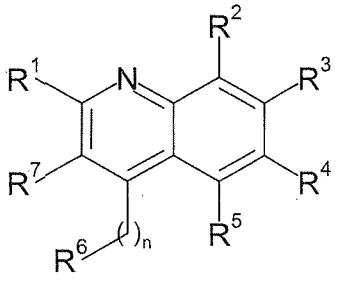
pharmaceutical compositions, medicaments containing the said compounds, their pharmaceutically acceptable salts or esters, the use of the said compounds, salts or esters for the treatment or prophylaxis of illnesses, especially in the treatment or prophylaxis of lipodystrophy, such as genetic and iatrogenic lipodystrophy, cancer, eye diseases supported by endothelial proliferation and angiogenesis, such as macular degeneration and retinopathy, lung diseases, such as asthma, bronchopulmonary dysplasia and chronic obstructive pulmonary disease, sarcoidosis, chronic renal diseases, such as vasculitis, focal segmental glomerulosclerosis, diabetic nephropathy, lupus nephritis, polycystic kidney disease and drug or toxin-induced chronic tubulointerstitial nephritis, preeclampsia and polycystic ovary syndrome, and the use of the said compounds, salts or esters for the production of medicaments for the treatment or prophylaxis of lipodystrophy, such as genetic and iatrogenic lipodystrophy, cancer, eye diseases supported by endothelial proliferation and angiogenesis, such as macular degeneration and retinopathy, lung diseases, such as asthma, bronchopulmonary dysplasia and chronic obstructive pulmonary disease, sarcoidosis, chronic renal diseases, such as vasculitis, focal segmental glomerulosclerosis, diabetic nephropathy, lupus nephritis, polycystic kidney disease and drug or toxin-induced chronic tubulointerstitial nephritis, preeclampsia and polycystic ovary syndrome

Compounds of the present invention are FABP 4 and/or 5 inhibitors, more particularly dual FABP 4 and 5 inhibitors. In particular, they are also selective FABP 4 and/or 5 inhibitors compared to FABP3 and/or 1.

In a first aspect, there is provided compounds of formula (I)



(I)

wherein

R^1 is alkyl, haloalkyl, cycloalkyl, ~~halocycloalkyl, alkoxy,~~ haloalkoxy, cycloalkoxy, ~~halocycloalkoxy,~~ hydroxyalkyl, heterocycloalkyl, substituted heterocycloalkyl, substituted amino~~, aminocarbonyl~~ or substituted aminocarbonyl, wherein substituted heterocycloalkyl is substituted with one to three substituents independently selected from oxo, halogen~~,~~ or alkyl, ~~cycloalkyl and haloalkyl,~~ and wherein substituted amino and substituted aminocarbonyl are

substituted on the nitrogen atom with one to two substituents independently selected from alkyl, ~~cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl,~~ hydroxyalkyl and alkoxyalkyl, with the proviso that R^1 is not methyl or ethyl;

R^2 is hydrogen, halogen, alkyl, haloalkyl, ~~cycloalkyl, halocycloalkyl,~~ alkoxy, ~~haloalkoxy, cycloalkoxy, halocycloalkoxy, nitro, cyano, amino, aminoalkyl,~~ or substituted amino ~~or substitued aminoalkyl~~, wherein substituted amino is ~~and substitued aminoalkyl are~~ substituted on the nitrogen atom with one to two ~~substituents independently selected from~~ alkyl, ~~cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl~~;

R^3 is hydrogen, ~~halogen, alkyl, haloalkyl, cycloalkyl, halocycloalkyl,~~ alkoxy or halogen, ~~haloalkoxy, cycloalkoxy, halocycloalkoxy, nitro, cyano, amino, aminoalkyl, substituted amino or substitued aminoalkyl, wherein substituted amino and substitued aminoalkyl are substituted on the nitrogen atom with one to two substituents independently selected from alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl~~;

R^4 is hydrogen, halogen, alkyl, ~~haloalkyl, cycloalkyl, halocycloalkyl, alkoxy, haloalkoxy, cycloalkoxy, halocycloalkoxy,~~ nitro, or cyano, ~~amino, aminoalkyl, substituted amino or substitued aminoalkyl, wherein substituted amino and substitued aminoalkyl are substituted on the nitrogen atom with one to two substituents independently selected from alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl~~;

