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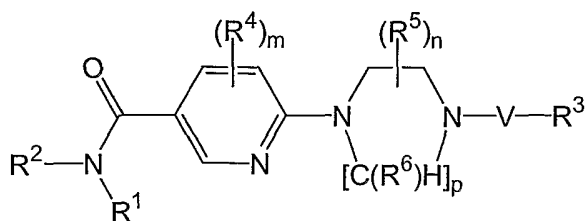
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(54) Title: NICOTINAMIDE DERIVATIVES AND THEIR USE AS THERAPEUTIC AGENTS



(1)

(57) Abstract: Methods of treating an SCD-medi-  
ated disease or condition in a mammal, preferably a  
human, are disclosed, wherein the methods comprise  
administering to a mammal in need thereof a com-  
pound of formula (I): where m, n, p, V, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>,  
R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are defined herein. Pharmaceutical  
compositions comprising the compounds of formula  
(I) are also disclosed.

WO 2006/014168 A1

## NICOTINAMIDE DERIVATIVES AND THEIR USE AS THERAPEUTIC AGENTS

### FIELD OF THE INVENTION

The present invention relates generally to the field of inhibitors of stearyl-CoA desaturase, such as nicotinamide derivatives, and uses for such compounds in treating  
5 and/or preventing various human diseases, including those mediated by stearyl-CoA desaturase (SCD) enzymes, preferably SCD1, especially diseases related to elevated lipid levels, cardiovascular disease, diabetes, obesity, metabolic syndrome and the like.

### BACKGROUND OF THE INVENTION

10 Acyl desaturase enzymes catalyze the formation of double bonds in fatty acids derived from either dietary sources or *de novo* synthesis in the liver. Mammals synthesize at least three fatty acid desaturases of differing chain length specificity that catalyze the addition of double bonds at the delta-9, delta-6, and delta-5 positions. Stearyl-CoA desaturases (SCDs) introduce a double bond in the C9-C10 position of  
15 saturated fatty acids. The preferred substrates are palmitoyl-CoA (16:0) and stearyl-CoA (18:0), which are converted to palmitoleoyl-CoA (16:1) and oleoyl-CoA (18:1), respectively. The resulting mono-unsaturated fatty acids are substrates for incorporation into phospholipids, triglycerides, and cholesteryl esters.

A number of mammalian SCD genes have been cloned. For example, two  
20 genes have been cloned from rat (SCD1, SCD2) and four SCD genes have been isolated from mouse (SCD1, 2, 3, and 4). While the basic biochemical role of SCD has been known in rats and mice since the 1970's (Jeffcoat, R. *et al.*, *Elsevier Science* (1984), Vol. 4, pp. 85-112; de Antueno, RJ, *Lipids* (1993), Vol. 28, No. 4, pp. 285-290), it has only recently been directly implicated in human disease processes.

25 A single SCD gene, SCD1, has been characterized in humans. SCD1 is described in Brownlie *et al*, PCT published patent application, WO 01/62954, the disclosure of which is hereby incorporated by reference in its entirety. A second human SCD isoform has recently been identified, and because it bears little sequence homology to alternate mouse or rat isoforms it has been named human SCD5 or  
30 hSCD5 (PCT published patent application, WO 02/26944, incorporated herein by reference in its entirety).

To date, no small-molecule, drug-like compounds are known that specifically

inhibit or modulate SCD activity. Certain long-chain hydrocarbons have been used historically to study SCD activity. Known examples include thia-fatty acids, cyclopropenoid fatty acids, and certain conjugated linoleic acid isomers. Specifically, *cis*-12, *trans*-10 conjugated linoleic acid is believed to inhibit SCD enzyme activity and  
5 reduce the abundance of SCD1 mRNA while *cis*-9, *trans*-11 conjugated linoleic acid does not. Cyclopropenoid fatty acids, such as those found in stercula and cotton seeds, are also known to inhibit SCD activity. For example, sterculic acid (8-(2-octylcyclopropenyl)octanoic acid) and malvalic acid (7-(2-octylcyclopropenyl)heptanoic acid) are C18 and C16 derivatives of sterculoyl- and malvaloyl fatty acids, respectively,  
10 having cyclopropene rings at their C9-C10 position. These agents are believed to inhibit SCD enzymatic activity by direct interaction with the enzyme, thus inhibiting delta-9 desaturation. Other agents that may inhibit SCD activity include thia-fatty acids, such as 9-thiastearic acid (also called 8-nonylthiooctanoic acid) and other fatty acids with a sulfoxy moiety.

15 These known modulators of delta-9 desaturase activity are not useful for treating the diseases and disorders linked to SCD1 biological activity. None of the known SCD inhibitor compounds are selective for SCD or delta-9 desaturases, as they also inhibit other desaturases and enzymes. The thia-fatty acids, conjugated linoleic acids and cyclopropene fatty acids (malvalic acid and sterculic acid) are neither useful  
20 at reasonable physiological doses, nor are they specific inhibitors of SCD1 biological activity, rather they demonstrate cross inhibition of other desaturases, in particular the delta-5 and delta-6 desaturases by the cyclopropene fatty acids.

The absence of small molecule inhibitors of SCD enzyme activity is a major scientific and medical disappointment because evidence is now compelling that SCD  
25 activity is directly implicated in common human disease processes: See *e.g.*, Attie, A.D. *et al.*, "Relationship between stearoyl-CoA desaturase activity and plasma triglycerides in human and mouse hypertriglyceridemia", *J. Lipid Res.* (2002) Vol. 43, No. 11, pp. 1899-907; Cohen, P. *et al.*, "Role for stearoyl-CoA desaturase-1 in leptin-mediated weight loss", *Science* (2002), Vol. 297, No. 5579, pp. 240-3, Ntambi, J. M. *et al.*, "Loss of stearoyl-CoA desaturase-1 function protects mice against adiposity", *Proc. Natl. Acad. Sci. U S A.* (2002), Vol. 99, No. 7, pp. 11482-6.  
30

The present invention solves this problem by presenting new classes of compounds that are useful in modulating SCD activity and regulating lipid levels, especially plasma lipid levels, and which are useful in the treatment of SCD-mediated  
35 diseases such as diseases related to dyslipidemia and disorders of lipid metabolism,

especially diseases related to elevated lipid levels, cardiovascular disease, diabetes, obesity, metabolic syndrome and the like.

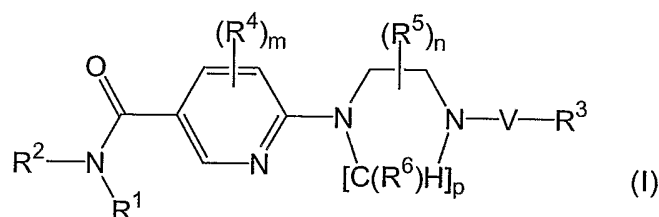
### Related Literature

U.S. Patent No. 6,677,452 discloses novel pyridine carboxamide or  
5 sulfonamide derivative compounds.

### SUMMARY OF THE INVENTION

The present invention provides methods of using nicotinamide derivatives to modulate the activity of stearyl-CoA desaturase. Pharmaceutical compositions comprising such derivatives are also encompassed.

10 Accordingly, one object of the present invention provides methods of treating an SCD-mediated disease or condition in a mammal, wherein the methods comprise administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I):



15 wherein:

m is 1, 2 or 3;

n is 1, 2, 3 or 4;

p is 2, 3 or 4;

V is -C(O)-, -S(O)- or -S(O)<sub>2</sub>-;

20 R<sup>1</sup> is hydrogen, alkyl, alkenyl, aryl, heteroaryl, aralkyl, aralkenyl or cycloalkyl;

R<sup>2</sup> is selected from the group consisting of hydrogen, -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

R<sup>3</sup> is selected from the group consisting of hydrogen, -R<sup>9</sup>-OR<sup>8</sup>, -R<sup>9</sup>-N(R<sup>8</sup>)<sub>2</sub>, alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted

aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl,  
optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally  
substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally  
substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted  
5 heteroarylalkenyl;

each R<sup>4</sup> is independently hydrogen, alkyl, alkenyl, halo, haloalkyl, aryl, cyano,  
nitro, -R<sup>9</sup>-OR<sup>8</sup>, -R<sup>9</sup>-N(R<sup>8</sup>)<sub>2</sub> or -S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2);

each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or  
aryl;

10 or one R<sup>5</sup> and one R<sup>6</sup> may together form an straight or branched alkylene  
bridge;

each R<sup>7</sup> is independently a straight or branched alkylene or alkenylene chain;

each R<sup>8</sup> is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl,  
cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl;

15 each R<sup>9</sup> is independently a direct bond or a straight or branched alkylene or  
alkenylene chain; and

R<sup>10</sup> is alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,  
heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl;

20 as a single stereoisomer, a mixture of stereoisomers, a racemic mixture thereof  
of stereoisomers, or as a tautomer;

or as a, pharmaceutically acceptable salt, prodrug, solvate or polymorph  
thereof.

The present invention further relates to a method for treating a patient for, or  
protecting a patient from developing, a disease or condition mediated by stearoyl-CoA  
25 desaturase (SCD), which method comprises administering to a patient afflicted with  
such disease or condition, or at risk of developing such disease or condition, a  
therapeutically effective amount of a compound that inhibits activity of SCD in a patient  
when administered thereto.

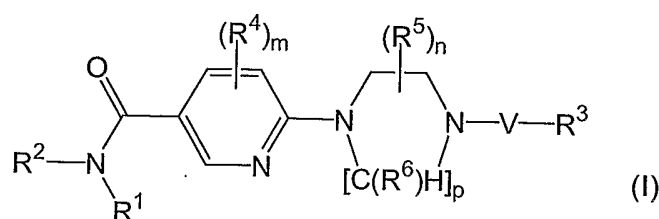
The present invention further relates to methods for treating a range of  
30 diseases involving lipid metabolism utilizing compounds identified by the methods  
disclosed herein. In accordance therewith, there is disclosed herein a range of  
compounds having said activity, based on a screening assay for identifying, from a  
library of test compounds, a therapeutic agent which modulates the biological activity  
of said SCD and is useful in treating a human disorder or condition relating to serum  
35 levels of lipids, such as triglycerides, VLDL, HDL, LDL, and/or total cholesterol.

It is a still further object of the present invention to provide compounds or pharmaceutical compositions useful in treating, preventing and/or diagnosing a disease or condition relating to SCD biological activity such as the diseases encompassed by cardiovascular disorders and/or metabolic syndrome (including dyslipidemia, insulin resistance and obesity).

It is yet a further object of the present invention to provide methods of preventing or treating a disease or condition related to elevated lipid levels, such as plasma lipid levels, especially elevated triglyceride or cholesterol levels, in a patient afflicted with such elevated levels, comprising administering to said patient a therapeutically or prophylactically effective amount of a composition as disclosed herein. The present invention also relates to novel compounds having therapeutic ability to reduce lipid levels in an animal, especially triglyceride and cholesterol levels.

The present invention also relates to pharmaceutical compositions comprising the compounds of formula (I) as set forth above and pharmaceutically acceptable excipients. In one embodiment, the present invention relates to a pharmaceutical composition comprising a compound of the invention in a pharmaceutically acceptable carrier and in an amount effective to modulate triglyceride level, or to treat diseases related to dyslipidemia and disorders of lipid metabolism, when administered to an animal, preferably a mammal, most preferably a human patient. In an embodiment of such composition, the patient has an elevated lipid level, such as elevated plasma triglycerides or cholesterol, before administration of said compound and said compound is present in an amount effective to reduce said lipid level.

The present invention also relates to compounds of formula (I):



25

wherein:

m is 1, 2 or 3;

n is 1, 2, 3 or 4;

p is 2, 3 or 4;

V is -C(O)-, -S(O)- or -S(O)<sub>2</sub>;

30

R<sup>1</sup> is hydrogen, alkyl, alkenyl, aryl, aralkyl, aralkenyl or cycloalkyl;

R<sup>2</sup> is selected from the group consisting of hydrogen, -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>,

-R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

R<sup>3</sup> is selected from the group consisting of cycloalkyl substituted by one or more substituents independently selected from the group consisting of alkyl, alkenyl, halo, haloalkyl, haloalkenyl, cyano, nitro, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -R<sup>9</sup>-OR<sup>8</sup>, -R<sup>9</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>9</sup>-C(O)R<sup>8</sup>, -R<sup>9</sup>-C(O)OR<sup>8</sup>, -R<sup>9</sup>-C(O)N(R<sup>8</sup>)<sub>2</sub>, -R<sup>9</sup>-N(R<sup>8</sup>)C(O)OR<sup>10</sup>, -R<sup>9</sup>-N(R<sup>8</sup>)C(O)R<sup>10</sup>, -R<sup>9</sup>-N(R<sup>8</sup>)(S(O)<sub>t</sub>R<sup>10</sup>) (where t is 1 or 2), -R<sup>9</sup>-S(O)<sub>t</sub>OR<sup>10</sup> (where t is 1 or 2), -R<sup>9</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), and -R<sup>9</sup>-S(O)<sub>t</sub>N(R<sup>8</sup>)<sub>2</sub> (where t is 1 or 2);

each R<sup>4</sup> is independently hydrogen, alkyl, alkenyl, halo, haloalkyl, aryl, cyano, nitro, -R<sup>9</sup>-OR<sup>8</sup>, -R<sup>9</sup>-N(R<sup>8</sup>)<sub>2</sub> or -S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2);

each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl;

or one R<sup>5</sup> and one R<sup>6</sup> may together form an straight or branched alkylene bridge;

each R<sup>7</sup> is independently a straight or branched alkylene or alkenylene chain;

each R<sup>8</sup> is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl;

each R<sup>9</sup> is independently a direct bond or a straight or branched alkylene or alkenylene chain; and

R<sup>10</sup> is alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl;

as a single stereoisomer, a mixture of stereoisomers, a racemic mixture thereof of stereoisomers, or as a tautomer;

or as a pharmaceutically acceptable salt, prodrug, solvate or polymorph thereof.

#### BRIEF DESCRIPTION OF THE DRAWING

Figure 1 shows dose response curves for two of the compounds of the invention. The compound at the left of the chart shows much greater inhibitory ability (with IC<sub>50</sub> of 100 nM) than the compound at the right (with IC<sub>50</sub> of 2.4 μM).

DETAILED DESCRIPTION OF THE INVENTIONDefinitions

As used in the specification and appended claims, unless specified to the contrary, the following terms have the meaning indicated:

- 5 "Alkyl" refers to a straight or branched hydrocarbon chain radical consisting solely of carbon and hydrogen atoms, containing no unsaturation, having from one to twelve carbon atoms, preferably one to eight carbon atoms, and which is attached to the rest of the molecule by a single bond, e.g., methyl, ethyl, *n*-propyl, 1-methylethyl (*iso*-propyl), *n*-butyl, *n*-pentyl, 1,1-dimethylethyl (*t*-butyl), and the like.
- 10 "Alkenyl" refers to a straight or branched hydrocarbon chain radical group consisting solely of carbon and hydrogen atoms, containing at least one double bond, having from two to twelve carbon atoms, preferably one to eight carbon atoms and which is attached to the rest of the molecule by a single bond, e.g., ethenyl, prop-1-enyl, but-1-enyl, pent-1-enyl, penta-1,4-dienyl, and the like.
- 15 "Aryl" refers to aromatic monocyclic or multicyclic hydrocarbon ring system consisting only of hydrogen and carbon and containing from 6 to 19 carbon atoms, where the ring system may be partially or fully saturated. Aryl groups include, but are not limited to groups such as fluorenyl, phenyl and naphthyl.. Unless stated otherwise specifically in the specification, the term "aryl" or the prefix "ar-" (such as in "aralkyl") is
- 20 meant to include aryl radicals optionally substituted by one or more substituents independently selected from the group consisting of alkyl, alkenyl, halo, haloalkyl, haloalkenyl, cyano, nitro, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl,  $-R^9-OR^8$ ,  $-R^9-N(R^8)_2$ ,  $-R^9-C(O)R^8$ ,  $-R^9-C(O)OR^8$ ,  $-R^9-C(O)N(R^8)_2$ ,  $-R^9-N(R^8)C(O)OR^{10}$ ,  $-R^9-N(R^8)C(O)R^{10}$ ,
- 25  $-R^9-N(R^8)(S(O)_tR^{10})$  (where *t* is 1 or 2),  $-R^9-S(O)_tOR^{10}$  (where *t* is 1 or 2),  $-R^9-S(O)_tR^{10}$  (where *t* is 0, 1 or 2), and  $-R^9-S(O)_tN(R^8)_2$  (where *t* is 1 or 2) where each  $R^8$ ,  $R^9$  and  $R^{10}$  are as defined above in the Summary of the Invention.
- "Aralkyl" refers to a radical of the formula  $-R_aR_b$  where  $R_a$  is an alkyl radical as defined above and  $R_b$  is one or more aryl radicals as defined above, e.g., benzyl,
- 30 diphenylmethyl and the like. The aryl radical(s) may be optionally substituted as described above.
- "Aralkenyl" refers to a radical of the formula  $-R_cR_b$  where  $R_c$  is an alkenyl radical as defined above and  $R_b$  is one or more aryl radicals as defined above, which may be



optionally substituted as described above.

"Alkylene" and "alkylene chain" refer to a straight or branched divalent hydrocarbon chain, linking the rest of the molecule to a radical group, consisting solely of carbon and hydrogen, containing no unsaturation and having from one to twelve  
5 carbon atoms, preferably having from one to eight carbons, *e.g.*, methylene, ethylene, propylene, *n*-butylene, and the like. The alkylene chain may be attached to the rest of the molecule and to the radical group can be through any two carbons within the chain.

"Alkylene" and "alkylene bridge" refer to a straight or branched divalent hydrocarbon bridge, linking two different carbons of the same ring structure, consisting  
10 solely of carbon and hydrogen, containing no unsaturation and having from one to twelve carbon atoms, preferably having from one to eight carbons, *e.g.*, methylene, ethylene, propylene, *n*-butylene, and the like. The alkylene bridge may link any two carbons within the ring structure.

"Alkenylene" and "alkenylene chain" refer to a straight or branched divalent  
15 hydrocarbon chain linking the rest of the molecule to a radical group, consisting solely of carbon and hydrogen, containing at least one double bond and having from two to seven carbon atoms, *e.g.*, ethenylene, propenylene, *n*-butenylene, and the like. The alkenylene chain is attached to the rest of the molecule through a single bond and to the radical group through a double bond or a single bond. The points of attachment of  
20 the alkenylene chain to the rest of the molecule and to the radical group can be through any two carbons within the chain.

"Cycloalkyl" refers to a stable non-aromatic monocyclic or bicyclic hydrocarbon radical consisting solely of carbon and hydrogen atoms, having from three to fifteen carbon atoms, preferably having from three to ten carbon atoms, and which is  
25 saturated or unsaturated and attached to the rest of the molecule by a single bond, *e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, decalanyl and the like. Unless otherwise stated specifically in the specification, the term "cycloalkyl" is meant to include cycloalkyl radicals which are optionally substituted by one or more substituents independently selected from the group consisting of alkyl, alkenyl, halo, haloalkyl,  
30 haloalkenyl, cyano, nitro, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl,  $-R^9-OR^8$ ,  $-R^9-N(R^8)_2$ ,  $-R^9-C(O)R^8$ ,  $-R^9-C(O)OR^8$ ,  $-R^9-C(O)N(R^8)_2$ ,  $-R^9-N(R^8)C(O)OR^{10}$ ,  $-R^9-N(R^8)C(O)R^{10}$ ,  $-R^9-N(R^8)(S(O)_tR^{10})$  (where *t* is 1 or 2),  $-R^9-S(O)_tOR^{10}$  (where *t* is 1 or 2),  $-R^9-S(O)_tR^{10}$  (where *t* is 0, 1 or 2), and  $-R^9-S(O)_tN(R^8)_2$  (where *t* is 1 or 2) where each  $R^8$ ,  $R^9$  and  $R^{10}$   
35 are as defined above in the Summary of the Invention.

"Cycloalkylalkyl" refers to a radical of the formula  $-R_aR_d$  where  $R_a$  is an alkyl radical as defined above and  $R_d$  is a cycloalkyl radical as defined above. The alkyl radical and the cycloalkyl radical may be optionally substituted as defined above.

"Halo" refers to bromo, chloro, fluoro or iodo.

5 "Haloalkyl" refers to an alkyl radical, as defined above, that is substituted by one or more halo radicals, as defined above, e.g., trifluoromethyl, difluoromethyl, trichloromethyl, 2,2,2-trifluoroethyl, 1-fluoromethyl-2-fluoroethyl, 3-bromo-2-fluoropropyl, 1-bromomethyl-2-bromoethyl, and the like.

10 "Haloalkenyl" refers to an alkenyl radical, as defined above, that is substituted by one or more halo radicals, as defined above, e.g., 2-bromoethenyl, 3-bromoprop-1-enyl, and the like.

"Heterocyclyl" refers to a stable 3- to 18-membered non-aromatic ring radical which consists of carbon atoms and from one to five heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur. For purposes of this invention, the  
 15 heterocyclyl radical may be a monocyclic, bicyclic, tricyclic or tetracyclic ring system, which may include fused or bridged ring systems; and the nitrogen, carbon or sulfur atoms in the heterocyclyl radical may be optionally oxidized; the nitrogen atom may be optionally quaternized; and the heterocyclyl radical may be partially or fully saturated. Examples of such heterocyclyl radicals include, but are not limited to, dioxolanyl,  
 20 decahydroisoquinolyl, imidazolyl, imidazolidinyl, isothiazolidinyl, isoxazolidinyl, morpholinyl, octahydroindolyl, octahydroisoindolyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolidinyl, oxazolidinyl, piperidinyl, piperazinyl, 4-piperidonyl, pyrrolidinyl, pyrazolidinyl, thiazolidinyl, tetrahydrofuryl, trithianyl, tetrahydropyranlyl, thiomorpholinyl, thiamorpholinyl, 1-oxo-thiomorpholinyl, and 1,1-dioxo-thiomorpholinyl. Unless stated  
 25 otherwise specifically in the specification, the term "heterocyclyl" is meant to include heterocyclyl radicals as defined above which are optionally substituted by one or more substituents independently selected from the group consisting of alkyl, alkenyl, halo, haloalkyl, haloalkenyl, cyano, nitro, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl,  $-R^9-OR^8$ ,  $-R^9-N(R^8)_2$ ,  
 30  $-R^9-C(O)R^8$ ,  $-R^9-C(O)OR^8$ ,  $-R^9-C(O)N(R^8)_2$ ,  $-R^9-N(R^8)C(O)OR^{10}$ ,  $-R^9-N(R^8)C(O)R^{10}$ ,  $-R^9-N(R^8)(S(O)_tR^{10})$  (where t is 1 or 2),  $-R^9-S(O)_tOR^{10}$  (where t is 1 or 2),  $-R^9-S(O)_tR^{10}$  (where t is 0, 1 or 2), and  $-R^9-S(O)_tN(R^8)_2$  (where t is 1 or 2) where each  $R^8$ ,  $R^9$  and  $R^{10}$  are as defined above in the Summary of the Invention.

35 "Heterocyclylalkyl" refers to a radical of the formula  $-R_aR_e$  where  $R_a$  is an alkyl radical as defined above and  $R_e$  is a heterocyclyl radical as defined above, and if the

heterocyclyl is a nitrogen-containing heterocyclyl, the heterocyclyl may be attached to the alkyl radical at the nitrogen atom. The heterocyclyl radical may be optionally substituted as defined above.

"Heteroaryl" refers to a 3- to 18-membered aromatic ring radical which consists of carbon atoms and from one to five heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur. For purposes of this invention, the heteroaryl radical may be a monocyclic, bicyclic, tricyclic or tetracyclic ring system, which may include fused or bridged ring systems; and the nitrogen, carbon or sulfur atoms in the heteroaryl radical may be optionally oxidized; the nitrogen atom may be optionally quaternized. Examples include, but are not limited to, azepinyl, acridinyl, benzimidazolyl, benzthiazolyl, benzindolyl, benzothiadiazolyl, benzonaphthofuranyl, benzoxazolyl, benzodioxolyl, benzodioxinyl, benzopyranyl, benzopyranonyl, benzofuranyl, benzofuranonyl, benzothieryl (benzothiophenyl), benzotriazolyl, benzo[4,6]imidazo[1,2-a]pyridinyl, carbazolyl, cinnolinyl, dibenzofuranyl, furanyl, furanonyl, isothiazolyl, imidazolyl, indolyl, indazolyl, isoindolyl, indolinyl, isoindolinyl, indoliziny, isoxazolyl, naphthyridinyl, oxadiazolyl, 2-oxoazepinyl, oxazolyl, oxiranyl, phenazinyl, phenothiazinyl, phenoxazinyl, phthalazinyl, pteridinyl, purinyl, pyrrolyl, pyrazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, quinazoliny, quinoxaliny, quinolinyl, quinuclidinyl, isoquinolinyl, thiazolyl, thiadiazolyl, triazolyl, tetrazolyl, triazinyl, and thiophenyl. Unless stated otherwise specifically in the specification, the term "heteroaryl" is meant to include heteroaryl radicals as defined above which are optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, halo, haloalkyl, haloalkenyl, cyano, nitro, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl,  $-R^9-OR^8$ ,  $-R^9-N(R^8)_2$ ,  $-R^9-C(O)R^8$ ,  $-R^9-C(O)OR^8$ ,  $-R^9-C(O)N(R^8)_2$ ,  $-R^9-N(R^8)C(O)OR^{10}$ ,  $-R^9-N(R^8)C(O)R^{10}$ ,  $-R^9-N(R^8)(S(O)_tR^{10})$  (where t is 1 or 2),  $-R^9-S(O)_tOR^{10}$  (where t is 1 or 2),  $-R^9-S(O)_tR^{10}$  (where t is 0, 1 or 2), and  $-R^9-S(O)_tN(R^8)_2$  (where t is 1 or 2) where each  $R^8$ ,  $R^9$  and  $R^{10}$  are as defined above in the Summary of the Invention.

"Heteroarylalkyl" refers to a radical of the formula  $-R_aR_f$  where  $R_a$  is an alkyl radical as defined above and  $R_f$  is a heteroaryl radical as defined above. The heteroaryl radical may be optionally substituted as defined above.

"Heteroarylalkenyl" refers to a radical of the formula  $-R_bR_f$  where  $R_b$  is an alkenyl radical as defined above and  $R_f$  is a heteroaryl radical as defined above. The heteroaryl radical may be optionally substituted as defined above.

"Prodrugs" is meant to indicate a compound that may be converted under

physiological conditions or by solvolysis to a biologically active compound of the invention. Thus, the term "prodrug" refers to a metabolic precursor of a compound of the invention that is pharmaceutically acceptable. A prodrug may be inactive when administered to a subject in need thereof, but is converted *in vivo* to an active compound  
5 of the invention. Prodrugs are typically rapidly transformed *in vivo* to yield the parent compound of the invention, for example, by hydrolysis in blood. The prodrug compound often offers advantages of solubility, tissue compatibility or delayed release in a mammalian organism (see, Bundgard, H., Design of Prodrugs (1985), pp. 7-9, 21-24 (Elsevier, Amsterdam).

10 A discussion of prodrugs is provided in Higuchi, T., *et al.*, "Pro-drugs as Novel Delivery Systems," A.C.S. Symposium Series, Vol. 14, and in Bioreversible Carriers in Drug Design, ed. Edward B. Roche, American Pharmaceutical Association and Pergamon Press, 1987, both of which are incorporated in full by reference herein.

