 268) 2-(Cyclopropanecarbonyl-amino)-4-methyl-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid amide;
- (Compound 269) 6-*tert*-Butyl 2-(cyclopropanecarbonyl-amino)-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid amide;
- 5 (Compound 270) 2-(Cyclopropanecarbonyl-amino)-6-methyl-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid amide;
- (Compound 271) 2-(Cyclopropylmethyl-amino)-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid amide;
- 10 (Compound 272) *N*-(3-Cyano-4,5,6,7-tetrahydrobenzo-[b]-thiophen-2-yl)-acetamide;
- (Compound 273) *N*-(3-Cyano-4,5,6,7-tetrahydrobenzo-[b]-thiophen-2-yl)-benzamide;
- (Compound 274) 5-Bromo-furan-2-carboxylic acid (3-cyano-4,5,6,7-tetrahydrobenzo-[b]-thiophen-2-yl)-amide;
- 15 (Compound 275) *N*-(3-Cyano-4,5,6,7-tetrahydrobenzo-[b]-thiophen-2-yl)-2,2,2-trifluoro-acetamide;
- (Compound 276) 2-[(Furan-2-ylmethylene)-amino]-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carbonitrile;
- 20 (Compound 277) *N*-(3-Cyano-6-methyl-4,5,6,7-tetrahydrobenzo-[b]-thiophen-2-yl)-acetamide;
- (Compound 278) 2-[(Pyrazine-2-carbonyl)-amino]-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid methyl ester;
- (Compound 279) 2-Isobutyrylamino-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid methyl ester;
- 25 (Compound 280) 6-Methyl-2-[(thiophene-2-carbonyl)-amino]-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid;
- (Compound 281) 2-[(Thiophene-2-carbonyl)-amino]-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid;
- 30 (Compound 282) 2-(Cyclopropanecarbonyl-amino)-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid;
- (Compound 283) 2-(Cyclohexanecarbonyl-amino)-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid amide;
- (Compound 284) 2-Acetylamino-6-methyl-4,5,6,7-tetrahydrobenzo-[b]-thiophene-3-carboxylic acid amide;
- 35 (Compound 285) 2-Amino-4,7-dihydro-5*H*-thieno[2,3-*c*]-thiopyran-3-carboxylic acid amide;
- (Compound 286) 2-(Cyclopropanecarbonyl-amino)-4,7-dihydro-5*H*-thieno[2,3-*c*]-thiopyran-3-carboxylic acid amide;

(Compound 287) 2-(Cyclopropanecarbonyl-amino)-6-oxo-4,5,6,7-tetrahydro-6 λ^4 -thieno[2,3-c]thiopyran-3-carboxylic acid amide.

- 5 10. Use according to claim 8 or 9, for treating diseases and/or infections, particularly virally and/or bacterially induced diseases or infections.
11. Use according to claim 10, wherein the bacterially induced disease or infection is caused by a mycobacterium.
- 10 12. Use according to claim 11, wherein the mycobacterium is *Mycobacterium tuberculosis*.
13. Use according to claim 11 or 12, wherein the disease is tuberculosis.
- 15 14. Use of at least one compound according to claim 8 or 9 as an inhibitor for a protein kinase.
15. Use according to claim 14, wherein the protein kinase is secreted from a cell to an environment of the cell.
- 20 16. Use according to claim 14 or 15, wherein the protein kinase is a mycobacterial kinase.
17. Use according to claim 16, wherein the mycobacterial kinase is from *Mycobacterium tuberculosis*.
- 25 18. Use according to claim 17, wherein the mycobacterial kinase from *Mycobacterium tuberculosis* is protein kinase G (PknG).
- 30 19. Use of at least one compound of the general formula (I)



wherein the substituents R¹ to R⁶ represent the residues as defined in claim 1 and/or a pharmaceutically active salt of one of these compounds for the preparation of a pharmaceutical composition.

- 5 20. Use according to claim 19, wherein these compounds are selected from the group comprising
- (Compound 1) 2-{3-[1-(2-Chloro-acetyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 2) 2-[3-(1-Butyryl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 3) 2-[3-(1-Propanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 4) 2-[3-(1-Benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 5) 2-{3-[1-(2-Chloro-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 6) 2-[3-(1-Isobutyryl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 7) 2-{3-[1-(4-Methyl-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 8) 2-[3-(1-Cyclohexanecarbonyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 9) 2-[3-(1-Cyclopropanecarbonyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 25 (Compound 10) 2-[3-(1-Hexanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 11) 2-{3-[1-(2-Methyl-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 12) 2-{3-[1-(3-Chloro-2,2-dimethyl-propionyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 30 (Compound 13) 2-{3-[1-(3,5,5-Trimethyl-hexanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 14) 2-{3-[1-(2-Ethyl-hexanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 35 (Compound 15) 2-{3-[1-(2-Phenyl-butyryl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 16) 2-[3-(1-Cyclopentylcarbonyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

- (Compound 17) 2-{3-[1-(2-Chloro-2-phenyl-acetyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 18) 2-{3-[1-(4-Butyl-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 19) 2-[3-(1-Decanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 20) 2-[3-(1-Heptanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 21) 2-[3-(1-Nonanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 22) 2-[3-(1-Dodecanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 23) 2-{3-[1-(3-Methy-butyryl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 24) 2-[3-(1-Tetradecanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 25) 2-[3-(1-Cyclohexylcarbamoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 26) 2-[3-(1-Phenylcarbamoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 27) 2-[3-(1-Benzylcarbamoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 28) 2-{3-[1-(4-Ethoxycarbonyl-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 25 (Compound 29) 2-{3-[1-(3-Bromo-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 30) 2-{3-[1-(2-Methoxy-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 30 (Compound 31) 2-{3-[1-(2-Methyl-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 32) 2-{3-[1-(4-Chloro-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 35 (Compound 33) 2-{3-[1-(4-Fluoro-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 34) 2-{3-[1-(4-Methyl-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