R^5 is hydrogen, ~~halogen, alkyl, haloalkyl, cycloalkyl, halocycloalkyl, alkoxy, haloalkoxy, cycloalkoxy, halocycloalkoxy, nitro, cyano, amino, aminoalkyl, substituted amino or substitued aminoalkyl, wherein substituted amino and substitued aminoalkyl are substituted on the nitrogen atom with one to two substituents independently selected from alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl~~;

R^6 is phenyl, substituted phenyl, pyridinyl or substituted pyridinyl, wherein substituted phenyl and substituted pyridinyl are substituted with one to three substituent independently selected from alkyl, cycloalkyl, alkylcycloalkyl, cycloalkylalkyl, cycloalkylalkoxy, cycloalkylalkoxyalkyl, cycloalkoxy, cycloalkoxyalkyl, alkylcycloalkylalkyl, halocycloalkyl, halocycloalkylalkyl, halogen, cyano, haloalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, haloalkoxy, hydroxyalkoxy, alkoxyalkoxy, alkoxyalkoxyalkyl, hydroxyhaloalkyl, amino and

substituted amino, wherein substituted amino is substituted with one to two substituents independently selected from alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl;

R^7 is -COOH, tetrazol-5-yl, 3H-[1,3,4]oxadiazol-2-on-5-yl, or 3H-[1,3,4]oxadiazole-2-thion-5-yl, ~~4H-[1,2,4]oxadiazol-5-on-3-yl, 4H-[1,2,4]oxadiazole-5-thion-3-yl, 3H-[1,2,3,5]oxathiadiazole-2-oxide-4-yl, 4H-[1,2,4]thiadiazol-5-on-3-yl, isoxazol-3-ol-5-yl, 5-alkylisoxazol-3-ol-4-yl, 5-cycloalkylisoxazol-3-ol-4-yl, furazan-3-ol-4-yl, 5-alkylsulfonylamino-[1,3,4]oxadiazol-2-yl, 5-cycloalkylsulfonylamino-[1,3,4]oxadiazol-2-yl, 5-alkylsulfonylamino-2H-[1,2,4]triazol-3-yl, 5-cycloalkylsulfonylamino-2H-[1,2,4]triazol-3-yl, 5-alkylisothiazol-3-ol-4-yl, 5-cycloalkylisothiazol-3-ol-4-yl, [1,2,5]thiadiazol-3-ol-4-yl, 1,4-dihydro-tetrazol-5-on-1-yl, 2H-tetrazol-5-ylcarbamoyl, 2H-tetrazole-5-carbonyl, [1,2,4]oxadiazolidine-3,5-dion-2-y, 4H-[1,2,4]oxadiazol-5-on-3-yl, 2,4-dihydro-[1,2,4]triazol-3-on-5-sulfanyl, 4H-[1,2,4]triazole-3-sulfanyl, 4H-[1,2,4]triazole-3-sulfinyl, 4H-[1,2,4]triazole-3-sulfonyl, 4-alkyl-pyrazol-1-ol-5-yl, 4-cycloalkyl-pyrazol-1-ol-5-yl, 4-alkyl-[1,2,3]triazol-1-ol-5-yl, 4-cycloalkyl-[1,2,3]triazol-1-ol-5-yl, 5-alkyl-imidazol-1-ol-2-yl, 5-cycloalkyl-imidazol-1-ol-2-yl, 4-alkyl-imidazol-1-ol-5-yl, 4-cycloalkyl-imidazol-1-ol-5-yl, 4-alkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, 4,4-dialkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, 4-cycloalkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, 4,4-dicycloalkyl-1,1-dioxo-1$\lambda^6$1,2,5]thiadiazolidin-3-on-5-yl, thiazolidine-2,4-dion-5-yl, oxazolidine-2,4-dion-5-yl, 3-[1-Hydroxy-meth-(E)-ylidene]-pyrrolidine-2,4-dion-1-yl, 3-[1-Hydroxy-meth-(Z)-ylidene]-pyrrolidine-2,4-dion-1-yl, 5-methyl-4-hydroxy-5H-furan-2-on-3-yl, 5,5-dialkyl-4-hydroxy-5H-furan-2-on-3-yl, 5-cycloalkyl-4-hydroxy-5H-furan-2-on-3-yl, 5,5-dicycloalkyl-4-hydroxy-5H-furan-2-on-3-yl, 3-hydroxy-cyclobut-3-ene-1,2-dion-4-yl or 3-hydroxy-cyclobut-3-ene-1,2-dion-4-amino~~;