The term "prodrug" is also meant to include any covalently bonded carriers which  
15 release the active compound of the invention *in vivo* when such prodrug is administered to a mammalian subject. Prodrugs of a compound of the invention may be prepared by modifying functional groups present in the compound of the invention in such a way that the modifications are cleaved, either in routine manipulation or *in vivo*, to the parent compound of the invention. Prodrugs include compounds of the invention wherein a  
20 hydroxy, amino or mercapto group is bonded to any group that, when the prodrug of the compound of the invention is administered to a mammalian subject, cleaves to form a free hydroxy, free amino or free mercapto group, respectively. Examples of prodrugs include, but are not limited to, ester and amide derivatives of hydroxy, carboxy, mercapto or amino functional groups in the compounds of the invention and the like.

25 "Stable compound" and "stable structure" are meant to indicate a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

"Mammal" includes humans and domestic animals, such as cats, dogs, swine, cattle, sheep, goats, horses, rabbits, and the like.

30 "Optional" or "optionally" means that the subsequently described event of circumstances may or may not occur, and that the description includes instances where said event or circumstance occurs and instances in which it does not. For example, "optionally substituted aryl" means that the aryl radical may or may not be substituted and that the description includes both substituted aryl radicals and aryl radicals having no  
35 substitution.

"Pharmaceutically acceptable carrier, diluent or excipient" includes without limitation any adjuvant, carrier, excipient, glidant, sweetening agent, diluent, preservative, dye/colorant, flavor enhancer, surfactant, wetting agent, dispersing agent, suspending agent, stabilizer, isotonic agent, solvent, or emulsifier which has been approved by the  
5 United States Food and Drug Administration as being acceptable for use in humans or domestic animals.

"Pharmaceutically acceptable salt" includes both acid and base addition salts.

"Pharmaceutically acceptable acid addition salt" refers to those salts which retain the biological effectiveness and properties of the free bases, which are not biologically or  
10 otherwise undesirable, and which are formed with inorganic acids such as, but not limited to, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, and organic acids such as, but not limited to, acetic acid, 2,2-dichloroacetic acid, adipic acid, alginic acid, ascorbic acid, aspartic acid, benzenesulfonic acid, benzoic acid, 4-acetamidobenzoic acid, camphoric acid, camphor-10-sulfonic acid, capric acid, caproic  
15 acid, caprylic acid, carbonic acid, cinnamic acid, citric acid, cyclamic acid, dodecylsulfuric acid, ethane-1,2-disulfonic acid, ethanesulfonic acid, 2-hydroxyethanesulfonic acid, formic acid, fumaric acid, galactaric acid, gentisic acid, glucoheptonic acid, gluconic acid, glucuronic acid, glutamic acid, glutaric acid, 2-oxo-glutaric acid, glycerophosphoric acid, glycolic acid, hippuric acid, isobutyric acid, lactic acid, lactobionic acid, lauric acid, maleic  
20 acid, malic acid, malonic acid, mandelic acid, methanesulfonic acid, mucic acid, naphthalene-1,5-disulfonic acid, naphthalene-2-sulfonic acid, 1-hydroxy-2-naphthoic acid, nicotinic acid, oleic acid, orotic acid, oxalic acid, palmitic acid, pamoic acid, propionic acid, pyroglutamic acid, pyruvic acid, salicylic acid, 4-aminosalicylic acid, sebacic acid, stearic acid, succinic acid, tartaric acid, thiocyanic acid, *p*-toluenesulfonic acid, trifluoroacetic  
25 acid, undecylenic acid, and the like.

"Pharmaceutically acceptable base addition salt" refers to those salts which retain the biological effectiveness and properties of the free acids, which are not biologically or otherwise undesirable. These salts are prepared from addition of an inorganic base or an  
30 organic base to the free acid. Salts derived from inorganic bases include, but are not limited to, the sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, aluminum salts and the like. Preferred inorganic salts are the ammonium, sodium, potassium, calcium, and magnesium salts. Salts derived from organic bases include, but are not limited to, salts of primary, secondary, and tertiary  
35 amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as ammonia, isopropylamine,

trimethylamine, diethylamine, triethylamine, tripropylamine, diethanolamine, ethanolamine, deanol, 2-dimethylaminoethanol, 2-diethylaminoethanol, dicyclohexylamine, lysine, arginine, histidine, caffeine, procaine, hydrabamine, choline, betaine, benethamine, benzathine, ethylenediamine, glucosamine, methylglucamine, 5 theobromine, triethanolamine, tromethamine, purines, piperazine, piperidine, *N*-ethylpiperidine, polyamine resins and the like. Particularly preferred organic bases are isopropylamine, diethylamine, ethanolamine, trimethylamine, dicyclohexylamine, choline and caffeine.

The compounds of the invention may, and typically do, exist as solids, including 10 crystalline solids which can be crystallized from common solvents such as ethanol, *N,N*-dimethylformamide, water, or the like. The crystallization process may, depending on the crystallization conditions, provide various polymorphic structures. Typically, a more thermodynamically stable polymorph is advantageous to the commercial scale manufacture of a compound of the invention, and is a preferred form of the compound. 15 Such polymorphs are considered to be within the scope of the invention.

Often crystallizations produce a solvate of the compound of the invention. As used herein, the term "solvate" refers to an aggregate that comprises one or more molecules of a compound of the invention with one or more molecules of solvent. The solvent may be water, in which case the solvate may be a hydrate. Alternatively, the 20 solvent may be an organic solvent. Thus, the compounds of the present invention may exist as a hydrate, including a monohydrate, dihydrate, hemihydrate, sesquihydrate, trihydrate, tetrahydrate and the like, as well as the corresponding solvated forms. The compound of the invention may be true solvates, while in other cases, the compound of the invention may merely retain adventitious water or be a mixture of water plus 25 some adventitious solvent.

A "pharmaceutical composition" refers to a formulation of a compound of the invention and a medium generally accepted in the art for the delivery of the biologically active compound to mammals, e.g., humans. Such a medium includes all pharmaceutically acceptable carriers, diluents or excipients therefor.

30 "Therapeutically effective amount" refers to that amount of a compound of the invention which, when administered to a mammal, preferably a human, is sufficient to effect treatment, as defined below, of an SCD-mediated disease or condition in the mammal, preferably a human. The amount of a compound of the invention which constitutes a "therapeutically effective amount" will vary depending on the compound, the 35 condition and its severity, and the age of the mammal to be treated, but can be

determined routinely by one of ordinary skill in the art having regard to his own knowledge and to this disclosure.

"Treating" or "treatment" as used herein covers the treatment of the disease or condition of interest in a mammal, preferably a human, having the disease or disorder of  
5 interest, and includes:

- (i) preventing the disease or condition from occurring in a mammal, in particular, when such mammal is predisposed to the condition but has not yet been diagnosed as having it;
- (ii) inhibiting the disease or condition, *i.e.*, arresting its development; or
- 10 (iii) relieving the disease or condition, *i.e.*, causing regression of the disease or condition.

As used herein, the terms "disease" and "condition" may be used interchangeably or may be different in that the particular malady or condition may not have a known causative agent (so that etiology has not yet been worked out) and it is  
15 therefore not yet recognized as a disease but only as an undesirable condition or syndrome, wherein a more or less specific set of symptoms have been identified by clinicians.

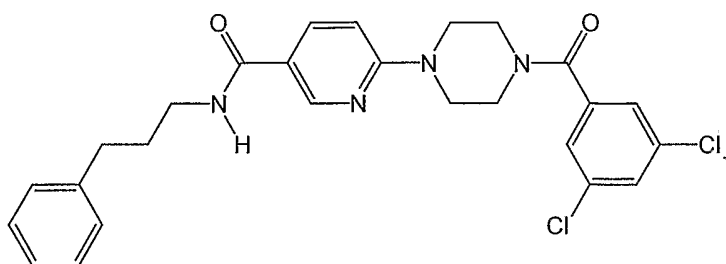
The compounds of the invention, or their pharmaceutically acceptable salts may contain one or more asymmetric centers and may thus give rise to enantiomers,  
20 diastereomers, and other stereoisomeric forms that may be defined, in terms of absolute stereochemistry, as (*R*)- or (*S*)- or, as (*D*)- or (*L*)- for amino acids. The present invention is meant to include all such possible isomers, as well as their racemic and optically pure forms. Optically active (+) and (-), (*R*)- and (*S*)-, or (*D*)- and (*L*)- isomers may be prepared using chiral synthons or chiral reagents, or resolved  
25 using conventional techniques, such as HPLC using a chiral column. When the compounds described herein contain olefinic double bonds or other centers of geometric asymmetry, and unless specified otherwise, it is intended that the compounds include both *E* and *Z* geometric isomers. Likewise, all tautomeric forms are also intended to be included.

30 A "stereoisomer" refers to a compound made up of the same atoms bonded by the same bonds but having different three-dimensional structures, which are not interchangeable. The present invention contemplates various stereoisomers and mixtures thereof and includes "enantiomers", which refers to two stereoisomers whose molecules are nonsuperimposable mirror images of one another.

35 A "tautomer" refers to a proton shift from one atom of a molecule to another

atom of the same molecule. The present invention includes tautomers of any said compounds.

The chemical naming protocol and structure diagrams used herein employ and rely the chemical naming features as utilized by Chemdraw version 7.0.1. (available  
 5 from Cambridgesoft Corp., Cambridge, MA). For complex chemical names employed herein, a substituent group is named before the group to which it attaches. In chemical structure diagrams, all bonds are identified, except for some carbon atoms which are assumed to be bonded to sufficient hydrogen atoms to complete the valency. For example, a compound of the following formula:



10

is named herein as 6-[4-(3,5-dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide.

#### Embodiments of the Invention

Of the various embodiments of the invention as set forth above in the Summary  
 15 of the Invention, one group of embodiments is directed to the methods of treating an SCD-mediated disease or condition in a mammal are methods wherein the compound of formula (I) is a compound of formula (I) wherein *m* is 1 or 2; *n* is 1 or 2; *p* is 2 or 3; *V* is -C(O)- or -S(O)<sub>2</sub>-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of hydrogen, -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where *t* is 0, 1 or 2), alkyl, alkenyl,  
 20 optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted  
 25 heteroarylalkenyl; R<sup>3</sup> is alkyl, alkenyl or -R<sup>9</sup>-N(R<sup>8</sup>)<sub>2</sub>; each R<sup>4</sup> is independently hydrogen, alkyl, alkenyl, halo, haloalkyl, aryl or -R<sup>9</sup>-OR<sup>8</sup>; each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl; or one R<sup>5</sup> and one R<sup>6</sup> may together form an straight or branched alkylene bridge; each R<sup>7</sup> is independently a straight or branched alkylene or alkenylene chain; each R<sup>8</sup> is independently hydrogen,



alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl or heteroarylalkyl; each  $R^9$  is independently a direct bond or a straight or branched alkylene chain; and  $R^{10}$  is alkyl, aryl or aralkyl.

Of this group of embodiments, one subgroup of embodiments is directed to the methods wherein the compound of formula (I) is a compound of formula (I) wherein m is 1 or 2; n is 1 or 2; p is 2; V is -C(O)-;  $R^1$  is hydrogen or alkyl;  $R^2$  is selected from the group consisting of  $-R^7-OR^8$ ,  $-R^7-N(R^8)_2$ ,  $-R^7-S(O)_tR^{10}$  (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl or optionally substituted cycloalkylalkenyl;  $R^3$  is alkyl; each  $R^4$  is independently hydrogen, alkyl, halo, or haloalkyl; each  $R^5$  and  $R^6$  is independently hydrogen, oxo, alkyl, halo or haloalkyl; each  $R^7$  is a straight or branched alkylene chain; each  $R^8$  is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl and aralkyl; and  $R^{10}$  is alkyl, aryl or aralkyl.

Of this subgroup of embodiments, one class of embodiments is directed to the methods wherein the compound of formula (I) is a compound of formula (I) wherein m is 1; n is 1; p is 2; V is -C(O)-;  $R^1$  is hydrogen or alkyl;  $R^2$  is selected from the group consisting of  $-R^7-OR^8$ ,  $-R^7-N(R^8)_2$ ,  $-R^7-S(O)_tR^{10}$  (where t is 0, 1 or 2) or alkyl;  $R^3$  is alkyl;  $R^4$  is hydrogen;  $R^5$  is hydrogen; each  $R^6$  is hydrogen;  $R^7$  is a straight or branched alkylene chain;  $R^8$  is hydrogen or alkyl; and  $R^{10}$  is alkyl, aryl or aralkyl.

Of the group of embodiments set forth above, another subgroup of embodiments is directed to the methods wherein the compound of formula (I) is a compound of formula (I) wherein m is 1 or 2; n is 1 or 2; p is 2 or 3; V is -C(O)- or -S(O)<sub>2</sub>-;  $R^1$  is hydrogen or alkyl;  $R^2$  is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclalkyl, optionally substituted heterocyclalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;  $R^3$  is alkyl or  $-R^7-N(R^8)_2$ ; each  $R^4$  is independently hydrogen, alkyl, halo, or haloalkyl; and each  $R^5$  and  $R^6$  is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl; or one  $R^5$  and one  $R^6$  may together form an straight or branched alkylene bridge;  $R^7$  is a direct bond; and each  $R^8$  is independently hydrogen or alkyl.

Of this subgroup of embodiments, one class of embodiments is directed to the methods wherein the compound of formula (I) is a compound of formula (I) wherein m is 1; n is 1; p is 2 or 3; V is -C(O)- or -S(O)<sub>2</sub>-;  $R^1$  is hydrogen or alkyl;  $R^2$  is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl,

optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heteroaryl and optionally substituted heteroarylalkyl;  $R^3$  is alkyl or  $-R^7-N(R^8)_2$ ;  $R^4$  is hydrogen, alkyl, halo or haloalkyl; and each  $R^5$  and  $R^6$  is independently hydrogen, oxo, alkyl, halo or haloalkyl; or one  $R^5$  and one  $R^6$  may together form a methylene bridge;  $R^7$  is a direct bond; and each  $R^8$  is independently hydrogen or alkyl.

Of the various embodiments of the invention as set forth above in the Summary of the Invention, another group of embodiments is directed to the methods of treating an SCD-mediated disease or condition in a mammal wherein the compound of formula (I) is a compound of formula (I) wherein  $m$  is 1 or 2;  $n$  is 1 or 2;  $p$  is 2;  $V$  is  $-C(O)-$ ;  $R^1$  is hydrogen or alkyl;  $R^2$  is selected from the group consisting of hydrogen,  $-R^7-OR^8$ ,  $-R^7-N(R^8)_2$ ,  $-R^7-S(O)_tR^{10}$  (where  $t$  is 0, 1 or 2), alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;  $R^3$  is optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, or optionally substituted cycloalkylalkenyl; each  $R^4$  is independently hydrogen, alkyl, alkenyl, halo, haloalkyl, aryl or  $-R^9-OR^8$ ; each  $R^5$  and  $R^6$  is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl; each  $R^7$  is independently a straight or branched alkylene or alkenylene chain; each  $R^8$  is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl;  $R^9$  is a direct bond or a straight or branched alkylene chain; and  $R^{10}$  is alkyl, aryl or aralkyl.

Of this group of embodiments, a subgroup of embodiments is directed to the methods wherein the compound of formula (I) is a compound of formula (I) wherein  $m$  is 1 or 2;  $n$  is 1 or 2;  $p$  is 2;  $V$  is  $-C(O)-$ ;  $R^1$  is hydrogen or alkyl;  $R^2$  is selected from the group consisting of  $-R^7-OR^8$ ,  $-R^7-N(R^8)_2$ ,  $-R^7-S(O)_tR^{10}$  (where  $t$  is 0, 1 or 2), alkyl, alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl or optionally substituted cycloalkylalkenyl;  $R^3$  is optionally substituted cycloalkyl or optionally substituted cycloalkylalkyl; each  $R^4$  is independently hydrogen, alkyl, halo, or haloalkyl; each  $R^5$  and  $R^6$  is independently hydrogen, oxo, alkyl, halo or haloalkyl; each  $R^7$  is a straight or branched alkylene chain; each  $R^8$  is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl and aralkyl; and  $R^{10}$  is alkyl, aryl or aralkyl.

Of this subgroup of embodiments, a class of embodiments is directed to the

methods wherein the compound of formula (I) is a compound of formula (I) wherein m is 1; n is 1; p is 2; V is -C(O)-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0 to 2) or alkyl; R<sup>3</sup> is optionally substituted cycloalkyl or optionally substituted cycloalkylalkyl; R<sup>4</sup> is hydrogen; R<sup>5</sup> is hydrogen; each R<sup>6</sup> is hydrogen; R<sup>7</sup> is a straight or branched alkylene chain; R<sup>8</sup> is hydrogen or alkyl; and R<sup>10</sup> is alkyl, aryl or aralkyl.

Of the group of embodiments set forth above, another subgroup of embodiments is directed to the methods wherein the compound of formula (I) is a compound of formula (I) wherein m is 1 or 2; n is 1 or 2; p is 2; V is -C(O)-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl; R<sup>3</sup> is optionally substituted cycloalkyl or optionally substituted cycloalkylalkyl; each R<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl; and each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl.

Of this subgroup of embodiments, a class of embodiments is directed to the methods wherein the compound of formula (I) is a compound of formula (I) wherein m is 1; n is 1; p is 2; V is -C(O)-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heteroaryl and optionally substituted heteroarylalkyl; R<sup>3</sup> is optionally substituted cycloalkyl or optionally substituted cycloalkylalkyl; R<sup>4</sup> is hydrogen, alkyl, halo or haloalkyl; R<sup>5</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl; and each R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl.

Of the various embodiments of the invention as set forth above in the Summary of the Invention, another group of embodiments is directed to the methods of treating an SCD-mediated disease or condition in a mammal wherein the compound of formula (I) is a compound of formula (I) wherein m is 1 or 2; n is 1 or 2; p is 2; V is -C(O)-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of hydrogen, -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted

heterocyclalkyl, optionally substituted heterocyclalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl; R<sup>3</sup> is optionally substituted aryl; each R<sup>4</sup> is independently hydrogen, alkyl, alkenyl, halo, haloalkyl, aryl or -R<sup>9</sup>-OR<sup>8</sup>; each R<sup>5</sup> and R<sup>6</sup> is independently  
5 hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl; each R<sup>7</sup> is independently a straight or branched alkylene or alkenylene chain; each R<sup>8</sup> is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocycl, heterocyclalkyl, heteroaryl or heteroarylalkyl; R<sup>9</sup> is a direct bond or a straight or branched alkylene chain; and R<sup>10</sup> is alkyl, aryl or aralkyl.

10 Of this group of embodiments, a subgroup of embodiments is directed to the methods wherein the compound of formula (I) is a compound of formula (I) wherein m is 1 or 2; n is 1 or 2; p is 2; V is -C(O)-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0 to 2), alkyl, alkenyl,  
15 optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl or optionally substituted cycloalkylalkenyl; R<sup>3</sup> is optionally substituted aryl; each R<sup>4</sup> is independently hydrogen, alkyl, halo, haloalkyl or -R<sup>9</sup>-OR<sup>8</sup>; each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl; each R<sup>7</sup> is a straight or branched alkylene chain; each R<sup>8</sup> is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl and aralkyl; R<sup>9</sup> is a direct bond or a straight or branched alkylene chain; and R<sup>10</sup> is alkyl, aryl or  
20 aralkyl.

Of this subgroup of embodiments, a class of embodiments is directed to the methods wherein the compound of formula (I) is a compound of formula (I) wherein m is 1 or 2; n is 1; p is 2; V is -C(O)-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl,  
25 optionally substituted cycloalkyl or optionally substituted cycloalkylalkyl; R<sup>3</sup> is optionally substituted aryl; each R<sup>4</sup> is independently hydrogen, halo, haloalkyl or -R<sup>9</sup>-OR<sup>8</sup>; R<sup>5</sup> is hydrogen; each R<sup>6</sup> is hydrogen; R<sup>7</sup> is a straight or branched alkylene chain; R<sup>8</sup> is hydrogen or alkyl; R<sup>9</sup> is a direct bond or a straight or branched alkylene chain; and R<sup>10</sup> is alkyl, aryl or aralkyl.

30 Of the group of embodiments set forth above, another subgroup of embodiments is directed to the methods wherein the compound of formula (I) is a compound of formula (I) wherein m is 1 or 2; n is 1 or 2; p is 2; V is -C(O)-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally  
35 substituted heterocycl, optionally substituted heterocyclalkyl, optionally substituted

heterocyclalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;  $R^3$  is optionally substituted aryl; each  $R^4$  is independently hydrogen, alkyl, halo, or haloalkyl; and each  $R^5$  and  $R^6$  is independently hydrogen, oxo, alkyl, halo or haloalkyl.

5           Of this subgroup of embodiments, a class of embodiments is directed to the methods wherein the compound of formula (I) is a compound of formula (I) wherein m is 1 or 2; n is 1; p is 2; V is -C(O)-;  $R^1$  is hydrogen or alkyl;  $R^2$  is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted heterocycl, optionally substituted heterocyclalkyl, optionally substituted  
10 heteroaryl and optionally substituted heteroarylalkyl;  $R^3$  is optionally substituted aryl; each  $R^4$  is independently hydrogen, alkyl, halo or haloalkyl;  $R^5$  is hydrogen, oxo, alkyl, halo or haloalkyl; and each  $R^6$  is independently hydrogen, alkyl, halo or haloalkyl.

          Of the various embodiments of the invention as set forth above in the Summary of the Invention, another group of embodiments is directed to the methods of treating  
15 an SCD-mediated disease or condition in a mammal wherein the compound of formula (I) is a compound of formula (I) wherein m is 1 or 2; n is 1 or 2; p is 2; V is -C(O)-;  $R^1$  is hydrogen or alkyl;  $R^2$  is selected from the group consisting of hydrogen,  $-R^7-OR^8$ ,  $-R^7-N(R^8)_2$ ,  $-R^7-S(O)_tR^{10}$  (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted  
20 cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocycl, optionally substituted heterocyclalkyl, optionally substituted heterocyclalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;  $R^3$  is optionally substituted heteroaryl, optionally substituted  
25 heteroarylalkyl or optionally substituted heteroarylalkenyl; each  $R^4$  is independently hydrogen, alkyl, alkenyl, halo, haloalkyl or aryl; each  $R^5$  and  $R^6$  is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl; each  $R^7$  is independently a straight or branched alkylene or alkenylene chain; each  $R^8$  is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocycl, heterocyclalkyl,  
30 heteroaryl or heteroarylalkyl; and  $R^{10}$  is alkyl, aryl or aralkyl.

          Of this group of embodiments, a subgroup of embodiments is directed to the methods wherein the compound of formula (I) is a compound wherein m is 1 or 2; n is 1 or 2; p is 2; V is -C(O)-;  $R^1$  is hydrogen or alkyl;  $R^2$  is selected from the group consisting of  $-R^7-OR^8$ ,  $-R^7-N(R^8)_2$ ,  $-R^7-S(O)_tR^{10}$  (where t is 0, 1 or 2), alkyl, alkenyl,  
35 optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl or optionally

substituted cycloalkylalkenyl; R<sup>3</sup> is optionally substituted heteroaryl, optionally substituted heteroarylalkyl or optionally substituted heteroarylalkenyl; each R<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl; each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl; each R<sup>7</sup> is a straight or branched alkylene chain; each R<sup>8</sup> is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl and aralkyl; and R<sup>10</sup> is alkyl, aryl or aralkyl.

Of this subgroup of embodiments, a class of embodiments is directed to the methods wherein the compound of formula (I) is a compound wherein m is 1 or 2; n is 1; p is 2; V is -C(O)-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2) or alkyl; R<sup>3</sup> is optionally substituted heteroaryl, optionally substituted heteroarylalkyl or optionally substituted heteroarylalkenyl; each R<sup>4</sup> is independently hydrogen, halo or haloalkyl; R<sup>5</sup> is hydrogen; each R<sup>6</sup> is hydrogen; R<sup>7</sup> is a straight or branched alkylene chain; R<sup>8</sup> is hydrogen or alkyl; and R<sup>10</sup> is alkyl, aryl or aralkyl.

Of the group of embodiments set forth above, another subgroup of embodiments is directed to the methods wherein the compound of formula (I) is a compound of formula (I) wherein m is 1 or 2; n is 1 or 2; p is 2; V is -C(O)-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl; R<sup>3</sup> is optionally substituted heteroaryl, optionally substituted heteroarylalkyl or optionally substituted heteroarylalkenyl; each R<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl; and each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl.

Of this subgroup of embodiments, a class of embodiments is directed to the methods wherein the compound of formula (I) is a compound of formula (I) wherein m is 1 or 2; n is 1; p is 2; V is -C(O)-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heteroaryl and optionally substituted heteroarylalkyl; R<sup>3</sup> is optionally substituted heteroaryl, optionally substituted heteroarylalkyl or optionally substituted heteroarylalkenyl; each R<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl; R<sup>5</sup> is hydrogen, oxo, alkyl, halo or haloalkyl; and each R<sup>6</sup> independently hydrogen, oxo, alkyl, halo or haloalkyl.

Of the various embodiments of the invention as set forth above in the Summary of the Invention, another group of embodiments is directed to the methods of treating an SCD-mediated disease or condition in a mammal wherein the compound of formula (I) is a compound of formula (I) wherein m is 1 or 2; n is 1 or 2; p is 2; V is -C(O)-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of hydrogen, -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl; R<sup>3</sup> is optionally substituted aralkyl or optionally substituted aralkenyl; each R<sup>4</sup> is independently hydrogen, alkyl, alkenyl, halo, haloalkyl, aryl or -R<sup>9</sup>-OR<sup>8</sup>; each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl; each R<sup>7</sup> is independently a straight or branched alkylene or alkenylene chain; each R<sup>8</sup> is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl; R<sup>9</sup> is a direct bond or a straight or branched alkylene chain; and R<sup>10</sup> is alkyl, aryl or aralkyl.

Of the group of embodiments set forth above, a subgroup of embodiments is directed to the methods wherein the compound of formula (I) is a compound of formula (I) wherein m is 1 or 2; n is 1 or 2; p is 2; V is -C(O)-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl or optionally substituted cycloalkylalkenyl; R<sup>3</sup> is optionally substituted aralkyl or optionally substituted aralkenyl; each R<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl; each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl; each R<sup>7</sup> is a straight or branched alkylene chain; each R<sup>8</sup> is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl and aralkyl; and R<sup>10</sup> is alkyl, aryl or aralkyl.

Of this subgroup of embodiments, a class of embodiments is directed to the methods wherein the compound of formula (I) is a compound of formula (1) wherein m is 1 or 2; n is 1; p is 2; V is -C(O)-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2) or alkyl; R<sup>3</sup> is optionally substituted aralkyl or optionally substituted aralkenyl; each R<sup>4</sup> is independently hydrogen, halo or haloalkyl; R<sup>5</sup> is hydrogen; each R<sup>6</sup> is hydrogen; R<sup>7</sup> is a

straight or branched alkylene chain; R<sup>8</sup> is hydrogen or alkyl; and R<sup>10</sup> is alkyl, aryl or aralkyl.

Of the group of embodiments set forth above, another subgroup of embodiments is directed to the methods wherein the compound of formula (I) is a compound wherein m is 1 or 2; n is 1 or 2; p is 2; V is -C(O)-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl; R<sup>3</sup> is optionally substituted aralkyl or optionally substituted aralkenyl; each R<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl; and each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl.

Of this subgroup of embodiments, a class of embodiments is directed to the methods wherein the compound of formula (I) is a compound of formula (1) wherein m is 1 or 2; n is 1; p is 2; V is -C(O)-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heteroaryl and optionally substituted heteroarylalkyl; R<sup>3</sup> is optionally substituted aralkyl or optionally substituted aralkenyl; each R<sup>4</sup> is independently hydrogen, alkyl, halo or haloalkyl; and R<sup>5</sup> is hydrogen, oxo, alkyl, halo or haloalkyl; and each R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl.