- (Compound 35) 2-{3-[1-Naphtalene-1-sulfonyl]-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 36) 2-{3-[1-(4-Chloro-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 37) 2-{3-[1-(2,5-Dichloro-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 38) 2-{3-[1-(2,2-Dichloro-acetyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 39) 2-{3-[1-(3,3-Dimethyl-butyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 40) 2-{3-[1-(Ethoxycarbonylmethyl-carbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 41) 2-{3-[1-(3-Methoxy-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 42) 2-{3-[1-(3,5-Bis-trifluoromethyl-benzoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 43) 2-{3-[1-Phenylacetyl-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 44) 2-{3-[1-(3,4-Dichloro-benzoyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 25 (Compound 45) 2-{3-[1-(2,4,6-Trimethyl-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 46) 2-{3-[1-(4-Methoxy-benzenesulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 30 (Compound 47) 2-{3-[1-(Naphtalene-2-sulfonyl)-piperidin-4-ylmethyl]-ureido}-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 48) 2-(3-Piperidin-4-ylmethyl-ureido)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 49) 2-(3-{1-[2-(4-Chloro-phenoxy)-acetyl]-piperidin-4-ylmethyl}-ureido)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 35 (Compound 50) 2-(3-{1-[3-(4-Nitro-phenoyl)-acryloyl]-piperidin-4-ylmethyl}-ureido)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;

- (Compound 51) 2-[3-(1-Octanoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 52) 2-[3-(1-Benzenesulfonyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 53) 2-[3-(1-Ethyllylcarbamoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 54) 2-[3-[1-(3-Fluoro-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 55) 2-[3-[1-(4-Chloro-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 56) 4-[3-(3-ethoxycarbonyl-4,5,6,7-tetrahydro-benzo [b] thiophene-2-yl)-ureidomethyl]-piperidine-1-carboxylic acid phenyl ester;
- (Compound 57) 2-[3-[1-(3-Trifluoromethyl-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 58) 2-[3-[1-(3-Bromo-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 59) 2-[3-[1-(2,4-Dichloro-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 60) 2-[3-[1-(2-Trifluoromethyl-phenylcarbamoyl)-piperidin-4-ylmethyl]-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 61) 2-[3-[1-(4-*tert*-Butyl-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 25 (Compound 62) 2-[3-[1-(3-Nitro-benzoyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 63) 2-[3-(1-Cyclobutanecarbonyl-piperidin-4-ylmethyl)-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 64) 2-[3-[1-(2-Thiophen-2-ylacetyl)-piperidin-4-ylmethyl]-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 30 (Compound 65) 2-[3-[1-(Naphthalene-2-carbonyl)-piperidin-4-ylmethyl]-ureido]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 66) 5,6,7,8-Tetrahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidine-2,4-dione;
- 35 (Compound 67) 4-Oxo-3,4,5,6,7,8-hexahydro-benzo[4,5]thieno[2,3-*d*]pyrimidine-2-carboxylic acid ethyl ester;
- (Compound 68) 2-Acetylamino-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester;

- (Compound 69) 2-Amino-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester;
- (Compound 70) 2-Amino-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- 5 (Compound 71) 2-Acetylamino-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid;
- (Compound 72) 2-(Toluene-4-sulfonylamino)-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- (Compound 73) 7-Methyl-1,3,4,9-tetrahydro-2*H*-11-thia-5a,6,9,10-tetraaza-benzo [*b*]fluorene-5,8-dione;
- 10 (Compound 74) 7-Phenyl-1,3,4,9-tetrahydro-2*H*-11-thia-5a,6,9,10-tetraaza-benzo [*b*]fluorene-5,8-dione;
- (Compound 75) 2-(5-Nitro-furan-2-yl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- 15 (Compound 76) 2-[(5-Bromo-2-hydroxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- (Compound 77) 2-[(4,5-Dibromo-2-hydroxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester;
- (Compound 78) 2-[(2-Chloro-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- 20 (Compound 79) 2-[1-(3-Oxo-3*H*-benzo[b]thiophen-2-ylidene)-ethylamino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic ethyl ester;
- (Compound 80) 2-Heptanoylamino-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester;
- 25 (Compound 81) 2-(3-Bromo-benzoylamino)-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester;
- (Compound 82) 2-Ethyl-5,6,7,8-tetrahydro-3-oxa-9-thia-1-aza-fluoren-4-one;
- (Compound 83) Furan-2-carboxylic acid [3-(4-methoxy-phenylcarbamoyl)-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl]-amide;
- 30 (Compound 84) 2-Pyridin-3-yl-5,6,7,8-tetrahydro-3-oxa-9-thia-1-aza-fluoren-4-one;
- (Compound 85) 2-Propionylamino-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic phenylamide;
- 35 (Compound 86) 1-Allylsulfanyl-4-phenyl-6,7,8,9-tetrahydro-4*H*-10-thia-2,3,4,10b-tetraaza-cyclopenta[*a*]fluoren-5-one;
- (Compound 87) 2-[2-(1-Phenyl-1*H*-tetrazol-5-ylsulfanyl)-acetylamino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester;

- (Compound 88) 2-[3-(4-Methoxy-phenyl)-3-(2,2,2-trifluoro-acetylamino)-propionyl-amino]-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid amide;
- 5 (Compound 89) 2-(3-Chloro-benzylamino)-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 90) 2-[[1-(4-Carboxy-butyryl)-1*H*-indol-3-ylmethylene]-amino]-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 91) 2-(7-Ethyl-4-oxo-3-phenyl-3,4,5,6,7,8-hexahydro-benzo)[4,5]thieno [2,3-*d*]pyrimidin-2-ylsulfanyl)-N-(2-isopropoxy-phenyl)-acetamide;
- 10 (Compound 92) N,N-Diethyl-2-(7-ethyl-4-oxo-3-phenyl-3,4,5,6,7,8-hexahydro-benzo)[4,5]thieno[2,3-*d*]pyrimidin-2-ylsulfanyl)-acetamide;
- (Compound 93) 3-[(4-Hydroxy-3-methoxy-benzylidene)-amino]-2-methyl-5,6,7,8-tetrahydro-3*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- 15 (Compound 94) 6-Ethyl-2-(3-phenyl-thioureido)-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 95) 2-[3-(Adamantane-1-carbonyl)-thioureido]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 96) 2-[(3,5-Dibromo-2,4-dihydroxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 97) Benzoic acid 2-ethoxy-4-(4-oxo-1,2,3,4,4a,5,6,7,8,9a-decahydro-benzo [4,5]thieno[2,3-*d*]pyrimidin-2-yl)-phenylester;
- (Compound 98) 2-(1-Acetylamino-2,2,2-trichloro-ethylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 25 (Compound 99) 2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 100) 4-Oxo-3,4,5,6,7,8-hexahydro-benzo[4,5]thieno[2,3-*d*]pyrimidine-2-carboxylic acid [1-(3-nitro-phenyl)-ethylidene]-hydrazide;
- (Compound 101) 2-[(Pyridine-4-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo[*b*]thio-phenene-3-carboxylic acid ethyl ester;
- 30 (Compound 102) 2-(2,2,3,3-Tetrafluoro-propionylamino)-4,5,6,7-tetrahydro-benzo[*b*] thiophene-3-carboxylic acid amide;
- (Compound 103) 2-[3-(1-Acetylamino-2,2,2-trichloro-ethyl)-thioureido]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 35 (Compound 104) 2-[3-(2,2,2-Trichloro-1-propionylamino-ethyl)-thioureido]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid amide;
- (Compound 105) 2-(3-Chloro-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;