n is zero or 1;

with the proviso that at least one of R^2, R^3, R^4 and R^5 is different from hydrogen and that 6-methoxy-4-phenyl-2-trifluoromethyl-quinoline-3-carboxylic acid
and 4-(3,4-dimethoxy-phenyl)-2-hydroxymethyl-6,7-dimethoxy-quinoline-3-carboxylic acid are excluded;

or pharmaceutically acceptable salts or esters.

In a second aspect, there is provided a process to prepare a compound as defined above comprising the reaction of

In a fifth aspect, there is provided a compound as defined above for the treatment or prophylaxis of type 2 diabetes, atherosclerosis, cancer, chronic renal disease and non-alcoholic steatohepatitis.

In a sixth aspect, there is provided use of a compound as defined above for the preparation of a medicament for the treatment or prophylaxis of type 2 diabetes, atherosclerosis, cancer, chronic renal disease and non-alcoholic steatohepatitis.

~~In a seventh aspect, there is provided a compound as defined above, when manufactured according to a process as defined above.~~

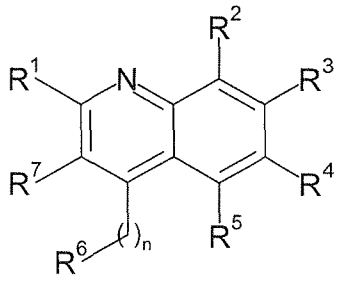
The term "alkoxy" denotes a group of the formula -O-R', wherein R' is an alkyl group. Examples of alkoxy group include methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy and tert-butoxy. Particular alkoxy group include methoxy , ethoxy and isopropoxy. More particular alkoxy group is isopropoxy.

The term "alkoxyalkoxy" denotes an alkoxy group wherein at least one of the hydrogen atoms of the alkoxy group has been replaced by another alkoxy group. Examples of alkoxyalkoxy group include methoxymethoxy, ethoxymethoxy, methoxyethoxy, ethoxyethoxy, methoxypropoxy and ethoxypropoxy. Particular alkoxyalkoxy groups include methoxymethoxy and methoxyethoxy.

The term "alkoxyalkoxyalkyl" denotes an alkyl group wherein at least one of the hydrogen atoms of the alkyl group has been replaced by an alkoxyalkoxy group. Examples

CLAIMS

1. Compounds of formula (I)



(I)

wherein

R^1 is alkyl, haloalkyl, cycloalkyl, ~~halocycloalkyl, alkoxy,~~ haloalkoxy, cycloalkoxy, ~~halocycloalkoxy,~~ hydroxyalkyl, heterocycloalkyl, substituted heterocycloalkyl, substituted amino~~, aminocarbonyl~~ or substituted aminocarbonyl, wherein substituted heterocycloalkyl is substituted with one to three substituents independently selected from oxo, halogen~~,~~ or alkyl, ~~cycloalkyl and haloalkyl,~~ and wherein substituted amino and substituted aminocarbonyl are substituted on the nitrogen atom with one to two substituents independently selected from alkyl, ~~cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl,~~ hydroxyalkyl and alkoxyalkyl, with the proviso that R^1 is not methyl or ethyl;

R^2 is hydrogen, halogen, alkyl, haloalkyl, ~~cycloalkyl, halocycloalkyl,~~ alkoxy~~,~~ ~~haloalkoxy, cycloalkoxy, halocycloalkoxy, nitro, cyano, amino, aminoalkyl,~~or substituted amino ~~or substitued aminoalkyl~~, wherein substituted amino ~~and substitued aminoalkyl are~~is substituted on the nitrogen atom with one to two ~~substituents independently selected from~~ alkyl, ~~cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl~~;

