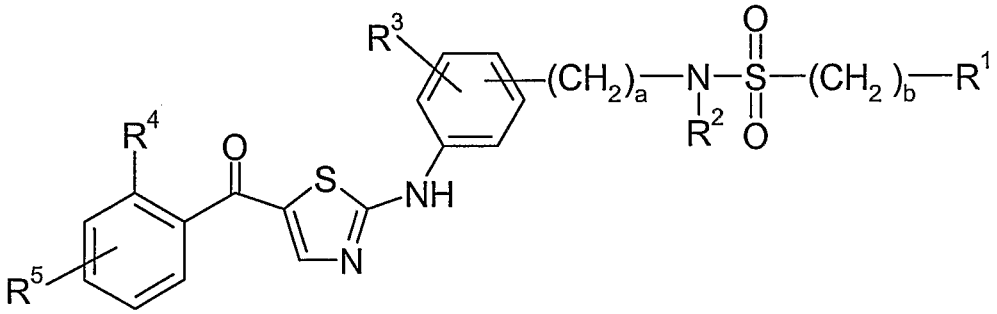
2-AMINO-5-BENZOYLTHIAZOLE NPY ANTAGONISTS

The present invention is concerned with novel thiazole derivatives useful as neuropeptide Y (NPY) receptor ligands, particularly neuropeptide Y (NPY) antagonists.

The invention is concerned especially with compounds of formula I and pharmaceutically acceptable salts and esters thereof



(I)

wherein

R^1 is amino, aryl or heteroaryl;

R^2 is hydrogen or alkyl;

R^3 is hydrogen, alkyl or halogen;

R^4 is alkyl or halogen;

R^5 is hydrogen, alkyl or halogen;

a is zero or 1; and

b is zero, 1 or 2.

The compounds of formula I and their pharmaceutically acceptable salts and esters and are novel and have valuable pharmacological properties. They are neuropeptide ligands, for example neuropeptide receptor antagonists and in particular, they are selective neuropeptides Y Y5 receptor antagonists.

Neuropetide Y is a 36 amino acid peptide that is widely distributed in the central and peripheral nervous systems. This peptide mediates a number of physiological effects through its various receptor subtypes. Studies in animals have shown that neuropeptide Y is a powerful stimulus of food intake, and it has been demonstrated that activation of neuropeptide Y Y5 receptors results in hyperphagia and decreased thermogenesis. Therefore compounds that antagonise neuropetide Y at the Y5 receptor subtype represent an approach to the treatment of eating disorders such as obesity and hyperphagia.

The current approach is aiming at medical intervention to induce weight loss or prevention of weight gain. This is achieved by interfering with appetite control, which is mediated by the Hypothalamus, an important brain region proven to control food intake. Herein, neuropeptide Y (NPY) has been proven to be one of the strongest central mediators of food intake in several animal species. Increased NPY levels result in profound food intake. Various receptors of neuropeptide Y (NPY) have been described to play a role in appetite control and weight gain. Interference with these receptors is likely to reduce appetite and consequently weight gain. Reduction and long-term maintenance of body weight can also have beneficial consequences on con associated risk factors such as arthritis, cardiovascular diseases, diabetes and renal failure.

Accordingly, the compounds of formula I can be used in the prophylaxis or treatment of of arthritis, cardiovascular diseases, diabetes, renal failure and particularly eating disorders and obesity.

Objects of the present invention are the compounds of formula I and their aforementioned salts and esters per se and their use as therapeutically active substances, a process for the manufacture of the said compounds, intermediates, pharmaceutical compositions, medicaments containing the said compounds, their pharmaceutically acceptable salts and esters, the use of the said compounds, esters and salts for the prophylaxis and/or therapy of illnesses, especially in the treatment or prophylaxis of arthritis, cardiovascular diseases, diabetes, renal failure and particularly eating disorders such as hyperphagia and particularly obesity, and the use of the said compounds, salts and

esters for the production of medicaments for the treatment or prophylaxis of arthritis, cardiovascular diseases, diabetes, renal failure and particularly eating disorders and obesity.

In the present description the term "alkyl", alone or in combination, signifies a straight-chain or branched-chain alkyl group with 1 to 8 carbon atoms, preferably a straight or branched-chain alkyl group with 1 to 6 carbon atoms and particularly preferred a straight or branched-chain alkyl group with 1 to 4 carbon atoms Examples of straight-chain and branched C_1-C_8 alkyl groups are methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert.-butyl, the isomeric pentyls, the isomeric hexyls, the isomeric heptyls and the isomeric octyls, preferably methyl and ethyl and most preferred methyl.

The term "cycloalkyl", alone or in combination, signifies a cycloalkyl ring with 3 to 8 carbon atoms and preferably a cycloalkyl ring with 3 to 6 carbon atoms. Examples of C_3-C_8 cycloalkyl are cyclopropyl, methyl-cyclopropyl, dimethylcyclopropyl, cyclobutyl, methyl-cyclobutyl, cyclopentyl, methyl-cyclopentyl, cyclohexyl, methyl-cyclohexyl, dimethyl-cyclohexyl, cycloheptyl and cyclooctyl, preferably cyclopropyl.

The term "alkoxy", alone or in combination, signifies a group of the formula alkyl-O- in which the term "alkyl" has the previously given significance, such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, sec. butoxy and tert.butoxy, preferably methoxy and ethoxy and most preferred methoxy.

The term "aryl", alone or in combination, signifies a phenyl or naphthyl group, preferably a phenyl group which optionally carries one or more substituents, preferably one to three, each independently selected from halogen, trifluoromethyl, trifluoromethoxy, amino, alkyl, alkoxy, alkylcarbonyl, cyano, carbamoyl, alkoxycarbamoyl, methylendioxy, carboxy, alkoxycarbonyl, aminocarbonyl, alkyaminocarbonyl, dialkylaminocarbonyl, hydroxy, nitro, alkyl-SO_2-, amino-SO_2-, cycloalkyl and the like. Preferred is phenyl or naphthyl, particularly phenyl optionally substituted with one to three, preferably one or two substituents independently selected from alkyl, halogen, alkoxy, trifluoromethoxy, nitro and trifluoromethyl.

The term "heteroaryl", alone or in combination, signifies aromatic 5- to 10-membered heterocycle which comprises one or more, preferably one or two, particularly preferred one hetero atom selected from nitrogen, oxygen and sulfur, wherein nitrogen is preferred. It can be substituted on one or more carbon atoms by cyano, trifluoromethyl, trifluoromethoxy, alkyl-SO_2-, amino-SO_2-, halogen, alkoxy, hydroxy, amino, cycloalkyl,

alkylcarbonyl, aminocarbonyl nitro, alkyl, and/or alkoxycarbonyl. Preferred heteroaryl cycles are thiophenyl or pyrrolidinyl, wherein thiophenyl and pyrrolidinyl are optionally substituted with one to three substituents, preferably one or two independently selected from alkyl, halogen, alkoxy, trifluoromethoxy, nitro and trifluoromethyl.

The term "amino", alone or in combination, signifies a primary, secondary or tertiary amino group bonded via the nitrogen atom, with the secondary amino group carrying an alkyl or cycloalkyl substituent and the tertiary amino group carrying two similar or different alkyl or cycloalkyl substituents or the two nitrogen substitutents together forming a ring, such as, for example, $-NH_2$, methylamino, ethylamino, dimethylamino, diethylamino, methyl-ethylamino, pyrrolidin-1-yl or piperidino etc., preferably primary amino, dimethylamino and diethylamino and particularly dimethylamino.

The term "halogen" signifies fluorine, chlorine, bromine or iodine and preferably fluorine, chlorine or bromine.

The term "carbonyl", alone or in combination signifies the -C(O)- group.

The term "nitro", alone or in combination signifies the $-NO_2$ group.

The term "cyano", alone or in combination signifies the group -CN.

The term "pharmaceutically acceptable salts" refers to those salts which retain the biological effectiveness and properties of the free bases or free acids, which are not biologically or otherwise undesirable. The salts are formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, preferably hydrochloric acid, and organic acids such as acetic acid, propionic acid, glycolic acid, pyruvic acid, oxylic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid, N-acetylcystein and the like. In addition these salts may be prepared form addition of an inorganic base or an organic base to the free acid. Salts derived from an inorganic base include, but are not limited to, the sodium, potassium, lithium, ammonium, calcium, magnesium salts and the like. Salts derived from organic bases include, but are not limited to salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, ethanolamine, lysine, arginine, N-ethylpiperidine, piperidine, polymine resins and the like. The compound of

formula I can also be present in the form of zwitterions. Particularly preferred pharmaceutically acceptable salts of compounds of formula I are the hydrochloride salts.

The compounds of formula I can also be solvated, e.g. hydrated. The solvation can be effected in the course of the manufacturing process or can take place e.g. as a consequence of hygroscopic properties of an initially anhydrous compound of formula I (hydration). The term pharmaceutically acceptable salts also includes physiologically acceptable solvates.

"Pharmaceutically acceptable esters" means that compounds of general formula (I) may be derivatised at functional groups to provide derivatives which are capable of conversion back to the parent compounds in vivo. Examples of such compounds include physiologically acceptable and metabolically labile ester derivatives, such as methoxymethyl esters, methylthiomethyl esters and pivaloyloxymethyl esters. Additionally, any physiologically acceptable equivalents of the compounds of general formula (I), similar to the metabolically labile esters, which are capable of producing the parent compounds of general formula (I) in vivo, are within the scope of this invention.

The term "lipase inhibitor" refers to compounds which are capable of inhibiting the action of lipases, for example gastric and pancreatic lipases. For example orlistat and lipstatin as described in U.S. Patent No. 4,598,089 are potent inhibitor of lipases. Lipstatin is a natural product of microbial origin, and orlistat is the result of a hydrogenation of lipstatin. Other lipase inhibitors include a class of compound commonly referred to as panclicins. Panclicins are analogues of orlistat (Mutoh et al, 1994). The term "lipase inhibitor" refers also to polymer bound lipase inhibitors for example described in International Patent Application WO99/34786 (Geltex Pharmaceuticals Inc.). These polymers are characterized in that they have been substituted with one or more groups that inhibit lipases. The term "lipase inhibitor" also comprises pharmaceutically acceptable salts of these compounds. The term "lipase inhibitor" preferably refers to orlistat.