- (Compound 106) 2-(2-Chloro-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 107) 2-Anthracene-9-yl-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*] pyrimidin-4-one;
- 5 (Compound 108) 2-(3,5-Dibromo-2-methoxy-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 109) 2-[5-(4-Bromo-phenyl)-furan-2-yl]-2,3,4a,5,6,7,8,9a-octahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 110) 2-(2,4-Dichlorophenoxy)-*N*-(4-oxo-2-propyl-5,6,7,8-
- 10 tetrahydro-4*H*-benzo[4,5]thieno [2,3-*d*]pyrimidin-3-yl)-acetamide;
- (Compound 111) 2-(3,4-Dimethoxy-benzoylamino)-4,5,6,7-tetrahydro-benzo[*b*]thio- phene-3-carboxylic acid ethyl ester;
- (Compound 112) 2-[3-(2-Chloro-phenyl)-acryloylamino]-4,5,6,7-tetrahydro-benzo[*b*] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 113) 3-(3-Ethoxycarbonyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-2-ylcarb-amoyl)-pyrazine-2-carboxylic acid;
- (Compound 114) 2-(3-{2,2,2-Trichloro-1-[(furan-2-carbonyl)-amino]-ethyl}-thioureido)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 20 (Compound 115) 2-(1-Methyl-2-phenyl-vinyl)-2,3,4a,5,6,7,8,9a-octahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 116) 2-(2-Methoxy-naphtalen-1-yl)-2,3,4a,5,6,7,8,9a-octahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 117) 2-(1,2-Dimethyl-1*H*-indol-3-yl)-2,3,4a,5,6,7,8,9a-
- 25 octahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 118) 2-(Cyclohexanecarbonyl-amino)-6-methyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 119) 3-Bromo-benzoic acid 3-(4-oxo-1,2,3,4,5,6,7,8-octahydro-benzo[4,5]thieno[2,3-*d*]pyrimidin-2-yl)-phenyl ester;
- 30 (Compound 120) 3-Thioxo-2,3,5,6,7,8-hexahydro-1*H*-9-thia-1,2,3a,10-tetraaza-cyclopenta[*b*]fluorene-4-one;
- (Compound 121) 2-(2,3-Dibromo-5-ethoxy-4-hydroxy-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 122) 2-[2-(4-Chloro-phenoxy)-acetylamino]-6-methyl-4,5,6,7-
- 35 tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 123) 4-Phenyl-5a,6,7,8,9,10a-hexahydro-4*H*-10-thia-1,2,3,4,10b-pentaaza-cyclopenta[*a*]fluoren-5-one;
- (Compound 124) 6-Methyl-2-[(thiophene-2-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid amide;

- (Compound 125) 3-Allyl-2-(2-oxo-2-thiophen-2-yl-ethylsulfanyl)-5,6,7,8-tetrahydro-3*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 126) 2-[(2-Chloro-4-nitro-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 127) 2-(2-Methyl-3,5-dinitro-benzoylamino)-4,5,6,7-tetrahydro-benzo[*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 128) 2-(4-Acetyl-benzoylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 129) 2-Benzoylamino-7-hydroxyimino-4,5,6,7-tetrahydro-benzo
- 10 [*b*] thio-phene-3-carboxylic acid ethyl ester;
- (Compound 130) 2-Formylamino-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 131) 5-Oxo-1,2,3,4,6,7,8,9-octahydro-5*H*-11-thia-5a,10-diaza-benzo[*b*]fluorene-9-carboxylic acid ethyl ester;
- 15 (Compound 132) 2-Benzoylamino-7-oxo-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 133) 2-(2-Phenylsulfanyl-acetylamino)-4,5,6,7-tetrahydro-benzo [*b*] thio-phene-3-carboxylic acid ethyl ester;
- (Compound 134) 2-(4-Nitro-benzylamino)-4,5,6,7-tetrahydro-
- 20 benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- (Compound 135) 2-[2-(4-Ethyl-piperazin-1-yl)-acetylamino]-7-oxo-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 136) 2-Phenylsulfanyl-3,4,7,8,9,10-hexahydro-2*H*,6*H*-12-thia-5,11-diaza-cyclohepta[*b*]fluorene-1,5-dione;
- 25 (Compound 137) 7-Hydroxy-2-(4-nitro-benzoylamino)-4,5,6,7-tetrahydro-benzo[*b*] thio- phene-3-carboxylic acid ethyl ester;
- (Compound 138) 2-(2-Cyclohexylamino-acetylamino)-7-oxo-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 139) 2-(2-Azepan-1-yl-acetylamino)-7-oxo-4,5,6,7-tetrahydro-
- 30 benzo[*b*] thio- phene-3-carboxylic acid ethyl ester;
- (Compound 140) 7-Hydroxyimino-2-pentanoylamino-4,5,6,7-tetrahydro-benzo[*b*] thio- phene-3-carboxylic acid ethyl ester;
- (Compound 141) 2-(2-Morpholin-4-yl-acetylamino)-7-oxo-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 35 (Compound 142) 2-Benzoyloxyimion-4,5,7,8,9,10,11-heptahydro-3*H*-1-thia-6a,12-diaza-cyclohepta[*b*]fluorene-6-one;
- (Compound 143) 2-(3-Acetylsulfanyl-propionylamino)-4,5,6,7-tetrahydro-benzo[*b*] thio-phene-3-carboxylic acid ethyl ester;