R^3 is hydrogen, ~~halogen, alkyl, haloalkyl, cycloalkyl, halocycloalkyl,~~ alkoxy~~,~~ ~~haloalkoxy, cycloalkoxy, halocycloalkoxy, nitro, cyano, amino, aminoalkyl, substituted amino or substitued aminoalkyl, wherein substituted amino and substitued aminoalkyl are substituted on the nitrogen atom with one to two substituents independently selected from alkyl, cycloalkyl, haloalkyl,~~

~~alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl~~or halogen;

R^4 is hydrogen, halogen, alkyl, ~~haloalkyl, cycloalkyl, halocycloalkyl, alkoxy, haloalkoxy, cycloalkoxy, halocycloalkoxy,~~ nitro~~,~~ or cyano~~, amino, aminoalkyl, substituted amino or substitued aminoalkyl, wherein substituted amino and substitued aminoalkyl are substituted on the nitrogen atom with one to two substituents independently selected from alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl~~;

R^5 is hydrogen~~, halogen, alkyl, haloalkyl, cycloalkyl, halocycloalkyl, alkoxy, haloalkoxy, cycloalkoxy, halocycloalkoxy, nitro, cyano, amino, aminoalkyl, substituted amino or substitued aminoalkyl, wherein substituted amino and substitued aminoalkyl are substituted on the nitrogen atom with one to two substituents independently selected from alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl~~;

R^6 is phenyl, substituted phenyl, pyridinyl or substituted pyridinyl, wherein substituted phenyl and substituted pyridinyl are substituted with one to three substituent independently selected from alkyl, cycloalkyl, alkylcycloalkyl, cycloalkylalkyl, cycloalkylalkoxy, cycloalkylalkoxyalkyl, cycloalkoxy, cycloalkoxyalkyl, alkylcycloalkylalkyl, halocycloalkyl, halocycloalkylalkyl, halogen, cyano, haloalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, haloalkoxy, hydroxyalkoxy, alkoxyalkoxy, alkoxyalkoxyalkyl, hydroxyhaloalkyl, amino and substituted amino, wherein substituted amino is substituted with one to two substituents independently selected from alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl;

R^7 is -COOH, tetrazol-5-yl, 3H-[1,3,4]oxadiazol-2-on-5-yl, or 3H-[1,3,4]oxadiazole-2-thion-5-yl~~, 4H-[1,2,4]oxadiazol-5-on-3-yl, 4H-[1,2,4]oxadiazole-5-thion-3-yl, 3H-[1,2,3,5]oxathiadiazole-2-oxide-4-yl, 4H-[1,2,4]thiadiazol-5-on-3-yl, isoxazol-3-ol-5-yl, 5-alkylisoxazol-3-ol-4-yl, 5-cycloalkylisoxazol-3-ol-4-yl, furazan-3-ol-4-yl, 5-alkylsulfonylamino-[1,3,4]oxadiazol-2-yl, 5-~~