Of the various embodiments of the invention as set forth above in the Summary of the Invention, another group of embodiments is directed to the methods of treating an SCD-mediated disease or condition in a mammal wherein the mammal is a human. Of this group of embodiments, a subgroup of embodiments is directed to the method wherein the disease or condition is a disease or condition related to serum levels of triglyceride, VLDL, HDL, LDL, total cholesterol or the process of reverse cholesterol transport. Another subgroup of embodiments is directed to the method wherein the disease or condition is a disease or condition related to serum triglyceride levels. Another subgroup of embodiments is directed to the method wherein the disease or condition is a disease or condition related to serum cholesterol levels. Another subgroup of embodiments is directed to the method wherein the disease or condition is selected from the group consisting of Type II diabetes, impaired glucose tolerance, insulin resistance, hypertension, obesity, hypertriglyceridemia, low HDL, lipidemia, dyslipidemia, microalbuminemia, hyperuricaemia, hypercoagulability,



hyperleptinaemia, metabolic syndrome and any combination of these. Of these subgroups of embodiments, classes of embodiments are directed to the methods wherein the disease or condition is Type II diabetes, obesity, dyslipidemia and/or metabolic syndrome.

5 Of the pharmaceutical compositions of the invention set forth above in the Summary of the Invention, one group of embodiments is directed to the pharmaceutical compositions wherein the therapeutically effective amount of the compound of formula (I) is an amount effective to modulate a lipid level in a mammal when administered to the mammal. Of this group of embodiments, a subgroup of embodiments is wherein the  
10 lipid is triglyceride. Another subgroup of embodiments is wherein the lipid is cholesterol. Another group of embodiments is directed to pharmaceutical compositions wherein the therapeutically effective amount of the compound of formula (I) is an amount effective to modulate HDL-cholesterol levels when administered to a mammal.

Of the compounds of formula (I) set forth above in the Summary of the  
15 Invention, one group of embodiments is directed to the compounds of formula (I) wherein m is 1, 2 or 3; n is 1, 2, 3 or 4; p is 2, 3 or 4; V is -C(O)-, -S(O)- or -S(O)<sub>2</sub>-; R<sup>1</sup> is hydrogen, alkyl, alkenyl, aryl, aralkyl, aralkenyl or cycloalkyl; R<sup>2</sup> is selected from the group consisting of hydrogen, -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally  
20 substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl; R<sup>3</sup> is selected from the  
25 group consisting of cycloalkyl substituted by one or more substituents independently selected from the group consisting of alkyl, alkenyl, halo, haloalkyl, haloalkenyl, cyano, nitro, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -R<sup>9</sup>-OR<sup>8</sup>, -R<sup>9</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>9</sup>-C(O)R<sup>8</sup>, -R<sup>9</sup>-C(O)OR<sup>8</sup>, -R<sup>9</sup>-C(O)N(R<sup>8</sup>)<sub>2</sub>, -R<sup>9</sup>-N(R<sup>8</sup>)C(O)OR<sup>10</sup>, -R<sup>9</sup>-N(R<sup>8</sup>)C(O)R<sup>10</sup>, -R<sup>9</sup>-N(R<sup>8</sup>)(S(O)<sub>t</sub>R<sup>10</sup>) (where t is 1 or 2),  
30 -R<sup>9</sup>-S(O)<sub>t</sub>OR<sup>10</sup> (where t is 1 or 2), -R<sup>9</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), and -R<sup>9</sup>-S(O)<sub>t</sub>N(R<sup>8</sup>)<sub>2</sub> (where t is 1 or 2); each R<sup>4</sup> is independently hydrogen, alkyl, alkenyl, halo, haloalkyl, aryl, cyano, nitro, -R<sup>9</sup>-OR<sup>8</sup>, -R<sup>9</sup>-N(R<sup>8</sup>)<sub>2</sub> or -S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2); each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl; or one R<sup>5</sup> and one R<sup>6</sup> may together form an straight or branched alkylene bridge; each  
35 R<sup>7</sup> is independently a straight or branched alkylene or alkenylene chain; each R<sup>8</sup> is

independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocylylalkyl, heteroaryl or heteroarylalkyl; each  $R^9$  is independently a direct bond or a straight or branched alkylene or alkenylene chain; and  $R^{10}$  is alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocylylalkyl, heteroaryl or heteroarylalkyl.

Of this group of embodiments, a subgroup of embodiments is directed to the compounds wherein  $R^3$  is cyclopropyl substituted by optionally substituted aryl or optionally substituted heteroaryl.

Of this subgroup of embodiments, a class of embodiments is directed to the compounds wherein  $m$  is 1 or 2;  $n$  is 1 or 2;  $p$  is 2;  $V$  is  $-C(O)-$ ;  $R^1$  is hydrogen or alkyl;  $R^2$  is selected from the group consisting of hydrogen,  $-R^7-OR^8$ ,  $-R^7-N(R^8)_2$ ,  $-R^7-S(O)_tR^{10}$  (where  $t$  is 0, 1 or 2), alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl; each  $R^4$  is independently hydrogen, alkyl, alkenyl, halo, haloalkyl, aryl or  $-R^9-OR^8$ ; each  $R^5$  and  $R^6$  is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl; each  $R^7$  is independently a straight or branched alkylene or alkenylene chain; each  $R^8$  is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocylylalkyl, heteroaryl or heteroarylalkyl;  $R^9$  is a direct bond or a straight or branched alkylene chain; and  $R^{10}$  is alkyl, aryl or aralkyl.

Of this class of embodiments, a subclass of embodiments is directed to the compounds wherein  $m$  is 1 or 2;  $n$  is 1 or 2;  $p$  is 2;  $V$  is  $-C(O)-$ ;  $R^1$  is hydrogen or alkyl;  $R^2$  is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl; each  $R^4$  is independently hydrogen, alkyl, halo, or haloalkyl; and each  $R^5$  and  $R^6$  is independently hydrogen, oxo, alkyl, halo or haloalkyl.

Of this subclass of embodiments, a set of embodiments is directed to the compounds wherein  $m$  is 1;  $n$  is 1;  $p$  is 2;  $V$  is  $-C(O)-$ ;  $R^1$  is hydrogen or alkyl;  $R^2$  is optionally substituted aralkyl, optionally substituted heteroarylalkyl, or optionally substituted heterocyclylalkyl;  $R^3$  is cyclopropyl substituted by phenyl;  $R^4$  is hydrogen,

alkyl, halo or haloalkyl; R<sup>5</sup> is hydrogen, oxo, alkyl, halo or haloalkyl; and each R<sup>6</sup> is hydrogen.

Of the class of embodiments set forth above, another subclass of embodiments is directed to the compounds wherein m is 1 or 2; n is 1 or 2; p is 2; V is -C(O)-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl or optionally substituted cycloalkylalkenyl; each R<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl; each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl; each R<sup>7</sup> is a straight or branched alkylene chain; each R<sup>8</sup> is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl and aralkyl; and R<sup>10</sup> is alkyl, aryl or aralkyl.

Of this subclass of embodiments, a set of embodiments is directed to the compounds wherein m is 1; n is 1; p is 2; V is -C(O)-; R<sup>1</sup> is hydrogen or alkyl; R<sup>2</sup> is selected from the group consisting of alkyl, -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, or -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0); R<sup>3</sup> is cyclopropyl substituted by phenyl; R<sup>4</sup> is hydrogen; R<sup>5</sup> is hydrogen; each R<sup>6</sup> is hydrogen; R<sup>7</sup> is a straight or branched alkylene chain; R<sup>8</sup> is hydrogen or alkyl; and R<sup>10</sup> is alkyl, aryl or aralkyl.

Of the compounds described above, the most preferred are selected from the group consisting of the following:

6-[4-(2-Phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-N-(3-phenyl-propyl)-nicotinamide;

N-(4-Phenyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

N-(1-Methyl-3-phenyl-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

N-Phenethyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2-Phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-N-(tetrahydro-furan-2-ylmethyl)-nicotinamide;

N-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

N-(3-Imidazol-1-yl-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

N-(3-Ethoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

*N*-(2-Ethylsulfanyl-ethyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

*N*-(1,3-Dimethylbutyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

5 *N*-(3-Methyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Methoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

10 *N*-(3-Butoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

*N*-Pentyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Dimethylamino-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

15 *N*-(3-Isopropoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide

*N*-(1-Methyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

*N*-Butyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

*N*-Hexyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

20 and

*N*-(2-Methyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide. In addition to the foregoing compounds, other specific embodiments of the invention are set below in Example 10.

25 In another embodiment, the methods of the invention are directed towards the treatment and/or prevention of diseases mediated by stearoyl-CoA desaturase (SCD), especially human SCD (hSCD), preferably diseases related to dyslipidemia and disorders of lipid metabolism, and especially a disease related to elevated plasma lipid levels, cardiovascular disease, diabetes, obesity, metabolic syndrome and the like by administering an effective amount of an agent of the invention.

### 30 Utility and Testing of the Compounds of the Invention

The present invention relates to compounds, pharmaceutical compositions and methods of using the compounds and pharmaceutical compositions for the treatment and/or prevention of diseases mediated by stearoyl-CoA desaturase (SCD), especially human SCD (hSCD), preferably diseases related to dyslipidemia and disorders of lipid

metabolism, and especially a disease related to elevated plasma lipid levels, especially cardiovascular disease, diabetes, obesity, metabolic syndrome and the like, by administering to a patient in need of such treatment an effective amount of an SCD-modulating, especially inhibiting, agent.

5           In general, the present invention provides a method for treating a patient for, or protecting a patient from developing, a disease related to dyslipidemia and/or a disorder of lipid metabolism, wherein lipid levels in an animal, especially a human being, are outside the normal range (*i.e.*, abnormal lipid level, such as elevated plasma lipid levels), especially levels higher than normal, preferably where said lipid is a fatty  
10   acid, such as a free or complexed fatty acid, triglycerides, phospholipids, or cholesterol, such as where LDL-cholesterol levels are elevated or HDL-cholesterol levels are reduced, or any combination of these, where said lipid-related condition or disease is an SCD-mediated disease or condition, comprising administering to an animal, such as a mammal, especially a human patient, a therapeutically effective  
15   amount of a compound of formula (I) or a pharmaceutical composition comprising a compound of formula (I) wherein the compound modulates the activity of SCD, preferably human SCD1.

          All of these compounds modulate, preferably inhibit, the activity of human SCD enzymes, especially human SCD1.

20           The general value of the compounds of the invention in modulating, especially inhibiting, the activity of SCD is demonstrated by the data of Table 3 in Example 10 below, wherein the ability of a sample of such compounds to inhibit SCD biological activity is disclosed. Alternatively, the general value of the compounds in treating disorders and diseases may be established in industry standard animal models for  
25   demonstrating the efficacy of compounds in treating obesity, diabetes or elevated triglyceride or cholesterol levels or for improving glucose tolerance. Such models include Zucker obese *fa/fa* rats (available from Harlan Sprague Dawley, Inc. (Indianapolis, Indiana)), or the Zucker diabetic fatty rat (*ZDF/GmiCrI-fa/fa*) (available from Charles River Laboratories (Montréal, Quebec)).

30           The present invention also relates to pharmaceutical composition containing the novel compounds disclosed herein. In one embodiment, the present invention relates to a composition comprising compounds of the invention in a pharmaceutically acceptable carrier and in an amount effective to modulate triglyceride level or to treat diseases related to dyslipidemia and disorders of lipid metabolism, when administered  
35   to an animal, preferably a mammal, most preferably a human patient. In an

embodiment of such composition, the patient has an elevated lipid level, such as elevated triglycerides or cholesterol, before administration of said compound of the invention and the compound of the invention is present in an amount effective to reduce said lipid level.

5           The compounds of the instant invention are inhibitors of delta-9 desaturases and are useful for treating diseases and disorders in humans and other organisms, including all those human diseases and disorders which are the result of aberrant delta-9 desaturase biological activity or which may be ameliorated by modulation of delta-9 desaturase biological activity.

10           As defined herein, an SCD-mediated disease or condition includes but is not limited to a disease or condition which is, or is related to, cardiovascular disease, dyslipidemias (including but not limited to disorders of serum levels of triglycerides, hypertriglyceridemia, VLDL, HDL, LDL, fatty acid Desaturation Index (e.g. the ratio of 18:1/18:0 fatty acids, or other fatty acids, as defined elsewhere herein), cholesterol, 15 and total cholesterol, hypercholesterolemia, as well as cholesterol disorders (including disorders characterized by defective reverse cholesterol transport), familial combined hyperlipidemia, coronary artery disease, atherosclerosis, heart disease, cerebrovascular disease (including but not limited to stroke, ischemic stroke and transient ischemic attack (TIA)), peripheral vascular disease, and ischemic retinopathy.

20           In a preferred embodiment, compounds of the invention will, in a patient, increase HDL levels and/or decrease triglyceride levels and/or decrease LDL or non-HDL-cholesterol levels.

          An SCD-mediated disease or condition also includes metabolic syndrome (including but not limited to dyslipidemia, obesity and insulin resistance, hypertension, 25 microalbuminemia, hyperuricaemia, and hypercoagulability), Syndrome X, diabetes, insulin resistance, decreased glucose tolerance, non-insulin-dependent diabetes mellitus, Type II diabetes, Type I diabetes, diabetic complications, body weight disorders (including but not limited to obesity, overweight, cachexia and anorexia), weight loss, body mass index and leptin related diseases. In a preferred 30 embodiment, compounds of the invention will be used to treat diabetes mellitus and obesity.

          As used herein, the term "metabolic syndrome" is a recognized clinical term used to describe a condition comprising combinations of Type II diabetes, impaired glucose tolerance, insulin resistance, hypertension, obesity, increased abdominal girth, 35 hypertriglyceridemia, low HDL, hyperuricaemia, hypercoagulability and/or

microalbuminemia.

An SCD-mediated disease or condition also includes fatty liver, hepatic steatosis, hepatitis, non-alcoholic hepatitis, non-alcoholic steatohepatitis (NASH), alcoholic hepatitis, acute fatty liver, fatty liver of pregnancy, drug-induced hepatitis, erythrohepatic protoporphyria, iron overload disorders, hereditary hemochromatosis, hepatic fibrosis, hepatic cirrhosis, hepatoma and conditions related thereto.

An SCD-mediated disease or condition also includes but is not limited to a disease or condition which is, or is related to primary hypertriglyceridemia, or hypertriglyceridemia secondary to another disorder or disease, such as hyperlipoproteinemias, familial histiocytic reticulosis, lipoprotein lipase deficiency, apolipoprotein deficiency (such as ApoCII deficiency or ApoE deficiency), and the like, or hypertriglyceridemia of unknown or unspecified etiology.

An SCD-mediated disease or condition also includes a disorder of polyunsaturated fatty acid (PUFA) disorder, or a skin disorder, including but not limited to eczema, acne, psoriasis, keloid scar formation or prevention, diseases related to production or secretions from mucous membranes, such as monounsaturated fatty acids, wax esters, and the like.

An SCD-mediated disease or condition also includes inflammation, sinusitis, asthma, pancreatitis, osteoarthritis, rheumatoid arthritis, cystic fibrosis, and pre-menstrual syndrome.

An SCD-mediated disease or condition also includes but is not limited to a disease or condition which is, or is related to cancer, neoplasia, malignancy, metastases, tumours (benign or malignant), carcinogenesis, hepatomas and the like.

An SCD-mediated disease or condition also includes a condition where increasing lean body mass or lean muscle mass is desired, such as is desirable in enhancing performance through muscle building. Myopathies and lipid myopathies such as carnitine palmitoyltransferase deficiency (CPT I or CPT II) are also included herein. Such treatments are useful in humans and in animal husbandry, including for administration to bovine, porcine or avian domestic animals or any other animal to reduce triglyceride production and/or provide leaner meat products and/or healthier animals.

An SCD-mediated disease or condition also includes a disease or condition which is, or is related to, neurological diseases, psychiatric disorders, multiple sclerosis, eye diseases, and immune disorders.

An SCD-mediated disease or condition also includes a disease or condition

which is, or is related to, viral diseases or infections including but not limited to all positive strand RNA viruses, coronaviruses, SARS virus, SARS-associated coronavirus, Togaviruses, Picornaviruses, Coxsackievirus, Yellow Fever virus, Flaviviridae, ALPHAVIRUS (TOGAVIRIDAE) including Rubella virus, Eastern equine encephalitis virus, Western equine encephalitis virus, Venezuelan equine encephalitis virus, Sindbis virus, Semliki forest virus, Chikungunya virus, O'nyong'nyong virus, Ross river virus, Mayaro virus, Alphaviruses; ASTROVIRIDAE including Astrovirus, Human Astroviruses; CALICIVIRIDAE including Vesicular exanthema of swine virus, Norwalk virus, Calicivirus, Bovine calicivirus, Pig calcivirus, Hepatitis E; CORONAVIRIDAE including Coronavirus, SARS virus, Avian infectious bronchitis virus, Bovine coronavirus, Canine coronavirus, Feline infectious peritonitis virus, Human coronavirus 299E, Human coronavirus OC43, Murine hepatitis virus, Porcine epidemic diarrhea virus, Porcine hemagglutinating encephalomyelitis virus, Porcine transmissible gastroenteritis virus, Rat coronavirus, Turkey coronavirus, Rabbit coronavirus, Berne virus, Breda virus; FLAVIVIRIDAE including Hepatitis C virus, West Nile virus, Yellow Fever virus, St. Louis encephalitis virus, Dengue Group, Hepatitis G virus, Japanese B encephalitis virus, Murray Valley encephalitis virus, Central European tick-borne encephalitis virus, Far Eastern tick-borne encephalitis virus, Kyasanur forest virus, Louping ill virus, Powassan virus, Omsk hemorrhagic fever virus, Kumilinge virus, Absetarov anzalova hypr virus, Ilheus virus, Rocio encephalitis virus, Langat virus, Pestivirus, Bovine viral diarrhea, Hog cholera virus, Rio Bravo Group, Tyuleniy Group, Ntaya Group, Uganda S Group, Modoc Group; PICORNAVIRIDAE including Coxsackie A virus, Rhinovirus, Hepatitis A virus, Encephalomyocarditis virus, Mengovirus, ME virus, Human poliovirus 1, Coxsackie B; POTYVIRIDAE including Potyvirus, Rymovirus, Bymovirus. Additionally it can be a disease or infection caused by or linked to Hepatitis viruses, Hepatitis B virus, Hepatitis C virus, human immunodeficiency virus (HIV) and the like. Treatable viral infections include those where the virus employs an RNA intermediate as part of the replicative cycle (hepatitis or HIV); additionally it can be a disease or infection caused by or linked to RNA negative strand viruses such as influenza and parainfluenza viruses.

The compounds identified in the instant specification inhibit the desaturation of various fatty acids (such as the C9-C10 desaturation of stearoyl-CoA) which is accomplished by delta-9 desaturases, such as stearoyl-CoA desaturase 1 (SCD1). As such these compounds inhibit the formation of various fatty acids and downstream metabolites thereof. This may lead to an accumulation of stearoyl-CoA or palmitoyl-



CoA and other upstream precursors of various fatty acids; which may possibly result in a negative feedback loop causing an overall change in fatty acid metabolism. Any of these consequences may ultimately be responsible for the overall therapeutic benefit provided by these compounds.

5           Typically, a successful SCD inhibitory therapeutic agent will meet some or all of the following criteria. Oral availability should be at or above 20%. Animal model efficacy is less than about 2 mg/Kg, 1 mg/Kg, or 0.5 mg/Kg and the target human dose is between 50 and 250 mg/70 Kg, although doses outside of this range may be acceptable. ("mg/Kg" means milligrams of compound per kilogram of body mass of the  
10           subject to whom it is being administered). The therapeutic index (or ratio of toxic dose to therapeutic dose) should be greater than 100. The potency (as expressed by IC<sub>50</sub> value) should be less than 10 μM, preferably below 1 μM and most preferably below 50 nM. The IC<sub>50</sub> ("Inhibitory Concentration – 50%") is a measure of the amount of compound required to achieve 50% inhibition of SCD activity, over a specific time  
15           period, in an SCD biological activity assay. Any process for measuring the activity of SCD enzymes, preferably mouse or human SCD enzymes, may be utilized to assay the activity of the compounds useful in the methods of the invention in inhibiting said SCD activity. Compounds of the invention demonstrate an IC<sub>50</sub> in a 15 minute  
20           microsomal assay of preferably less than 10 μM, less than 5 μM, less than 2.5 μM, less than 1 μM, less than 750 nM, less than 500 nM, less than 250 nM, less than 100 nM, less than 50 nM, and most preferably less than 20 nM. The compound of the invention may show reversible inhibition (*i.e.*, competitive inhibition) and preferably does not inhibit other iron binding proteins. The required dosage should preferably be no more than about once or twice a day or at meal times.

25           The identification of compounds of the invention as SCD inhibitors was readily accomplished using the SCD enzyme and microsomal assay procedure described in Brownlie et al, *supra*.

            Data showing inhibition of SCD by compounds of the invention as tested in this assay are presented in Table 3 in Example 10 below. In particular, Table 3 sets forth  
30           the % remaining SCD activity at 10 μM of of a compound of the invention in the indicated assay.

            These results provide the basis for analysis of the structure-activity relationship (SAR) between test compounds and SCD. Certain R groups tend to provide more potent inhibitory compounds. SAR analysis is one of the tools those skilled in the art

may now employ to identify preferred embodiments of the compounds of the invention for use as therapeutic agents.

Other methods of testing the compounds disclosed herein are also readily available to those skilled in the art. Thus, in addition, said contacting may be accomplished *in vivo*. In one such embodiment, said contacting in step (a) is accomplished by administering said chemical agent to an animal afflicted with a triglyceride (TG)- or very low density lipoprotein (VLDL)-related disorder and subsequently detecting a change in plasma triglyceride level in said animal thereby identifying a therapeutic agent useful in treating a triglyceride (TG)- or very low density lipoprotein (VLDL)-related disorder. In such embodiment, the animal may be a human, such as a human patient afflicted with such a disorder and in need of treatment of said disorder.

In specific embodiments of such *in vivo* processes, said change in SCD1 activity in said animal is a decrease in activity, preferably wherein said SCD1 modulating agent does not substantially inhibit the biological activity of a delta-5 desaturase, delta-6 desaturase or fatty acid synthetase.

The model systems useful for compound evaluation may include, but are not limited to, the use of liver microsomes, such as from mice that have been maintained on a high carbohydrate diet, or from human donors, including persons suffering from obesity. Immortalized cell lines, such as HepG2 (from human liver), MCF-7 (from human breast cancer) and 3T3-L1 (from mouse adipocytes) may also be used. Primary cell lines, such as mouse primary hepatocytes, are also useful in testing the compounds of the invention. Where whole animals are used, mice used as a source of primary hepatocyte cells may also be used wherein the mice have been maintained on a high carbohydrate diet to increase SCD activity in microsomes and/or to elevate plasma triglyceride levels (i.e., the 18:1/18:0 ratio); alternatively mice on a normal diet or mice with normal triglyceride levels may be used. Mouse models employing transgenic mice designed for hypertriglyceridemia are also available as is the mouse phenome database. Rabbits and hamsters are also useful as animal models, especially those expressing CETP (cholesterol ester transfer protein).

Another suitable method for determining the *in vivo* efficacy of the compounds of the invention is to indirectly measure their impact on inhibition of SCD enzyme by measuring a subject's Desaturation Index after administration of the compound. "Desaturation Index" as employed in this specification means the ratio of the product over the substrate for the SCD enzyme as measured from a given tissue sample. This

may be calculated using three different equations 18:1n-9/18:0 (oleic acid over stearic acid); 16:1n-7/16:0 (palmitoleic acid over palmitic acid); and/or 16:1n-7 + 18:1n-7/16:0 (measuring all reaction products of 16:0 desaturation over 16:0 substrate).

Desaturation Index is primarily measured in liver or plasma triglycerides, but may also  
5 be measured in other selected lipid fractions from a variety of tissues. Desaturation Index, generally speaking, is a tool for plasma lipid profiling.

A number of human diseases and disorders are the result of aberrant SCD1 biological activity and may be ameliorated by modulation of SCD1 biological activity using the therapeutic agents of the invention.

10 Inhibition of SCD expression may also affect the fatty acid composition of membrane phospholipids, as well as production or levels of triglycerides and cholesterol esters. The fatty acid composition of phospholipids ultimately determines membrane fluidity, while the effects on the composition of triglycerides and cholesterol esters can affect lipoprotein metabolism and adiposity.

15 In carrying out the procedures of the present invention it is of course to be understood that reference to particular buffers, media, reagents, cells, culture conditions and the like are not intended to be limiting, but are to be read so as to include all related materials that one of ordinary skill in the art would recognize as being of interest or value in the particular context in which that discussion is presented.  
20 For example, it is often possible to substitute one buffer system or culture medium for another and still achieve similar, if not identical, results. Those of skill in the art will have sufficient knowledge of such systems and methodologies so as to be able, without undue experimentation, to make such substitutions as will optimally serve their purposes in using the methods and procedures disclosed herein.

## 25 Pharmaceutical Compositions of the Invention and Administration

The present invention also relates to pharmaceutical composition containing the compounds of the invention disclosed herein. In one embodiment, the present invention relates to a composition comprising compounds of the invention in a pharmaceutically acceptable carrier and in an amount effective to modulate triglyceride  
30 level or to treat diseases related to dyslipidemia and disorders of lipid metabolism, when administered to an animal, preferably a mammal, most preferably a human patient. In an embodiment of such composition, the patient has an elevated lipid level, such as elevated triglycerides or cholesterol, before administration of said compound of the invention and the compound of the invention is present in an amount effective to

reduce said lipid level.

The pharmaceutical compositions useful herein also contain a pharmaceutically acceptable carrier, including any suitable diluent or excipient, which includes any pharmaceutical agent that does not itself induce the production of antibodies harmful to the individual receiving the composition, and which may be administered without undue toxicity. Pharmaceutically acceptable carriers include, but are not limited to, liquids, such as water, saline, glycerol and ethanol, and the like. A thorough discussion of pharmaceutically acceptable carriers, diluents, and other excipients is presented in REMINGTON'S PHARMACEUTICAL SCIENCES (Mack Pub. Co., N.J. current edition).

Those skilled in the art know how to determine suitable doses of the compounds for use in treating the diseases and disorders contemplated herein. Therapeutic doses are generally identified through a dose ranging study in humans based on preliminary evidence derived from animal studies. Doses must be sufficient to result in a desired therapeutic benefit without causing unwanted side-effects for the patient. The preferred dosage range for an animal is 0.001 mg/Kg to 10,000 mg/Kg, including 0.5 mg/Kg, 1.0 mg/Kg and 2.0 mg/Kg, though doses outside this range may be acceptable. The dosing schedule may be once or twice per day, although more often or less often may be satisfactory.

Those skilled in the art are also familiar with determining administration methods (oral, intravenous, inhalation, sub-cutaneous, etc.), dosage forms, suitable pharmaceutical excipients and other matters relevant to the delivery of the compounds to a subject in need thereof.

In an alternative use of the invention, the compounds of the invention can be used in *in vitro* or *in vivo* studies as exemplary agents for comparative purposes to find other compounds also useful in treatment of, or protection from, the various diseases disclosed herein.

#### Preparation of the Compounds of Formula (I)

It is understood that in the following description, combinations of substituents and/or variables of the depicted formulae are permissible only if such contributions result in stable compounds.

It will also be appreciated by those skilled in the art that in the process described below the functional groups of intermediate compounds may need to be protected by suitable protecting groups. Such functional groups include hydroxy,

amino, mercapto and carboxylic acid. Suitable protecting groups for hydroxy include trialkylsilyl or diarylalkylsilyl (e.g., *t*-butyldimethylsilyl, *t*-butyldiphenylsilyl or trimethylsilyl), tetrahydropyranyl, benzyl, and the like. Suitable protecting groups for amino, amidino and guanidino include *t*-butoxycarbonyl, benzyloxycarbonyl, and the like. Suitable protecting groups for mercapto include -C(O)-R" (where R" is alkyl, aryl or arylalkyl), *p*-methoxybenzyl, trityl and the like. Suitable protecting groups for carboxylic acid include alkyl, aryl or arylalkyl esters.