- (Compound 144) 2-[3-(3,4-Dichloro-phenyl-ureido)]-4,5,6,7-tetrahydro-benzo [b] thio- phene-3-carboxylic acid amide;
- (Compound 145) 2-(2-Chloro-5-iodo-benzoylamino)-4,5,6,7-tetrahydro-benzo [b] thio-phene-3-carboxylic acid ethyl ester;
- 5 (Compound 146) 2-[(5-Benzyl-2-hydroxy-3-nitro-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 147) 2-[(Pyridine-3-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo[b] thiophene -3-carboxylic acid ethyl ester;
- (Compound 148) 2-(3-Thiophen-2-yl-propionylamino)-4,5,6,7-tetrahydro-10 benzo [b] thio- phene-3-carboxylic acid ethyl ester;
- (Compound 149) 6-Methyl-2-(3-methyl-4-nitro-benzoylamino)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 150) 2-Isopropyl-5,6,7,8-tetrahydro-3-oxa-9-thia-1-aza-fluor-4-one;
- 15 (Compound 151) 2-(2-Piperidin-1-yl-acetylamino)-4,5,6,7-tetrahydro-benzo [b] thio-phene-3-carboxylic acid amide;
- (Compound 152) 3-Allyl-2-prop-2-ynylsulfanyl-5,6,7,8-tetrahydro-3*H*-benzo [4,5] thieno [2,3-*d*]pyrimidin-4-one;
- (Compound 153) 2-(Trifluoromethyl)-5,6,7,8-tetrahydro-3*H*-20 benzo[4,5]thieno[2,3-*d*] pyrimidin-4-one;
- (Compound 154) 2-[2-(4-Methyl-piperazin-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid amide;
- (Compound 155) Furan-2-carboxylic acid-(3-phenylcarbamoyl-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-amide;
- 25 (Compound 156) 3-Phenyl-5,6,7,8-tetrahydro-3*H*-benzo [4,5] thieno [2,3-*d*]pyrimidin-4-one;
- (Compound 157) 2-(4-Oxo-3-phenyl-3,4,5,6,7,8-hexahydro-benzo[4,5]thieno[2,3-*d*] pyrimidin-2-ylsulfanyl)-*N*-phenethyl-acetamide;
- (Compound 158) 2-(3-Benzoylsulfanyl-acetylamino)-4,5,6,7-tetrahydro-benzo[b] -thiophene-3-carboxylic acid ethyl ester;
- 30 (Compound 159) 2-(5-Hydroxy-2-nitro-phenyl)-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5] thieno[2,3-*d*]pyrimidin-4-one;
- (Compound 160) 2-[2-(2-Benzoylamino-2-carboxy-ethylsulfanyl)-acetylamino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 35 (Compound 161) 2-[(5-Bromo-2-hydroxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 162) 3-[(2,4-Dihydroxy-benzylidene)-amino]-2-methyl-5,6,7,8-tetrahydro-3*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one;

- (Compound 163) *N*-(4-Oxo-2-pentyl-5-pentyl-5,6,7,8-tetrahydro-4*H*-benzo[4,5]thieno [2,3-*d*]pyrimidin-3-yl)-2-phenyl-acetamide;
- (Compound 164) 2-[(2,3-Dihydro-benzo[1,4]dioxine-5-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 165) 2-[(3,5-Dichloro-4-methoxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 166) 2-Iodo-5-phenyl-2,3,4a,5,6,7,8,9,10-octahydro-1*H*-4,11-dithia-5,11b-diaza-benzo[*a*]fluoren-6-one;
- (Compound 167) 2-Benzoylamino-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-10 carboxylic acid;
- (Compound 168) 2-(2,2,2-Trichloro-1-phenylacetyl-amino-ethyl-amino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 169) 2-(3-Furan-2-yl-acryloylamino)-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid amide;
- 15 (Compound 170) 3-[(3-Bromo-4-hydroxy-5-methoxy-benzylidene)-amino]-2-methyl-5,6,7,8-tetrahydro-3*H*-benzo[4,5] thieno [2,3-*d*]pyrimidin-4-one;
- (Compound 171) 3-[(3-Chloro-4-hydroxy-5-methoxy-benzylidene)-amino]-2-methyl-5,6,7,8-tetrahydro-3*H*-benzo[4,5] thieno [2,3-*d*]pyrimidin-4-one;
- (Compound 172) 2-[3-(4-Chloro-2-methyl-phenoxy)-propionylamino]-4,5,6,7-20 tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 173) 2-Amino-6-methyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 174) 7-Benzoyloxyimino-2-pyrrol-1-yl-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid ethyl ester;
- 25 (Compound 175) 2-(2-Formyl-pyrrol-1-yl)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid;
- (Compound 176) 2-(5-Chloro-pentanoylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 177) 3-Allyl-6-methyl-2-thioxo-2,3,5,6,7,8-hexahydro-1*H*-30 benzo[4,5]thieno [2,3-*d*]pyrimidin-4-one;
- (Compound 178) (3-Allyl-6-methyl-4-oxo-3,4,5,6,7,8-hexahydro-benzo[4,5]thieno[2,3-*d*]pyrimidin-2-ylsulfanyl)-acetic acid;
- (Compound 179) 2-[2-(4-Bromo-phenyl-2-oxo-ethylsulfanyl)]-6-methyl-3-phenyl-5,6,7,8-tetrahydro-3*H*-benzo [4,5] thieno [2,3-*d*]pyrimidin-4-one;
- 35 (Compound 180) 2-Amino-5-methyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 181) 2-(2-Bromo-benzoylamino)-7-oxo-4,5,6,7-tetrahydro-benzo[*b*]thio- phene-3-carboxylic acid ethyl ester;