Orlistat is a known compound useful for the control or prevention of obesity and hyperlipidemia. See, U.S. Patent No. 4,598,089, issued July 1, 1986, which also discloses processes for making orlistat and U.S. Patent No. 6,004,996, which discloses appropriate pharmaceutical compositions. Further suitable pharmaceutical compositions are described for example in International Patent Applications WO 00/09122 and WO 00/09123. Additional processes for the preparation of orlistat are disclosed in European Patent Applications Publication Nos. 185,359, 189,577, 443,449, and 524,495.

Orlistat is preferably orally administered from 60 to 720 mg per day in divided doses two to three times per day. Preferred is wherein from 180 to 360 mg, most preferably 360 mg per day of a lipase inhibitor is administered to a subject, preferably in divided doses two or, particularly, three times per day. The subject is preferably an obese or overweight human, i.e. a human with a body mass index of 25 or greater. Generally, it is preferred that the lipase inhibitor be administered within about one or two hours of ingestion of a meal containing fat. Generally, for administering a lipase inhibitor as defined above it is preferred that treatment be administered to a human who has a strong family history of obesity and has obtained a body mass index of 25 or greater.

Orlistat can be administered to humans in conventional oral compositions, such as, tablets, coated tablets, hard and soft gelatin capsules, emulsions or suspensions. Examples of carriers which can be used for tablets, coated tablets, dragées and hard gelatin capsules are lactose, other sugars and sugar alcohols like sorbitol, mannitol, maltodextrin, or other fillers; surfactants like sodium lauryle sulfate, Brij 96, or Tween 80; disintegrants like sodium starch glycolate, maize starch or derivatives thereof; polymers like povidone, crospovidone; talc; stearic acid or its salts and the like. Suitable carriers for soft gelatin capsules are, for example, vegetable oils, waxes, fats, semi-solid and liquid polyols and the like. Moreover, the pharmaceutical preparations can contain preserving agents, solubilizers, stabilizing agents, wetting agents, emulsifying agents, sweetening agents, coloring agents, flavoring agents, salts for varying the osmotic pressure, buffers, coating agents and antioxidants. They can also contain still other therapeutically valuable substances. The formulations may conveniently be presented in unit dosage form and may be prepared by any methods known in the pharmaceutical art. Preferably, orlistat is administered according to the formulation shown in the Examples and in U.S. Patent No. 6,004,996, respectively.

The compounds of formula I can contain several asymmetric centers and can be present in the form of optically pure enantiomers, mixtures of enantiomers such as, for example, racemates, optically pure diastereioisomers, mixtures of diastereoisomers, diastereoisomeric racemates or mixtures of diastereoisomeric racemates.

Preferred are the compounds of formula I and pharmaceutically acceptable salts thereof, particularly the compounds of formula I.

Further preferred are compounds according to formula I, wherein R^2 is hydrogen or methyl. Particularly preferred are those compounds of formula I, wherein R^2 is hydrogen.

Another preferred embodiment of the present invention are compounds of formula I, wherein R^3 is hydrogen or alkyl, particularly hydrogen, methyl or ethyl. Particularly preferred are those compounds according to formula I, wherein R^3 is hydrogen.

Further preferred are compounds of formula I, wherein R^4 is alkyl, particularly methyl or ethyl. Particularly preferred are those, wherein R^4 is methyl.

Also preferred are compounds of formula I, wherein R^5 is hydrogen or alkyl. Particularly preferred are the compounds of formula I, wherein R^5 is hydrogen.

Further preferred are the compounds of formula I, wherein b is zero or 1. Particularly preferred are those, wherein b is zero.

Another preferred object of the present invention are the compounds according to formula I, wherein a is zero. Further preferred are those compounds of formula I, wherein a is 1.

Preferred are the compounds according to formula I, wherein R^1 is monoalkylamino, dialkylamino, phenyl, thiophenyl or pyrrolidinyl, wherein phenyl, thiophenyl and pyrrolidinyl are optionally substituted with one to three substituents independently selected from alkyl, halogen, alkoxy, trifluoromethoxy, nitro and trifluoromethyl.

Particularly preferred are the compounds according to formula I, wherein R^1 is thiophene-3-yl, 3-fluorophenyl, 4-fluorophenyl, 2-methylphenyl, 2-methoxy-5-methylphenyl, dimethylamino, thiophene-2-yl, 5-fluoro-2-methylphenyl, 2,4-difluorophenyl, 5-chloro-2-methoxyphenyl, 2-fluorophenyl, 3-fluorophenyl, 2-chloro-5-trifluoromethylphenyl, 3-nitrophenyl, 4-nitrophenyl or 4-methoxyphenyl.

Examples of preferred compounds of formula (I) are:

1. thiophene-2-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

2. thiophene-3-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

3. 5-chloro-thiophene-2-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

4. 2-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

5. 3-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

6. 4-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

7. 2,4-difluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

8. 2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

9. 2,5-dimethyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

10. 5-fluoro-2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

11. 3-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

12. 4-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

13. 2-methoxy-5-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

14. 2,5-dimethoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

15. 5-chloro-2-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

16. N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-4-trifluoromethoxy-benzenesulfonamide;

17. N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-3-nitro-benzenesulfonamide;

18. 2-chloro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-5-trifluoromethyl-benzenesulfonamide;

19. 4-chloro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

20. N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-4-nitro-benzenesulfonamide;

21. pyrrolidine-1-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

22. dimethylamine-1-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

23. thiophene-2-sulfonic acid {3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

24. 5-chloro-thiophene-2-sulfonic acid {3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

25. 3-fluoro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

26. 4-fluoro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

27. 2-methyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

28. 2,5-dimethyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

29. 5-fluoro-2-methyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

30. 3-methoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

31. 4-methoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

32. 2-methoxy-5-methyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

33. 2-chloro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-4-trifluoromethyl-benzenesulfonamide;

34. 4-chloro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

35. N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-3-nitro-benzenesulfonamide;

36. dimethylamine-1-sulfonic acid {3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

37. 5-fluoro-2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

38. 2,4-difluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

39. 5-chloro-thiophene-2-sulfonic acid 4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide;

40. 5-chloro-2-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

41. 2-chloro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-4-trifluoromethyl-benzenesulfonamide;

42. thiophene-3-sulfonic acid 4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide;

43. 4-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

44. 2-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

45. 3-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

46. 2-chloro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-5-trifluoromethyl-benzenesulfonamide;

47. N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-3-nitro-benzenesulfonamide;

48. 4-chloro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

49. N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-4-nitro-benzenesulfonamide;

50. dimethylamine-1-sulfonic acid 4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide;

51. 2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

52. 2,5-dimethyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

53. 4-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

54. 3-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

55. 5-fluoro-2-methyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

56. 2,4-difluoro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

57. 5-chloro-thiophene-2-sulfonic acid 3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide;

58. 5-chloro-2-methoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

59. 2-chloro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-4-trifluoromethyl-benzenesulfonamide;

60. 2,5-dimethoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

61. 3-methoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

62. 2-chloro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-5-trifluoromethyl-benzenesulfonamide;

63. N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-3-nitro-benzenesulfonamide;

64. 4-chloro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

65. N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-4-nitro-benzenesulfonamide;

66. C-(4-fluoro-phenyl)-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-methanesulfonamide;

67. 4-methoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

68. 2,5-dimethyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

69. pyrrolidine-1-sulfonic acid 3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide;

70. thiophene-2-sulfonic acid 3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide;

71. thiophene-3-sulfonic acid 3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide;

72. 2-methyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

73. 2-fluoro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide; and

74. 3-fluoro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide.

Examples of particularly preferred compounds of formula (I) are:

thiophene-3-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

3-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

4-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

2-methoxy-5-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

dimethylamine-1-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

thiophene-2-sulfonic acid {3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

5-fluoro-2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

2,4-difluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

5-chloro-2-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

2-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

3-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

2-chloro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-5-trifluoromethyl-benzenesulfonamide;

N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-3-nitro-benzenesulfonamide;

N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-4-nitro-benzenesulfonamide;

dimethylamine-1-sulfonic acid 4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide;

2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide; and

4-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide.

Processes for the manufacture of compounds of formula I are an object of the invention.

The preparation of compounds of formula I of the present invention may be carried out in sequential or convergent synthetic routes. Syntheses of the invention are shown in the following Schemes. The skills required for carrying out the reaction and purification of the resulting products are known to those in the art. The substituents and indices used in the following description of the processes have the significance given above unless indicated to the contrary.

Compounds of general formula I, wherein a is zero can be prepared according to scheme 1 as follows:

a) Nitrothioureas IA, either commercially available or easily synthetically available for example from the respective nitroanilin and benzoylisothioccyanate followed by basic aqueous work-up (reaction conditions described in literature affecting such a reaction see for example: Tetrahedron 1963, 19, 1603), are conveniently reacted with N,N-dimethylformamide dimethyl acetal in the presence or the absence of a solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or the reagents involved and that it can dissolve the reagents, at least to some extent. Examples for suitable solvents include: DMF and dioxane and the like. The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. We find it convenient to carry out the reaction with heating from ambient temperature to reflux. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents. However, a period of from 0.5 h to several days will usually suffice to yield the dimethylaminomethylene-thioureido derivatives IB. For reaction conditions described in literature affecting such a reaction see for example: Heterocycles 11, 313-318; 1978.

b) Dimethylaminomethylene-thioureido derivatives IB can be converted to thiazole derivatives IC by reaction of IB with α-bromoketones (a known compound or compound prepared by known methods. The source for α-bromoketones employed is indicated as appropriate) in a solvent such as ethanol, and the like, in the presence or the absence of a base. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or the reagents involved and that it can dissolve the reagents, at least to some extent. Examples for suitable solvents include: dichloromethane, chloroform, or dioxane, methanol, ethanol