~~cycloalkylsulfonylamino-[1,3,4]oxadiazol-2-yl, 5-alkylsulfonylamino-2H-[1,2,4]triazol-3-yl, 5-cycloalkylsulfonylamino-2H-[1,2,4]triazol-3-yl, 5-alkylisothiazol-3-ol-4-yl, 5-cycloalkylisothiazol-3-ol-4-yl, [1,2,5]thiadiazol-3-ol-4-yl, 1,4-dihydro-tetrazol-5-on-1-yl, 2H-tetrazol-5-ylcarbamoyl, 2H-tetrazole-5-carbonyl, [1,2,4]oxadiazolidine-3,5-dion-2-y, 4H-[1,2,4]oxadiazol-5-on-3-yl, 2,4-dihydro-[1,2,4]triazol-3-on-5-sulfanyl, 4H-[1,2,4]triazole-3-sulfanyl, 4H-[1,2,4]triazole-3-sulfinyl, 4H-[1,2,4]triazole-3-sulfonyl, 4-alkyl-pyrazol-1-ol-5-yl, 4-cycloalkyl-pyrazol-1-ol-5-yl, 4-alkyl-[1,2,3]triazol-1-ol-5-yl, 4-cycloalkyl-[1,2,3]triazol-1-ol-5-yl, 5-alkyl-imidazol-1-ol-2-yl, 5-cycloalkyl-imidazol-1-ol-2-yl, 4-alkyl-imidazol-1-ol-5-yl, 4-cycloalkyl-imidazol-1-ol-5-yl, 4-alkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, 4,4-dialkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, 4-cycloalkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, 4,4-dicycloalkyl-1,1-dioxo-1$\lambda^6$1,2,5]thiadiazolidin-3-on-5-yl, thiazolidine-2,4-dion-5-yl, oxazolidine-2,4-dion-5-yl, 3-[1-Hydroxy-meth-(E)-ylidene]-pyrrolidine-2,4-dion-1-yl, 3-[1-Hydroxy-meth-(Z)-ylidene]-pyrrolidine-2,4-dion-1-yl, 5-methyl-4-hydroxy-5H-furan-2-on-3-yl, 5,5-dialkyl-4-hydroxy-5H-furan-2-on-3-yl, 5-cycloalkyl-4-hydroxy-5H-furan-2-on-3-yl, 5,5-dicycloalkyl-4-hydroxy-5H-furan-2-on-3-yl, 3-hydroxy-cyclobut-3-ene-1,2-dion-4-yl or 3-hydroxy-cyclobut-3-ene-1,2-dion-4-amine~~;

n is zero or 1;

with the proviso that at least one of R^2, R^3, R^4 and R^5 is different from hydrogen and that 6-methoxy-4-phenyl-2-trifluoromethyl-quinoline-3-carboxylic acid and 4-(3,4-dimethoxy-phenyl)-2-hydroxymethyl-6,7-dimethoxy-quinoline-3-carboxylic acid are excluded;

or pharmaceutically acceptable salts or esters.

~~2. A compound according to claim 1, wherein R^1 is alkyl, haloalkyl, cycloalkyl, alkoxy, haloalkoxy, cycloalkoxy, hydroxyalkyl, heterocycloalkyl, substituted heterocycloalkyl, substituted amino or substituted aminocarbonyl, wherein substituted heterocycloalkyl is substituted with one to three substituents independently selected from oxo, halogen or alkyl, and wherein substituted amino and substituted aminocarbonyl are substituted on the nitrogen atom with one to two~~

~~substituents independently selected from alkyl, hydroxyalkyl and alkoxyalkyl, with the proviso that R^1 is not methyl or ethyl.~~

32. A compound according to claim 1 ~~or 2~~, wherein R^1 is ~~alkoxy,~~ heterocycloalkyl, substituted heterocycloalkyl or substituted amino, wherein substituted heterocycloalkyl is substituted with one alkyl, and wherein substituted amino is substituted on the nitrogen atom with two alkyl.

43. A compound according to any one of claims 1 to ~~3~~2, wherein R^1 is piperidinyl or methylpyrrolidinyl.

54. A compound according to any one of claims 1 to 43, wherein R^1 is substituted amino, wherein substituted amino is substituted on the nitrogen atom with one to two alkyl.

~~6. A compound according to any one of claims 1 to 5, wherein R^2 is hydrogen, halogen, alkyl, haloalkyl, alkoxy or substituted amino, wherein substituted amino is substituted on the nitrogen atom with one to two alkyl.~~

75. A compound according to any one of claims 1 to ~~6~~4, wherein R^2 is hydrogen or halogen.

~~8. A compound according to any one of claims 1 to 7, wherein R^3 is hydrogen, alkoxy or halogen.~~

~~9. A compound according to any one of claims 1 to 8, wherein R^3 is hydrogen.~~

~~10. A compound according to any one of claims 1 to 9, wherein R^4 is hydrogen, halogen, alkyl, nitro or cyano.~~

~~11. A compound according to any one of claims 1 to 10, wherein R^4 is halogen.~~

~~12. A compound according to any one of claims 1 to 11, wherein R^5 is hydrogen.~~