Protecting groups may be added or removed in accordance with standard techniques, which are well-known to those skilled in the art and as described herein.

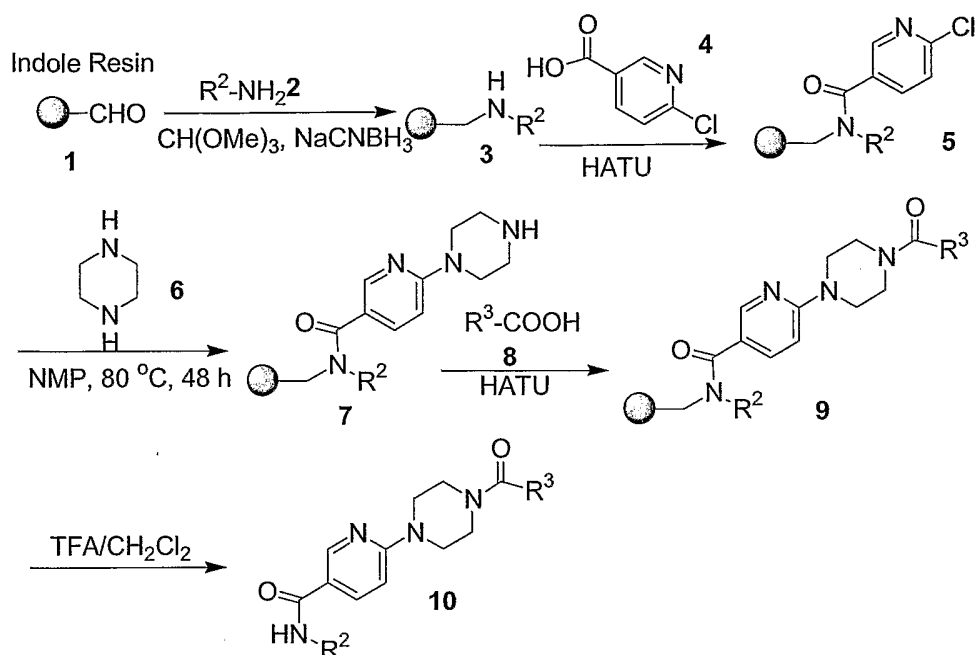
10 The use of protecting groups is described in detail in Green, T.W. and P.G.M. Wutz, *Protective Groups in Organic Synthesis* (1999), 3rd Ed., Wiley. The protecting group may also be a polymer resin such as a Wang resin or a 2-chlorotrityl-chloride resin.

15 It will also be appreciated by those skilled in the art, although such protected derivatives of compounds of this invention may not possess pharmacological activity as such, they may be administered to a mammal and thereafter metabolized in the body to form compounds of the invention which are pharmacologically active. Such derivatives may therefore be described as "prodrugs". All prodrugs of compounds of this invention are included within the scope of the invention.

20 The following Reaction Schemes illustrate methods to make compounds of this invention. The various R groups in the Reaction Schemes have the same meaning as described above in the Summary of the Invention unless otherwise noted. It is understood that one of those skilled in the art would be able to make these compounds by similar methods or by methods known to one skilled in the art. In general, starting components may be obtained from sources such as Sigma Aldrich, Lancaster  
25 Synthesis, Inc., Maybridge, Matrix Scientific, TCI, and Fluorochem USA, etc. or synthesized according to sources known to those skilled in the art (see, e.g., *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 5th edition (Wiley, December 2000)) or prepared as described in this invention.

30 The following Reaction Scheme 1 illustrates a method of preparing the compounds of the invention by solid phase technology.

## REACTION SCHEME 1 - Solid Phase Approach

5 Experimental Procedures - Solid Phase Approach

A preferred synthetic scheme employs solid phase synthesis using Kan™ reactors. Kan™ reactors are rigid containers with mesh side walls. A single compound is synthesized in each one, and each one contains a unique, miniature radiofrequency label along with the actual solid phase resin.

10 Kan reactors are designed to be loaded with solid phase resin beads and an Rf tag. The synthesis takes place by allowing reagents to flow through the outer mesh walls of the Kan. Syntheses are performed using normal laboratory glassware and apparatus for heating, cooling, mixing, etc.

15 There are 3 sizes of Kan reactors available which may be used interchangeably with the AccuTag system - MicroKans, MiniKans, and MacroKans. Typically about 30-300 mg of most commercial resins are loaded into a Kan leaving enough space available for the resin to swell and still remain loose within the Kan.

20 Synthesis takes place by the flow of reagents through the mesh walls of the Kan. The Kan reactors permit virtually any synthetic chemistry which can be performed using loose solid phase resin and conventional laboratory glassware to be done using the AccuTag system.

The Kan is made of high-grade polypropylene with a polypropylene mesh side

wall. The Kan is filled with the solid phase resin and the radiofrequency tag before being used in the synthesis. The appropriate Kan size can be selected by one skilled in the art familiar with the Kan technology.

Further information on the Irori Kan technology can be obtained from Discovery  
5 Partners, Inc., at [www.discoverypartners.com](http://www.discoverypartners.com).

All of the reagents, amines and carboxylic acids necessary to carry out the syntheses described below are commercially available from widely available sources.

Kans **1** (12 Kans) containing indole resin (90 mg per Kan, 0.9 mmol/g) were suspended in anhydrous trimethylorthoformate (40 mL). The amine **2** (10 mmol, 10  
10 eq) was added, and the reaction was shaken at ambient temperature for 16 hours. Sodium cyanoborohydride (1.3 g, 20 eq) was added and the reaction was shaken at ambient temperature for 1 hour. Aqueous acetic acid (3.2 mL, 8% v/v) was slowly added and the reaction was shaken at ambient temperature for 3 h. The MiniKans **3** were washed alternately with MeOH and DCM for four cycles and dried under vacuum.

15 Kans containing **3** from seven reactions (total 84 MiniKans) were suspended in anhydrous DMF (250 mL). 6-Chloronicotinic acid (11.2 g, 10 eq), diisopropylethylamine (25 mL, 20 eq) and HATU (26.2 g, 10 eq) were added and the reaction was shaken at ambient temperature for 24 hours. The Kans **5** were washed alternately with MeOH and DCM for four cycles and dried under vacuum.

20 The Kans containing **5** were suspended in anhydrous *N*-methylpyrrolidinone (250 mL). Piperazine **6** (12.0 g, 20 eq) and diisopropylethylamine (49 mL, 40 eq) were added and the reaction mixture was heated at 80°C for 48 h. The MiniKans containing **7** were washed alternately with MeOH and DCM for 4 cycles and dried under vacuum.

After sorting, Kans containing **7** (12 Kans) were suspended in anhydrous DMF  
25 (40 mL). The carboxylic acid **8** (10 mmol, 10 eq), diisopropylethylamine (3.5 mL, 20 eq) and HATU (3.8 g, 10 eq) were added and the reaction was shaken at ambient temperature for 24 hours. The Kans containing **9** were then washed alternately with MeOH and DCM for five cycles and dried under vacuum.

30 Kans containing **9** (3 Kans) were treated with 20 % TFA/DCM (9 mL) at ambient temperature for 2 hour. Pyridylpiperazine **10** was obtained and purified by HPLC.

This solid phase approach is used to prepare compounds of this invention. Examples of amine and carboxylic acids that can be used in this solid phase approach to produce compounds of the invention are set forth below in Tables 1 and 2.

35

TABLE 1. EXAMPLES OF AMINES

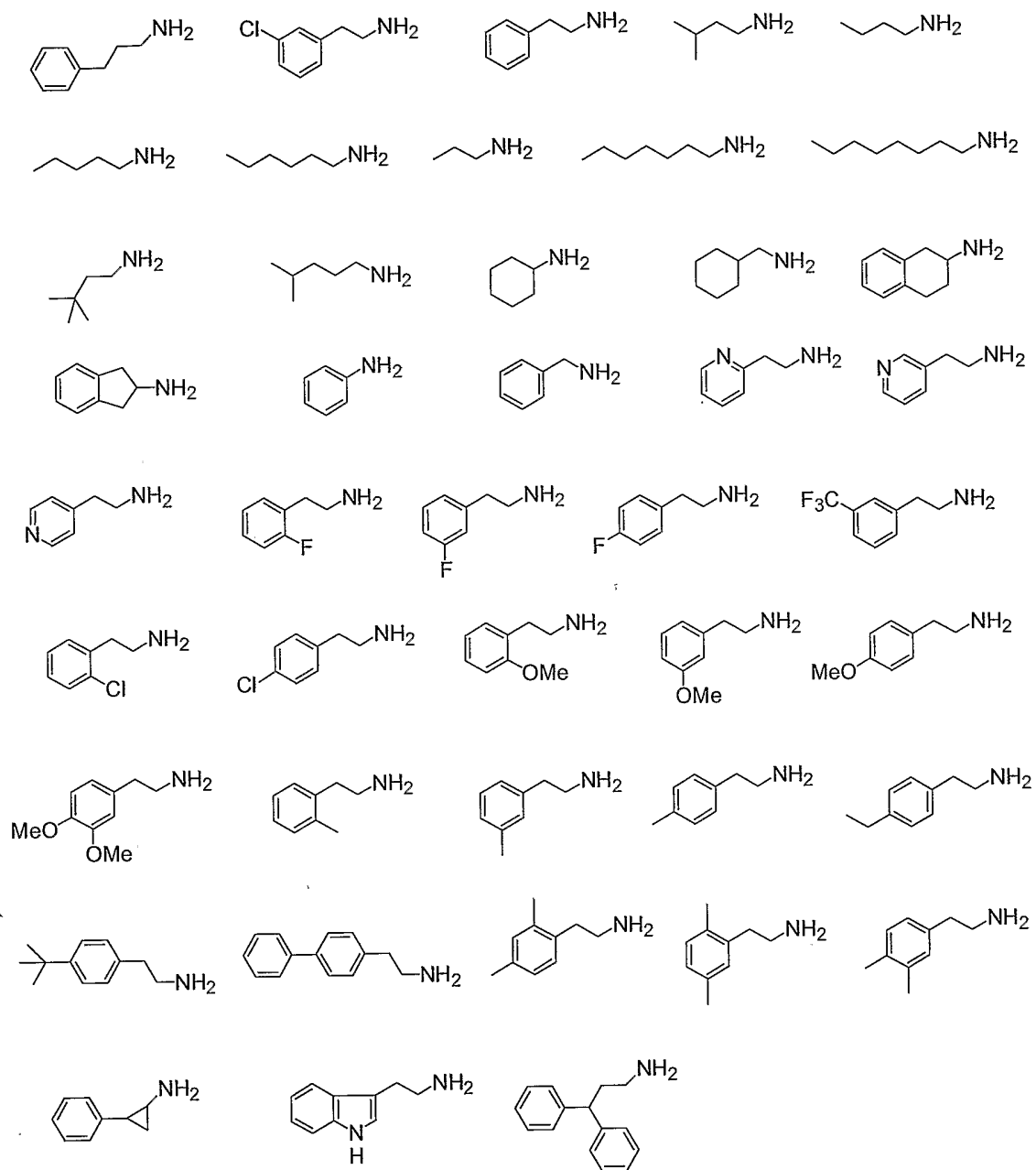
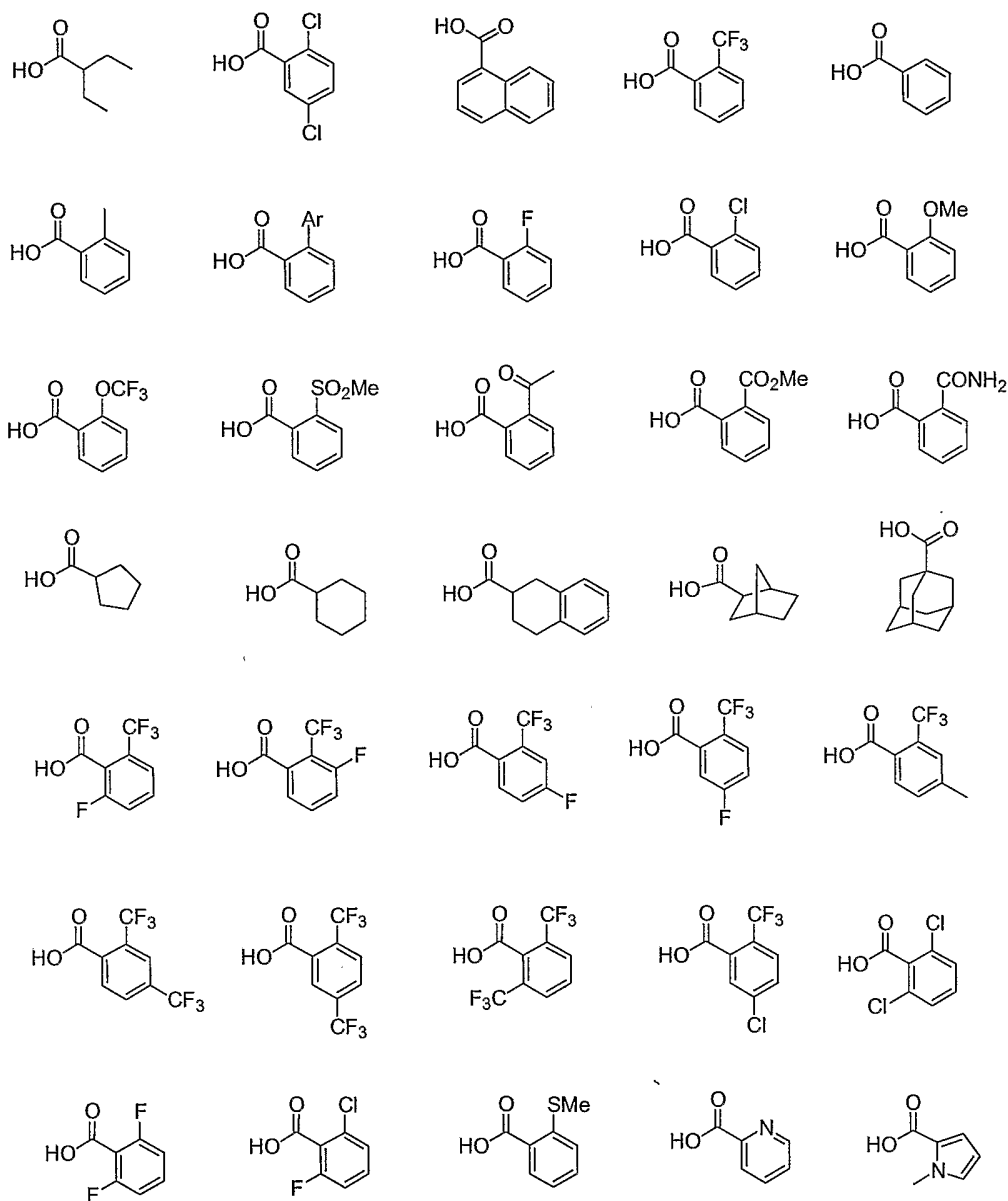




TABLE 2. EXAMPLES OF CARBOXYLIC ACIDS



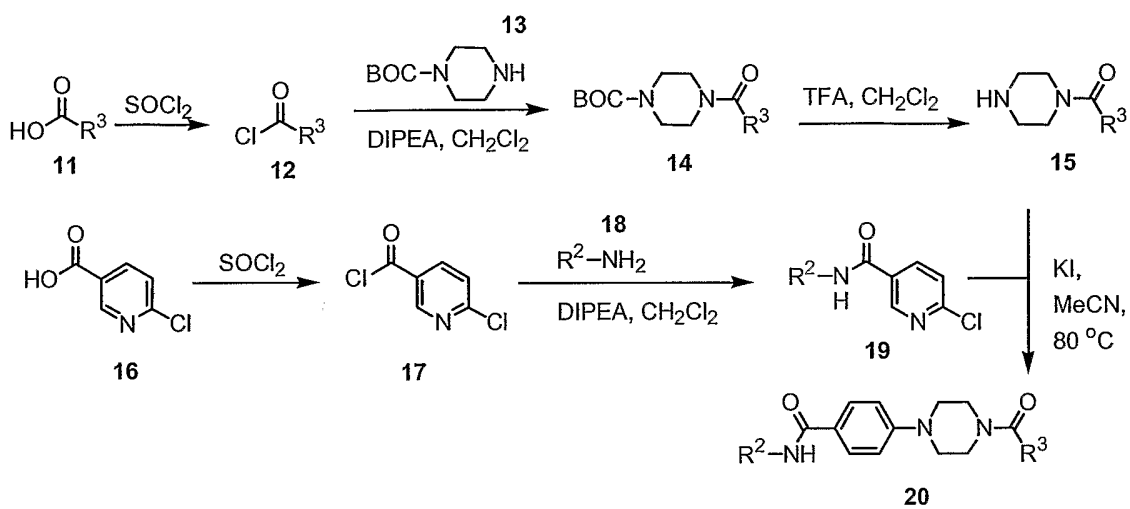
An alternative synthetic scheme for the preparation of the compounds of the  
5 invention, as set forth below in Reaction Scheme 2, includes a convergent solution-  
phase approach. For example, the acyl chloride **12** can be prepared from the  
corresponding acid **11** by reacting with thionyl chloride under conditions known to one  
skilled in the art or can be purchased from a commercial source, such as Aldrich  
Chemical Co. Reaction of **12** with piperazine **13** under conditions known to one skilled  
10 in the art generates the amide bond of **14**, in which the protecting group can be  
removed in an acidic media under conditions known to one skilled in the art, such as

trifluoroacetic acid in dichloromethane, to give compound **15**. On the other hand, 6-chloronicotinic acid (**16**) is converted to its chloride **17** under conditions known to one skilled in the art, which is then coupled with amine **18** to afford nicotinamide **19**.

Coupling of **15** with **19** under conditions known to one skilled in the art gives the final

5 product **20**.

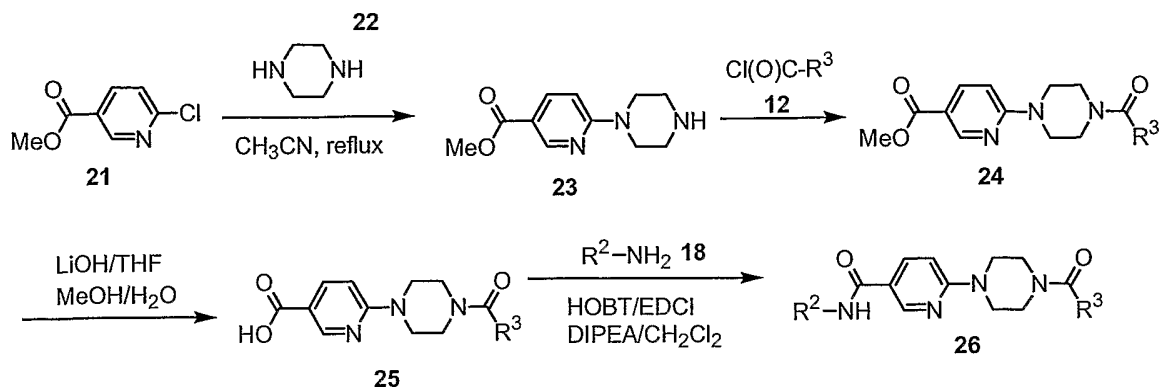
### REACTION SCHEME 2



10 Alternatively, the compounds of this invention can be prepared according to the synthetic approach set forth in Reaction Scheme 3 below. 6-Chloronicotinic methyl ester (**21**) couples with piperazine **22** under conditions known to one skilled in the art to give compound **23** followed by reaction with acyl chloride **12** under conditions known to one skilled in the art to generate compound **24**. Hydrolysis of methyl ester by using a

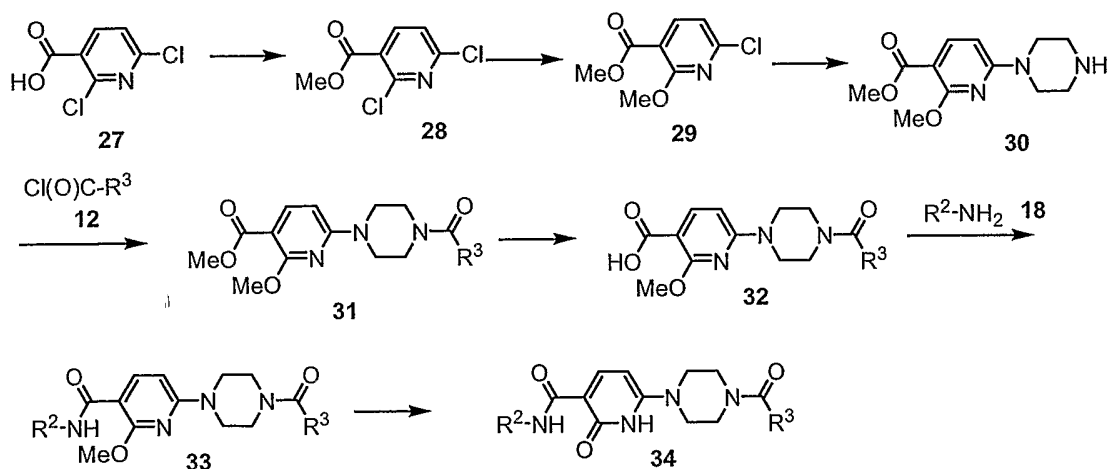
15 base under conditions known to one skilled in the art, such as lithium hydroxide, gives acid **25**, which can react with amine **18** under conditions known to one skilled in the art to afford the final product **26**.

## REACTION SCHEME 3



- Alternatively, compounds of the invention where  $\text{R}^4$  is  $-\text{OCH}_3$  or  $-\text{OH}$  can be prepared according to the synthetic approach set forth in Reaction Scheme 4 below.
- 5 2,6-Dichloronicotinic acid 27 is converted to its ester 28 under conditions known to one skilled in the art, in which the 2-position chloro group can then be substituted with a methoxy group under conditions known to one skilled in the art to generate compound 29. Coupling of 29 with piperazine under conditions known to one skilled in the art
- 10 gives compound 30, which can then react with acyl chloride 12 under conditions known to one skilled in the art to generate compound 31. After hydrolysis, acid 32 reacts with amine 18 under conditions known to one skilled in the art to produce nicotinamide 33. The methyl group in compound 33 can be removed by using a Lewis acid under conditions known to one skilled in the art, such as *in situ* generated trimethylsilyl iodide, to afford compound 34.
- 15

## REACTION SCHEME 4



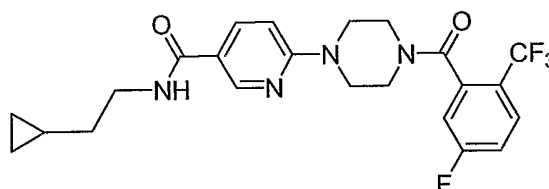
All reagents and reaction conditions employed in these syntheses are known to those skilled in the art and are available from ordinary commercial sources. Other compounds of the invention can be prepared according to the methods described above by one skilled in the art utilizing known starting materials and experimental parameters, or by the methods disclosed in the following experimentals. In addition, one skilled in the art can prepare the compounds of the invention by the methods disclosed in U.S. Patent No. 6,677,452, which is incorporated herein in full by reference.

All compounds of the invention as prepared above and below which exist in free base or acid form may be converted to their pharmaceutically acceptable salt by treatment with the appropriate inorganic or organic base or acid. Salts of the compounds prepared herein may be converted to their free base or acid by standard techniques.

The following specific examples are provided as a guide to assist in the practice of the invention and are not intended as a limitation on the scope of the invention.

#### EXAMPLE 1

*N*-(2-Cyclopropylethyl)-6-[4-(5-fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]nicotinamide



20

To a solution of 6-[4-(5-fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]nicotinic acid (0.100 g, 0.25 mmol), 1-hydroxy benzotriazole hydrate (0.041 g, 0.30 mmol) in dichloromethane (20 mL) were added 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide (0.047 g, 0.30 mmol) and ethyldiisobutylamine (0.065 g, 0.50 mmol). The resulted mixture was stirred for 15 minutes at ambient temperature, followed by the addition of a solution of 2-cyclopropylethyl amine (0.021 g, 0.25 mmol) in 5 mL of dichloromethane. The reaction mixture was stirred at ambient temperature for 24 hours, and then diluted with dichloromethane (50 mL). The organic phase was washed with water, followed by brine solution, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo* to generate a white solid. This was purified by column chromatography (2:1,

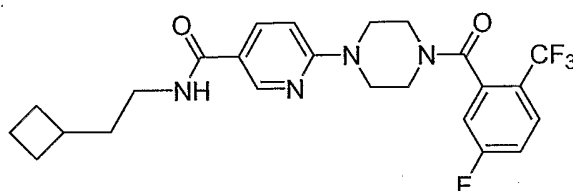
30

ethyl acetate: hexane) to obtain title compound as a white solid (0.087 g, 75% yield);  
<sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 8.52 (d, J = 2.4 Hz, 1H), 7.92 (dd, J = 2.4, 6.6 Hz, 1H),  
 7.72 (d, J = 7.8 Hz, 1H), 7.61-7.5 (m, 2H), 7.34 (d, J = 7.5 Hz, 1H), 6.62 (d, J = 9 Hz,  
 1H), 6.14 (t, J = 5.1 Hz, 1H), 3.98-3.92 (m, 1H), 3.87-3.78 (m, 1H), 3.75-3.66 (m, 2H),  
 5 3.6-3.47 (m, 4H), 3.29-3.25 (m, 2H), 1.52-1.45 (m, 2H), 0.72-0.65 (m, 1H), 0.49-0.43  
 (m, 2H), 0.1-0.04 (m, 2H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 167.5, 165.7, 159.7, 147.1,  
 136.9, 134.4, 134.3, 132.3, 129.3, 127.4, 126.74, 126.68, 126.62, 120.0, 105.8, 46.5,  
 44.4, 41.3, 40.1, 34.3, 8.6, 4.1 (2 peaks). MS (ES+) *m/z* 447 (M+1).

10

## EXAMPLE 2

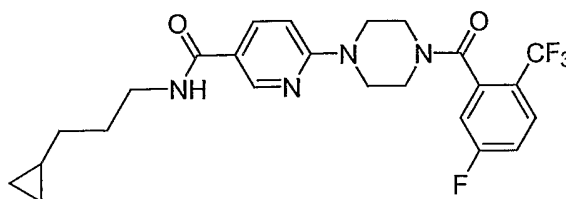
*N*-(2-Cyclobutylethyl)-6-[4-(5-fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]nicotinamide



Following the procedure set forth above in Example 1, the title compound was  
 15 obtained as a white solid (0.053g, 44% yield); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz): δ 8.51-8.50  
 (m, 1H), 7.94-7.90 (m, 1H), 7.75-7.7 (m, 1H), 7.21-7.19 (m, 1H), 7.07-7.04 (m, 1H),  
 6.63 (d, J = 9 Hz, 1H), 5.94 (t, J = 5.5 Hz, 1H), 3.96-3.89 (m, 1H), 3.87-3.77 (m, 1H),  
 3.75-3.68 (m, 2H), 3.65-3.58 (m, 2H), 3.37-3.27 (m, 4H), 2.38-2.28 (m, 1H), 2.12-1.98  
 (m, 2H), 1.94-1.73 (m, 3H), 1.7-1.58 (m, 3H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz): δ 165.9,  
 20 165.6, 162.5, 159.5, 146.9, 137.1, 136.95, 129.6, 129.5, 129.48, 129.42, 125.0, 121.4,  
 120.1, 116.7, 116.4, 114.9, 114.6, 105.99, 46.5, 44.5, 41.4, 38.2, 36.5, 33.85, 28.3,  
 18.7. MS (ES+): *m/z* 479.1 (M+1)

## EXAMPLE 3

*N*-(3-Cyclopropyl propyl)-6-[4-(5-fluoro-2-trifluoromethyl benzoyl)-piperazin-1-yl] nicotinamide

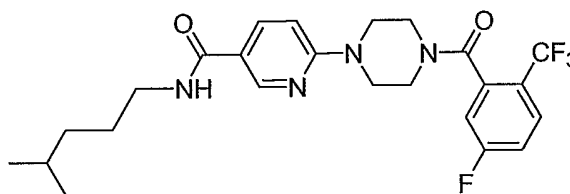


5 Following the procedure set forth above in Example 1, the title compound was obtained as a white solid (0.086 g, 77% yield); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 8.53 (s, 1H), 7.94-7.9 (m, 1H), 7.74-7.7 (m, 1H), 7.21-7.18 (m, 1H), 7.07-7.03 (m, 1H), 6.61 (d, J = 8.7 Hz, 1H), 6.18 (t, J = 5.4 Hz, 1H), 3.97-3.58 (m, 6H), 3.46-3.39 (m, 2H), 3.29-3.26 (m, 2H), 1.72-1.63 (m, 2H), 1.28-1.21 (m, 2H), 0.70-0.61 (m, 1H), 0.43-0.37 (m, 10 2H), 0.01-0.04 (m, 2H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 165.9, 165.7, 162.4, 159.5, 147.2, 136.9, 129.5, 129.5, 129.4, 129.35, 128.6, 124.95, 123.1, 122.7, 121.3, 120.1, 116.6, 116.3, 114.8, 114.5, 105.8, 46.4, 44.3, 41.3, 39.6, 31.9, 29.5, 10.4, 4.4. MS (ES<sup>+</sup>) *m/z* 479.0 (M+1).