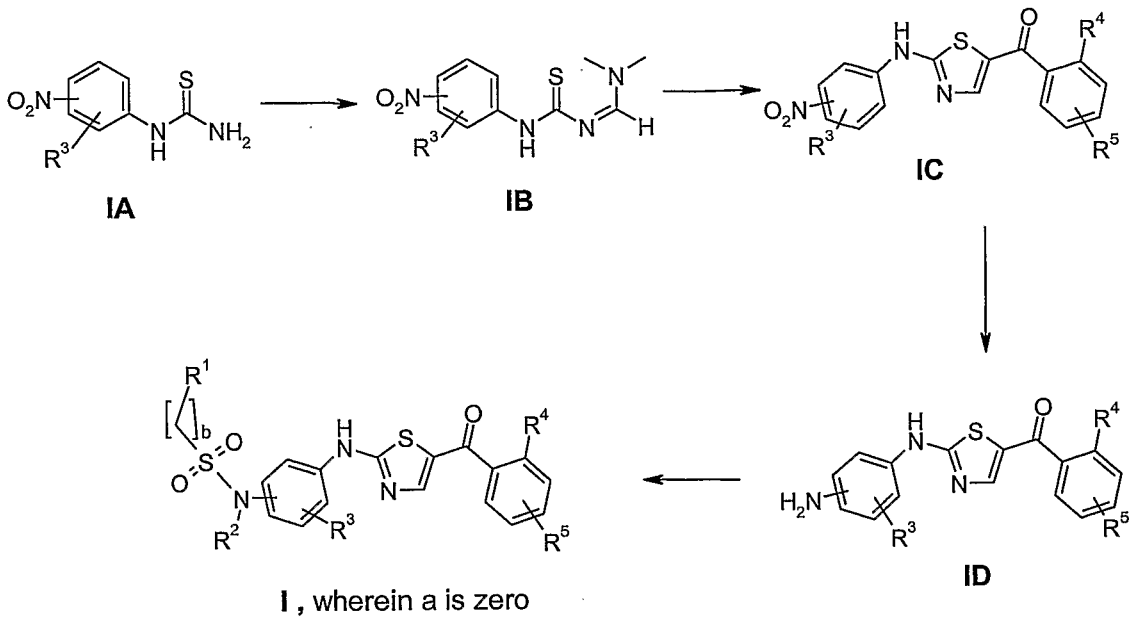
and the like. There is no particular restriction on the nature of the base used in this stage, and any base commonly used in this type of reaction may equally be employed here. Examples of such bases include triethylamine and diisopropylethylamine, and the like. The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. We find it convenient to carry out the reaction with heating from ambient temperature to reflux. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents. However, a period of from 0.5 h to several days will usually suffice to yield the thiazole derivatives **IC**. For reaction conditions described in literature affecting such a reaction see for example: J. Heterocycl. Chem., 16(7), 1377-83; 1979. The resulting compound of formula IC is a compound of the present invention and may be the desired product; alternatively it may be subjected to consecutive reactions like reduction of the nitro-group by methods described widely in literature to yield the desired thiazole derivatives **ID**.

c) We find it convenient to reduce the nitro-group in **IC** with hydrogen over Pd/C in a solvent or with $SnCl_2$ in a solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or the reagents involved and that it can dissolve the reagents, at least to some extent. Examples for suitable solvents include: DMF or dioxane, methanol, ethanol and the like. The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. We find it convenient to carry out the reaction with heating from ambient temperature to reflux. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents. However, a period of from 0.5 h to several days will usually suffice to yield the amino-derivatives ID. For reaction conditions described in literature affecting such a reaction see for example: Tetrahedron Lett 1984, 25, 3415; J Med Chem 1983, 26, 1747. However, the resulting compound of formula ID is a compound of the present invention and may be the desired product; alternatively it may be subjected to consecutive reactions.

d) Sulfonamides and sulfonic acid derivatives **I** can be prepared from suitable starting materials according to methods known in the art. The conversion of the amino-moiety in **ID** to access sulfonamides or sulfonic acid derivatives can be affected by methods described in literature. For example the conversion of the amine derivatives **ID** or their respective salts to access compounds of the general formula **I** is affected by reaction of **ID** with suitable sulfonyl chlorides, or sulfamoyl chlorides (compounds known or compound prepared by known methods) respectively in a solvent like dichloromethane and / or MeOH and the like and in the presence or the absence of a

base. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or the reagents involved and that it can dissolve the reagents, at least to some extent. Examples for suitable solvents include: DCM, chloroform, MeOH or dioxane, THF, and the like. There is no particular restriction on the nature of the base used in this stage, and any base commonly used in this type of reaction may equally be employed here. Examples of such bases include triethylamine and diisopropylethylamine, and the like. The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. We find it convenient to carry out the reaction with heating from ambient temperature to reflux. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents. However, a period of from 0.5 h to several days will usually suffice to yield thiazole derivatives **I**. For reaction conditions described in literature affecting such reactions see for example: Comprehensive Organic Transformations: A Guide to Functional Group Preparations, 2nd Edition, Richard C. Larock. John Wiley & Sons, New York, NY. 1999. However, the resulting compound of formula I (R2 = H) is a compound of the present invention and may be the desired product; alternatively it may be subjected to consecutive reactions like alkylation of the sulphonamide under suitable conditions. Sulfonamides I (R2 = H) are converted to sulfonamides I (R2=alkyl) by reaction of I (R2 = H) with suitable electophiles such as alkyl halogenids under basic conditions. The reaction can be carried out in the presence or absence of a solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or the reagents involved and that it can dissolve the reagents, at least to some extent. Examples for suitable solvents include: chloroform, or dioxane, THF, and the like. There is no particular restriction on the nature of the base used in this stage, and any base commonly used in this type of reaction may equally be employed here. Examples of such bases include NaH, triethylamine and diisopropylethylamine, and the like. The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. We find it convenient to carry out the reaction with heating from ambient temperature to reflux. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents. However, a period of from 0.5 h to several days will usually suffice to yield thiazole derivatives **I** (R2=alkyl). For reaction conditions described in literature affecting such a reaction see for example: J Org Chem 1984, 49, 249.

Scheme 1



Compounds of general formula I, wherein a is 1 can be prepared according to scheme 2 as follows:

a) Benzophenons IIA (either commercially available or synthetically accessible via various methods described in the art) can be formylated under various reaction conditions. We find it convenient to formylate IIA with ethyl formate under basic conditions in the presence or the absence of a solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or the reagents involved and that it can dissolve the reagents, at least to some extent. Examples for suitable solvents include: MeOH, ethanol or dioxane, THF, and the like. There is no particular restriction on the nature of the base used in this stage, and any base commonly used in this type of reaction may equally be employed here. Examples of such bases include sodium methoxide, and the like. The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. We find it convenient to carry out the reaction from 0 °C to heating to reflux. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents. However, a period of from 0.5 h to several days will usually suffice to yield derivatives **IIB**. For reaction conditions described in literature affecting such reactions see for example: J Am Chem Soc 1947, 69, 2942.

b) Compounds **IIB** can be brominated under various reaction conditions described in literature. We find it convenient to brominate **IIB** with Br_2 at low temperatures in a solvent to yield derivatives **IIC**. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or the reagents involved and that it can dissolve the reagents, at least to some extent. Examples for suitable solvents include: DCM, THF, and the like. The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. We find it convenient to carry out the reaction from -78 °C to heating to reflux. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents. However, a period of from 0.5 h to several days will usually suffice to yield derivatives IIC. For reaction conditions described in literature affecting such reactions see for example: J Org Chem 1984, 49, 566.

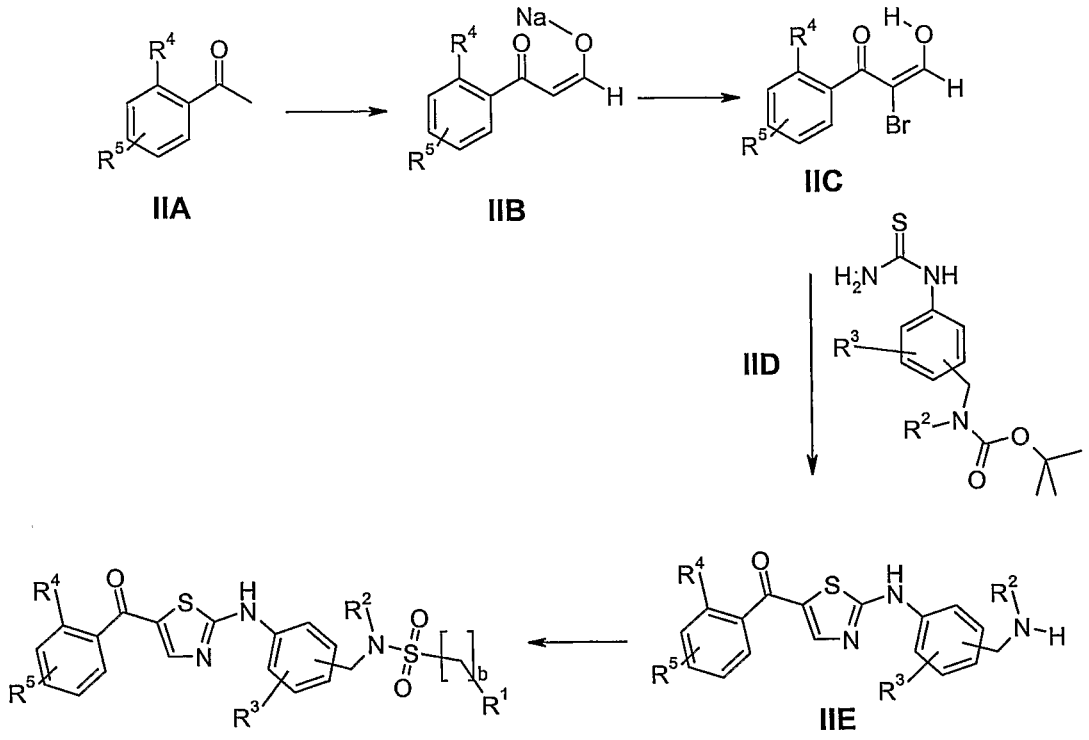
c) Thioureas IID are synthetically accessible via convergent or linear synthetic routes starting from various commercially available starting materials. We find it convenient to react amino-benzyl carbamic acid tert butyl esters (which are either commercially available or easily synthetically accessible via reaction of aminomethylanilins with Boc_2O under various reaction conditions described in the art like for example: Bioorg Med Chem Lett 2002, 12, 1439) with suitable electophiles such as alkyl halogenids under basic conditions in the case that R2=H is to be converted to R2= alkyl. The reaction can be carried out in the presence or absence of a solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or the reagents involved and that it can dissolve the reagents, at least to some extent. Examples for suitable solvents include: DMF, chloroform, or dioxane, THF, and the like. There is no particular restriction on the nature of the base used in this stage, and any base commonly used in this type of reaction may equally be employed here. Examples of such bases include NaH, triethylamine and diisopropylethylamine, and the like. The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. We find it convenient to carry out the reaction with heating from ambient temperature to reflux. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents. However, a period of from 0.5 h to several days will usually suffice to yield the anilinic intermediates (R2=alkyl). For reaction conditions described in literature affecting such a reaction see for example: Org Lett 2001, 3, 3379. Subsequent conversion of the aniline moiety of the intermediates to the thiourea moiety can be affected by several methods described in the literature.