~~13. A compound according to any one of claims 1 to 12, wherein R^6 is phenyl or phenyl substituted with one to three substituent independently selected from alkyl, halogen, haloalkyl, alkoxy or haloalkoxy.~~

~~14. A compound according to any one of claims 1 to 13, wherein R^6 is pyridinyl or pyridinyl substituted with one to three substituent independently selected from alkyl, halogen, haloalkyl, alkoxy or haloalkoxy.~~

~~15. A compound according to any one of claims 1 to 14, wherein R^7 is -COOH, tetrazol-5-yl, 3H-[1,3,4]oxadiazol-2-on-5-yl, 3H-[1,3,4]oxadiazole-2-thion-5-yl, 4H-[1,2,4]oxadiazol-5-on-3-yl, 4H-[1,2,4]oxadiazole-5-thion-3-yl, 3H-[1,2,3,5]oxathiadiazole-2-oxide-4-yl or 4H-[1,2,4]thiadiazol-5-on-3-yl.~~

~~16. A compound according to any one of claims 1 to 15, wherein R^7 is -COOH, tetrazol-5-yl, 3H-[1,3,4]oxadiazol-2-on-5-yl or 3H-[1,3,4]oxadiazole-2-thion-5-yl.~~

~~17~~16. A compound according to any one of claims 1 to ~~16~~5, wherein R^7 is -COOH.

~~18~~17. A compound according to any one of claims 1 to ~~16~~5, wherein R^7 is tetrazol-5-yl.

~~19~~18. A compound according to any one of claims 1 to ~~18~~7, selected from

6-Chloro-2-cyclopropyl-4-phenyl-quinoline-3-carboxylic acid;

6-Chloro-2-isopropyl-4-phenyl-quinoline-3-carboxylic acid;

2-Ethoxy-6-nitro-4-phenyl-quinoline-3-carboxylic acid;

6-Chloro-2-ethoxy-4-phenyl-quinoline-3-carboxylic acid;

6-Chloro-4-phenyl-2-piperidin-1-yl-quinoline-3-carboxylic acid;

6-Chloro-4-(3-chloro-phenyl)-2-cyclopropyl-quinoline-3-carboxylic acid;

7-Chloro-4-(2-fluoro-phenyl)-2-isopropyl-quinoline-3-carboxylic acid;

7-Chloro-2-cyclopropyl-4-(2-fluoro-phenyl)-quinoline-3-carboxylic acid;

6-Chloro-2-methylcarbamoyl-4-phenyl-quinoline-3-carboxylic acid;

6-Chloro-4-(2-chloro-benzyl)-2-cyclopropyl-quinoline-3-carboxylic acid;

6-Chloro-4-phenyl-2-(2,2,2-trifluoro-ethoxy)-quinoline-3-carboxylic acid;

6-Chloro-4-(2-chloro-benzyl)-2-(2,2,2-trifluoro-1-methyl-ethoxy)-quinoline-3-carboxylic acid;

6-Chloro-4-(3-chloro-phenyl)-2-(2,2,2-trifluoro-1-methyl-ethoxy)-quinoline-3-carboxylic acid;

6-Chloro-4-(3-chloro-phenyl)-2-isopropoxy-quinoline-3-carboxylic acid;

[6-Chloro-4-(3-isopropyl-phenyl)-3-(1H-tetrazol-5-yl)-quinolin-2-yl]-diethyl-amine;

[6-Chloro-4-(3-isopropyl-phenyl)-3-(1H-tetrazol-5-yl)-quinolin-2-yl]-ethyl-methyl-amine;

and pharmaceutically acceptable salts thereof.