- (Compound 182) 2-(3-Methyl-benzoylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 183) 2-(4-Benzoyl-benzoylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 184) 2-[(2-Ethoxy-benzylidene)-amino]-4,5,6,7-tetrahydro-benzo[*b*]thio- phene-3-carboxylic acid amide;
- (Compound 185) 2-[2-Amino-3-cyano-7,7-dimethyl-4-(3-nitro-phenyl)-5-oxo-4a,5,6,7,8,8a-hexahydro-4*H*-quinolin-1-yl]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 10 (Compound 186) 2-[2-Amino-3-cyano-7,7-dimethyl-4-(4-chloro-phenyl)-5-oxo-4a,5,6,7,8,8a-hexahydro-4*H*-quinolin-1-yl]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 187) 2-[2-Amino-3-cyano-7,7-dimethyl-4-(4-ethyl-phenyl)-5-oxo-4a,5,6,7,8,8a-hexahydro-4*H*-quinolin-1-yl]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 188) 2-[2-Amino-3-cyano-7,7-dimethyl-4-(4-nitro-phenyl)-5-oxo-4a,5,6,7,8,8a-hexahydro-4*H*-quinolin-1-yl]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 189) (3-Allyl--4-oxo-3,4,5,6,7,8-hexahydro-benzo[4,5]thieno [2,3-*d*]pyrimidin-2-ylsulfanyl)-acetic acid methyl ester;
- 20 (Compound 190) 2-(2-Hydroxy-ethylsulfanyl)-5,6,7,8-tetrahydro-3*H*-benzo[4,5]thieno [2,3-*d*]pyrimidin-4-one;
- (Compound 191) Thiophene-2-carboxylic acid 2-ethoxy-4-(4-oxo-3,4,5,6,7,8-hexahydro-benzo-[4,5]thieno-[2,3-*d*]pyrimidin-2-ylsulfanyl)-phenyl ester;
- 25 (Compound 192) 2-(2-Fluoro-benzoylamino)-6-methyl-4,5,6,7-tetrahydro-benzo[*b*] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 193) 3a,7a-Dihydro-benzo[1,3]dioxole-5-carboxylic acid (3-carbamoyl-5-methyl-4,5,6,7-tetrahydro-benzo[*b*]thiophen-2-yl)-amide;
- 30 (Compound 194) 2-[(3a,7a-Dihydro-benzo[1,3]dioxole-5-carbonyl)-amino]-6-methyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 195) 2-[(3a,7a-Dihydro-benzo[1,3]dioxole-5-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid isopropyl ester;
- 35 (Compound 196) 6-Methyl-2-(3-phenyl-propionylamino)-4,5,6,7-tetrahydro-benzo[*b*] thiophene-3-carboxylic acid amide;
- (Compound 197) 2-(2,4-Dichloro-benzoylamino)-6-Methyl-4,5,6,7-tetrahydro-benzo[*b*] thiophene-3-carboxylic acid isopropyl ester;

- (Compound 198) 2-(4-Methoxy-benzoylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 199) Tetrahydro-fruan-2-carboxylic acid (3-carbamoyl-6-methyl-4,5,6,7-tetrahydro-benzo[*b*]thiophen-2-yl)-amide;
- 5 (Compound 200) 2-[2-(5-Methyl-3-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 201) 2-(4-Fluoro-benzenesulfonylamino)-4,5,6,7-tetrahydro-benzo[*b*]thio- phene-3-carboxylic acid amide;
- (Compound 202) 6-*tert*-Butyl-2-(3-phenyl-3-phenylsulfanyl-propionylamino)-10 4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 203) 2-[2-(3,5-Dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-6-methyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 204) 2-[2-(3,5-Dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-15 4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 205) 6-Methyl-2-(3,3-diphenyl-propionylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 206) 2-(3,5-Dimethoxy-benzoylamino)-6-(1,1-dimethyl-propyl)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 207) 6-*tert*-Butyl-2-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-20 acetyl-amino]-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carboxylic acid amide;
- (Compound 208) 6-*tert*-Butyl-2-(3-phenyl-3-phenylsulfanyl-propionylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 209) 2-[2-(5-Methyl-3-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid isopropyl ester;
- 25 (Compound 210) 6-*tert*-Butyl-2-[2-(3-nitro-[1,2,4]triazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 211) 6-*tert*-Butyl-2-[2-(3,5-dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- 30 (Compound 212) 6-Methyl-2-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 213) 6-Methyl-2-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- 35 (Compound 214) 6-*tert*-Butyl-2-[2-(5-methyl-3-trifluoromethyl-pyrazol-1-yl)-acetyl- amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;

- (Compound 215) 6-*tert*-Butyl-2-[2-(3,5-dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid amide;
- (Compound 216) 6-*tert*-Butyl-2-(3-carboxy-acryloylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- 5 (Compound 217) 6-*tert*-Butyl-2-(4-carboxy-butyrylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 218) 2-[(4-Iodo-2-methyl-2*H*-pyrazole-3-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 219) 2-[4-(4-Chloro-2-methyl-phenoxy)-butyrylamino]-6-methyl-10 4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 220) 2-(2-Phenyl-2-phenylsulfanyl-acetylamino)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 221) 2-[(5-Methyl-3-phenyl-isoxazole-4-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- 15 (Compound 222) 6-Methyl-2-[2-(3-nitro-[1,2,4]triazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 223) 6-Methyl-2-[2-(3-nitro-[1,2,4]triazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 224) 2-Amino-6-*tert*-butyl-4,5,6,7-tetrahydro-benzo [*b*] 20 thiophene-3-carboxylic acid methyl ester;
- (Compound 225) 2-Amino-6-*tert*-butyl-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid amide;
- (Compound 226) 6-Methyl-2-[2-(5-methyl-3-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- 25 (Compound 227) 2-[2-(3,5-Dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 228) 2-[2-(3,5-Dimethyl-4-nitro-pyrazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid amide;
- (Compound 229) 2-[2-(5-Methyl-3-trifluoromethyl-pyrazol-1-yl)-acetylamino]-30 4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid methyl ester;
- (Compound 230) 6-Methyl-2-[2-(3-nitro-[1,2,4]triazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid ethyl ester;
- (Compound 231) 2-[(2-Carboxy-cyclohexanecarbonyl)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid isopropyl ester;
- 35 (Compound 232) 2-(3-Carboxy-acryloylamino)-6-(1,1-dimethyl-propyl)-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid amide;
- (Compound 233) 6-(1,1-Dimethyl-propyl)-2-[(5-methyl-furan-2-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [*b*] thiophene-3-carboxylic acid amide;

- (Compound 234) 6-Methyl-2-[(2-methyl-furan-3-carbonyl)-amino]-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid isopropyl ester;
- (Compound 235) 2-(4-Chloro-benzoylamino)-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- 5 (Compound 236) 2-Benzoylamino-4,5,6,7-tetrahydro-benzo [b] thiophene-3-carboxylic acid ethyl ester;
- (Compound 237) 2-(Cyclopropanecarbonyl-amino)-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- (Compound 238) 2-[2-(4-Nitrophenyl)-acetylamino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- 10 (Compound 239) 6-Methyl-2-[2-(3-nitro-[1,2,4]triazol-1-yl)-acetylamino]-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid amide;
- (Compound 240) Furan-2-carboxylic acid [3-(2-hydroxy-ethylcarbonyl)-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl]-amide;
- 15 (Compound 241) Cyclopropanecarboxylic acid (3-ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-amide;
- (Compound 242) *N*-(3-Ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-acet-amide;
- (Compound 243) *N*-(3-Ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-propion-amide;
- 20 (Compound 244) *N*-(3-Ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-2-methyl-acrylamide;
- (Compound 245) 3-Methyl-but-2-enoic acid (3-ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-amide;
- 25 (Compound 246) But-2-enoic acid (3-ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-amide;
- (Compound 247) *N*-(3-ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-2,2-dimethyl-propionamide;
- (Compound 248) Thiophene-2-carboxylic acid (3-ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-amide;
- 30 (Compound 249) Furan-2-carboxylic acid (3-ethoxy-4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl)-amide;
- (Compound 250) 2-Acetyl-amino-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylic acid amide;
- 35 (Compound 251) 2-(2,2,-Dimethyl-propionylamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylic acid amide;
- (Compound 252) 2-(Cyclopropanecarbonyl-amino)-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid;