However, we find it convenient to react the intermediates with benzoylisothiocanate in a solvent and subsequenty basic removal of the benzoyl group to liberate the thioureas IID. For reaction conditions described in literature affecting such a reaction see for example: Tetrahedron 1963, 19, 1603.

d) The reaction of **IIC** with **IID** to access the protected precursor of **IIE** can be affected by various methods described in literature. However, we find it convenient to react **IIC** with **IID** in the presence or the absence of a solvent in the presence of a base. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or the reagents involved and that it can dissolve the reagents, at least to some extent. Examples for suitable solvents include: acetone, methanol and dioxane THF, and the like. There is no particular restriction on the nature of the base used in this stage, and any base commonly used in this type of reaction may equally be employed here. The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. We find it convenient to carry out the reaction with heating from ambient temperature to reflux. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents. However, a period of from 0.5 h to several days will usually suffice to yield the protected precursor of **IIE**. However, the resulting intermediate is a compound of the present invention and may be the desired product; alternatively it may be subjected to consecutive reactions like deprotection, possible under various reaction conditions, to liberate IIE. We find it convenient to remove the Boc-protecting group under acidic conditions in the presence or absence of a solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or the reagents involved and that it can dissolve the reagents, at least to some extent. Examples for suitable solvents include: dioxane, THF, and the like. There is no particular restriction on the nature of the acid used in this stage, and any acid commonly used in this type of reaction may equally be employed here. Examples of such acids include HCl, TFA and the like. The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. We find it convenient to carry out the reaction with heating from ambient temperature to reflux. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents. However, a period of from 0.5 h to several days will usually suffice to yield thiazole **IIE** or the respective salt thereof. For reaction conditions described in literature affecting such reactions see for example: Heterocycles 1991, 32, 1699.

e) Sulfonamides and sulfonic acid derivatives **I** can be prepared from suitable starting materials according to methods known in the art. The conversion of the amino-moiety in **IE** to access sulfonamides or sulfonic acid derivatives can be affected by methods described in literature. For example the conversion of the amine derivatives **IIE** or their respective salts to access compounds of the general formula **I** is affected by reaction of **IIE** with suitable sulfonyl chlorides, or sulfamoyl chlorides (compounds known or compound prepared by known methods) respectively in a solvent like dichloromethane and / or MeOH and the like and in the presence or the absence of a base. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or the reagents involved and that it can dissolve the reagents, at least to some extent. Examples for suitable solvents include: DCM, chloroform, MeOH or dioxane, THF, and the like. There is no particular restriction on the nature of the base used in this stage, and any base commonly used in this type of reaction may equally be employed here. Examples of such bases include triethylamine and diisopropylethylamine, and the like. The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. We find it convenient to carry out the reaction with heating from ambient temperature to reflux. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents. However, a period of from 0.5 h to several days will usually suffice to yield thiazole derivatives **I**. For reaction conditions described in literature affecting such reactions see for example: Comprehensive Organic Transformations: A Guide to Functional Group Preparations, 2nd Edition, Richard C. Larock. John Wiley & Sons, New York, NY. 1999.

Scheme 2

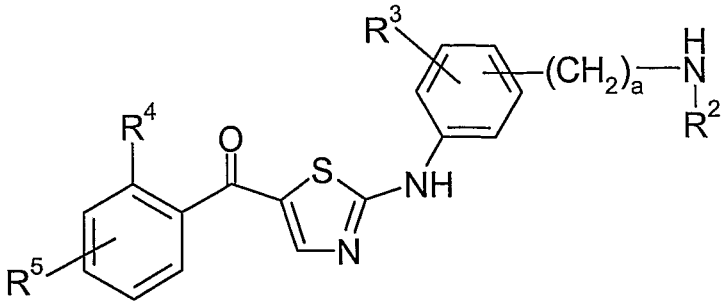


I ,wherein a is 1

The conversion of a compound of formula I into a pharmaceutically acceptable salt can be carried out by treatment of such a compound with an inorganic acid, for example a hydrohalic acid, such as, for example, hydrochloric acid or hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid etc., or with an organic acid, such as, for example, acetic acid, citric acid, maleic acid, fumaric acid, tartaric acid, methanesulfonic acid or p-toluenesulfonic acid. The corresponding carboxylate salts can also be prepared from the compounds of formula I by treatment with physiologically compatible bases.

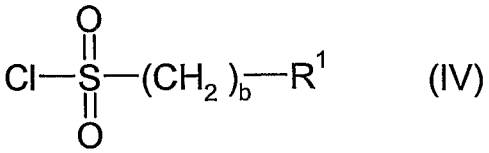
The conversion of compounds of formula I into pharmaceutically acceptable esters or amides can be carried out e.g. by treatment of suited amino or hydroxyl groups present in the molecules with an carboxylic acid such as acetic acid, with a condensating reagent such as benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (BOP) or N,N-dicylohexylcarbodiimide (DCCI) to produce the carboxylic ester or carboxylic amide.

A preferred process for the preparation of a compound of formula I comprises the reaction of a compound according to formula



(III)

in the presence of a compound according to formula



(IV)

in order to obtain a compound of formula I, wherein R^1 to R^5, a and b are defined as in claim 1. Particularly preferred is the above reaction, wherein the solvent is e.g. dichloromethane and / or MeOH in the presence or the absence of a base. Preferred bases are e.g. triethylamine and diisopropylethylamine.

Preferred intermediates are:

[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone

[2-(3-Amino-phenylamino)-thiazol-5-yl]-o-tolyl-methanone

[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride

[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride

The compounds of formula I described above for use as therapeutically active substances are a further object of the invention.

Also an object of the invention are compounds described above for the production of medicaments for the prophylaxis and therapy of illnesses which are caused by disorders associated with the NPY receptor, particularly for the production of medicaments for the prophylaxis and therapy of arthritis, cardiovascular diseases, diabetes, renal failure and particularly eating disorders and obesity.

Likewise an object of the invention are pharmaceutical compositions containing a compound of formula I described above and a therapeutically inert carrier.

An object of the invention is also the use of the compounds described above for the production of medicaments, particularly for the treatment and prophylaxis of arthritis, cardiovascular diseases, diabetes, renal failure and particularly eating disorders and obesity.

A further object of the invention comprises compounds which are manufactured according to one of the described processes.

A further object of the invention is a method for the treatment and prophylaxis of arthritis, cardiovascular diseases, diabetes, renal failure and particularly eating disorders and obesity whereby an effective amount of a compound described above is administered.

According to a further aspect of the invention there is provided a method of treatment of obesity in a human in need of such treatment which comprises administration to the human a therapeutically effective amount of a compound according to formula I and a therapeutically effective amount of a lipase inhibitor, particularly preferred, wherein the lipase inhibitor is orlistat. Also subject of the present invention is the mentioned method, wherein the administration is simultaneous, separate or sequential.

A further preferred embodiment of the present invention is the use of a compound of the formula I in the manufacture of a medicament for the treatment and prevention of obesity in a patient who is also receiving treatment with a lipase inhibitor, particularly preferred, wherein the lipase inhibitor is orlistat.

Also an object of the invention are compounds described above for the production of medicaments for the prophylaxis and therapy of alcoholism.

A further object of the invention is a method for the treatment and prophylaxis of alcoholism.

Assay Procedures

Cloning of mouse NPY5 receptor cDNAs:

The full-length cDNA encoding the mouse NPY5 (mNPY5) receptor was amplified from mouse brain cDNA using specific primers, designed based on the published sequence, and Pfu DNA-Polymerase. The amplification product was subcloned into the mammalian expression vector pcDNA3 using Eco RI and XhoI restriction sites. Positive clones were sequenced and one clone, encoding the published sequence was selected for generation of stable cell clones.

Stable transfection:

Human embryonic kidney 293 (HEK293) cells were transfected with 10 µg mNPY5 DNA using the lipofectamine reagent. Two days after transfection, geneticin selection (1 mg/ml) was initiated and several stable clones were isolated. One clone was further used for pharmacological characterization.

Radioligand competition binding:

Human embryonic kidney 293 cells (HEK293), expressing recombinant mouse NPY5-receptor (mNPY5) were broken by three freeze/thawing cycles in hypotonic Tris buffer (5 mM, pH 7.4, 1 mM $MgCl_2$), homogenized and centrifuged at 72,000 x g for 15 min. The pellet was washed twice with 75 mM Tris buffer, pH 7.4, containing 25 mM $MgCl_2$ and 250 mM sucrose, 0.1 mM phenylmethylsulfonylfluoride and 0.1 mM 1,10-pheneanthrolin, resuspended in the same buffer and stored in aliquots at -80°C. Protein was determined according to the method of Lowry using bovine serum albumine (BSA) as a standard.

Radioligand competition binding assays were performed in 250 µl 25 mM Hepes buffer (pH 7.4, 2.5 mM $CaCl_2$, 1 mM $MgCl_2$, 1 % bovine serum albumine, and 0.01 % NaN_3 containing 5 µg protein, 100 pM [^{125}I]labelled peptide YY (PYY) and 10 µL DMSO containing increasing amounts of unlabelled test compounds. After incubation for 1 h at

22°C, bound and free ligand are separated by filtration over glass fibre filters. Non specific binding is assessed in the presence of 1 μM unlabelled PYY. Specific binding is defined as the difference between total binding and non specific binding. IC_{50} values are defined as the concentration of antagonist that displaces 50 % of the binding of [^{125}I]labelled neuropeptide Y. It is determined by linear regression analysis after logit/log transformation of the binding data.

Results obtained in the foregoing test using representative compounds of the invention as the test compounds are shown in the following table:

Compound	NPY5-R (mouse) IC_{50} (nM)
Example 5: 3-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	0.74
Example 23: thiophene-2-sulfonic acid {3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide	0.54
Example 37: 5-fluoro-2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	0.99

Compounds as described above have IC_{50} values below 1000 nM; more preferred compounds have IC_{50} values below 100 nM, particularly below 10 nM. Most preferred compounds have IC_{50} values below 2 nM. These results have been obtained by using the foregoing test.