~~209~~. A compound according to any one of claims 1 to ~~187~~, selected from

6-Chloro-8-fluoro-4-phenyl-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)quinoline;

6-Chloro-2-(pentan-3-yl)-4-phenyl-3-(1H-tetrazol-5-yl)quinoline;

4-Phenyl-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6-(trifluoromethyl)quinoline;

Diethyl-[4-phenyl-3-(2H-tetrazol-5-yl)-6-trifluoromethyl-quinolin-2-yl]-amine;

6-Chloro-2-cyclobutyl-4-phenyl-3-(1H-tetrazol-5-yl)quinoline;

6-Chloro-2-cyclopentyl-7-fluoro-4-phenyl-3-(2H-tetrazol-5-yl)quinoline;

6-Chloro-7-fluoro-2-(pentan-3-yl)-4-phenyl-3-(2H-tetrazol-5-yl)quinoline;

6-Chloro-7-fluoro-4-phenyl-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)quinoline;

6-Chloro-N,N-diethyl-7-fluoro-4-phenyl-3-(2H-tetrazol-5-yl)quinolin-2-amine;

6-Chloro-4-(3-chlorophenyl)-2-(pentan-3-yl)-3-(1H-tetrazol-5-yl)quinoline;

6-Chloro-2-cyclohexyl-4-phenyl-3-(1H-tetrazol-5-yl)quinoline;

6-Chloro-4-(3-chlorophenyl)-2-cyclobutyl-3-(1H-tetrazol-5-yl)quinoline;

2-(Pentan-3-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)quinoline;

2-Cyclopentyl-4-phenyl-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)quinoline;

6-Chloro-2-cyclohexyl-7-fluoro-4-phenyl-3-(2H-tetrazol-5-yl)quinoline;

2-Cyclohexyl-4-phenyl-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)quinoline;

6-Chloro-4-(3-chlorophenyl)-2-isopropyl-3-(1H-tetrazol-5-yl)quinoline;

6-Chloro-4-(3-chlorophenyl)-2-cyclopropyl-3-(1H-tetrazol-5-yl)quinoline;

6-Chloro-2-(3,3-difluoropiperidin-1-yl)-7-fluoro-4-phenyl-3-(2H-tetrazol-5-yl)quinoline;

6-Chloro-2-(3,3-difluoroazetidin-1-yl)-7-fluoro-4-phenyl-3-(2H-tetrazol-5-yl)quinoline;

1-(6-Chloro-4-phenyl-3-(2H-tetrazol-5-yl)quinolin-2-yl)piperidin-2-one;

7-Methoxy-2-(pentan-3-yl)-4-phenyl-3-(1H-tetrazol-5-yl)quinoline;

2-Cyclopentyl-7-methoxy-4-phenyl-3-(1H-tetrazol-5-yl)quinoline;

7-Methoxy-4-phenyl-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)quinoline;

1-(6-Chloro-4-phenyl-3-(2H-tetrazol-5-yl)quinolin-2-yl)pyrrolidin-2-one;

2-Cyclopentyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)quinoline;

6-Chloro-2-cyclohexyl-4-(2-methyl-pyridin-4-yl)-3-(2H-tetrazol-5-yl)-quinoline;

6-Chloro-2-cyclopentyl-4-(2-methyl-pyridin-4-yl)-3-(2H-tetrazol-5-yl)-quinoline;

6-Chloro-4-(2-methylpyridin-4-yl)-2-(pentan-3-yl)-3-(2H-tetrazol-5-yl)quinoline;

and pharmaceutically acceptable salts thereof.

~~21~~10. A compound according to any one of claims 1 to ~~19~~8, selected from

6-Chloro-4-phenyl-2-piperidin-1-yl-quinoline-3-carboxylic acid;

6-Chloro-4-phenyl-2-piperidin-1-yl-3-(1H-tetrazol-5-yl)-quinoline;

6,8-Dichloro-2-(2-methyl-pyrrolidin-1-yl)-4-phenyl-quinoline-3-carboxylic acid;

6-Chloro-2-(2-methyl-pyrrolidin-1-yl)-4-phenyl-3-(1H-tetrazol-5-yl)-quinoline;

5-(6-Chloro-4-phenyl-2-piperidin-1-yl-quinolin-3-yl)-3H-[1,3,4]oxadiazole-2-thione;

6-Chloro-4-(2-chloro-benzyl)-2-diethylamino-quinoline-3-carboxylic acid;

6-Chloro-4-(3-chloro-phenyl)-2-diethylamino-quinoline-3-carboxylic acid;

6-Chloro-4-(3-chloro-phenyl)-2-isopropoxy-quinoline-3-carboxylic acid;

and pharmaceutically acceptable salts thereof.