15

## EXAMPLE 4

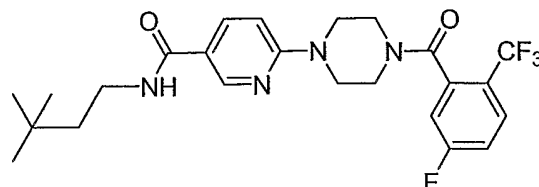
6-[4-(5-Fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]-*N*-(4-methylpentyl)-nicotinamide



Following the procedure set forth above in Example 1, the title compound was obtained as a white solid (0.075g, 66% yield); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 8.52 (s, 20 1H), 7.94-7.91 (m, 1H), 7.72-7.7 (m, 1H), 7.21-7.18 (m, 1H), 7.06-7.04 (m, 1H), 6.62 (d, J = 9 Hz, 1H), 6.02 (br. t, 1H), 3.98-3.55 (m, 6H), 3.43-3.34 (m, 2H), 3.3-3.26 (m, 2H), 1.62-1.48 (m, 3H), 1.25-1.18 (m, 2H), 0.86 (d, J = 6.6 Hz, 6H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 165.9, 165.7, 162.5, 159.5, 147.1, 137.02, 129.6, 129.5, 129.4, 129.38, 128.6, 127.6, 124.5, 122.7, 121.4, 120.1, 117.7, 116.6, 116.4, 114.8, 114.5, 105.8, 25 46.4, 44.4, 41.3, 40.1, 36.0, 27.7, 27.5, 22.4. MS (ES<sup>+</sup>): *m/z* 481.1 (M+1).

## EXAMPLE 5

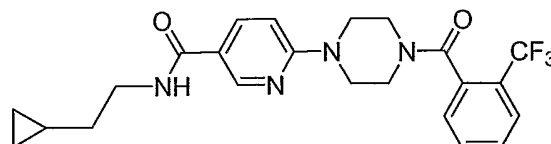
*N*-(3,3-Dimethylbutyl)-6-[4-(5-fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]-nicotinamide



- 5 Following the procedure set forth above in Example 1, the title compound was obtained as a white solid (0.085 g, 76% yield); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 8.52 (s, 1H), 7.93-7.89 (m, 1H), 7.75-7.7 (m, 1H), 7.24-7.18 (m, 1H), 7.06-7.03 (m, 1H), 6.61 (d, *J* = 9 Hz, 1H), 5.94 (br, 1H), 3.98-3.75 (m, 2H), 3.75-3.66 (m, 2H), 3.63-3.56 (m, 2H), 3.48-3.35 (m, 2H), 3.32-3.23 (m, 2H), 1.51-1.46 (m, 2H), 0.93 (s, 9H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 165.9, 165.6, 162.5, 159.5, 147.2, 136.9, 129.6, 129.5, 129.4, 129.37, 128.6, 124.96, 123.2, 122.3, 120.1, 116.6, 116.3, 114.8, 114.5, 105.8, 46.4, 44.3, 43.1, 41.3, 36.5, 29.8, 29.3. MS (ES<sup>+</sup>) *m/z* 481.0 (M+1),
- 10

## EXAMPLE 6

- 15 *N*-(2-Cyclopropylethyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide

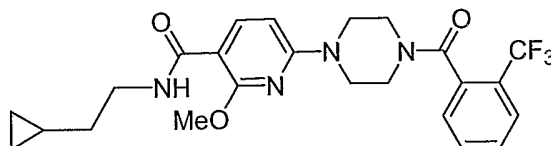


- A mixture of 6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinic acid (280 mg, 0.738 mmol), diisopropylethylamine (0.19 mL, 1.1 mmol), 1-hydroxybenzotriazole hydrate (130 mg, 0.96 mmol) and EDCI (0.19 mL, 1.1 mmol) in dichloromethane (5 mL) was stirred for 15 min, 2-cyclopropylethylamine (70 mg, 0.82 mmol) was added. After stirring for 10 h at ambient temperature, the reaction mixture was diluted with dichloromethane (50 mL), washed with water, saturated NaHCO<sub>3</sub> and brine, dried (anhydrous Na<sub>2</sub>SO<sub>4</sub>) and concentrated. Purification via flash chromatography over silica gel(ethyl acetate) afforded *N*-(2-cyclopropyl-ethyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide (264 mg, 80%). <sup>1</sup>H NMR:(400 MHz, CDCl<sub>3</sub>) δ: 8.52 (d, *J* = 1.9, 1H), 7.94 (dd, *J* = 1.9, 8.7 Hz, 1H), 7.73 (d, *J* = 9.2 Hz, 1H), 7.63 (t, *J* = 8.5 Hz, 1H), 7.56 (t, *J* = 8.5 Hz, 1H), 7.37 (d, *J* = 8.7 Hz, 1H), 6.62 (d, *J* = 9.2 Hz, 1H),
- 20
- 25

6.14 (br, 1H), 4.02-3.27 (m, 10H), 1.52(q,  $J = 6.7$  Hz, 2H), 0.78-0.70 (m, 1H), 0.53-0.48 (m, 2H), 0.13-0.08 (m, 2H). MS (ES+)  $m/z$  447.2 ( $M+1$ ).

## EXAMPLE 7

5 *N*-(2-cyclopropylethyl)-2-methoxy-6-(4-(2-trifluoromethylbenzoyl)piperazin-1-yl]nicotinamide



- A. To a solution of 2,6-dichloronicotinic acid (5.0 g, 26 mmol) in MeOH (100 mL) was added  $\text{SOCl}_2$  (0.1 mL). The reaction mixture was heated to reflux overnight. The solvent was removed by evaporation. The residue was dissolved in ethyl acetate and washed with saturated  $\text{NaHCO}_3$  and brine; dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated to afford 2,6-dichloronicotinic acid methyl ester (5.37 g, 100%);  $^1\text{H}$ NMR:(300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.13 (d,  $J = 8.1$  Hz, 1H), 7.33 (d,  $J = 8.1$  Hz, 1H), 3.94 (s, 3H).
- 10
- B. A solution of 2,6-dichloronicotinic acid methyl ester (2.39 g, 11.6 mmol) and NaOMe (800 mg, 14.06 mmol) in THF (15 mL) was stirred at ambient temperature for 3 days. The reaction mixture was quenched by adding 10 mL of 10%  $\text{NH}_4\text{Cl}$  solution and extracted with ether. The combined organic layers was dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated to afford an unseparable mixture (1.7 g),
- 15
- 20 containing 6-chloro-2-methoxynicotinic acid methyl ester.
- C. The above crude material was dissolved in  $\text{CH}_3\text{CN}$  (30 ml) followed by the addition of piperazine (3.0 g, 34.8 mmol). The reaction mixture was heated at reflux overnight. Acetonitrile was removed by evaporation to afford crude 2-methoxy-6-piperazin-1-yl-nicotinic acid methyl ester (1.82 g). To the solution of the residue in dichloromethane (20 mL) was added  $\text{Et}_3\text{N}$  (1 mL, 7.17 mmol) and cooled to  $0^\circ\text{C}$ . 2-Trifluoromethylbenzoic chloride (0.6 mL, 4.05 mmol) was added. The reaction mixture was stirred at ambient temperature for 2 hours, diluted with ethyl acetate and washed with water; dried over anhydrous  $\text{Na}_2\text{SO}_4$ , and concentrated. The residue was purified over silica gel chromatography to give 2-methoxy-6-(4-(2-
- 25
- 30 trifluoromethylbenzoyl)piperazin-1-yl]nicotinic acid methyl ester (1.46 g, 30% over 3 steps);  $^1\text{H}$ NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.04 (d,  $J = 8.7$  Hz, 1H), 7.72 (d,  $J = 7.8$  Hz, 1H),



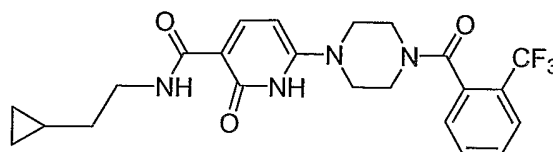
7.61 (dd,  $J = 7.5, 7.8$  Hz, 1H), 7.53 (dd,  $J = 7.5, 7.8$  Hz, 1H), 7.34 (d,  $J = 7.8$  Hz, 1H), 6.14 (d,  $J = 8.7$  Hz, 1H), 4.00-3.59 (m, 12H), 3.29-3.26 (m, 2H). MS ( $ES^+$ )  $m/z$  446.0 (M+Na).

D. Lithium hydroxide hydrate (476 mg, 11.34 mmol) was added to a  
5 solution of 2-methoxy-6-(4-(2-trifluoromethylbenzoyl)piperazin-1-yl)nicotinic acid methyl ester (1.2 g, 2.83 mmol) in THF (30 mL) and water (10 mL). The reaction mixture was heated to reflux for 8 hours. THF was removed by evaporation. The residue was neutralized with 5% HCl solution and extracted with ethyl acetate. The combined organic phase was washed with water and brine; dried over anhydrous  
10  $Na_2SO_4$  and concentrated to give 2-methoxy-6-(4-(2-trifluoromethylbenzoyl)piperazin-1-yl)nicotinic acid (1.08 g, 96%);  $^1H$ NMR (300 MHz,  $CDCl_3$ )  $\delta$  8.19 (d,  $J = 8.7$  Hz, 1H), 7.73 (d,  $J = 7.8$  Hz, 1H), 7.62 (dd,  $J = 7.5, 7.8$  Hz, 1H), 7.53 (dd,  $J = 7.5, 7.8$  Hz, 1H), 7.34 (d,  $J = 7.8$  Hz, 1H), 6.29 (d,  $J = 8.7$  Hz, 1H), 4.13-3.57 (m, 9H), 3.36-3.28 (m, 2H); MS ( $ES^+$ )  $m/z$  432.1 (M+1).

E. To a solution of 2-methoxy-6-(4-(2-trifluoromethylbenzoyl)piperazin-1-yl)nicotinic acid (440 mg, 1.07 mmol) in dichloromethane (20 mL) was added diisopropylethylamine (0.5 mL, 2.8 mmol), 1-hydroxybenzotriazole hydrate (215 mg, 1.5 mmol) and EDCI (0.28 mL, 1.5 mmol). The resulting mixture was stirred for 15  
15 min; and then cyclopropylethylamine (110 mg, 1.2 mmol) was added. After stirring for 20 hours, the reaction mixture was diluted with dichloromethane (100 mL), washed with water, brine, dried over anhydrous  $Na_2SO_4$  and concentrated. Purification via flash chromatography over silica gel (ethyl acetate) and recrystallization from ethyl acetate and hexanes gave *N*-(2-cyclopropylethyl)-2-methoxy-6-(4-(2-trifluoromethylbenzoyl)piperazin-1-yl)nicotinamide (340 mg, 67%); m.p. 49-51°C.  $^1H$   
25 NMR(300 MHz,  $CDCl_3$ )  $\delta$  8.32 (d,  $J = 8.7$  Hz, 1H), 7.80 (t,  $J = 4.8$  Hz, 1H), 7.72(d,  $J = 7.8$  Hz, 1H), 7.63-7.50(m, 2H), 7.34(d,  $J = 7.5$  Hz, 1H), 6.25 (d,  $J = 8.7$  Hz, 1H), 3.96-3.80(m, 4H), 3.74-3.66(m, 2H), 3.56-3.47(m, 4H), 3.29-3.26(m, 2H), 1.49 (q,  $J = 6.0$  Hz, 2H), 0.76-0.66(m, 1H), 0.49-0.43(m, 2H), 0.12-0.07(m, 2H);  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz)  $\delta$  167.5, 164.3, 160.0, 158.1, 143.5, 134.5, 132.3, 129.3, 127.2, 126.8, 104.9,  
30 99.1, 53.4, 46.5, 44.5, 44.4, 41.3, 39.8, 34.4, 8.9, 4.1. MS ( $ES^+$ )  $m/z$  477.4 (M+1).

## EXAMPLE 8

2-Oxo-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-1,2-dihydro-pyridine-3-carboxylic acid (2-cyclopropylethyl)amide



- 5 Chlorotrimethylsilane (0.28 mL, 2.2 mmol) was added to a mixture of *N*-(2-cyclopropylethyl)-2-methoxy-6-(4-(2-trifluoromethylbenzoyl)piperazin-1-yl)nicotinamide (270 mg, 0.56 mmol) and sodium iodide (332 mg, 2.2 mmol) in CH<sub>3</sub>CN (5 mL) and 1 drop water at 0°C. The reaction mixture was stirred at ambient temperature overnight. The reaction was quenched by addition of 5 mL MeOH at 0°C and concentrated. The residue was purified over silica gel chromatography (ethyl acetate) and recrystallized from ethyl acetate and hexanes to give *N*-(2-cyclopropylethyl)-2-hydroxy-6-(4-(2-trifluoromethylbenzoyl)piperazin-1-yl)nicotinamide (79 mg, 30%); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.02(d, *J* = 8.7 Hz, 1H), 7.80(t, *J* = 7.5 Hz, 1H), 7.64(t, *J* = 7.5 Hz, 1H), 7.50(d, *J* = 7.5 Hz, 1H), 5.92(br, 1H), 3.75-3.05(m, 10H), 1.34(q, *J* = 1.34 Hz, 2H), 0.71-0.57(m, 1H), 0.44-0.28(m, 2H), 0.08-0.03 (m, 2H); MS (ES<sup>+</sup>) *m/z* 463.1 (M+1).
- 10
- 15

## EXAMPLE 9

The following representative compounds of the invention can be prepared according to the synthetic approaches set forth above in Reaction Schemes 1 and 2, or in a similar manner to the methods disclosed herein by utilizing the appropriately substituted starting materials, or by methods known to one skilled in the art:

20

6-[4-(2-Ethylbutyryl)piperazin-1-yl]-*n*-(3-phenylpropyl)nicotinamide; 423.3 (M+1);

25 6-[4-(4-Methyl-hexanoyl)piperazin-1-yl]-*n*-(3-phenylpropyl)nicotinamide; 423.2 (M+1);

6-[4-(2-Ethylbutyryl)-3-methylpiperazin-1-yl]-*n*-(3-phenylpropyl)nicotinamide; 437.3 (M+1);

6-[4-(2-Phenylcyclopropanecarbonyl)piperazin-1-yl]-*n*-(3-phenylpropyl)nicotinamide; 469.1 (M+1);

30 6-[4-(3-Cyclohexylpropionyl)piperazin-1-yl]-*n*-(3-methylbutyl)nicotinamide;

- 415.3 (M+1);  
6-[4-(2-Cyclohexylacetyl)piperazin-1-yl]-*n*-hexyl-nicotinamide; 415.2 (M+1);  
*N*-Butyl-6-[4-(3-cyclohexylpropionyl)piperazin-1-yl]nicotinamide; 401.2 (M+1);  
6-[4-(2-Cyclohexylacetyl)piperazin-1-yl]-*n*-pentyl-nicotinamide; 401.2 (M+1);  
5 6-[4-(3-Cyclohexylpropionyl)piperazin-1-yl]-*n*-pentyl-nicotinamide; 415.2 (M+1);  
*N*-[2-(3-Chlorophenyl)ethyl]-6-[4-(3-cyclohexylpropionyl)piperazin-1-yl]nicotinamide; 483.1 (M+1);  
*N*-[2-(3-Chlorophenyl)ethyl]-6-[4-(2-cyclohexylacetyl)piperazin-1-yl]nicotinamide; 469.1 (M+1);  
10 *N*-Butyl-6-[4-(2-mercapto-benzoyl)piperazin-1-yl]nicotinamide; 447.2 (M+1);  
*N*-(3-Methylbutyl)-6-[4-(2-*o*-tolylacetyl)piperazin-1-yl]nicotinamide; 409.2 (M+1);  
6-[4-[2-(2,4-Dimethylphenyl)-acetyl]-piperazin-1-yl]-*N*-(3-methylbutyl)nicotinamide; 409.2 (M+1);  
6-[4-(2-Bromo-benzoyl)piperazin-1-yl]-*n*-(3-ethoxy-propyl)nicotinamide; 475.1  
15 (M+1);  
6-[4-[2-(2-Chloro-6-fluorophenyl)-acetyl]-piperazin-1-yl]-*N*-(3-methylbutyl)nicotinamide; 447.1 (M+1);  
*N*-(3-Methylbutyl)-6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]nicotinamide; 449.0 (M+1);  
20 *N*-(3-Methylbutyl)-6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]nicotinamide hydrochloride; 448.7 (M-HCl);  
*N*-(3-Methylbutyl)-4-trifluoromethyl-6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]nicotinamide; 517.3 (M+1);  
2-Chloro-5-fluoro-*N*-(3-methylbutyl)-6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]nicotinamide; 501.1 (M+1);  
25 2-Chloro-*N*-(3-methylbutyl)-6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]nicotinamide; 483.1 (M+1);  
*N*-(3-Methylbutyl)-6-[3-oxo-4-(2-trifluoromethylbenzyl)piperazin-1-yl]nicotinamide; 449.2 (M+1);  
30 6-[4-(2,5-Dichloro-benzoyl)piperazin-1-yl]-*n*-(3-imidazol-1-ylpropyl)nicotinamide; 487.0 (M+1);  
6-[4-(2,4-Dichloro-benzoyl)piperazin-1-yl]-*n*-(3-imidazol-1-ylpropyl)nicotinamide; 487.1 (M+1);  
6-[4-(2-Bromo-5-methoxy-benzoyl)piperazin-1-yl]-*n*-(3-phenylpropyl)nicotinamide; 539.0 (M+1);  
35

- 6-[4-(2-Bromo-benzoyl)piperazin-1-yl]-*n*-[2-(3H-imidazol-4-yl)ethyl]nicotinamide; 483.0 (M+1);  
*N*-[2-(3-Chlorophenyl)ethyl]-6-[4-(2,4-dichloro-benzoyl)piperazin-1-yl]nicotinamide; 519.1 (M+3);
- 5 6-[2-Oxo-4-(2-trifluoromethylbenzoyl)piperazin-1-yl]-*n*-(3-phenylpropyl)nicotinamide; 511.2 (M+1);  
*N*-(3-Methylbutyl)-6-[2-oxo-4-(2-trifluoromethylbenzoyl)piperazin-1-yl]nicotinamide; 463.1 (M+1);
- 10 6-[4-(3-Methyl-3H-1H-thiophene-2-carbonyl)piperazin-1-yl]-*n*-pentyl-nicotinamide; 401.1 (M+1);  
*N*-[2-(3-Chlorophenyl)ethyl]-6-[4-(3-methyl-thiophene-2-carbonyl)piperazin-1-yl]nicotinamide; 469.1 (M+1);
- 15 6-[4-(2-(4-Chlorophenyl)propionyl)-piperazin-1-yl]-*N*-(3-methylbutyl)nicotinamide; 443.0 (M+1);  
6-[4-(2-Phenylbutyryl)piperazin-1-yl]-*n*-(3-phenylpropyl)nicotinamide; 471.3 (M+1);  
*N*-Pentyl-6-[4-(2-phenylcyclopropanecarbonyl)piperazin-1-yl]nicotinamide; 421.2 (M+1);
- 20 *N*-(3-Methylbutyl)-6-[4-(naphthalene-1-carbonyl)piperazin-1-yl]nicotinamide; 431.5 (M+1);  
*N*-(3-Methylbutyl)-6-[4-(naphthalene-1-carbonyl)piperazin-1-yl]nicotinamide; 431.2 (M+1);  
*N*-[2-(3-Chlorophenyl)ethyl]-6-[4-(2-phenylcyclopropanecarbonyl)piperazin-1-yl]nicotinamide; 489.2 (M+1);
- 25 6-[5-(2-Ethylbutyryl)-2,5-diaza-bicyclo[2.2.1]hept-2-yl]-*n*-(3-phenylpropyl)nicotinamide; 435.3 (M+1);  
6-[4-(2-Ethylbutyl)piperazin-1-yl]-*n*-(3-phenylpropyl)nicotinamide; 409.3 (M+1);  
6-[4-(Butane-1-sulfonyl)piperazin-1-yl]-*n*-(3-phenylpropyl)nicotinamide; 444.9 (M+1);
- 30 4-[5-(3-Phenylpropylcarbamoyl)pyridin-2-yl]-piperazine-1-carboxylic acid butylamide; 424.3 (M+1);  
*N*-(3-Ethoxy-propyl)-6-[4-(2-ethylbutyryl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Ethoxy-propyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-(3-Ethoxy-propyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]nicotinamide
- 35 *N*-(3-Butoxy-propyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide

- N*-(3-Methyl-butyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-nicotinamide  
6-[4-(3-Methyl-pentanoyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;  
*N*-Butyl-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-nicotinamide  
*N*-Butyl-6-[4-(2-ethylbutyryl)-piperazin-1-yl]-nicotinamide  
5 *N*-(3-Methyl-butyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-(2-Ethylsulfanyl-ethyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-(3-Methoxy-propyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-nicotinamide;  
6-(4-Pentanoyl-piperazin-1-yl)-*N*-pentyl-nicotinamide;  
*N*-Hexyl-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-nicotinamide;  
10 *N*-(1,3-Dimethylbutyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-nicotinamide;  
*N*-(1-Methyl-butyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-(3-Dimethylamino-propyl)-6-[4-(2-ethylbutyryl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Methoxy-propyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
15 *N*-(2-Methyl-butyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(2-ethylbutyryl)-piperazin-1-yl]-nicotinamide;  
6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(3-methylbutyl)-nicotinamide;  
*N*-Butyl-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(2-methylbutyl)-nicotinamide;  
20 *N*-(3-Isopropoxy-propyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-(2-Ethylsulfanyl-ethyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-ethyl)-nicotinamide;  
6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-hexyl-nicotinamide;  
6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(1-methylbutyl)-nicotinamide;  
25 *N*-(2-Methyl-butyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-[4-(2-ethylbutyryl)-piperazin-1-yl]-nicotinamide;  
6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;  
*N*-(3-Isopropoxy-propyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Dimethylamino-propyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-  
30 nicotinamide;  
6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(3-methoxy-propyl)-nicotinamide;  
6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(3-isopropoxy-propyl)-nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-nicotinamide;  
*N*-(1-Methyl-butyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-nicotinamide;  
35 *N*-Hexyl-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;

- N*-(3-Dimethylamino-propyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-[2-(3-Chlorophenyl)-1-methylethyl]-6-[4-(2-ethylbutyryl)-piperazin-1-yl]-  
 nicotinamide  
*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-  
 5 nicotinamide;  
*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2-ethylbutyryl)-piperazin-1-yl]-nicotinamide;  
 6-(4-Pentanoyl-piperazin-1-yl)-*N*-(4-phenyl-butyl)-nicotinamide;  
*N*-[2-(3-Chlorophenyl)-ethyl]-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
 6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;  
 10 6-[4-(3-Methyl-pentanoyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;  
 6-(4-Pentanoyl-piperazin-1-yl)-*N*-(3-phenyl-propyl)nicotinamide;  
*N*-(1-Methyl-3-phenyl-propyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
 6-[4-(3-Methyl-pentanoyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-  
 nicotinamide;  
 15 6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-  
 nicotinamide;  
 6-(4-Pentanoyl-piperazin-1-yl)-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;  
 6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide;  
*N*-(3-Imidazol-1-yl-propyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
 20 6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(3-imidazol-1-yl-propyl)-nicotinamide;  
*N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-  
 nicotinamide;  
 6-(4-Pentanoyl-piperazin-1-yl)-*N*-phenethyl-nicotinamide;  
 25 6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-[2-(3H-imidazol-4-yl)-ethyl]-nicotinamide;  
*N*-(3-Imidazol-1-yl-propyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-  
 nicotinamide;  
 6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(3-ethoxy-propyl)-nicotinamide;  
*N*-Butyl-6-[4-(2-cyclohexyl-acetyl)-piperazin-1-yl]-nicotinamide;  
 30 6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(3-methoxy-propyl)-  
 nicotinamide;  
*N*-Pentyl-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
 6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-nicotinamide;  
 6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(3-isopropoxy-propyl)-  
 35 nicotinamide;

- 6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(1,3-dimethylbutyl)-nicotinamide;  
6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(1-methylbutyl)-nicotinamide;  
6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(3-methylbutyl)-nicotinamide;  
6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-ethyl)-nicotinamide;  
5 *N*-(3-Butoxy-propyl)-6-[4-(2-cyclohexyl-acetyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-ethyl)-  
nicotinamide;  
6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(3-methoxy-propyl)-nicotinamide;  
6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(1-methylbutyl)-nicotinamide;  
10 6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(3-isopropoxy-propyl)-nicotinamide;  
6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(3-ethoxy-propyl)-nicotinamide;  
6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(1,3-dimethylbutyl)-  
nicotinamide;  
6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-nicotinamide;  
15 6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-hexyl-nicotinamide;  
6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(3-dimethylamino-propyl)-  
nicotinamide;  
*N*-(3-Ethoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-  
nicotinamide  
20 *N*-(2-Ethylsulfanyl-ethyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(3-Methyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-  
25 nicotinamide;  
*N*-(3-Methoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-  
nicotinamide;  
30 *N*-(3-Dimethylamino-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-  
yl]-nicotinamide;  
*N*-(3-Isopropoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(1-Methyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-  
35 nicotinamide;

- N*-Butyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-Hexyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(2-Methyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-  
nicotinamide;
- 5 6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(3-dimethylamino-propyl)-  
nicotinamide;  
6-[4-(2-Phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-  
nicotinamide;  
*N*-(4-Phenyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-  
10 nicotinamide;  
6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;  
*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-  
yl]-nicotinamide  
*N*-(1-Methyl-3-phenyl-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-  
15 1-yl]-nicotinamide  
*N*-Phenethyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-  
nicotinamide;  
6-[4-(2-Phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-  
ylmethyl)-nicotinamide;
- 20 *N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-  
1-yl]-nicotinamide;  
*N*-(3-Imidazol-1-yl-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-  
nicotinamide;
- 25 6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-[2-(3H-imidazol-4-yl)-ethyl]-  
nicotinamide;  
6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide;  
6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;  
6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide;  
6-[4-(3-Methyl-pentanoyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide;
- 30 6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide;  
6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(1-methyl-3-phenyl-propyl)-  
nicotinamide;  
6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-[2-(3H-imidazol-4-yl)-ethyl]-  
nicotinamide;
- 35 6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-