The compounds of formula I and their pharmaceutically acceptable salts and esters can be used as medicaments (e.g. in the form of pharmaceutical preparations). The pharmaceutical preparations can be administered internally, such as orally (e.g. in the form of tablets, coated tablets, dragées, hard and soft gelatin capsules, solutions, emulsions or suspensions), nasally (e.g. in the form of nasal sprays) or rectally (e.g. in the form of suppositories). However, the administration can also be effected parentally, such as intramuscularly or intravenously (e.g. in the form of injection solutions).

The compounds of formula I and their pharmaceutically acceptable salts and esters can be processed with pharmaceutically inert, inorganic or organic adjuvants for the

production of tablets, coated tablets, dragées and hard gelatin capsules. Lactose, corn starch or derivatives thereof, talc, stearic acid or its salts etc. can be used, for example, as such adjuvants for tablets, dragées and hard gelatin capsules.

Suitable adjuvants for soft gelatin capsules, are, for example, vegetable oils, waxes, fats, semi-solid substances and liquid polyols, etc.

Suitable adjuvants for the production of solutions and syrups are, for example, water, polyols, saccharose, invert sugar, glucose, etc.

Suitable adjuvants for injection solutions are, for example, water, alcohols, polyols, glycerol, vegetable oils, etc.

Suitable adjuvants for suppositories are, for example, natural or hardened oils, waxes, fats, semi-solid or liquid polyols, etc.

Moreover, the pharmaceutical preparations can contain preservatives, solubilizers, viscosity-increasing substances, stabilizers, wetting agents, emulsifiers, sweeteners, colorants, flavorants, salts for varying the osmotic pressure, buffers, masking agents or antioxidants. They can also contain still other therapeutically valuable substances.

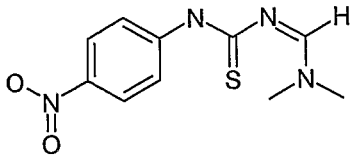
In accordance with the invention the compounds of formula I and their pharmaceutically acceptable salts can be used for the prophylaxis and treatment of arthritis, cardiovascular diseases, diabetes, renal failure and particularly eating disorders and obesity. The dosage can vary in wide limits and will, of course, be fitted to the individual requirements in each particular case. In general, in the case of oral administration a daily dosage of about 0.1 mg to 20 mg per kg body weight, preferably about 0.5 mg to 4 mg per kg body weight (e.g. about 300 mg per person), divided into preferably 1-3 individual doses, which can consist, for example, of the same amounts, should be appropriate. It will, however, be clear that the upper limit given above can be exceeded when this is shown to be indicated.

The invention is illustrated hereinafter by Examples, which have no limiting character.

Examples

Example A

1-Dimethylaminomethylene-3-(4-nitro-phenyl)-thiourea



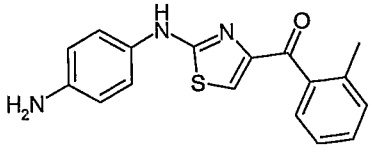
A mixture of 5 g (25.3 mmol) (4-nitro-phenyl)-thiourea and 33.8 ml (253 mmol) N,N-Dimethylformamide dimethyl acetal was heated to 100 °C for 1 h. The precipitate was filtered off, washed with diethyl ether and dried to yield 4.74 g (74 %) the title compound as orange solid.

1-H-NMR (300 MHz, DMSO d6) δ= 3.13 (s, 3H, NMe_2), 3.30 (s, 3H, NMe_2), 8.05 (s, br, 2H, Ar), 8.18 (d, 2H, J=9.2, Ar), 8.79 (s, 1H, PhNH), 10.95 (s, 1H, N=C<u>H</u>-NMe_2).

MS (m/e): 253.2 (MH^+, 100%)

Example B

[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone



A mixture of 0.6 g (2.4 mmol) 1-dimethylaminomethylene-3-(4-nitro-phenyl)-thiourea, 0.61 g (2.88 mmol) 2-bromo-1-o-tolyl-ethanone (WO9907666) and 1002 ul (7.2 mmol) NEt_3 in 3 ml EtOH was heated to 90 °C for 16 h. After concentration under vacuum the mixture was treated with diluted aqueous diluted $NaHCO_3$ solution and extracted with ethyl acetate. The combined organic layers were filtered through a plug of silica topped with a layer of $MgSO_4$ and concentrated under vacuum to yield 549 mg (67 %) of the intermediate [2-(4-nitro-phenylamino)-thiazol-5-yl]-o-tolyl-methanone. The residue was

taken up in MeOH and hydrogenated with 1 bar H_2 over Pd/C at room temperature to yield after filtration and evaporation 388 mg (78 %) of the title compound.

MS (m/e): 310.2 (MH^+, 100%)

Example 1

Thiophene-2-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide

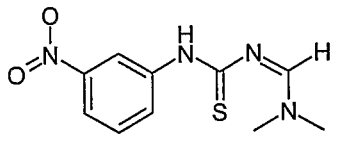
A mixture of 31 mg (0.1 mmol) [2-(4-amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 44 ul (0.32 mmol) NEt_3 in 1 ml MeOH was treated with 21.9 mg (0.12 mmol) thiophene-2-sulfonyl chloride (commercially available) in 3 ml DCM and heated to 60 °C for 16 h. After evaporation of the volatiles the residue was taken up in 1.5 ml of MeOH / formic acid 3 / 2 and subjected to reversed phase HPLC purification eluting with a gradient of acetonitrile / water. After evaporation of the product fractions 7 mg (16 %) of the title compound was obtained.

MS (m/e): 454.2 (MH^-, 100%)

Examples 2 to 22 have been prepared according to the procedure described for the synthesis of Example 1 (see table 1).

Example C

1-Dimethylaminomethylene-3-(3-nitro-phenyl)-thiourea



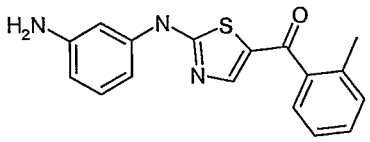
A mixture of 5 g (25.3 mmol) (4-nitro-phenyl)-thiourea and 38.2 ml (286 mmol) N,N-dimethylformamide dimethyl acetal was heated to 100 °C for 1 h. The precipitate was filtered off, washed wit diethyl ether and dried to yield 6.31 g (99 %) the title compound as white solid.

1-H-NMR (300 MHz, DMSO d6) δ= 3.13 (s, 3H, NMe_2), 3.26 (s, 3H, NMe_2), 7.56 ppm (t, 2H, J=8.1, H-5), 7.89 (m br, 2H, H-4/H-6), 8.81 (s, 1H, H-2) 8.94 (s, br, 1H, PhNH), 10.83 (s br, 1H, N=CH-NMe_2).

MS (m/e): 253.3 (MH^+, 100%)

Example D

[2-(3-Amino-phenylamino)-thiazol-5-yl]-o-tolyl-methanone



A mixture of 0.6 g (2.4 mmol) 1-dimethylaminomethylene-3-(3-nitro-phenyl)-thiourea, 0.61 g (2.88 mmol) 2-bromo-1-o-tolyl-ethanone (WO9907666) and 1002 ul (7.2 mmol) NEt_3 in 3 ml EtOH was heated to 90 °C for 16 h. After concentration under vacuum the mixture was treated with diluted aqueous diluted $NaHCO_3$ solution and extracted with ethyl acetate. The combined organic layers were filtered through a plug of silica topped with a layer of $MgSO_4$ and concentrated in vacuo to yield 570 mg (70 %) of the intermediate [2-(4-Nitro-phenylamino)-thiazol-5-yl]-o-tolyl-methanone. The residue was taken up in H_2O / THF and reduced with $SnCl_2$.H2O at room temperature during 16 h to yield after filtration and evaporation 493 mg (95 %) of the title compound.

MS (m/e): 310.2 (MH^+, 100%)

Example 23

Thiophene-2-sulfonic acid {3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide

A mixture of 31 mg (0.1 mmol) [2-(3-amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 44 ul (0.32 mmol) NEt_3 in 1 ml MeOH was treated with 21.9 mg (0.12 mmol) thiophene-2-sulfonyl chloride (commercially available) in 3 ml DCM and heated to 60 °C for 16 h. After evaporation of the volatiles the residue was taken up in 1.5 ml of MeOH / formic acid 3 / 2 and subjected to reversed phase HPLC purification eluting with

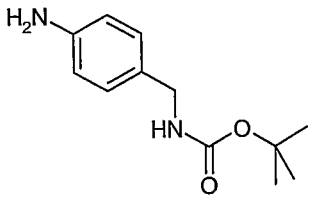
a gradient of acetonitrile / water. After evaporation of the product fractions 6 mg (12 %) of the title compound was yielded.

MS (m/e): 454.2 (MH^-, 100%)

Examples 24 to 36 have been prepared according to the procedure described for the synthesis of Example 23 (see table 1).

Example E

(4-Amino-benzyl)-carbamic acid tert-butyl ester

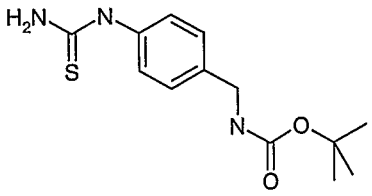


A mixture of 7 g (57.2 mmol) 4-aminobenzylamine (commercially available), 13.7 g (63 mmol) Boc_2O and 9.57 ml (68.7 mmol) NEt_3 in 100 ml aceton was further treated with 3.74 g (17.1 mmol) Boc_2O and stirred at room temperature for 16 h. After evaporation of all volatiles the residue was extracted with ethyl acetate and the organic fractions were washed with 0.5 N aqueous NaOH solution and dried with $MgSO_4$. Evaporation of the solvent yielded 12.14 (95 %) of the title compound.