- (Compound 253) Cyclopropanecarboxylic acid (3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thiophen-2-yl) amide;
- (Compound 254) 2-Amino-4,5,6,7-tetrahydro-benzo[*b*]thiophene-3-carbonitrile;
- 5 (Compound 255) 2-Isobutyrylamino-4,5,6,7-tetrahydrobenzo-*[b]*-thiophene-3-carboxylic acid amide;
- (Compound 256) 2-Isobutyrylamino-4,5,6,7-tetrahydrobenzo-*[b]*-thiophene-3-carboxylic acid ethyl ester;
- (Compound 257) 2-(Ethoxyoxalyl-amino)-4,5,6,7-tetrahydrobenzo-*[b]*-
10 thiophene-3-carboxylic acid ethyl ester;
- (Compound 258) 2-Amino-4-methyl-4,5,6,7-tetrahydrobenzo-*[b]*-thiophene-3-carboxylic acid ethyl ester;
- (Compound 259) 2-(Cyclopropanecarbonyl amino)-4-methyl-4,5,6,7-
15 tetrahydro-benzo-*[b]*-thiophene-3-carboxylic acid ethyl ester;
- (Compound 260) Oxo-(4,5,6,7-tetrahydrobenzo-*[b]*-thiophen-2-yl)-acetic acid;
- (Compound 261) 2-Chloro-1-(4,5,6,7-tetrahydrobenzo-*[b]*-thiophen-2-yl)-
ethanone;
- 20 (Compound 262) 2-Hydrazino-1-(4,5,6,7-tetrahydrobenzo-*[b]*-thiophen-2-yl)-ethanone;
- (Compound 263) 2-(2-Methyl-acryloylamino)-4,5,6,7-tetrahydrobenzo-*[b]*-
thiophene-3-carboxylic acid amide;
- (Compound 264) 2-[(Thiophene-2-carbonyl)-amino]- 4,5,6,7-
25 tetrahydrobenzo-*[b]*-thiophene-3-carboxylic acid amide;
- (Compound 265) Furan-2-carboxylic acid (3-carbamoyl-4,5,6,7-tetrahydrobenzo[*b*]thiophen-2-yl)-amide;
- (Compound 266) 2-(Cyclobutanecarbonyl-amino)-4,5,6,7-tetrahydrobenzo-
[b]-thiophene-3-carboxylic acid amide;
- 30 (Compound 267) 2-(2-Methyl-butyrylamino)- 4,5,6,7-tetrahydrobenzo-*[b]*-thiophene-3-carboxylic acid amide;
- (Compound 268) 2-(Cyclopropanecarbonyl-amino)-4-methyl-4,5,6,7-tetrahydrobenzo-*[b]*-thiophene-3-carboxylic acid amide;
- (Compound 269) 6-*tert*-Butyl 2-(cyclopropanecarbonyl-amino)- 4,5,6,7-
35 tetrahydrobenzo-*[b]*-thiophene-3-carboxylic acid amide;
- (Compound 270) 2-(Cyclopropanecarbonyl-amino)-6-methyl-4,5,6,7-tetrahydrobenzo-*[b]*-thiophene-3-carboxylic acid amide;
- (Compound 271) 2-(Cyclopropylmethyl-amino)- 4,5,6,7-tetrahydrobenzo-*[b]*-
thiophene-3-carboxylic acid amide;

- (Compound 272) *N*-(3-Cyano-4,5,6,7-tetrahydrobenzo-[*b*]-thiophen-2-yl)-acetamide;
- (Compound 273) *N*-(3-Cyano-4,5,6,7-tetrahydrobenzo-[*b*]-thiophen-2-yl)-benzamide;
- 5 (Compound 274) 5-Bromo-furan-2-carboxylic acid (3-cyano-4,5,6,7-tetrahydrobenzo-[*b*]-thiophen-2-yl)-amide;
- (Compound 275) *N*-(3-Cyano-4,5,6,7-tetrahydrobenzo-[*b*]-thiophen-2-yl)-2,2,2,-trifluoro-acetamide;
- (Compound 276) 2-[(Furan-2-ylmethylene)-amino]-4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carbonitrile;
- 10 (Compound 277) *N*-(3-Cyano-6-methyl-4,5,6,7-tetrahydrobenzo-[*b*]-thiophen-2-yl)-acetamide;
- (Compound 278) 2-[(Pyrazine-2-carbonyl)-amino]-4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid methyl ester;
- 15 (Compound 279) 2-Isobutyrylamino- 4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid methyl ester;
- (Compound 280) 6-Methyl-2-[(thiophene-2-carbonyl)-amino]- 4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid;
- (Compound 281) 2-[(Thiophene-2-carbonyl)-amino]- 4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid;
- 20 (Compound 282) 2-(Cyclopropanecarbonyl-amino) 4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid;
- (Compound 283) 2-(Cyclohexanecarbonyl-amino) 4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid amide.
- 25 (Compound 284) 2-Acetylamino-6-methyl- 4,5,6,7-tetrahydrobenzo-[*b*]-thiophene-3-carboxylic acid amide;
- (Compound 285) 2-Amino-4,7-dihydro-5*H*-thieno[2,3-*c*]-thiopyran-3-carboxylic acid amide;
- (Compound 286) 2-(Cyclopropanecarbonyl-amino)-4,7-dihydro-5*H*-thieno[2,3-*c*]-thiopyran-3-carboxylic acid amide;
- 30 (Compound 287) 2-(Cyclopropanecarbonyl-amino)-6-oxo-4,5,6,7-tetrahydro-6λ⁴-thieno[2,3-*c*]thiopyran-3-carboxylic acid amide.
21. Use according to one of claims 19 or 20, wherein the pharmaceutical composition is suitable for the prophylaxis and/or treatment of diseases and
- 35 infections, particularly virally or bacterially induced disease and infections.
22. Use according to claim 21, wherein the bacterially induced disease or infection is induced by a mycobacterium.