- nicotinamide;  
 6-[4-(2-Cyclohexyl<sup>1</sup>-acetyl)-piperazin-1-yl]-N-(3-imidazol-1-yl-propyl)-  
 nicotinamide;  
 6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-N-(3-imidazol-1-yl-propyl)-  
 5 nicotinamide;  
 6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-N-(tetrahydro-furan-2-ylmethyl)-  
 nicotinamide;  
 6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-N-(3-methoxy-propyl)-nicotinamide;  
 6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-N-(3-dimethylamino-propyl)-  
 10 nicotinamide  
 6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-N-(3-methylbutyl)-nicotinamide  
 6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-N-(3-ethoxy-propyl)-nicotinamide  
 N-Butyl-6-[4-(3,5-dichloro-benzoyl)-piperazin-1-yl]-nicotinamide  
 6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-N-(3-ethoxy-propyl)-nicotinamide  
 15 6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-N-(2-ethylsulfanyl-ethyl)-  
 nicotinamide  
 N-(3-Ethoxy-propyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
 nicotinamide  
 N-(3-Dimethylamino-propyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-  
 20 nicotinamide  
 6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-N-(2-ethylsulfanyl-ethyl)-  
 nicotinamide;  
 N-(2-Ethylsulfanyl-ethyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
 nicotinamide  
 25 6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-N-(3-methylbutyl)-nicotinamide  
 N-Butyl-6-[4-(2,4-dimethyl-benzoyl)-piperazin-1-yl]-nicotinamide  
 6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-N-(3-isopropoxy-propyl)-  
 nicotinamide;  
 6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-N-(3-methylbutyl)-  
 30 nicotinamide  
 N-(3-Butoxy-propyl)-6-[4-(2,5-dichloro-benzoyl)-piperazin-1-yl]-nicotinamide;  
 N-(3-Methyl-butyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
 6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-N-(3-butoxy-propyl)-nicotinamide;  
 6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-N-pentyl-nicotinamide;  
 35 N-(3-Butoxy-propyl)-6-[4-(2,4-dimethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

- 6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(3-ethoxy-propyl)-nicotinamide;
- 6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-isopropoxy-propyl)-nicotinamide;
- 5 *N*-(3-Ethoxy-propyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- N*-Pentyl-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- N*-Butyl-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- N*-Butyl-6-[4-(2,5-dichloro-benzoyl)-piperazin-1-yl]-nicotinamide;
- 10 6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(3-isopropoxy-propyl)-nicotinamide;
- 6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-isopropoxy-propyl)-nicotinamide;
- N*-(3-Butoxy-propyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 15 6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-ethyl)-nicotinamide;
- N*-(3-Butoxy-propyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-methoxy-propyl)-nicotinamide;
- 20 6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(1,3-dimethylbutyl)-nicotinamide;
- 6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-nicotinamide;
- 6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-nicotinamide;
- 6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-ethyl)-nicotinamide;
- 25 *N*-(1,3-Dimethylbutyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-nicotinamide;
- N*-(3-Dimethylamino-propyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 30 *N*-Hexyl-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(1,3-dimethylbutyl)-nicotinamide;
- N*-(3-Isopropoxy-propyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 35 6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-hexyl-nicotinamide;

- 6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-hexyl-nicotinamide;  
*N*-(3-Isopropoxy-propyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;
- 5 6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(3-methoxy-propyl)-  
nicotinamide;  
6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(1-methylbutyl)-nicotinamide;  
6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-hexyl-nicotinamide;  
*N*-(3-Methoxy-propyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;
- 10 6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-hexyl-nicotinamide;  
*N*-(2-Ethylsulfanyl-ethyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-Pentyl-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
*N*-(2-Methyl-butyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 15 *N*-(2-Ethylsulfanyl-ethyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;  
6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-nicotinamide;  
6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(3-butoxy-propyl)-  
20 nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(3,5-dichloro-benzoyl)-piperazin-1-yl]-nicotinamide;
- 25 6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-butyl-nicotinamide;  
6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(3-Methoxy-propyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
30 nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(1-methylbutyl)-nicotinamide;  
6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-methoxy-propyl)-nicotinamide;  
*N*-(1-Methyl-butyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Dimethylamino-propyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
35 nicotinamide;

- 6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(1-methylbutyl)-nicotinamide;  
6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(1-methylbutyl)-nicotinamide;  
*N*-(1-Methyl-butyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-hexyl-nicotinamide;  
5 6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(3-methoxy-propyl)-nicotinamide;  
6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(1-methylbutyl)-nicotinamide;  
6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-methylbutyl)-nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
10 6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(3-isopropoxy-propyl)-  
nicotinamide;  
*N*-(1-Methyl-butyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
*N*-Butyl-6-[4-(2,4-dichloro-benzoyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(1,3-dimethylbutyl)-nicotinamide;  
15 *N*-Butyl-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(1,3-dimethylbutyl)-  
nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-hexyl-nicotinamide;  
6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(1,3-dimethylbutyl)-nicotinamide;  
20 *N*-(3-Butoxy-propyl)-6-[4-(2,4-dichloro-benzoyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Methoxy-propyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(3-ethoxy-propyl)-nicotinamide;  
6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-nicotinamide;  
25 *N*-Hexyl-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;  
6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(1,3-dimethylbutyl)-nicotinamide;  
*N*-Hexyl-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(3-methoxy-propyl)-nicotinamide;  
30 *N*-(2-Methyl-butyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(1-methylbutyl)-  
nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-nicotinamide;  
6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;  
35 *N*-(2-Methyl-butyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

- 6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-methylbutyl)-nicotinamide;  
6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-ethyl)-nicotinamide;  
6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-methoxy-propyl)-nicotinamide;  
6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(3-isopropoxy-propyl)-  
5 nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
10 *N*-Butyl-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;  
*N*-(1-Methyl-butyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(3-Methoxy-propyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
15 *N*-(3-Isopropoxy-propyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-Pentyl-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;  
*N*-(2-Methyl-butyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
20 *N*-Hexyl-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Methyl-butyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(2-Ethylsulfanyl-ethyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
25 *N*-(3-Ethoxy-propyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(3-Dimethylamino-propyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(3-Ethoxy-propyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
30 nicotinamide;  
6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-ethyl)-  
nicotinamide;  
*N*-(3-Methyl-butyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
*N*-Butyl-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
35 *N*-(3-Isopropoxy-propyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-

- nicotinamide;  
*N*-Pentyl-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-dimethylamino-propyl)-  
nicotinamide;
- 5 6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(3-dimethylamino-propyl)-  
nicotinamide;  
6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-dimethylamino-propyl)-  
nicotinamide;  
6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-dimethylamino-propyl)-
- 10 nicotinamide;  
*N*-(3-Dimethylamino-propyl)-6-[4-(2,4-dimethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(3-Ethoxy-propyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-  
nicotinamide;
- 15 6-[4-(2-Naphthalen-2-yl-acetyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide  
*N*-Butyl-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-nicotinamide  
*N*-(3-Butoxy-propyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-nicotinamide  
*N*-Butyl-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-nicotinamide;
- 20 *N*-(3-Methoxy-propyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(1-Methyl-butyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(Naphthalene-1-carbonyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;  
*N*-(3-Isopropoxy-propyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-
- 25 nicotinamide;  
*N*-(1-Methyl-butyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Methyl-butyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Dimethylamino-propyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-  
nicotinamide;
- 30 *N*-(3-Ethoxy-propyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-Hexyl-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(2-Ethylsulfanyl-ethyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-  
nicotinamide;
- 35 *N*-Hexyl-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-

- nicotinamide;  
N-(3-Isopropoxy-propyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
N-(1,3-Dimethylbutyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-  
5 nicotinamide;  
N-(1,3-Dimethylbutyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-  
nicotinamide;  
N-(2-Methyl-butyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-nicotinamide;  
N-(2-Ethylsulfanyl-ethyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-  
10 nicotinamide;  
N-(2-Methyl-butyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-nicotinamide;  
N-(3-Ethoxy-propyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
N-(2-Methyl-butyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
N-(3-Methyl-butyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
15 N-(3-Methoxy-propyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
N-Butyl-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
N-(3-Butoxy-propyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
N-(1-Methyl-butyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
20 N-(3-Isopropoxy-propyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
N-Hexyl-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
N-(3-Dimethylamino-propyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
25 N-(2-Ethylsulfanyl-ethyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
N-(3-Dimethylamino-propyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
N-(3-Methoxy-propyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-  
30 nicotinamide;  
N-(2-Cyclopropyl-ethyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide ;  
N-(2-Cyclopropyl-ethyl)-6-[4-(5-fluoro-2-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide ;  
35 N-(2-Cyclopropyl-ethyl)-2-hydroxy-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-

- yl]-nicotinamide ;  
*N*-(2-Cyclobutyl-ethyl)-6-[4-(5-fluoro-2-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
 nicotinamide ;  
*N*-(3-Cyclopropyl-propyl)-6-[4-(5-fluoro-2-trifluoromethyl-benzoyl)-piperazin-1-  
 5 yl]-nicotinamide ;  
 6-[4-(5-Fluoro-2-trifluoromethyl-benzoyl)-piperazin-1-yl]-*N*-(4-methyl-pentyl)-  
 nicotinamide ;  
*N*-(3,3-Dimethylbutyl)-6-[4-(5-fluoro-2-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
 nicotinamide ;  
 10 *N*-(1-Methyl-2-phenyl-ethyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
 nicotinamide;  
*N*-(1-Methyl-2-phenyl-ethyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
 nicotinamide;  
 6-[4-(Naphthalene-1-carbonyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-  
 15 nicotinamide  
*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-  
 yl]-nicotinamide;  
 6-[4-(Naphthalene-2-carbonyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide;  
*N*-(3-Imidazol-1-yl-propyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-  
 nicotinamide;  
 20 6-[4-(Naphthalene-1-carbonyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide;  
*N*-(1-Methyl-3-phenyl-propyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-  
 nicotinamide;  
 6-[4-(2-Naphthalen-2-yl-acetyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;  
*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-  
 25 nicotinamide;  
*N*-(1-Methyl-3-phenyl-propyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-  
 nicotinamide;  
 6-[4-(Naphthalene-1-carbonyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;  
*N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-  
 30 nicotinamide;  
 6-[4-(2-Naphthalen-2-yl-acetyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide;  
 6-[4-(Naphthalene-2-carbonyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide;  
*N*-(1-Methyl-3-phenyl-propyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-  
 nicotinamide;  
 35 *N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-



- nicotinamide;  
6-[4-(Naphthalene-2-carbonyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-  
nicotinamide;  
6-[4-(Naphthalene-1-carbonyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-  
5 nicotinamide;  
*N*-(3-Imidazol-1-yl-propyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
10 6-[4-(Naphthalene-2-carbonyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;  
6-[4-(Naphthalene-2-carbonyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide;  
*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(3-Imidazol-1-yl-propyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-  
15 nicotinamide;  
6-[4-(2-Naphthalen-2-yl-acetyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-  
nicotinamide;  
6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide;  
20 *N*-Phenethyl-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
6-[4-[2-(2,5-Dichloro-phenyl)-acetyl]-piperazin-1-yl]-*N*-(2-methyl-3-phenyl-  
propyl)-nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide;  
*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2-fluoro-4-methyl-benzoyl)-piperazin-1-yl]-  
25 nicotinamide;  
*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2,5-dichloro-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(3-Phenyl-propyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
30 6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(3-imidazol-1-yl-propyl)-nicotinamide;  
*N*-(4-Phenyl-butyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Phenyl-propyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-[2-(3-chloro-phenyl)-ethyl]-  
35 nicotinamide;

- 6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(2-methyl-3-phenyl-propyl)-nicotinamide;
- 6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(5-phenyl-pentyl)-nicotinamide;
- 5 6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-[2-(3-chloro-phenyl)-ethyl]-nicotinamide;
- N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- N*-(3-Phenyl-propyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 10 *N*-(4-Phenyl-butyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;
- 6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide;
- 6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;
- 15 6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(1-methyl-3-phenyl-propyl)-nicotinamide;
- 6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide;
- 6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(1-methyl-3-phenyl-propyl)-nicotinamide;
- 20 *N*-Phenethyl-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;
- N*-Phenethyl-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(1-methyl-3-phenyl-propyl)-nicotinamide;
- 25 6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide;
- 6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;
- 6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(3-imidazol-1-yl-propyl)-nicotinamide;
- 6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-imidazol-1-yl-propyl)-nicotinamide;
- 30 *N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;
- N*-Phenethyl-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;
- 35 6-[4-(3-Methyl-pentanoyl)-piperazin-1-yl]-*N*-(1-methyl-3-phenyl-propyl)-

- nicotinamide;  
6-[4-(2,3,4,5-Tetrafluoro-benzoyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;  
6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;  
5 *N*-(Tetrahydro-furan-2-ylmethyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(1-methyl-3-phenyl-propyl)-  
10 nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;  
6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;  
15 *N*-(1-Methyl-3-phenyl-propyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
*N*-Phenethyl-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;  
*N*-(4-Phenyl-butyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;  
20 *N*-(1-Methyl-3-phenyl-propyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;  
*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Phenyl-propyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-  
25 nicotinamide;  
6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-[2-(3H-imidazol-4-yl)-ethyl]-nicotinamide;  
30 *N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Imidazol-1-yl-propyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(3-imidazol-1-yl-propyl)-  
35 nicotinamide;

- 6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-[2-(3H-imidazol-4-yl)-ethyl]-nicotinamide;
- N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 5 6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-[2-(3H-imidazol-4-yl)-ethyl]-nicotinamide;
- 6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;
- N*-(3-Imidazol-1-yl-propyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 10 *N*-(Tetrahydro-furan-2-ylmethyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- N*-(Tetrahydro-furan-2-ylmethyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 15 6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;
- N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-[2-(3H-imidazol-4-yl)-ethyl]-nicotinamide;
- 20 *N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 25 *N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(3,5-dichloro-benzoyl)-piperazin-1-yl]-nicotinamide;
- N*-(4-Phenyl-butyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide;
- 6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide;
- 30 6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide;
- 6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;
- N*-(3-Imidazol-1-yl-propyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;
- 6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-[2-(3H-imidazol-4-yl)-ethyl]-nicotinamide;
- 35

- N*-(3-Imidazol-1-yl-propyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;
- N*-(3-Dimethylamino-propyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- 5 *N*-(3-Dimethylamino-propyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- 6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(3-ethoxy-propyl)-nicotinamide;
- 6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-ethyl)-
- 10 nicotinamide;
- 6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(3-methylbutyl)-nicotinamide;
- 6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(3-isopropoxy-propyl)-nicotinamide;
- 15 *N*-(2-Ethylsulfanyl-ethyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(3-Ethoxy-propyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(3-Methyl-butyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- 6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(3-methoxy-propyl)-
- 20 nicotinamide;
- N*-Pentyl-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- 6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-hexyl-nicotinamide;
- N*-(3-Isopropoxy-propyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- 25 *N*-(1-Methyl-butyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- N*-Hexyl-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(1,3-Dimethylbutyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- N*-Butyl-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(3-Methoxy-propyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- 30 6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(1,3-dimethylbutyl)-nicotinamide;
- N*-Butyl-6-[4-(2-chloro-pyridine-3-carbonyl)-piperazin-1-yl]-nicotinamide;
- 6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-nicotinamide;
- 35 *N*-(2-Methyl-butyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;

- 6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(1-methylbutyl)-nicotinamide;
- N*-(1,3-Dimethylbutyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- 5 *N*-Butyl-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(3-Butoxy-propyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(3-Isopropoxy-propyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- 10 *N*-(3-Ethoxy-propyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(2-Methyl-butyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(2-Ethylsulfanyl-ethyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- 15 *N*-(3-Methoxy-propyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(1-Methyl-butyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- 20 *N*-(3-Methyl-butyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(3-Butoxy-propyl)-6-[4-(2-chloro-pyridine-3-carbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(3-Butoxy-propyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- 25 6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;
- N*-Hexyl-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- 6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(3-dimethylamino-propyl)-nicotinamide;
- N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-[2-(2-chloro-pyridin-3-yl)-acetyl]-piperazin-1-yl]-nicotinamide;
- 30 6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide;
- N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;
- 35 6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-

- nicotinamide;  
*N*-(3-Phenyl-propyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-Phenethyl-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(1-Methyl-3-phenyl-propyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-  
5 nicotinamide;  
*N*-(4-Phenyl-butyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(1-methyl-3-phenyl-  
propyl)-nicotinamide;  
6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;  
10 6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-  
ylmethyl)-nicotinamide;  
6-[4-(3-Methyl-thiophene-2-carbonyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-  
nicotinamide;  
*N*-(1-Methyl-3-phenyl-propyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-  
15 yl]-nicotinamide;  
6-[4-(3-Methyl-thiophene-2-carbonyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-  
nicotinamide;  
6-[4-(3-Methyl-thiophene-2-carbonyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;  
6-[4-(3-Methyl-thiophene-2-carbonyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-  
20 ylmethyl)-nicotinamide;  
*N*-(3-Imidazol-1-yl-propyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(Tetrahydro-furan-2-ylmethyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
25 *N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(3-Imidazol-1-yl-propyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-  
30 yl]-nicotinamide;  
6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(3-imidazol-1-yl-propyl)-  
nicotinamide;  
6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-[2-(3H-imidazol-4-yl)-  
ethyl]-nicotinamide;  
35 6-[4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl]-*N*-(3-ethoxy-propyl)-

- nicotinamide;  
6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-(3-dimethylamino-propyl)-nicotinamide;  
6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-(3-ethoxy-propyl)-  
5 nicotinamide;  
6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-N-(3-ethoxy-propyl)-  
nicotinamide;  
N-(3-Ethoxy-propyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
N-(2-Ethylsulfanyl-ethyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
10 6-[4-(3-Methyl-pentanoyl)-piperazin-1-yl]-N-(4-phenyl-butyl)-nicotinamide;  
N-Butyl-6-{4-[3-(3,4-difluoro-phenyl)-propionyl]-piperazin-1-yl}-nicotinamide;  
6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-N-(3-dimethylamino-propyl)-nicotinamide;  
6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-(2-ethylsulfanyl-ethyl)-  
15 nicotinamide;  
N-(3-Methoxy-propyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
N-Butyl-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
N-(3-Butoxy-propyl)-6-{4-[2-(4-chloro-phenyl)-propionyl]-piperazin-1-yl}-  
nicotinamide;  
20 N-(3-Methoxy-propyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
N-(3-Methyl-butyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
N-(1-Methyl-butyl)-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
N-Butyl-6-{4-[2-(2-chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-nicotinamide;  
N-(2-Methyl-butyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
25 6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-(2-methylbutyl)-  
nicotinamide;  
N-(3-Isopropoxy-propyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-(3-methylbutyl)-  
nicotinamide;  
30 6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-(3-methoxy-propyl)-  
nicotinamide;  
N-(1-Methyl-butyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-N-(2-methylbutyl)-  
nicotinamide;  
35 6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-N-(1-methylbutyl)-



- nicotinamide;  
*N*-(2-Methyl-butyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
 6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-(2-methylbutyl)-  
 5 nicotinamide;  
 6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-(3-isopropoxy-propyl)-nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
 6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-*N*-hexyl-nicotinamide;  
 10 *N*-(1-Methyl-butyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
 6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-(1-methylbutyl)-  
 nicotinamide;  
 6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-(1,3-dimethylbutyl)-  
 nicotinamide;  
 15 *N*-Butyl-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
 6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-(1,3-dimethylbutyl)-  
 nicotinamide;  
*N*-(3-Methyl-butyl)-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
 20 *N*-Butyl-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
*N*-Pentyl-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
*N*-Pentyl-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
 25 *N*-(2-Ethylsulfanyl-ethyl)-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
 6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-(2-ethylsulfanyl-ethyl)-  
 nicotinamide;  
*N*-(3-Ethoxy-propyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
 6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-(3-methoxy-propyl)-  
 30 nicotinamide;  
 6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-*N*-(3-isopropoxy-propyl)-  
 nicotinamide;  
 6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-pentyl-nicotinamide;  
*N*-(3-Butoxy-propyl)-6-{4-[2-(2-chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-  
 35 nicotinamide;

- 6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-hexyl-nicotinamide;  
6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-(3-methoxy-propyl)-  
nicotinamide;  
*N*-Hexyl-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;
- 5 6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-*N*-(4-phenyl-butyl)-  
nicotinamide;  
*N*-(3-Isopropoxy-propyl)-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-*N*-(1-methylbutyl)-  
nicotinamide;
- 10 6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-*N*-pentyl-nicotinamide;  
6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-hexyl-nicotinamide;  
*N*-Butyl-6-{4-[2-(4-chloro-phenyl)-propionyl]-piperazin-1-yl}-nicotinamide;  
6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-(2-ethylsulfanyl-  
ethyl)-nicotinamide;
- 15 6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-pentyl-nicotinamide;  
*N*-Hexyl-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Isopropoxy-propyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
*N*-Pentyl-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
*N*-Hexyl-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;
- 20 6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-*N*-(1,3-dimethylbutyl)-  
nicotinamide;  
6-[4-(Naphthalene-2-carbonyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;  
6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-(3-dimethylamino-propyl)-  
nicotinamide;
- 25 *N*-(3-Dimethylamino-propyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(3-Dimethylamino-propyl)-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Dimethylamino-propyl)-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-[3-(3,4-difluoro-phenyl)-propionyl]-piperazin-1-yl]-
- 30 nicotinamide;  
*N*-(3-Methoxy-propyl)-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
*N*-(2-Methyl-butyl)-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-(3-isopropoxy-propyl)-
- 35 nicotinamide;

- 6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-*N*-phenethyl-nicotinamide;
- N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide
- 6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-(3-phenyl-propyl)-
- 5 nicotinamide
- N*-(1-Methyl-3-phenyl-propyl)-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide
- N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide
- 6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-phenethyl-nicotinamide
- 10 *N*-(3-Phenyl-propyl)-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide
- 6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-[2-(3-chloro-phenyl)-ethyl]-nicotinamide
- 6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-(3-phenyl-propyl)-nicotinamide
- 15 6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-(1-methyl-3-phenyl-propyl)-nicotinamide
- N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-[2-(4-chloro-phenyl)-propionyl]-piperazin-1-yl]-nicotinamide
- N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide
- 20 *N*-Phenethyl-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide
- N*-(3-Phenyl-propyl)-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide
- N*-(1-Methyl-3-phenyl-propyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide
- 6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-(4-phenyl-butyl)-
- 25 nicotinamide
- N*-(4-Phenyl-butyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide
- 6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-(1-methyl-3-phenyl-propyl)-nicotinamide
- 6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-*N*-(3-phenyl-propyl)-
- 30 nicotinamide
- N*-Phenethyl-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide
- 6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-*N*-(1-methyl-3-phenyl-propyl)-nicotinamide;
- N*-(4-Phenyl-butyl)-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;
- 35 *N*-(3-Imidazol-1-yl-propyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;

- 6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-N-(4-phenyl-butyl)-  
nicotinamide;
- 6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-N-[2-(3H-imidazol-4-yl)-  
ethyl]-nicotinamide;
- 5 6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-N-(3-imidazol-1-yl-  
propyl)-nicotinamide;
- N-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-  
nicotinamide;
- 6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-N-(3-imidazol-1-yl-propyl)-  
10 nicotinamide;
- N-(2-Ethylsulfanyl-ethyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;
- N-(1-Methyl-3-phenyl-propyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;
- 6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-phenethyl-  
nicotinamide;
- 15 N-Phenethyl-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;
- N-(Tetrahydro-furan-2-ylmethyl)-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-  
nicotinamide;
- 6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-N-(tetrahydro-furan-2-  
ylmethyl)-nicotinamide;
- 20 N-(4-Phenyl-butyl)-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;
- 6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-(tetrahydro-furan-2-  
ylmethyl)-nicotinamide;
- N-(Tetrahydro-furan-2-ylmethyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-  
nicotinamide;
- 25 6-[4-(2-Phenyl-butyryl)-piperazin-1-yl]-N-(tetrahydro-furan-2-ylmethyl)-  
nicotinamide;
- 6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-[2-(3H-imidazol-4-yl)-  
ethyl]-nicotinamide;
- N-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-  
30 nicotinamide;
- N-(3-Imidazol-1-yl-propyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;
- 6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-(3-imidazol-1-yl-  
propyl)-nicotinamide;
- N-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-  
35 nicotinamide;

- N*-(3-Imidazol-1-yl-propyl)-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
6-[4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;
- 5 6-[4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl]-*N*-[2-(3H-imidazol-4-yl)-ethyl]-nicotinamide;
- N*-(4-Phenyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(1-Methyl-3-phenyl-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide
- 10 *N*-Phenethyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;
- 6-[4-(2-Phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;
- N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;
- 15 *N*-(3-Imidazol-1-yl-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(3-Ethoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide
- 20 *N*-(2-Ethylsulfanyl-ethyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(1,3-Dimethylbutyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(3-Methyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;
- 25 *N*-(3-Methoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(3-Butoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;
- 30 *N*-Pentyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(3-Dimethylamino-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;
- N*-(3-Isopropoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;
- 35 *N*-(1-Methyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-

nicotinamide;

*N*-Butyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

*N*-Hexyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

and

5        *N*-(2-Methyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-  
nicotinamide. .

#### EXAMPLE 10

The identification of compounds of the invention as SCD inhibitors was readily  
10 accomplished using the SCD enzymes and microsomal assay procedure described in  
Brownlie *et al*, PCT published patent application, WO 01/62954. Briefly, mouse or  
human liver microsomes (induced for SCD1 expression and containing cytochrome b<sub>5</sub>  
and cytochrome b<sub>5</sub> reductase) and NADH are suspended in buffer with a compound of  
the invention, and reaction is initiated by addition of 0.025 mM tritiated stearyl-CoA.  
15 This ligand is tritiated at the C9 and C10 position only. The reaction is allowed to  
proceed for between 5 and 20 minutes at ambient temperature, whereupon it is halted  
by addition of acid. Activated charcoal is then added, mixed, and centrifuged to  
separate labeled substrate from labeled water. An aliquot of supernatant is than tested  
for radioactivity using liquid scintillation counting. This is taken as a measure of delta-  
20 9 desaturase activity.

Data showing inhibition of SCD by compounds of the invention when tested by  
this assay are presented below in Table 3, which sets forth the % remaining SCD  
activity at 10 μM of test compound in the indicated assay. Compounds were tested in  
mouse liver microsomes, 100 μg, preincubation with the test compound for 15 minutes  
25 at ambient temperature, a desaturation period for 15 minutes at ambient temperature,  
utilizing the large volume bench-top tube method.

TABLE 3. SCD INHIBITORY ACTIVITY FOR SELECTED COMPOUNDS.