MS (m/e): 223.3 (MH^+, 100%)

Example F

(4-Thioureido-benzyl)-carbamic acid tert-butyl ester



A mixture of 3 g (13.5 mmol) (4-Amino-benzyl)-carbamic acid tert-butyl ester and 1.81 ml (13.5 mmol) benzoyl isothiocyanate in 60 ml THF was stirred at room temperature for

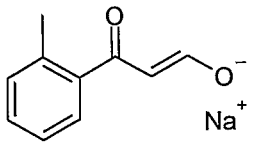
1 h and afterwards evaporated under reduced pressure. 80 ml MeOH and 5.6 g (40.5 mmol) potassium carbonate in 80 ml water were added and the mixture was stirred at room temperature for 16 h. The mixture was concentrated under reduced pressure and extracted with ethyl acetate. The organic layers were washed with saturated $NaHCO_3$ solution and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica eluting with a gradient of hexane / ethyl acetate to yield after evaporation of the product fractions 3.67 g (97 %) of the title compound as yellow amorphous solid.

1-H-NMR (300 MHz, DMSO d6) δ=1.39 (s, 9H, Boc), 4.08 (d, J=6.1Hz, 2H, CH_2), 7.17 (d, J= 8.2 Hz, 2H, H-3/H-5), 7.35 (d, J= 8.2 Hz, 2H, H-2/H-6), 7.36 (d, 1H, J=6.1Hz, NHBoc), 7.38 (s, br, 2H, NH_2), 9.62 (s, 1H, NH).

MS (m/e): 282.2 (MH^+, 100%)

Example G

Sodium; 3-oxo-3-o-tolyl-propen-1-olate



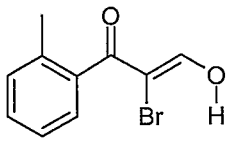
A suspension of 4.02 g (74.5 mmol) sodium methoxide in 200 ml diethyl ether was treated with 10 g (74.5 mmol) 2-methylacetophenone and 6 ml (74.5 mmol) ethyl formate under vigorous mechanical stirring at 30 °C. The suspension was stirred for 3 h at 30 °C and cooled to room temperature. The suspension was filtered and the precipitate was washed with diethyl ether and dried under reduced pressure to yield 8.09 g (59 %) of the title compound as white solid.

1-H-NMR (300 MHz, DMSO d6) δ= 2.18 (s, 3H, PhMe), 4.78 (d, J=10.1 Hz, 1H, CH), 7.07 (m, 4H, Ar), 8.50 (s, br, CH).

MS (m/e): 161.0 (MH^-, 100%)

Example H

2-Bromo-3-hydroxy-1-o-tolyl-propenone



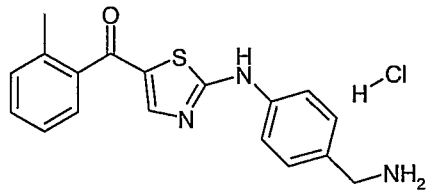
A solution of 8.09 g (43.9 mmol) sodium; 3-oxo-3-o-tolyl-propen-1-olate in 150 ml DCM at –78 °C was treated dropwise with 2.14 ml (41.7 mmol) Br_2 in 15 ml DCM and allowed to stirr for 2 h at –78 °C. The mixture was warmed to 0 °C and filtered. The filtrate was concentrated under reduced pressure at 5 °C to yield 7.92 g (75 %) of the title compound as white solid.

1-H-NMR (300 MHz, DMSO d6) δ= 2.18 (s, 3H, PhMe), 7.25 (m, 4H, Ar), 7.74 (s, br, 1H, CH), 11.9 (s, Br, 1H, OH).

MS (m/e): 240.0 (MH^-, 100%).

Example I

[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride



A mixture of 3.14 g (13 mmol) 2-bromo-3-hydroxy-1-o-tolyl-propenone and 3.67 g (13 mmol) (4-thioureido-benzyl)-carbamic acid tert-butyl ester in acetone was stirred at 60 °C for 16 h. After removal of all volatiles the residue was extracted with ethyl acetate and the organic layers washed with saturated aqueous $NaHCO_3$ solution, water and brine, dried with $MgSO_4$ and evaporated under reduced pressure. The residue was taken up in 150 ml dioxane and 20 ml of a 4 N HCl dioxane solution was added and stirred at room temperature for 16 h. After addition of diethyl ether the precipitate was filtered off, washed with diethyl ether and dried under vacuum to yield 2.79 g (59 %) of the title compound.

1-H-NMR (300 MHz, $CDCl_3$) δ= 2.36 (s, 3H, PhMe), 4.15 (d, J=6.0Hz, 2H, CH_2), 7.2-7.8 (m, 9H, Ar + NH), 8.07 (s, 1H, H-5 thiazole), 8.8 (s, br, 2H, NH_2).

MS (m/e): 324.2 (MH^+, 100%).

Example 37

5-Fluoro-2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide

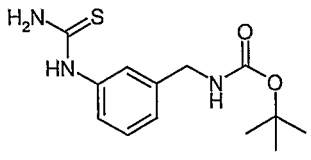
A mixture of 35.8 mg (0.1 mmol) [2-(4-aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride, 25 mg (0.12 mmol) 5-fluoro-2-methyl-benzenesulfonyl chloride (commercially available) and 69 ul (0.5 mmol) NEt_3 in 3 ml DCM was stirred at 60 °C for 16 h. After evaporation of the volatiles the residue was taken up in 1.5 ml MeOH/formic acid 2/1 and subjected to reversed phase HPLC purification eluting with a gradient of acetonitrile / water. After evaporation of the product fractions 10 mg (21 %) of the title compound was obtained.

MS (m/e): 494.1 (MH^-, 100%)

Examples 38 to 54 have been prepared according to the procedure described for the synthesis of Example 37 (see table 1).

Example J

(3-Thioureido-benzyl)-carbamic acid tert-butyl ester



A mixture of 3 g (13.5 mmol) (3-amino-benzyl)-carbamic acid tert-butyl ester (WO 9740028 A1) and 1.81 ml (13.5 mmol) benzoyl isothiocyanate in 60 ml THF was stirred at room temperature for 1 h and afterwards evaporated under reduced pressure. 80 ml MeOH and 5.6 g (40.5 mmol) potassium carbonate in 80 ml water were added and the mixture was stirred at room temperature for 16 h. The mixture was concentrated under reduced pressure and extracted with ethyl acetate. The organic layers were washed with

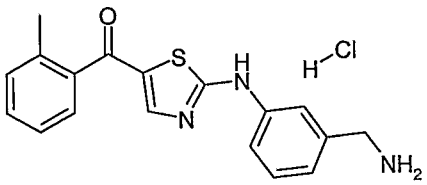
saturated $NaHCO_3$ solution and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica eluting with a gradient of hexane / ethyl acetate to yield after evaporation of the product fractions 3.56 g (94 %) of the title compound as yellow amorphous solid.

1-H-NMR (300 MHz, DMSO d6) δ= 1.39 (s, 9H, Boc), 4.10 (d, J=6.0Hz, 2H, CH2), 6.9-7.4 (m, 7H, Ar + NHBoc + NH_2), 9.69 ppm (s, 1H, NH).

MS (m/e): 282.0 (MH^+, 100%).

Example K

[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride



A mixture of 3.04 g (12.6 mmol) 2-bromo-3-hydroxy-1-o-tolyl-propenone and 3.56 g (12.6 mmol) (4-thioureido-benzyl)-carbamic acid tert-butyl ester in acetone was stirred at 60 °C for 16 h. After removal of all volatiles the residue was extracted with ethyl acetate and the organic layers washed with saturated aqueous $NaHCO_3$ solution, water and brine, dried with $MgSO_4$ and evaporated under reduced pressure. The residue was taken up in 150 ml dioxane and 20 ml of a 4 N HCl dioxane solution was added and stirred at room temperature for 16 h. After addition of diethyl ether the precipitate was filtered off, washed with diethyl ether and dried under vacuum to yield 2.81 g (62 %) of the title compound.

1-H-NMR (300 MHz, DMSO d6) δ= 2.5 (s, 3H, PhMe), 4.11 (m, br, 2H, CH_2), 7.2–7.7 (m, 10H, Ar + H-4 thiazole + NH), 8.36 (s, br, NH_2)

MS (m/e): 324.2 (MH^+, 100%)

Example 55

5-Fluoro-2-methyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide

A mixture of 35.8 mg (0.1 mmol) [2-(3-aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride, 25 mg (0.12 mmol) 5-fluoro-2-methyl-benzenesulfonyl chloride (commercially available) and 69 ul (0.5 mmol) NEt_3 in 3 ml DCM was stirred at 60 °C for 16 h. After evaporation of the volatiles the residue was taken up in 1.5 ml MeOH/formic acid 2/1 and subjected to reversed phase HPLC purification eluting with a gradient of acetonitrile / water. After evaporation of the product fractions 31 mg (62 %) of the title compound was obtained.

MS (m/e): 494.1 (MH^-, 100%)

Examples 56 to 74 have been prepared according to the procedure described for the synthesis of Example 55 (see table 1).

Table 1:

Ex	MW	name	starting materials	MW found
1	455.6	Thiophene-2-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and Thiophene-2-sulfonyl chloride (commercially available)	454.2 $(M-H)^-$
2	455.6	Thiophene-3-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and Thiophene-3-sulfonyl chloride (commercially available)	454.2 $(M-H)^-$
3	490	5-Chloro-thiophene-2-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 5-Chloro-thiophene-2-sulfonyl chloride (commercially available)	488.0 $(M-H)^-$

Ex	MW	name	starting materials	MW found
4	467.5	2-Fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 2-Fluoro-benzenesulfonyl chloride (commercially available)	466.1 $(M-H)^-$
5	467.5	3-Fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 3-Fluoro-benzenesulfonyl chloride (commercially available)	466.1 $(M-H)^-$
6	467.5	4-Fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 2-Fluoro-benzenesulfonyl chloride (commercially available)	466.1 $(M-H)^-$
7	485.5	2,4-Difluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 2,4-Difluoro-benzenesulfonyl chloride (commercially available)	484.1 $(M-H)^-$
8	463.6	2-Methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 2-Methyl-benzenesulfonyl chloride (commercially available)	462.1 $(M-H)^-$
9	477.6	2,5-Dimethyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 2,5-Dimethyl-benzenesulfonyl chloride (commercially available)	476.1 $(M-H)^-$

Ex	MW	name	starting materials	MW found
10	481.6	5-Fluoro-2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 5-Fluoro-2-methyl-benzenesulfonyl chloride (commercially available)	480.2 $(M-H)^-$
11	479.6	3-Methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 3-Methoxy-benzenesulfonyl chloride (commercially available)	478.1 $(M-H)^-$
12	479.6	4-Methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 4-Methoxy-benzenesulfonyl chloride (commercially available)	478.1 $(M-H)^-$
13	493.6	2-Methoxy-5-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 2-Methoxy-5-methyl-benzenesulfonyl chloride (commercially available)	492.1 $(M-H)^-$
14	509.6	2,5-Dimethoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 2,5Dimethoxy-benzenesulfonyl chloride (commercially available)	508.2 $(M-H)^-$