23. Use according to claim 22, wherein the mycobacterium is *Mycobacterium tuberculosis*.
- 5 24. Use according to one of claims 19 to 23, wherein the disease is tuberculosis.
25. Use according to claim 19 to 24, wherein the compound inhibits a protein kinase, particularly the protein serine/threonine kinase G (PknG) of *Mycobacterium tuberculosis*.
- 10 26. Use according to claim 25, wherein the protein serine/threonine kinase G (PknG) is secreted from the interior of the *Mycobacterium tuberculosis* to the environment of *Mycobacterium*.
- 15 27. Use of at least one protein serine/threonine kinase for developing methods for detection and/or determination of these kinases for recognising diseases, for monitoring diseases, and/or for controlling therapy of diseases.
- 20 28. Use according to claim 27, wherein the methods are immunochemical methods.
29. Use according to one of claims 27 or 28, wherein the protein serine/threonine kinase is a mycobacterial protein kinase.
- 25 30. Use according to claim 29, wherein the mycobacterial protein serine/threonine kinase is protein serine/threonine kinase G (PknG).
- 30 31. Use according to claim 30, wherein the mycobacterial protein serine/threonine kinase G (PknG) is secreted from the interior of a mycobacterial cell to the environment of this cell.
32. Use according to claim 30 or 31, wherein the mycobacterial protein serine/threonine kinase is from *Mycobacterium tuberculosis*.
- 35 33. Use according to claim 32, wherein the disease is tuberculosis.
34. Use of at least one kinase as target for medical intervention against bacterial infections of host cells.

35. Use according to claim 34, wherein the kinase is a protein kinase.
36. Use according to claim 35, wherein the protein kinase is secreted from the interior of a cell to the environment of the cell.
- 5 37. Use according to one of claims 35 or 36, wherein the protein kinase is a mycobacterial kinase.
- 10 38. Use according to claim 37, wherein the mycobacterial kinase is from *Mycobacterium tuberculosis*.
39. Use according to one of claims 37 or 38, wherein the mycobacterial kinase is protein kinase G (PknG).
- 15 40. A method for identifying a compound useful in the diagnosis or treatment of a disease, the method comprising the following steps:
- a) providing a bacterial protein kinase;
 - b) mixing the bacterial protein kinase with the compound to be tested;
 - 20 c) determining the binding affinity of the compound to be tested to the bacterial protein kinase; and
 - d) determining the kinase activity of the bacterial protein kinase by measuring the autophosphorylation.
- 25 41. A method for identifying compounds useful in the diagnosis or treatment of a disease, the method comprising the following steps:
- a) providing a first amount of a bacterial protein kinase;
 - b) mixing the first amount of the bacterial protein kinase with a substrate for the protein kinase;
 - 30 c) incubating the mixture of the first amount of the bacterial protein kinase and the substrate under conditions that are suitable for the binding of the substrate to the protein kinase;
 - d) determining a first binding affinity for the substrate to the protein kinase;
 - 35 e) providing a second amount of the bacterial protein kinase;
 - f) mixing the second amount of the bacterial protein kinase with the substrate and a compound to be tested;
 - g) incubating the mixture of the second amount of the bacterial protein kinase, the substrate, and the compound to be tested under conditions

- that are suitable for the binding of the substrate and the compound to be tested to the protein kinase;
- h) determining a second binding affinity for the substrate to the bacterial protein kinase in the presence of the compound to be tested;
- 5 i) determining the difference between the first and the second binding affinities;
- j) evaluating from the difference of the first binding affinity and the second binding affinity whether or not the compound tested is suitable for inhibiting the bacterial protein kinase; and
- 10 k) determining the kinase activity of the bacterial kinase by measuring the substrate phosphorylation.
42. Method according to one of claims 40 or 41, wherein the binding affinity is measured by means of the half-maximal inhibition constant (IC_{50}).
- 15 43. Method according to one of claims 40 to 42, wherein the bacterial protein kinase is a kinase from a mycobacterium.
44. Method according to claim 43, wherein the mycobacterium is *Mycobacterium tuberculosis*.
- 20 45. Method according to one of claims 40 to 44, wherein the bacterial protein kinase is protein kinase G (PknG).
- 25 46. Use of at least one protein kinase as virulence factor in a bacterium.
47. Use according to claim 46, wherein the protein kinase is secreted from the bacterium to the environment of the bacterium.
- 30 48. Use according to claim 46 or 47, wherein the bacterium is a mycobacterium.
49. Use according to claim 48, wherein the mycobacterium is *Mycobacterium tuberculosis*.
- 35 50. Use according to one of claims 46 to 49, wherein the protein kinase is protein kinase G (PknG).