Compound	% Activity 10 $\mu$ M	Mol. weight
6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-N-(2-ethylsulfanyl-ethyl)-nicotinamide	1.4	516.15
N-(3-Phenyl-propyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide	1.3	458.13
6-[4-(2-Naphthalen-2-yl-acetyl)-piperazin-1-yl]-N-pentyl-nicotinamide	0.7	496.21
6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-N-(3-methylbutyl)-nicotinamide	1.3	492.12
6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-N-(3-butoxy-propyl)-nicotinamide	0.8	448.21
N-Butyl-6-[4-(2-ethylbutyryl)-piperazin-1-yl]-nicotinamide	2.0	448.14
N-(3-Butoxy-propyl)-6-[4-(2,4-dimethyl-benzoyl)-piperazin-1-yl]-nicotinamide	0.7	482.19
N-(3-Methyl-butyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide	3.2	442.27
6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-N-(1-methyl-3-phenyl-propyl)-nicotinamide	2.7	434.19
6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-N-phenethyl-nicotinamide	1.1	496.14
6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-N-(3-methylbutyl)-nicotinamide	1.7	448.21
6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-N-pentyl-nicotinamide	1.2	482.13
N-(1,3-Dimethylbutyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide	1.8	458.13

Compound	% Activity 10 $\mu$ M	Mol. weight
6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]- <i>N</i> -(2-ethylsulfanyl-ethyl)-nicotinamide	1.4	448.14
6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]- <i>N</i> -(3-methoxy-propyl)-nicotinamide	1.2	462.22
6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]- <i>N</i> -(1-methylbutyl)-nicotinamide	2.1	430.24
6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]- <i>N</i> -(3-ethoxy-propyl)-nicotinamide	1.0	537.5
<i>N</i> -(1-Methyl-3-phenyl-propyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide	3.4	469
6-[4-(2-Phenyl-buteryl)-piperazin-1-yl]- <i>N</i> -(3-phenyl-propyl)-nicotinamide	3.6	445.4
<i>N</i> -(2-Ethylsulfanyl-ethyl)-6-[4-(2- <i>p</i> -tolyl-acetyl)-piperazin-1-yl]-nicotinamide	1.8	470.6
<i>N</i> -(3-Phenyl-propyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide	3.9	408.5

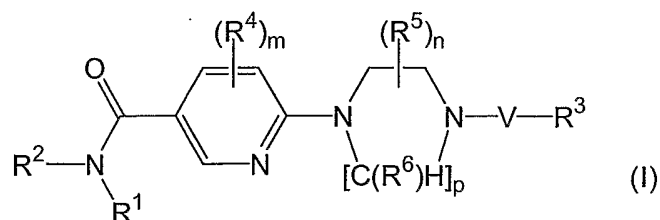
All of the U.S. patents, U.S. patent application publications, U.S. patent applications, foreign patents, foreign patent applications and non-patent publications referred to in this specification and/or listed in the Application Data Sheet are incorporated herein by reference, in their entirety.

From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.



## WHAT IS CLAIMED IS

1. A method of treating an SCD-mediated disease or condition in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I):



wherein:

m is 1, 2 or 3;

n is 1, 2, 3 or 4;

p is 2, 3 or 4;

V is -C(O)-, -S(O)- or -S(O)<sub>2</sub>-;

R<sup>1</sup> is hydrogen, alkyl, alkenyl, aryl, aralkyl, aralkenyl or cycloalkyl;

R<sup>2</sup> is selected from the group consisting of hydrogen, -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

R<sup>3</sup> is selected from the group consisting of hydrogen, -R<sup>9</sup>-OR<sup>8</sup>, -R<sup>9</sup>-N(R<sup>8</sup>)<sub>2</sub>, alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

each R<sup>4</sup> is independently hydrogen, alkyl, alkenyl, halo, haloalkyl, aryl, cyano, nitro, -R<sup>9</sup>-OR<sup>8</sup>, -R<sup>9</sup>-N(R<sup>8</sup>)<sub>2</sub> or -S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2);

each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl;

or one R<sup>5</sup> and one R<sup>6</sup> may together form a straight or branched alkylene bridge;

each R<sup>7</sup> is independently a straight or branched alkylene or alkenylene chain;

each R<sup>8</sup> is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl or heteroarylalkyl;

each R<sup>9</sup> is independently a direct bond or a straight or branched alkylene or alkenylene chain; and

R<sup>10</sup> is alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl or heteroarylalkyl;

as a single stereoisomer, a mixture of stereoisomers, a racemic mixture thereof of stereoisomers, or as a tautomer;

or as a pharmaceutically acceptable salt, prodrug, solvate or polymorph thereof.

2. The method of Claim 1 wherein the compound of formula (I) is a compound wherein:

m is 1 or 2;

n is 1 or 2;

p is 2 or 3;

V is -C(O)- or -S(O)<sub>2</sub>-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of hydrogen, -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclalkyl, optionally substituted heterocyclalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

R<sup>3</sup> is alkyl, alkenyl or -R<sup>9</sup>-N(R<sup>8</sup>)<sub>2</sub>;

each R<sup>4</sup> is independently hydrogen, alkyl, alkenyl, halo, haloalkyl, aryl or -R<sup>9</sup>-OR<sup>8</sup>;

each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl;

or one R<sup>5</sup> and one R<sup>6</sup> may together form an straight or branched alkylene bridge;

each R<sup>7</sup> is independently a straight or branched alkylene or alkenylene chain;

each R<sup>8</sup> is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocylalkyl, heteroaryl or heteroarylalkyl;

each R<sup>9</sup> is independently a direct bond or a straight or branched alkylene chain; and

R<sup>10</sup> is alkyl, aryl or aralkyl.

3. The method of Claim 2 wherein the compound of formula (I) is a compound wherein:

m is 1 or 2;

n is 1 or 2;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl or optionally substituted cycloalkylalkenyl;

R<sup>3</sup> is alkyl;

each R<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl;

each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl;

each R<sup>7</sup> is a straight or branched alkylene chain;

each R<sup>8</sup> is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl and aralkyl; and

R<sup>10</sup> is alkyl, aryl or aralkyl.

4. The method of Claim 3 wherein the compound of formula (I) is a compound wherein:

m is 1;

n is 1;

p is 2;

V is -C(O)-;  
 R<sup>1</sup> is hydrogen or alkyl;  
 R<sup>2</sup> is selected from the group consisting of -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>,  
 -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2) or alkyl;  
 R<sup>3</sup> is alkyl;  
 R<sup>4</sup> is hydrogen;  
 R<sup>5</sup> is hydrogen;  
 each R<sup>6</sup> is hydrogen;  
 R<sup>7</sup> is a straight or branched alkylene chain;  
 R<sup>8</sup> is hydrogen or alkyl; and  
 R<sup>10</sup> is alkyl, aryl or aralkyl.

5. The method of Claim 4 wherein the compound of formula (I) is selected from the group consisting of the following:

*N*-(3-Ethoxy-propyl)-6-[4-(2-ethylbutyryl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Ethoxy-propyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-(3-Ethoxy-propyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]nicotinamide  
*N*-(3-Butoxy-propyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide  
*N*-(3-Methyl-butyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-nicotinamide  
 6-[4-(3-Methyl-pentanoyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;  
*N*-Butyl-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-nicotinamide  
*N*-Butyl-6-[4-(2-ethylbutyryl)-piperazin-1-yl]-nicotinamide  
*N*-(3-Methyl-butyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-(2-Ethylsulfanyl-ethyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-(3-Methoxy-propyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-nicotinamide;  
 6-(4-Pentanoyl-piperazin-1-yl)-*N*-pentyl-nicotinamide;  
*N*-Hexyl-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-nicotinamide;  
*N*-(1-Methyl-butyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-(3-Dimethylamino-propyl)-6-[4-(2-ethylbutyryl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Methoxy-propyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-(2-Methyl-butyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(2-ethylbutyryl)-piperazin-1-yl]-nicotinamide;  
6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(3-methylbutyl)-nicotinamide;  
*N*-Butyl-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(2-methylbutyl)-nicotinamide;  
*N*-(3-Isopropoxy-propyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-(2-Ethylsulfanyl-ethyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-  
nicotinamide;  
6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-ethyl)-  
nicotinamide;  
6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-hexyl-nicotinamide;  
6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(1-methylbutyl)-nicotinamide;  
*N*-(2-Methyl-butyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-[4-(2-ethylbutyryl)-piperazin-1-yl]-nicotinamide;  
6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;  
*N*-(3-Isopropoxy-propyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(3-Dimethylamino-propyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-  
nicotinamide;  
6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(3-methoxy-propyl)-nicotinamide;  
6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(3-isopropoxy-propyl)-  
nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(1-Methyl-butyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-Hexyl-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide; and  
*N*-(3-Dimethylamino-propyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide

6. The method of Claim 2 wherein the compound of formula (I) is a compound wherein:

m is 1 or 2;

n is 1 or 2;

p is 2 or 3;

V is -C(O)- or -S(O)<sub>2</sub>-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

R<sup>3</sup> is alkyl or -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>;

each R<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl; and

each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl;

or one R<sup>5</sup> and one R<sup>6</sup> may together form an straight or branched alkylene bridge;

R<sup>7</sup> is a direct bond; and

each R<sup>8</sup> is independently hydrogen or alkyl.

7. The method of Claim 6 wherein the compound of formula (I) is a compound wherein:

m is 1;

n is 1;

p is 2 or 3;

V is -C(O)- or -S(O)<sub>2</sub>-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heteroaryl and optionally substituted heteroarylalkyl;

R<sup>3</sup> is alkyl or -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>;

R<sup>4</sup> is hydrogen, alkyl, halo or haloalkyl; and

each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl;

or one R<sup>5</sup> and one R<sup>6</sup> may together form a methylene bridge;

R<sup>7</sup> is a direct bond; and

each R<sup>8</sup> is independently hydrogen or alkyl.

8. The method of Claim 7 wherein the compound of formula (I) is selected from the group consisting of the following:

- 6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide;  
 6-[4-(4-Methyl-hexanoyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide;  
*N*-[2-(3-Chlorophenyl)-1-methylethyl]-6-[4-(2-ethylbutyryl)-piperazin-1-yl]-nicotinamide  
*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-nicotinamide;  
*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2-ethylbutyryl)-piperazin-1-yl]-nicotinamide;  
 6-(4-Pentanoyl-piperazin-1-yl)-*N*-(4-phenyl-butyl)-nicotinamide;  
*N*-[2-(3-Chlorophenyl)-ethyl]-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
 6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;  
 6-[4-(3-Methyl-pentanoyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;  
 6-(4-Pentanoyl-piperazin-1-yl)-*N*-(3-phenyl-propyl)nicotinamide;  
*N*-(1-Methyl-3-phenyl-propyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
 6-[4-(3-Methyl-pentanoyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;  
 6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;  
 6-(4-Pentanoyl-piperazin-1-yl)-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;  
 6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide;  
*N*-(3-Imidazol-1-yl-propyl)-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
 6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-(3-imidazol-1-yl-propyl)-nicotinamide;  
*N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-(4-pentanoyl-piperazin-1-yl)-nicotinamide;  
*N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-nicotinamide;

6-(4-Pentanoyl-piperazin-1-yl)-*N*-phenethyl-nicotinamide;  
 6-[4-(2-Ethylbutyryl)-piperazin-1-yl]-*N*-[2-(3H-imidazol-4-yl)-ethyl]-  
 nicotinamide;  
*N*-(3-Imidazol-1-yl-propyl)-6-[4-(3-methyl-pentanoyl)-piperazin-1-yl]-  
 nicotinamide;  
 6-[4-(2-Ethylbutyryl)-[1,4]diazepan-1-yl]-*N*-(3-phenyl-propyl)-  
 nicotinamide;  
 6-[4-(2-Ethylbutyryl)-3-methyl-piperazin-1-yl]-*N*-(3-phenyl-propyl)-  
 nicotinamide;  
 6-[5-(2-Ethylbutyryl)-2,5-diaza-bicyclo[2.2.1]hept-2-yl]-*N*-(3-phenyl-  
 proyl)-nicotinamide;  
 6-[4-(Butane-1-sulfonyl)-piperazine-1-yl]-*N*-(3-phenyl-propyl)-  
 nicotinamide;  
 4-[5-(3-Phenyl-propylcarbamoyl)-pyridin-2-yl]-piperazine-1-carboxylic  
 acid butylamide .

9. The method of Claim 1 wherein the compound of formula (I) is a compound wherein:

*m* is 1 or 2;

*n* is 1 or 2;

*p* is 2;

*V* is -C(O)-;

*R*<sup>1</sup> is hydrogen or alkyl;

*R*<sup>2</sup> is selected from the group consisting of hydrogen, -*R*<sup>7</sup>-OR<sup>8</sup>, -*R*<sup>7</sup>-N(*R*<sup>8</sup>)<sub>2</sub>, -*R*<sup>7</sup>-S(O)<sub>*t*</sub>*R*<sup>10</sup> (where *t* is 0, 1 or 2), alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

*R*<sup>3</sup> is optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, or optionally substituted cycloalkylalkenyl;

each *R*<sup>4</sup> is independently hydrogen, alkyl, alkenyl, halo, haloalkyl, aryl or -*R*<sup>9</sup>-OR<sup>8</sup>;



each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl;

each R<sup>7</sup> is independently a straight or branched alkylene or alkenylene chain;

each R<sup>8</sup> is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocylalkyl, heteroaryl or heteroarylalkyl;

R<sup>9</sup> is a direct bond or a straight or branched alkylene chain; and

R<sup>10</sup> is alkyl, aryl or aralkyl.

10. The method of Claim 9 wherein the compound of formula (I) is a compound wherein:

m is 1 or 2;

n is 1 or 2;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl or optionally substituted cycloalkylalkenyl;

R<sup>3</sup> is optionally substituted cycloalkyl or optionally substituted cycloalkylalkyl;

each R<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl;

each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl;

each R<sup>7</sup> is a straight or branched alkylene chain;

each R<sup>8</sup> is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl and aralkyl; and

R<sup>10</sup> is alkyl, aryl or aralkyl.

11. The method of Claim 10 wherein the compound of formula (I) is a compound wherein:

m is 1;

n is 1;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

$R^2$  is selected from the group consisting of  $-R^7-OR^8$ ,  $-R^7-N(R^8)_2$ ,  $-R^7-S(O)_tR^{10}$  (where  $t$  is 0 to 2) or alkyl;

$R^3$  is optionally substituted cycloalkyl or optionally substituted cycloalkylalkyl;

$R^4$  is hydrogen;

$R^5$  is hydrogen;

each  $R^6$  is hydrogen;

$R^7$  is a straight or branched alkylene chain;

$R^8$  is hydrogen or alkyl; and

$R^{10}$  is alkyl, aryl or aralkyl.

12. The method of Claim 11 wherein the compound of formula (I) is selected from the group consisting of the following:

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(3-ethoxy-propyl)-nicotinamide;

*N*-Butyl-6-[4-(2-cyclohexyl-acetyl)-piperazin-1-yl]-nicotinamide;

6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(3-methylbutyl)-nicotinamide;

6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(3-methoxy-propyl)-nicotinamide;

*N*-Pentyl-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-nicotinamide;

6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(3-isopropoxy-propyl)-nicotinamide;

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(1,3-dimethylbutyl)-nicotinamide;

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-hexyl-nicotinamide;

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(1-methylbutyl)-nicotinamide;

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(3-methylbutyl)-nicotinamide;

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-ethyl)-nicotinamide;

*N*-(3-Butoxy-propyl)-6-[4-(2-cyclohexyl-acetyl)-piperazin-1-yl]-

nicotinamide;

*N*-Butyl-6-[4-(3-cyclohexyl-propionyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;

6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-ethyl)-

nicotinamide;

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(3-methoxy-propyl)-

nicotinamide;

6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(1-methylbutyl)-

nicotinamide;

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(3-isopropoxy-propyl)-

nicotinamide;

6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(3-ethoxy-propyl)-

nicotinamide;

6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(1,3-dimethylbutyl)-

nicotinamide;

6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-

nicotinamide;

6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-hexyl-nicotinamide;

6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;

6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-*N*-(3-dimethylamino-

propyl)-nicotinamide;

*N*-(3-Ethoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-

yl]-nicotinamide

*N*-(2-Ethylsulfanyl-ethyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-

piperazin-1-yl]-nicotinamide;

*N*-(1,3-Dimethylbutyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-

1-yl]-nicotinamide;

*N*-(3-Methyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-

nicotinamide;

*N*-(3-Methoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-

1-yl]-nicotinamide;

*N*-(3-Butoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-

yl]-nicotinamide;

*N*-Pentyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-

nicotinamide;

*N*-(3-Dimethylamino-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Isopropoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

*N*-(1-Methyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

*N*-Butyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

*N*-Hexyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

*N*-(2-Methyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide; and

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-*N*-(3-dimethylamino-propyl)-nicotinamide .

13. The method of Claim 9 wherein the compound of formula (I) is a compound wherein:

*m* is 1 or 2;

*n* is 1 or 2;

*p* is 2;

*V* is -C(O)-;

*R*<sup>1</sup> is hydrogen or alkyl;

*R*<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

*R*<sup>3</sup> is optionally substituted cycloalkyl or optionally substituted cycloalkylalkyl;

each *R*<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl; and

each *R*<sup>5</sup> and *R*<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl.

14. The method of Claim 13 wherein the compound of formula (I) is a compound wherein:

*m* is 1;

n is 1;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted heterocyclyl, optionally substituted heterocyclalkyl, optionally substituted heteroaryl and optionally substituted heteroarylalkyl;

R<sup>3</sup> is optionally substituted cycloalkyl or optionally substituted cycloalkylalkyl;

R<sup>4</sup> is hydrogen, alkyl, halo or haloalkyl;

R<sup>5</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl; and

each R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl.

15. The method of Claim 14 wherein the compound of formula (I) is selected from the group consisting of the following:

6-[4-(2-Phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-N-(3-phenyl-propyl)-nicotinamide;

N-(4-Phenyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-N-phenethyl-nicotinamide;

N-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide

N-(1-Methyl-3-phenyl-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide

N-Phenethyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2-Phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-N-(tetrahydrofuran-2-ylmethyl)-nicotinamide;

N-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

N-(3-Imidazol-1-yl-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

N-[2-(3-Chlorophenyl)-ethyl]-6-[4-(3-cyclohexyl-propionyl)-piperazin-1-yl]-nicotinamide

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-N-[2-(3H-imidazol-4-yl)-ethyl]-nicotinamide;

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-N-(3-phenyl-propyl)-nicotinamide;

N-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2-cyclohexyl-acetyl)-piperazin-1-yl]-nicotinamide;

6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-N-phenethyl-nicotinamide;

6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-N-(3-phenyl-propyl)-nicotinamide;

6-[4-(3-Methyl-pentanoyl)-piperazin-1-yl]-N-(4-phenyl-butyl)-nicotinamide;

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-N-(4-phenyl-butyl)-nicotinamide;

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-N-(1-methyl-3-phenyl-propyl)-nicotinamide;

6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-N-[2-(3H-imidazol-4-yl)-ethyl]-nicotinamide;

6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-N-(tetrahydro-furan-2-ylmethyl)-nicotinamide;

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-N-(3-imidazol-1-yl-propyl)-nicotinamide;

6-[4-(3-Cyclohexyl-propionyl)-piperazin-1-yl]-N-(3-imidazol-1-yl-propyl)-nicotinamide; and

6-[4-(2-Cyclohexyl-acetyl)-piperazin-1-yl]-N-(tetrahydro-furan-2-ylmethyl)-nicotinamide .

16. The method of Claim 1 wherein the compound of formula (I) is a compound wherein:

m is 1 or 2;

n is 1 or 2;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of hydrogen, -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted aryl,

optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclalkyl, optionally substituted heterocyclalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

$R^3$  is optionally substituted aryl;

each  $R^4$  is independently hydrogen, alkyl, alkenyl, halo, haloalkyl, aryl or  $-R^9-OR^8$ ;

each  $R^5$  and  $R^6$  is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl;

each  $R^7$  is independently a straight or branched alkylene or alkenylene chain;

each  $R^8$  is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl or heteroarylalkyl;

$R^9$  is a direct bond or a straight or branched alkylene chain; and

$R^{10}$  is alkyl, aryl or aralkyl.

17. The method of Claim 16 wherein the compound of formula (I) is a compound wherein:

m is 1 or 2;

n is 1 or 2;

p is 2;

V is  $-C(O)-$ ;

$R^1$  is hydrogen or alkyl;

$R^2$  is selected from the group consisting of  $-R^7-OR^8$ ,  $-R^7-N(R^8)_2$ ,  $-R^7-S(O)_tR^{10}$  (where t is 0 to 2), alkyl, alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl or optionally substituted cycloalkylalkenyl;

$R^3$  is optionally substituted aryl;

each  $R^4$  is independently hydrogen, alkyl, halo, haloalkyl or  $-R^9-OR^8$ ;

each  $R^5$  and  $R^6$  is independently hydrogen, oxo, alkyl, halo or haloalkyl;

each  $R^7$  is a straight or branched alkylene chain;

each  $R^8$  is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl and aralkyl;

$R^9$  is a direct bond or a straight or branched alkylene chain; and

R<sup>10</sup> is alkyl, aryl or aralkyl.

18. The method of Claim 17 wherein the compound of formula (I) is a compound wherein:

m is 1 or 2;

n is 1;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, optionally substituted cycloalkyl or optionally substituted cycloalkylalkyl;

R<sup>3</sup> is optionally substituted aryl;

each R<sup>4</sup> is independently hydrogen, halo, haloalkyl or -R<sup>9</sup>-OR<sup>8</sup>;

R<sup>5</sup> is hydrogen;

each R<sup>6</sup> is hydrogen;

R<sup>7</sup> is a straight or branched alkylene chain;

R<sup>8</sup> is hydrogen or alkyl;

R<sup>9</sup> is a direct bond or a straight or branched alkylene chain; and

R<sup>10</sup> is alkyl, aryl or aralkyl.

19. The method of Claim 18 wherein the compound of formula (I) is selected from the group consisting of the following:

*N*-Butyl-6-[4-(2-mercapto-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Methyl-butyl)-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;

6-[4-[2-(2,4-Dimethyl-phenyl)-acetyl]-piperazin-1-yl]-*N*-(3-methylbutyl)-nicotinamide;

6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(3-ethoxypropyl)nicotinamide;

6-[4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl]-*N*-(3-methylbutyl)-nicotinamide;

6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-methoxy-propyl)-nicotinamide;

6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(3-dimethylamino-propyl)-nicotinamide

6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-methylbutyl)-



nicotinamide

6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-ethoxy-propyl)-

nicotinamide

*N*-Butyl-6-[4-(3,5-dichloro-benzoyl)-piperazin-1-yl]-nicotinamide

6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-ethoxy-propyl)-

nicotinamide

6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-ethyl)-

nicotinamide

*N*-(3-Ethoxy-propyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-

nicotinamide

*N*-(3-Dimethylamino-propyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-

1-yl]-nicotinamide

6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-

ethyl)-nicotinamide;

*N*-(2-Ethylsulfanyl-ethyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-

nicotinamide

6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(3-methylbutyl)-nicotinamide

*N*-Butyl-6-[4-(2,4-dimethyl-benzoyl)-piperazin-1-yl]-nicotinamide

6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-isopropoxy-propyl)-

nicotinamide;

6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(3-methylbutyl)-

nicotinamide

*N*-(3-Butoxy-propyl)-6-[4-(2,5-dichloro-benzoyl)-piperazin-1-yl]-

nicotinamide;

*N*-(3-Methyl-butyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-

nicotinamide;

*N*-(3-Methyl-butyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-

nicotinamide;

6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(3-butoxy-propyl)-

nicotinamide;

6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;

*N*-(3-Butoxy-propyl)-6-[4-(2,4-dimethyl-benzoyl)-piperazin-1-yl]-

nicotinamide;

6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(3-ethoxy-propyl)-

nicotinamide;

6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-isopropoxy-propyl)-nicotinamide;

*N*-(3-Ethoxy-propyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-Pentyl-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-Butyl-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-Butyl-6-[4-(2,5-dichloro-benzoyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(3-isopropoxy-propyl)-nicotinamide;

6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-isopropoxy-propyl)-nicotinamide;

*N*-(3-Butoxy-propyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-ethyl)-nicotinamide;

*N*-(3-Butoxy-propyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-methoxy-propyl)-nicotinamide;

6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(1,3-dimethylbutyl)-nicotinamide;

6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-nicotinamide;

6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-nicotinamide;

6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-ethyl)-nicotinamide;

*N*-(1,3-Dimethylbutyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-nicotinamide;

*N*-(3-Dimethylamino-propyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-Hexyl-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(1,3-dimethylbutyl)-

nicotinamide;

*N*-(3-Isopropoxy-propyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-

nicotinamide;

6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-hexyl-nicotinamide;

6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-hexyl-nicotinamide;

*N*-(3-Isopropoxy-propyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-

nicotinamide;

6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(3-methoxy-

propyl)-nicotinamide;

6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(1-methylbutyl)-nicotinamide;

6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-hexyl-nicotinamide;

*N*-(3-Methoxy-propyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-

nicotinamide;

6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-hexyl-nicotinamide;

*N*-(2-Ethylsulfanyl-ethyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-

nicotinamide;

*N*-Pentyl-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-(2-Methyl-butyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-

nicotinamide;

*N*-(2-Ethylsulfanyl-ethyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-

nicotinamide;

6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;

6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-nicotinamide;

6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(3-butoxy-propyl)-

nicotinamide;

*N*-(1,3-Dimethylbutyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-

nicotinamide;

6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;

*N*-(3-Butoxy-propyl)-6-[4-(3,5-dichloro-benzoyl)-piperazin-1-yl]-

nicotinamide;

6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-butyl-nicotinamide;

6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;

*N*-(1,3-Dimethylbutyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-

nicotinamide;

*N*-(3-Methoxy-propyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-

nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-N-(1-methylbutyl)-  
nicotinamide;  
6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-N-(3-methoxy-propyl)-  
nicotinamide;  
N-(1-Methyl-butyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
N-(3-Dimethylamino-propyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-  
yl]-nicotinamide;  
6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-N-(1-methylbutyl)-  
nicotinamide;  
6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-N-(1-methylbutyl)-  
nicotinamide;  
N-(1-Methyl-butyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-N-hexyl-nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-N-(3-methoxy-propyl)-  
nicotinamide;  
6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-N-(1-methylbutyl)-  
nicotinamide;  
6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-N-(3-methylbutyl)-  
nicotinamide;  
N-(3-Butoxy-propyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-N-(3-isopropoxy-propyl)-  
nicotinamide;  
N-(1-Methyl-butyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
N-Butyl-6-[4-(2,4-dichloro-benzoyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-N-(1,3-dimethylbutyl)-  
nicotinamide;  
N-Butyl-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-N-(1,3-dimethylbutyl)-  
nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-N-hexyl-nicotinamide;

6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(1,3-dimethylbutyl)-  
nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(2,4-dichloro-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(3-Methoxy-propyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(3-ethoxy-propyl)-  
nicotinamide;  
6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-  
nicotinamide;  
*N*-Hexyl-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;  
6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(1,3-dimethylbutyl)-  
nicotinamide;  
*N*-Hexyl-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(3-methoxy-propyl)-  
nicotinamide;  
*N*-(2-Methyl-butyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(1-methylbutyl)-  
nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-  
nicotinamide;  
6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-pentyl-  
nicotinamide;  
*N*-(2-Methyl-butyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-methylbutyl)-  
nicotinamide;  
6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-ethyl)-  
nicotinamide;  
6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-methoxy-propyl)-  
nicotinamide;  
6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(3-isopropoxy-  
propyl)-nicotinamide;

*N*-(3-Butoxy-propyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-(1,3-Dimethylbutyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-Butyl-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-(1-Methyl-butyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Methoxy-propyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Isopropoxy-propyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-Pentyl-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-(2-Methyl-butyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-Hexyl-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Methyl-butyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-(2-Ethylsulfanyl-ethyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Ethoxy-propyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Dimethylamino-propyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Ethoxy-propyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-ethyl)-nicotinamide;

*N*-(3-Methyl-butyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-Butyl-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Isopropoxy-propyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-Pentyl-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-dimethylamino-propyl)-nicotinamide;

6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(3-dimethylamino-propyl)-  
nicotinamide;

6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-dimethylamino-propyl)-  
nicotinamide;

6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-dimethylamino-propyl)-  
nicotinamide;

*N*-(3-Dimethylamino-propyl)-6-[4-(2,4-dimethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;

*N*-(3-Methyl-butyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide ;

*N*-(3-Methyl-butyl)-4-trifluoromethyl-6-[4-(2-trifluoromethyl-benzoyl)-  
piperazin-1-yl]-nicotinamide;

2-Chloro-5-fluoro-*N*-(3-methylbutyl)-6-[4-(2-trifluoromethyl-benzoyl)-  
piperazin-1-yl]-nicotinamide;

*N*-(3-Ethoxy-propyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-  
nicotinamide;

6-[4-(2-Naphthalen-2-yl-acetyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide  
*N*-Butyl-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-nicotinamide  
*N*-(3-Butoxy-propyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-  
nicotinamide

*N*-Butyl-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Butoxy-propyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-  
nicotinamide;

*N*-(3-Methoxy-propyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-  
nicotinamide;

*N*-(1-Methyl-butyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-  
nicotinamide;

6-[4-(Naphthalene-1-carbonyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;

*N*-(3-Isopropoxy-propyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-  
nicotinamide;

*N*-(1-Methyl-butyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-  
nicotinamide;

*N*-(3-Methyl-butyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-  
nicotinamide;

*N*-(3-Dimethylamino-propyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-

yl]-nicotinamide;  
N-(3-Ethoxy-propyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
N-Hexyl-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-nicotinamide;  
N-(2-Ethylsulfanyl-ethyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-  
nicotinamide;  
N-Hexyl-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-nicotinamide;  
N-(1,3-Dimethylbutyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
N-(3-Isopropoxy-propyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
N-(1,3-Dimethylbutyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
N-(1,3-Dimethylbutyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-  
nicotinamide;  
N-(2-Methyl-butyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
N-(2-Ethylsulfanyl-ethyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
N-(2-Methyl-butyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-  
nicotinamide;  
N-(3-Methyl-butyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
N-(3-Ethoxy-propyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
N-(2-Methyl-butyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
N-(3-Methyl-butyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
N-(3-Methoxy-propyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
N-Butyl-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
N-(3-Butoxy-propyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
N-(1-Methyl-butyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-



nicotinamide;  
*N*-(3-Isopropoxy-propyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-Hexyl-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Dimethylamino-propyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-  
yl]-nicotinamide;  
*N*-(2-Ethylsulfanyl-ethyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(3-Dimethylamino-propyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-  
yl]-nicotinamide;  
*N*-(3-Methyl-butyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-  
nicotinamide;  
*N*-(3-Methoxy-propyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-yl]-  
nicotinamide;  
2-Chloro-*N*-(3-methylbutyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-  
yl]-nicotinamide;  
*N*-(2-Cyclopropyl-ethyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide ;  
*N*-(2-Cyclopropyl-ethyl)-2-methoxy-6-[4-(2-trifluoromethyl-benzoyl)-  
piperazin-1-yl]-nicotinamide ;  
*N*-(2-Cyclopropyl-ethyl)-6-[4-(5-fluoro-2-trifluoromethyl-benzoyl)-  
piperazin-1-yl]-nicotinamide ;  
2-Oxo-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-1,2-dihydro-  
pyridine-3-carboxylic acid (2-cyclopropylethyl)amide;  
*N*-(2-Cyclopropyl-ethyl)-2-hydroxy-6-[4-(2-trifluoromethyl-benzoyl)-  
piperazin-1-yl]-nicotinamide ;  
*N*-(2-Cyclobutyl-ethyl)-6-[4-(5-fluoro-2-trifluoromethyl-benzoyl)-  
piperazin-1-yl]-nicotinamide ;  
*N*-(3-Cyclopropyl-propyl)-6-[4-(5-fluoro-2-trifluoromethyl-benzoyl)-  
piperazin-1-yl]-nicotinamide ;  
6-[4-(5-Fluoro-2-trifluoromethyl-benzoyl)-piperazin-1-yl]-*N*-(4-methyl-  
pentyl)-nicotinamide ; and  
*N*-(3,3-Dimethylbutyl)-6-[4-(5-fluoro-2-trifluoromethyl-benzoyl)-piperazin-  
1-yl]-nicotinamide .