Ex	MW	name	starting materials	MW found
15	514	5-Chloro-2-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 5-Chloro-2-methoxy-benzenesulfonyl chloride (commercially available)	512.0 $(M-H)^-$
16	533.5	N-{4-[5-(2-Methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-4-trifluoromethoxy-benzenesulfonamide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 4-Trifluoromethoxy-benzenesulfonyl chloride (commercially available)	532.0 $(M-H)^-$
17	494.6	N-{4-[5-(2-Methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-3-nitro-benzenesulfonamide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 3-Nitro-benzenesulfonyl chloride (commercially available)	493.1 $(M-H)^-$
18	552	2-Chloro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-5-trifluoromethyl-benzenesulfonamide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 2-Chloro-5-trifluoromethyl-benzenesulfonyl chloride (commercially available)	549.9 $(M-H)^-$
19	484	4-Chloro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 4-Chloro-benzenesulfonyl chloride (commercially available)	482.2 $(M-H)^-$
20	494.6	N-{4-[5-(2-Methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-4-nitro-benzenesulfonamide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 4-Nitro-benzenesulfonyl chloride (commercially available)	493.1 $(M-H)^-$

Ex	MW	name	starting materials	MW found
21	442.6	Pyrrolidine-1-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and Pyrrolidine-1-sulfonyl chloride (commercially available)	441.2 $(M-H)^-$
22	416.5	Dimethylamine-1-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide	[2-(4-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and Dimethylamine-1-sulfonyl chloride (commercially available)	415.2 $(M-H)^-$
23	455.6	Thiophene-2-sulfonic acid {3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide	[2-(3-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and Thiophene-2-sulfonyl chloride (commercially available)	454.2 $(M-H)^-$
24	490	5-Chloro-thiophene-2-sulfonic acid {3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide	[2-(3-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 5-Chloro-thiophene-2-sulfonyl chloride (commercially available)	488.0 $(M-H)^-$
25	467.5	3-Fluoro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(3-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 3-Fluoro-benzenesulfonyl chloride (commercially available)	466.1 $(M-H)^-$
26	467.5	4-Fluoro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(3-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 4-Fluoro-benzenesulfonyl chloride (commercially available)	466.1 $(M-H)^-$

Ex	MW	name	starting materials	MW found
27	463.6	2-Methyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(3-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 2-Methyl-benzenesulfonyl chloride (commercially available)	462.2 $(M-H)^-$
28	477.6	2,5-Dimethyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(3-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 2,5-Dimethyl-benzenesulfonyl chloride (commercially available)	476.1 $(M-H)^-$
29	481.6	5-Fluoro-2-methyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(3-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 5-Fluoro-2-methyl-benzenesulfonyl chloride (commercially available)	480.2 $(M-H)^-$
30	479.6	3-Methoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(3-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 3-Methoxy-benzenesulfonyl chloride (commercially available)	478.1 $(M-H)^-$
31	479.6	4-Methoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(3-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 3-Methoxy-benzenesulfonyl chloride (commercially available)	478.1 $(M-H)^-$
32	493.6	2-Methoxy-5-methyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(3-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 2-Methoxy-5-methyl-benzenesulfonyl chloride (commercially available)	492.1 $(M-H)^-$

Ex	MW	name	starting materials	MW found
33	552	2-Chloro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-4-trifluoromethyl-benzenesulfonamide	[2-(3-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 2-Chloro-4-trifluoromethyl-benzenesulfonyl chloride (commercially available)	549.9 $(M-H)^-$
34	484	4-Chloro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide	[2-(3-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 4-Chloro-benzenesulfonyl chloride (commercially available)	482.1 $(M-H)^-$
35	494.6	N-{3-[5-(2-Methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-3-nitro-benzenesulfonamide	[2-(3-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and 3-Nitro-benzenesulfonyl chloride (commercially available)	493.0 $(M-H)^-$
36	416.5	Dimethylamine-1-sulfonic acid {3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide	[2-(3-Amino-phenylamino)-thiazol-4-yl]-o-tolyl-methanone and Dimethylamine-1-sulfonyl chloride (commercially available)	415.1 $(M-H)^-$
37	495.6	5-Fluoro-2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 5-Fluoro-2-methyl-benzenesulfonyl chloride (commercially available)	494.1 $(M-H)^-$

Ex	MW	name	starting materials	MW found
38	499.6	2,4-Difluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 2,4-Difluoro-benzenesulfonyl chloride (commercially available)	498.0 $(M-H)^-$
39	504.1	5-Chloro-thiophene-2-sulfonic acid 4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 5-Chloro-thiophene-2-sulfonyl chloride (commercially available)	502.0 $(M-H)^-$
40	528.1	5-Chloro-2-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 5-Chloro-2-methoxy-benzenesulfonyl chloride (commercially available)	526.0 $(M-H)^-$
41	566	2-Chloro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-4-trifluoromethyl-benzenesulfonamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 2-Chloro-4-trifluoromethyl-benzenesulfonyl chloride (commercially available)	564.1 $(M-H)^-$

Ex	MW	name	starting materials	MW found
42	469.6	Thiophene-3-sulfonic acid 4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and Thiophene-3-sulfonyl chloride (commercially available)	468.0 $(M-H)^-$
43	481.6	4-Fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 4-Fluoro-benzenesulfonyl chloride (commercially available)	480.2 $(M-H)^-$
44	481.6	2-Fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 2-Fluoro-benzenesulfonyl chloride (commercially available)	480.2 $(M-H)^-$
45	481.6	3-Fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 3-Fluoro-benzenesulfonyl chloride (commercially available)	480.2 $(M-H)^-$
46	566	2-Chloro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-5-trifluoromethyl-benzenesulfonamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 2-Chloro-5-trifluoromethyl-benzenesulfonyl chloride (commercially available)	564.2 $(M-H)^-$

Ex	MW	name	starting materials	MW found
47	508.6	N-{4-[5-(2-Methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-3-nitro-benzenesulfonamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 3-Nitro-benzenesulfonyl chloride (commercially available)	507.2 $(M-H)^-$
48	498	4-Chloro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 4-Chloro-benzenesulfonyl chloride (commercially available)	496.0 $(M-H)^-$
49	508.6	N-{4-[5-(2-Methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-4-nitro-benzenesulfonamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 4-Nitro-benzenesulfonyl chloride (commercially available)	507.2 $(M-H)^-$
50	430.6	Dimethylamine-1-sulfonic acid 4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and Dimethylamine-1-sulfonyl chloride (commercially available)	429.3 $(M-H)^-$
51	477.6	2-Methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 2-Methyl-benzenesulfonyl chloride (commercially available)	476.1 $(M-H)^-$

Ex	MW	name	starting materials	MW found
52	491.6	2,5-Dimethyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 2,5-Dimethyl-benzenesulfonyl chloride (commercially available)	490.2 $(M-H)^-$
53	493.6	4-Methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 4-Methoxy-benzenesulfonyl chloride (commercially available)	492.1 $(M-H)^-$
54	493.6	3-Methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(4-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 3-Methoxy-benzenesulfonyl chloride (commercially available)	492.1 $(M-H)^-$
55	495.6	5-Fluoro-2-methyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 5-Fluoro-2-Methyl-benzenesulfonyl chloride (commercially available)	494.1 $(M-H)^-$

Ex	MW	name	starting materials	MW found
56	499.6	2,4-Difluoro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 2,4-Difluoro-benzenesulfonyl chloride (commercially available)	498.0 $(M-H)^-$
57	504.1	5-Chloro-thiophene-2-sulfonic acid 3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 5-Chloro-thiophene-2-sulfonyl chloride (commercially available)	502.0 $(M-H)^-$
58	528.1	5-Chloro-2-methoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 5-Chloro-2-methoxy-benzenesulfonyl chloride (commercially available)	526.0 $(M-H)^-$
59	566	2-Chloro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-4-trifluoromethyl-benzenesulfonamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 2-Chloro-4-trifluoromethyl-benzenesulfonyl chloride (commercially available)	564.2 $(M-H)^-$

Ex	MW	name	starting materials	MW found
60	523.6	2,5-Dimethoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 2,5-Dimethoxy-benzenesulfonyl chloride (commercially available)	522.1 $(M-H)^-$
61	493.6	3-Methoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 3-Methoxy-benzenesulfonyl chloride (commercially available)	492.1 $(M-H)^-$
62	566	2-Chloro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-5-trifluoromethyl-benzenesulfonamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 2-Chloro-5-trifluoromethyl-benzenesulfonyl chloride (commercially available)	564.1 $(M-H)^-$
63	508.6	N-{3-[5-(2-Methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-3-nitro-benzenesulfonamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 3-Nitro-benzenesulfonyl chloride (commercially available)	507.2 $(M-H)^-$
64	498	4-Chloro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 4-Chloro-benzenesulfonyl chloride (commercially available)	496.1 $(M-H)^-$

Ex	MW	name	starting materials	MW found
65	508.6	N-{3-[5-(2-Methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-4-nitro-benzenesulfonamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 4-Nitro-benzenesulfonyl chloride (commercially available)	507.2 $(M-H)^-$
66	495.6	C-(4-Fluoro-phenyl)-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-methanesulfonamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and (4-Fluoro-phenyl)-methanesulfonyl chloride (commercially available)	494.1 $(M-H)^-$
67	493.6	4-Methoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 4-Methoxy-benzenesulfonyl chloride (commercially available)	492.1 $(M-H)^-$
68	491.6	2,5-Dimethyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 2,5-Dimethyl-benzenesulfonyl chloride (commercially available)	490.2 $(M-H)^-$
69	456.6	Pyrrolidine-1-sulfonic acid 3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and Pyrrolidin-1-sulfonyl chloride (commercially available)	455.3 $(M-H)^-$