~~22~~11. A compound according to any one of claims 1 to ~~18~~7 and ~~20~~9, selected from

6-Chloro-8-fluoro-4-phenyl-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)quinoline;

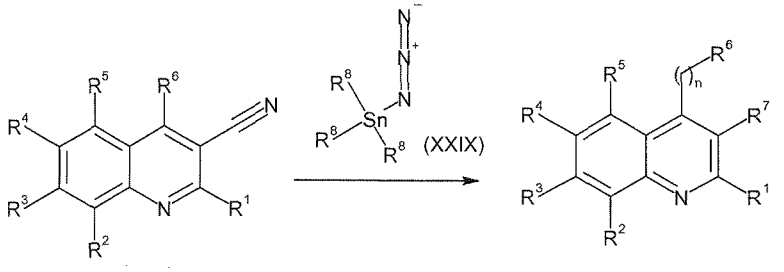
6-Chloro-2-cyclopentyl-7-fluoro-4-phenyl-3-(2H-tetrazol-5-yl)quinoline;

6-Chloro-4-(2-methylpyridin-4-yl)-2-(pentan-3-yl)-3-(2H-tetrazol-5-yl)quinoline;

and pharmaceutically acceptable salts thereof.

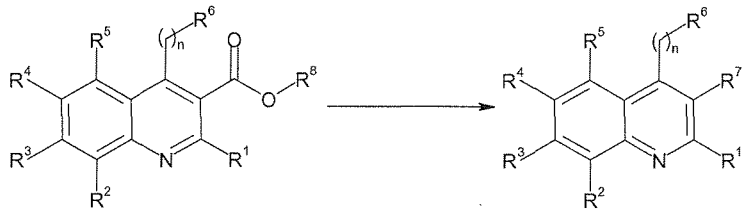
~~23~~12. A process to prepare a compound according to any one of claims 1 to ~~22~~11 comprising the reaction of

a) a compound of formula (XXIII) in the presence of a compound of formula (XXIX);



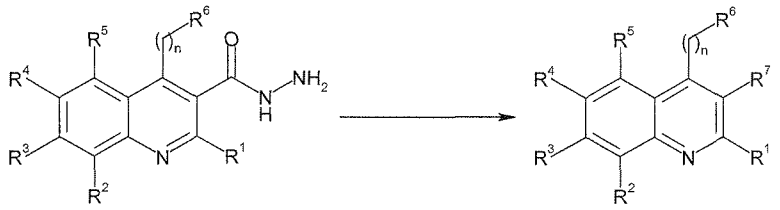
(XXIII) (I)

b) a compound of formula (XXX) in the presence of base or and acid;



(XXX) (I)

c) a compound of formula (XXVIII) in the presence of N,N'-carbonyldiimidazole or 1,1'-thiocarbonyldiimidazole;



(XXVIII) (I)

wherein R^1, R^2, R^3, R^4, R^5, R^6 and n are as defined in claim 1 and wherein R^8 is alkyl and wherein R^7 is tetrazolyl in step a), -COOH in step b) and 3H-[1,3,4]-oxadiazol-2-on-yl or 3H-[1,3,4]-oxadiazol-2-thion-yl in step c).

~~24~~13. A compound according to any one of claims 1 to ~~22~~ 11 for use as therapeutically active substance.

~~25~~14. A pharmaceutical composition comprising a compound according to any one of claims 1 to ~~22~~ 11 and a therapeutically inert carrier.

~~26~~15. A compound according to any one of claims 1 to ~~22~~ 11 for the treatment or prophylaxis of type 2 diabetes, atherosclerosis, cancer, chronic renal disease and non-alcoholic steatohepatitis.

~~27~~16. The use of a compound according to any one of claims 1 to ~~22~~ 11 for the preparation of a medicament for the treatment or prophylaxis of type 2 diabetes, atherosclerosis, cancer, chronic renal disease and non-alcoholic steatohepatitis.

28. A compound according to any one of claims 1 to 22, when manufactured according to a process of claim 23.