Fig. 1

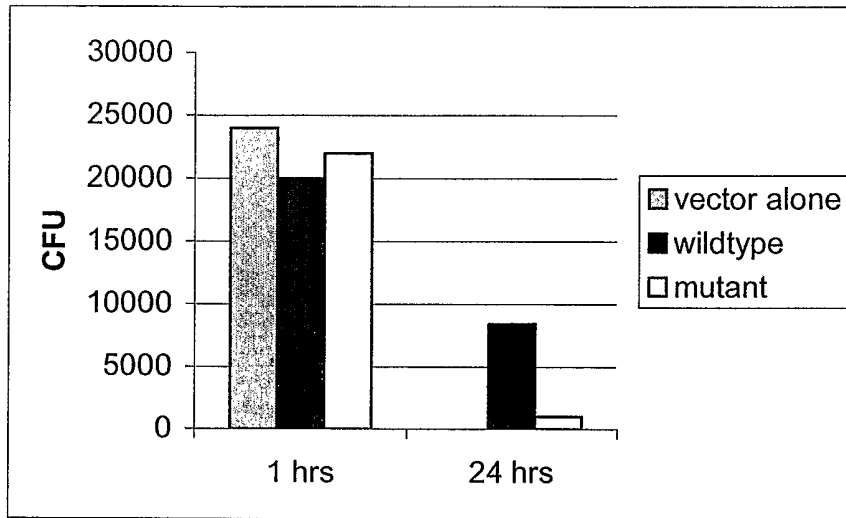


Fig. 2

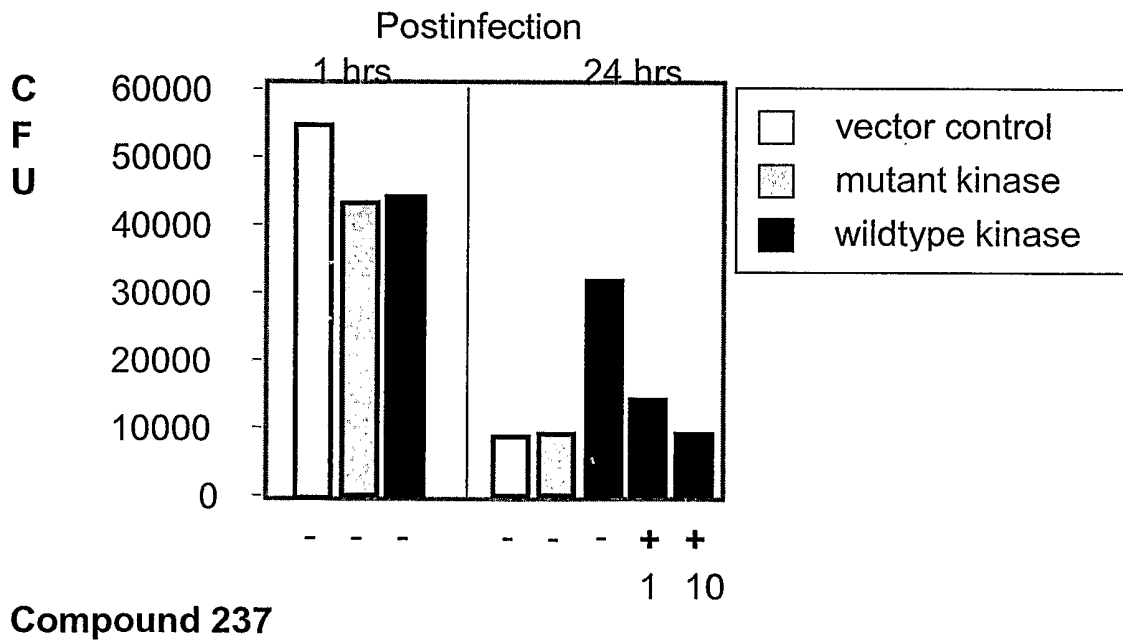
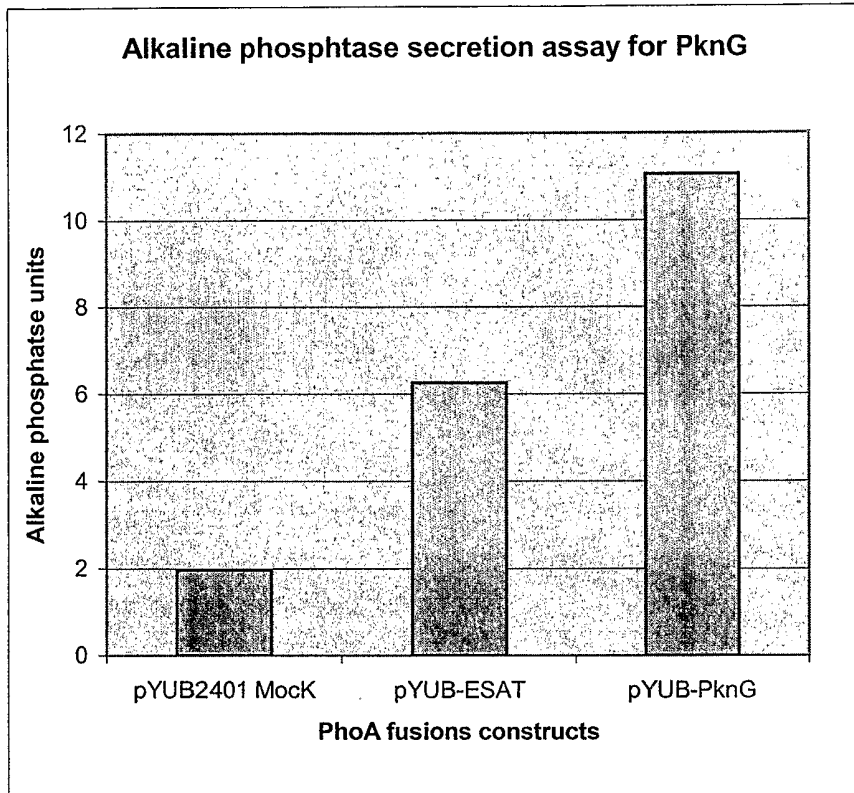


Fig. 3



A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D333/68 - C07D333/66 - C07D409/12 - C07D409/14 - C07D495/04 -
 C07D495/14 - A61K31/381 - A61P31/06 - //(C07D495/04, 333:00,
 239:00), (C07D495/04, 335:00, 333:00), (C07D495/14, 333:00, 249:00,

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01 38561 A (QUESTCOR PHARMACEUTICALS INC) 31 May 2001 (2001-05-31) page 19; claims 9,16,20-22 ---	1,20-50
P,A	WO 02 28829 A (QUESTCOR PHARMACEUTICALS INC) 11 April 2002 (2002-04-11) claims ---	1-50
P,A	WO 02 094796 A (AXXIMA PHARMACEUTICALS AG ;HABENBERGER PETER (DE); BACHER GERALD ()) 28 November 2002 (2002-11-28) claims -----	1-50

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

14 July 2003

Date of mailing of the international search report

23/07/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
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Authorized officer

Chouly, J

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 239:00)		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols)		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
<input type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in annex.		
° Special categories of cited documents :		
A document defining the general state of the art which is not considered to be of particular relevance *E* earlier document but published on or after the international filing date *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) *O* document referring to an oral disclosure, use, exhibition or other means *P* document published prior to the international filing date but later than the priority date claimed	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. *&* document member of the same patent family	
Date of the actual completion of the international search 14 July 2003	Date of mailing of the international search report	
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Chouly, J	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/03697

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 10-45 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/03697

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 0138561	A	31-05-2001	AU	1929301 A	04-06-2001
			WO	0138561 A1	31-05-2001
WO 0228829	A	11-04-2002	AU	3038502 A	15-04-2002
			WO	0228829 A2	11-04-2002
WO 02094796	A	28-11-2002	WO	02094796 A2	28-11-2002