Ex	MW	name	starting materials	MW found
70	469.6	Thiophene-2-sulfonic acid 3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and Thiophene-2-sulfonyl chloride (commercially available)	468.0 $(M-H)^-$
71	469.6	Thiophene-3-sulfonic acid 3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and Thiophene-3-sulfonyl chloride (commercially available)	468.0 $(M-H)^-$
72	477.6	2-Methyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 2-Methyl-benzenesulfonyl chloride (commercially available)	476.1 $(M-H)^-$
73	481.6	2-Fluoro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 2-Fluoro-benzenesulfonyl chloride (commercially available)	480.2 $(M-H)^-$
74	481.6	3-Fluoro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide	[2-(3-Aminomethyl-phenylamino)-thiazol-5-yl]-o-tolyl-methanone; hydrochloride and 3-Fluoro-benzenesulfonyl chloride (commercially available)	480.2 $(M-H)^-$

Example A

A compound of formula I can be used in a manner known per se as the active ingredient for the production of tablets of the following composition:

	Per tablet
Active ingredient	200 mg
Microcrystalline cellulose	155 mg
Corn starch	25 mg
Talc	25 mg
Hydroxypropylmethylcellulose	20 mg
	425 mg

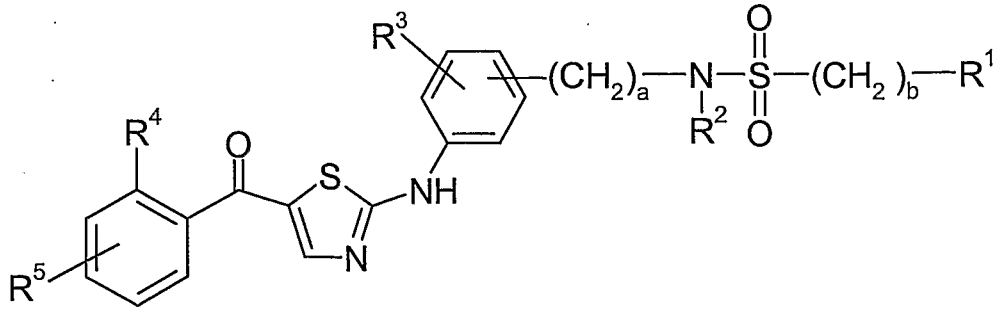
Example B

A compound of formula I can be used in a manner known per se as the active ingredient for the production of capsules of the following composition:

	Per capsule
Active ingredient	100.0 mg
Corn starch	20.0 mg
Lactose	95.0 mg
Talc	4.5 mg
Magnesium stearate	0.5 mg
	220.0 mg

CLAIMS

1. Compounds of formula I



(I)

wherein

R^1 is amino, aryl or heteroaryl;

R^2 is hydrogen or alkyl;

R^3 is hydrogen, alkyl or halogen;

R^4 is alkyl or halogen;

R^5 is hydrogen, alkyl or halogen;

a is zero or 1;

b is zero, 1 or 2;

and pharmaceutically acceptable salts and esters thereof.

2. Compounds according to claim 1, wherein R^2 is hydrogen.

3. Compounds according to claim 1 or 2, wherein R^3 is hydrogen.

4. Compounds according to any one of claims 1 to 3, wherein R^4 is alkyl.

5. Compounds according to claim 4, wherein R^4 is methyl.

6. Compounds according to any one of claims 1 to 5, wherein R^5 is hydrogen.

7. Compounds according to any one of claims 1 to 6, wherein b is zero.

8. Compounds according to any one of claims 1 to 7, wherein a is zero.

9. Compounds according to any one of claims 1 to 7, wherein a is 1.

10. Compounds according to any one of claims 1 to 9, wherein R^1 is monoalkylamino, dialkylamino, phenyl, thiophenyl or pyrrolidinyl, wherein phenyl, thiophenyl and pyrrolidinyl are optionally substituted with one to three substituents independently selected from alkyl, halogen, alkoxy, trifluoromethoxy, nitro and trifluoromethyl.

11. Compounds according to claim 10, wherein R^1 is thiophene-3-yl, 3-fluorophenyl, 4-fluorophenyl, 2-methylphenyl, 2-methoxy-5-methylphenyl, dimethylamino, thiophene-2-yl, 5-fluoro-2-methylphenyl, 2,4-difluorophenyl, 5-chloro-2-methoxyphenyl, 2-fluorophenyl, 3-fluorophenyl, 2-chloro-5-trifluoromethylphenyl, 3-nitrophenyl, 4-nitrophenyl or 4-methoxyphenyl.

12. Compounds according to any one of claims 1 to 11 selected from

thiophene-2-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

thiophene-3-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

5-chloro-thiophene-2-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

2-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

3-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

4-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

2,4-difluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

2,5-dimethyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

5-fluoro-2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

3-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

4-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

2-methoxy-5-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

2,5-dimethoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

5-chloro-2-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-4-trifluoromethoxy-benzenesulfonamide;

N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-3-nitro-benzenesulfonamide;

2-chloro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-5-trifluoromethyl-benzenesulfonamide;

4-chloro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-4-nitro-benzenesulfonamide;

pyrrolidine-1-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

dimethylamine-1-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

thiophene-2-sulfonic acid {3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

5-chloro-thiophene-2-sulfonic acid {3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

3-fluoro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

4-fluoro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

2-methyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

2,5-dimethyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

5-fluoro-2-methyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

3-methoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

4-methoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

2-methoxy-5-methyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

2-chloro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-4-trifluoromethyl-benzenesulfonamide;

4-chloro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-3-nitro-benzenesulfonamide;

dimethylamine-1-sulfonic acid {3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

5-fluoro-2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

2,4-difluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

5-chloro-thiophene-2-sulfonic acid 4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide;

5-chloro-2-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

2-chloro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-4-trifluoromethyl-benzenesulfonamide;

thiophene-3-sulfonic acid 4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide;

4-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

2-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

3-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

2-chloro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-5-trifluoromethyl-benzenesulfonamide;

N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-3-nitro-benzenesulfonamide;

4-chloro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-4-nitro-benzenesulfonamide;

dimethylamine-1-sulfonic acid 4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide;

2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

2,5-dimethyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

4-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

3-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

5-fluoro-2-methyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

2,4-difluoro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

5-chloro-thiophene-2-sulfonic acid 3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide;

5-chloro-2-methoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

2-chloro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-4-trifluoromethyl-benzenesulfonamide;

2,5-dimethoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

3-methoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

2-chloro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-5-trifluoromethyl-benzenesulfonamide;

N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-3-nitro-benzenesulfonamide;

4-chloro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-4-nitro-benzenesulfonamide;

C-(4-fluoro-phenyl)-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-methanesulfonamide;

4-methoxy-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

2,5-dimethyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

pyrrolidine-1-sulfonic acid 3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide;

thiophene-2-sulfonic acid 3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide;

thiophene-3-sulfonic acid 3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide;

2-methyl-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

2-fluoro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide; and

3-fluoro-N-{3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide.

13. Compounds according to any one of claims 1 to 12 selected from

thiophene-3-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

3-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

4-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

2-methoxy-5-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-benzenesulfonamide;

dimethylamine-1-sulfonic acid {4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

thiophene-2-sulfonic acid {3-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-phenyl}-amide;

5-fluoro-2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

2,4-difluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

5-chloro-2-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

2-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

3-fluoro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide;

2-chloro-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-5-trifluoromethyl-benzenesulfonamide;

N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-3-nitro-benzenesulfonamide;

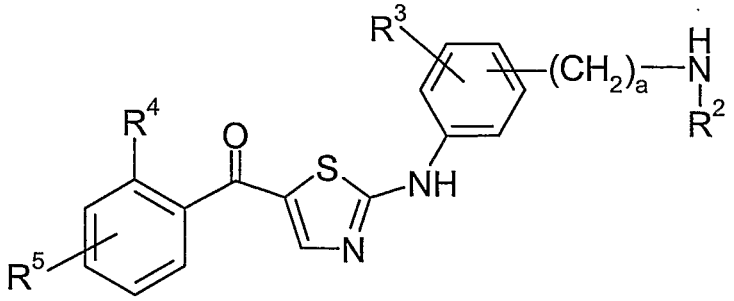
N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-4-nitro-benzenesulfonamide;

dimethylamine-1-sulfonic acid 4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzylamide;

2-methyl-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide; and

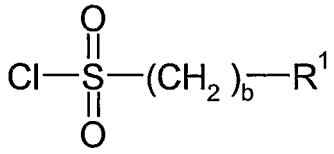
4-methoxy-N-{4-[5-(2-methyl-benzoyl)-thiazol-2-ylamino]-benzyl}-benzenesulfonamide.

14. A process for the preparation of a compound according to any one of claims 1 to 13 comprising the reaction of a compound according to formula



(III)

in the presence of a compound according to formula



(IV)

in order to obtain a compound of formula I, wherein R^1 to R^5, a and b are defined as in claim 1.

15. Compounds according to any one of claims 1 to 13 for use as therapeutically active substance.

16. Compounds according to any one of claims 1 to 13 for the preparation of medicaments for the prophylaxis and therapy of illnesses which are caused by disorders associated with the NPY receptor.

17. A pharmaceutical composition comprising a compound in accordance with any one of claims 1 to 13 and a therapeutically inert carrier.

18. The use of a compound according to any one of claims 1 to 13 for the preparation of medicaments for the treatment and prophylaxis of arthritis, diabetes, eating disorders and obesity.

19. A compound according to any one of claims 1 to 13, when manufactured according to a process of claim 14.

20. A method for the treatment and prophylaxis of arthritis, diabetes, eating disorders and obesity, which method comprises administering an effective amount of a compound as defined in any one of claims 1 to 13.

21. A method of treatment of obesity in a human in need of such treatment which comprises administration to the human a therapeutically effective amount of a compound as defined in any one of the claims 1 to 13 and a therapeutically effective amount of a lipase inhibitor.

22. The method according to claim 21, wherein the lipase inhibitor is orlistat.

23. The method according to claim 21 or 22 for simultaneous, separate or sequential administration.

24. The use of a compound according to any one of claims 1 to 13 in the manufacture of a medicament for the treatment and prevention of obesity in a patient who is also receiving treatment with a lipase inhibitor.

25. The use according to claim 24, wherein the lipase inhibitor is orlistat.

26. The pharmaceutical composition of claim 17 further comprising a therapeutically effective amount of a lipase inhibitor.

27. The pharmaceutical composition according to claim 26, wherein the lipase inhibitor is orlistat.

28. The invention as hereinbefore described.

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