20. The method of Claim 16 wherein the compound of formula (I) is a compound wherein:

m is 1 or 2;

n is 1 or 2;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

R<sup>3</sup> is optionally substituted aryl;

each R<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl; and

each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl.

21. The method of Claim 20 wherein the compound of formula (I) is a compound wherein:

m is 1 or 2;

n is 1;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heteroaryl and optionally substituted heteroarylalkyl;

R<sup>3</sup> is optionally substituted aryl;

each R<sup>4</sup> is independently hydrogen, alkyl, halo or haloalkyl;

R<sup>5</sup> is hydrogen, oxo, alkyl, halo or haloalkyl; and

each R<sup>6</sup> is independently hydrogen, alkyl, halo or haloalkyl.

22. The method of Claim 21 wherein the compound of formula (I) is selected from the group consisting of the following:

6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-N-(3-imidazol-1-yl-propyl)-

nicotinamide

6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-imidazol-1-yl-propyl)-

nicotinamide

6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-

nicotinamide;

6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-[2-(3H-imidazol-4-yl)-ethyl]-

nicotinamide

*N*-(1-Methyl-2-phenyl-ethyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-

yl]-nicotinamide;

*N*-(1-Methyl-2-phenyl-ethyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-

yl]-nicotinamide;

6-[4-(Naphthalene-1-carbonyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-

nicotinamide

*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-

yl]-nicotinamide

6-[4-(Naphthalene-2-carbonyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-

nicotinamide

*N*-(3-Imidazol-1-yl-propyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-1-

yl]-nicotinamide

6-[4-(Naphthalene-1-carbonyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-

nicotinamide

*N*-(1-Methyl-3-phenyl-propyl)-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-

1-yl]-nicotinamide;

6-[4-(2-Naphthalen-2-yl-acetyl)-piperazin-1-yl]-*N*-phenethyl-

nicotinamide;

*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(naphthalene-1-carbonyl)-piperazin-1-

yl]-nicotinamide;

*N*-(1-Methyl-3-phenyl-propyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-

yl]-nicotinamide;

6-[4-(Naphthalene-1-carbonyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;

*N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(2-naphthalen-2-yl-acetyl)-piperazin-

1-yl]-nicotinamide;

6-[4-(2-Naphthalen-2-yl-acetyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-

nicotinamide;

6-[4-(Naphthalene-2-carbonyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-

nicotinamide;

*N*-(1-Methyl-3-phenyl-propyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-nicotinamide;

*N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-nicotinamide;

6-[4-(Naphthalene-2-carbonyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;

6-[4-(Naphthalene-1-carbonyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;

*N*-(3-Imidazol-1-yl-propyl)-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-nicotinamide;

*N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-nicotinamide;

6-[4-(Naphthalene-2-carbonyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;

6-[4-(Naphthalene-2-carbonyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide;

*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(naphthalene-2-carbonyl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Imidazol-1-yl-propyl)-6-[4-(naphthalene-1-carbonyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2-Naphthalen-2-yl-acetyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;

6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide;

*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2,4-dichloro-benzoyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide

*N*-Phenethyl-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide

6-[4-[2-(2,5-Dichloro-phenyl)-acetyl]-piperazin-1-yl]-*N*-(2-methyl-3-phenyl-propyl)-nicotinamide

6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide

*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2-fluoro-4-methyl-benzoyl)-piperazin-1-yl]-nicotinamide

*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2,5-dichloro-benzoyl)-piperazin-1-yl]-  
 nicotinamide  
*N*-(3-Phenyl-propyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
 nicotinamide  
 6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(3-imidazol-1-yl-propyl)-  
 nicotinamide  
*N*-(4-Phenyl-butyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
 nicotinamide  
*N*-(3-Phenyl-propyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
 nicotinamide  
 6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-[2-(3-chloro-phenyl)-ethyl]-  
 nicotinamide  
 6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(2-methyl-3-phenyl-propyl)-  
 nicotinamide  
 6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(5-phenyl-pentyl)-  
 nicotinamide  
 6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-[2-(3-chloro-  
 phenyl)-ethyl]-nicotinamide  
*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-  
 1-yl]-nicotinamide  
*N*-(3-Phenyl-propyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
 nicotinamide  
*N*-(4-Phenyl-butyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
 nicotinamide  
 6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;  
 6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide;  
 6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;  
 6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(1-methyl-3-phenyl-  
 propyl)-nicotinamide;  
 6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-  
 nicotinamide;  
 6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(1-methyl-3-phenyl-propyl)-  
 nicotinamide;  
*N*-Phenethyl-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
 nicotinamide;

6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;  
*N*-Phenethyl-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(1-methyl-3-phenyl-propyl)-  
nicotinamide;  
6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-  
nicotinamide;  
6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-phenethyl-  
nicotinamide;  
6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(3-imidazol-1-yl-  
propyl)-nicotinamide;  
6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-imidazol-1-yl-propyl)-  
nicotinamide;  
*N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-  
piperazin-1-yl]-nicotinamide;  
*N*-Phenethyl-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;  
6-[4-(3-Methyl-pentanoyl)-piperazin-1-yl]-*N*-(1-methyl-3-phenyl-propyl)-  
nicotinamide;  
6-[4-(2,3,4,5-Tetrafluoro-benzoyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-  
ylmethyl)-nicotinamide;  
6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-  
2-ylmethyl)-nicotinamide;  
*N*-(Tetrahydro-furan-2-ylmethyl)-6-[4-(4-trifluoromethyl-benzoyl)-  
piperazin-1-yl]-nicotinamide;  
6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-  
nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(1-methyl-3-phenyl-  
propyl)-nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-  
ylmethyl)-nicotinamide;  
6-[4-(2-Bromo-benzoyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-  
nicotinamide;  
*N*-(1-Methyl-3-phenyl-propyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-

1-yl]-nicotinamide;  
N-Phenethyl-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
N-(4-Phenyl-butyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
N-(1-Methyl-3-phenyl-propyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-  
piperazin-1-yl]-nicotinamide;  
N-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-  
1-yl]-nicotinamide;  
N-(3-Phenyl-propyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-  
nicotinamide;  
6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-N-(tetrahydro-furan-2-  
ylmethyl)-nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-N-[2-(3H-imidazol-4-yl)-  
ethyl]-nicotinamide;  
N-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-  
1-yl]-nicotinamide;  
N-(3-Imidazol-1-yl-propyl)-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-  
yl]-nicotinamide;  
6-[4-(2,4-Dimethyl-benzoyl)-piperazin-1-yl]-N-(3-imidazol-1-yl-propyl)-  
nicotinamide;  
6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-N-[2-(3H-imidazol-4-yl)-ethyl]-  
nicotinamide;  
N-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-  
1-yl]-nicotinamide;  
6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-N-[2-(3H-imidazol-4-yl)-ethyl]-  
nicotinamide;  
6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-N-(tetrahydro-furan-2-  
ylmethyl)-nicotinamide;  
N-(3-Imidazol-1-yl-propyl)-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-  
yl]-nicotinamide;  
N-(Tetrahydro-furan-2-ylmethyl)-6-[4-(3-trifluoromethyl-benzoyl)-  
piperazin-1-yl]-nicotinamide;  
N-(Tetrahydro-furan-2-ylmethyl)-6-[4-(2-trifluoromethyl-benzoyl)-  
piperazin-1-yl]-nicotinamide;

6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;

*N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2-Bromo-5-methoxy-benzoyl)-piperazin-1-yl]-*N*-[2-(3H-imidazol-4-yl)-ethyl]-nicotinamide;

*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(3-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(3,5-dichloro-benzoyl)-piperazin-1-yl]-nicotinamide;

*N*-(4-Phenyl-butyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide;

6-[4-(2,4-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide;

6-[4-(2,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide;

6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;

*N*-(3-Imidazol-1-yl-propyl)-6-[4-(4-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide;

6-[4-(3,5-Dichloro-benzoyl)-piperazin-1-yl]-*N*-[2-(3H-imidazol-4-yl)-ethyl]-nicotinamide;

*N*-(3-Imidazol-1-yl-propyl)-6-[4-(2,3,4,5-tetrafluoro-benzoyl)-piperazin-1-yl]-nicotinamide;

6-[2-Oxo-4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide;

*N*-(3-Methyl-butyl)-6-[2-oxo-4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-nicotinamide .

23. The method of Claim 1 wherein the compound of formula (I) is a compound wherein:

m is 1 or 2;



n is 1 or 2;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of hydrogen, -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

R<sup>3</sup> is optionally substituted heteroaryl, optionally substituted heteroarylalkyl or optionally substituted heteroarylalkenyl;

each R<sup>4</sup> is independently hydrogen, alkyl, alkenyl, halo, haloalkyl or aryl;

each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl;

each R<sup>7</sup> is independently a straight or branched alkylene or alkenylene chain;

each R<sup>8</sup> is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl; and

R<sup>10</sup> is alkyl, aryl or aralkyl.

24. The method of Claim 23 wherein the compound of formula (I) is a compound wherein:

m is 1 or 2;

n is 1 or 2;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl or optionally substituted cycloalkylalkenyl;

R<sup>3</sup> is optionally substituted heteroaryl, optionally substituted

heteroarylalkyl or optionally substituted heteroarylalkenyl;

each R<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl;

each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl;

each R<sup>7</sup> is a straight or branched alkylene chain;

each R<sup>8</sup> is independently hydrogen, alkyl, haloalkyl, cycloalkyl,

cycloalkylalkyl, aryl and aralkyl; and

R<sup>10</sup> is alkyl, aryl or aralkyl.

25. The method of Claim 24 wherein the compound of formula (I) is a compound wherein:

m is 1 or 2;

n is 1;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>,

-R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2) or alkyl;

R<sup>3</sup> is optionally substituted heteroaryl, optionally substituted heteroarylalkyl or optionally substituted heteroarylalkenyl;

each R<sup>4</sup> is independently hydrogen, halo or haloalkyl;

R<sup>5</sup> is hydrogen;

each R<sup>6</sup> is hydrogen;

R<sup>7</sup> is a straight or branched alkylene chain;

R<sup>8</sup> is hydrogen or alkyl; and

R<sup>10</sup> is alkyl, aryl or aralkyl.

26. The method of Claim 25 wherein the compound of formula (I) is selected from the group consisting of the following:

6-[4-(3-Methyl-3H-1,4-thiophene-2-carbonyl)-piperazin-1-yl]-N-pentyl-nicotinamide;

N-(3-Dimethylamino-propyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide

N-(3-Dimethylamino-propyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide

6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-N-(3-ethoxy-propyl)-

nicotinamide

6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(2-ethylsulfanyl-

ethyl)-nicotinamide

6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(3-methylbutyl)-

nicotinamide;

6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(3-isopropoxy-

propyl)-nicotinamide

*N*-(2-Ethylsulfanyl-ethyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-

nicotinamide;

*N*-(3-Ethoxy-propyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-

nicotinamide;

*N*-(3-Methyl-butyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-

nicotinamide;

6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(3-methoxy-

propyl)-nicotinamide;

*N*-Pentyl-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-hexyl-nicotinamide;

*N*-(3-Isopropoxy-propyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-

nicotinamide;

*N*-(1-Methyl-butyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-

nicotinamide;

*N*-Hexyl-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;

*N*-(1,3-Dimethylbutyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-

nicotinamide;

*N*-Butyl-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Methoxy-propyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-

nicotinamide;

6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(1,3-dimethylbutyl)-

nicotinamide;

*N*-Butyl-6-[4-(2-chloro-pyridine-3-carbonyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(2-methylbutyl)-

nicotinamide;

*N*-(2-Methyl-butyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-

nicotinamide;

6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(1-methylbutyl)-

nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-Butyl-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Isopropoxy-propyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Ethoxy-propyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(2-Methyl-butyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(2-Ethylsulfanyl-ethyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Methoxy-propyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(1-Methyl-butyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Methyl-butyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(2-chloro-pyridine-3-carbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;  
6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-pentyl-nicotinamide;  
*N*-Hexyl-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide; and  
6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(3-dimethylamino-propyl)-nicotinamide .

27. The method of Claim 23 wherein the compound of formula (I) is a compound wherein:

m is 1 or 2;

n is 1 or 2;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

R<sup>3</sup> is optionally substituted heteroaryl, optionally substituted heteroarylalkyl or optionally substituted heteroarylalkenyl;

each R<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl; and

each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl.

28. The method of Claim 27 wherein the compound of formula (I) is a compound wherein:

m is 1 or 2;

n is 1;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heteroaryl and optionally substituted heteroarylalkyl;

R<sup>3</sup> is optionally substituted heteroaryl, optionally substituted heteroarylalkyl or optionally substituted heteroarylalkenyl;

each R<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl;

R<sup>5</sup> is hydrogen, oxo, alkyl, halo or haloalkyl; and

each R<sup>6</sup> independently hydrogen, oxo, alkyl, halo or haloalkyl.

29. The method of Claim 21 wherein the compound of formula (I) is selected from the group consisting of the following:

*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;

*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-[2-(2-chloro-pyridin-3-yl)-acetyl]-piperazin-1-yl]-nicotinamide

6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide

*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide

6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide

*N*-(3-Phenyl-propyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide

*N*-Phenethyl-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide

*N*-(1-Methyl-3-phenyl-propyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide

*N*-(4-Phenyl-butyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide

6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(1-methyl-3-phenyl-propyl)-nicotinamide;

6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;

6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;

6-[4-(3-Methyl-thiophene-2-carbonyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide;

*N*-(1-Methyl-3-phenyl-propyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;

6-[4-(3-Methyl-thiophene-2-carbonyl)-piperazin-1-yl]-*N*-(4-phenyl-butyl)-nicotinamide;

6-[4-(3-Methyl-thiophene-2-carbonyl)-piperazin-1-yl]-*N*-phenethyl-nicotinamide;

6-[4-(3-Methyl-thiophene-2-carbonyl)-piperazin-1-yl]-*N*-(tetrahydro-furan-2-ylmethyl)-nicotinamide;

*N*-(3-Imidazol-1-yl-propyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;

*N*-(Tetrahydro-furan-2-ylmethyl)-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;

*N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Imidazol-1-yl-propyl)-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;

*N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(3-methyl-thiophene-2-carbonyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-(3-imidazol-1-yl-propyl)-nicotinamide; and

6-[4-(2-Chloro-pyridine-3-carbonyl)-piperazin-1-yl]-*N*-[2-(3H-imidazol-4-yl)-ethyl]-nicotinamide .

30. The method of Claim 1 wherein the compound of formula (I) is a compound wherein:

*m* is 1 or 2;

*n* is 1 or 2;

*p* is 2;

*V* is -C(O)-;

*R*<sup>1</sup> is hydrogen or alkyl;

*R*<sup>2</sup> is selected from the group consisting of hydrogen, -*R*<sup>7</sup>-OR<sup>8</sup>, -*R*<sup>7</sup>-N(*R*<sup>8</sup>)<sub>2</sub>, -*R*<sup>7</sup>-S(O)<sub>*t*</sub>*R*<sup>10</sup> (where *t* is 0, 1 or 2), alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

*R*<sup>3</sup> is optionally substituted aralkyl or optionally substituted aralkenyl;

each *R*<sup>4</sup> is independently hydrogen, alkyl, alkenyl, halo, haloalkyl, aryl or -*R*<sup>9</sup>-OR<sup>8</sup>;

each *R*<sup>5</sup> and *R*<sup>6</sup> is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl;

each *R*<sup>7</sup> is independently a straight or branched alkylene or alkenylene chain;

each *R*<sup>8</sup> is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl;

$R^9$  is a direct bond or a straight or branched alkylene chain; and  
 $R^{10}$  is alkyl, aryl or aralkyl.

31. The method of Claim 30 wherein the compound of formula (I) is a compound wherein:

$m$  is 1 or 2;

$n$  is 1 or 2;

$p$  is 2;

$V$  is  $-C(O)-$ ;

$R^1$  is hydrogen or alkyl;

$R^2$  is selected from the group consisting of  $-R^7-OR^8$ ,  $-R^7-N(R^8)_2$ ,  $-R^7-S(O)_tR^{10}$  (where  $t$  is 0, 1 or 2), alkyl, alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl or optionally substituted cycloalkylalkenyl;

$R^3$  is optionally substituted aralkyl or optionally substituted aralkenyl;

each  $R^4$  is independently hydrogen, alkyl, halo, or haloalkyl;

each  $R^5$  and  $R^6$  is independently hydrogen, oxo, alkyl, halo or haloalkyl;

each  $R^7$  is a straight or branched alkylene chain;

each  $R^8$  is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl and aralkyl; and

$R^{10}$  is alkyl, aryl or aralkyl.

32. The method of Claim 31 wherein the compound of formula (I) is a compound wherein:

$m$  is 1 or 2;

$n$  is 1;

$p$  is 2;

$V$  is  $-C(O)-$ ;

$R^1$  is hydrogen or alkyl;

$R^2$  is selected from the group consisting of  $-R^7-OR^8$ ,  $-R^7-N(R^8)_2$ ,  $-R^7-S(O)_tR^{10}$  (where  $t$  is 0, 1 or 2) or alkyl;

$R^3$  is optionally substituted aralkyl or optionally substituted aralkenyl;

each  $R^4$  is independently hydrogen, halo or haloalkyl;

$R^5$  is hydrogen;

each  $R^6$  is hydrogen;

$R^7$  is a straight or branched alkylene chain;



R<sup>8</sup> is hydrogen or alkyl; and

R<sup>10</sup> is alkyl, aryl or aralkyl.

33. The method of Claim 32 wherein the compound of formula (I) is selected from the group consisting of the following:

6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-N-(3-methylbutyl)-nicotinamide;

6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-N-(3-ethoxy-propyl)-nicotinamide

6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-(3-dimethylamino-propyl)-nicotinamide

6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-(3-ethoxy-propyl)-nicotinamide

6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-N-(3-ethoxy-propyl)-nicotinamide

N-(3-Ethoxy-propyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide

N-(2-Ethylsulfanyl-ethyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide

6-[4-(3-Methyl-pentanoyl)-piperazin-1-yl]-N-(4-phenyl-butyl)-nicotinamide

N-Butyl-6-[4-[3-(3,4-difluoro-phenyl)-propionyl]-piperazin-1-yl]-nicotinamide

6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-N-(3-dimethylamino-propyl)-nicotinamide

6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-(2-ethylsulfanyl-ethyl)-nicotinamide;

N-(3-Methoxy-propyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;

N-Butyl-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;

N-(3-Butoxy-propyl)-6-[4-[2-(4-chloro-phenyl)-propionyl]-piperazin-1-yl]-nicotinamide

N-(3-Methoxy-propyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;

N-(3-Methyl-butyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;

N-(1-Methyl-butyl)-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;

N-Butyl-6-[4-[2-(2-chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl]-

nicotinamide;  
*N*-(2-Methyl-butyl)-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-*N*-(2-methylbutyl)-nicotinamide;  
*N*-(3-Isopropoxy-propyl)-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-*N*-(3-methylbutyl)-nicotinamide;  
6-[4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl]-*N*-(3-methoxy-propyl)-nicotinamide;  
*N*-(1-Methyl-butyl)-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-(2-methylbutyl)-nicotinamide;  
6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-(1-methylbutyl)-nicotinamide;  
*N*-(2-Methyl-butyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-(2-methylbutyl)-nicotinamide;  
6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-(3-isopropoxy-propyl)-nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-*N*-hexyl-nicotinamide;  
*N*-(1-Methyl-butyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-(1-methylbutyl)-nicotinamide;  
6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-(1,3-dimethylbutyl)-nicotinamide;  
*N*-Butyl-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-(1,3-dimethylbutyl)-nicotinamide;  
*N*-(3-Methyl-butyl)-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;

*N*-Butyl-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
*N*-Pentyl-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
*N*-Pentyl-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
*N*-(2-Ethylsulfanyl-ethyl)-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-  
nicotinamide;  
6-[4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl]-*N*-(2-ethylsulfanyl-  
ethyl)-nicotinamide;  
*N*-(3-Ethoxy-propyl)-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
6-[4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl]-*N*-(3-methoxy-  
propyl)-nicotinamide;  
6-[4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl]-*N*-(3-isopropoxy-  
propyl)-nicotinamide;  
6-[4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl]-*N*-pentyl-  
nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-[2-(2-chloro-6-fluoro-phenyl)-acetyl]-piperazin-  
1-yl]-nicotinamide;  
6-[4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl]-*N*-hexyl-  
nicotinamide;  
6-[4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl]-*N*-(3-methoxy-  
propyl)-nicotinamide;  
*N*-Hexyl-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
6-[4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl]-*N*-(4-phenyl-  
butyl)-nicotinamide;  
*N*-(3-Isopropoxy-propyl)-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-  
nicotinamide;  
6-[4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl]-*N*-(1-  
methylbutyl)-nicotinamide;  
6-[4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl]-*N*-pentyl-  
nicotinamide;  
6-[4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl]-*N*-hexyl-  
nicotinamide;  
*N*-Butyl-6-[4-[2-(4-chloro-phenyl)-propionyl]-piperazin-1-yl]-  
nicotinamide;

6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-N-(2-ethylsulfanyl-ethyl)-nicotinamide;  
6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-N-pentyl-nicotinamide;  
N-Hexyl-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
N-(3-Isopropoxy-propyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
N-Pentyl-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
N-Hexyl-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-(1,3-dimethylbutyl)-nicotinamide;  
6-[4-(Naphthalene-2-carbonyl)-piperazin-1-yl]-N-pentyl-nicotinamide;  
6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-N-(3-dimethylamino-propyl)-nicotinamide;  
N-(3-Dimethylamino-propyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;  
N-(3-Dimethylamino-propyl)-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
N-(3-Dimethylamino-propyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
N-(3-Butoxy-propyl)-6-{4-[3-(3,4-difluoro-phenyl)-propionyl]-piperazin-1-yl}-nicotinamide;  
N-(3-Methoxy-propyl)-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
N-(2-Methyl-butyl)-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
N-(3-Butoxy-propyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;  
and  
6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-N-(3-isopropoxy-propyl)-nicotinamide .

34. The method of Claim 30 wherein the compound of formula (I) is a compound wherein:

m is 1 or 2;

n is 1 or 2;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclalkyl, optionally substituted heterocyclalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

R<sup>3</sup> is optionally substituted aralkyl or optionally substituted aralkenyl; each R<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl; and each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl.

35. The method of Claim 34 wherein the compound of formula (I) is a compound wherein:

m is 1 or 2;

n is 1;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted heterocyclyl, optionally substituted heterocyclalkyl, optionally substituted heteroaryl and optionally substituted heteroarylalkyl;

R<sup>3</sup> is optionally substituted aralkyl or optionally substituted aralkenyl; each R<sup>4</sup> is independently hydrogen, alkyl, halo or haloalkyl; and R<sup>5</sup> is hydrogen, oxo, alkyl, halo or haloalkyl; and each R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl.

36. The method of Claim 35 wherein the compound of formula (I) is selected from the group consisting of the following:

6-[4-(2-Phenyl-butyryl)-piperazin-1-yl]-N-(3-phenyl-propyl)-nicotinamide;

6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-phenethyl-nicotinamide;

N-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide

6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-N-(3-phenyl-propyl)-nicotinamide

*N*-(1-Methyl-3-phenyl-propyl)-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide

*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide

6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-phenethyl-nicotinamide

*N*-(3-Phenyl-propyl)-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide

6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-[2-(3-chloro-phenyl)-ethyl]-nicotinamide

6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-(3-phenyl-propyl)-nicotinamide

6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-(1-methyl-3-phenyl-propyl)-nicotinamide

*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-[2-(4-chloro-phenyl)-propionyl]-piperazin-1-yl]-nicotinamide

*N*-[2-(3-Chlorophenyl)-ethyl]-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide

*N*-Phenethyl-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide

*N*-(3-Phenyl-propyl)-6-[4-(2-*p*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide

*N*-(1-Methyl-3-phenyl-propyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide

6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-*N*-(4-phenyl-butyryl)-nicotinamide

*N*-(4-Phenyl-butyryl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide

6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-(1-methyl-3-phenyl-propyl)-nicotinamide

6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-*N*-(3-phenyl-propyl)-nicotinamide

*N*-Phenethyl-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide

6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-*N*-(1-methyl-3-phenyl-propyl)-nicotinamide;

*N*-(4-Phenyl-butyryl)-6-[4-(2-*o*-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Imidazol-1-yl-propyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;

6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-*N*-(4-phenyl-

butyl)-nicotinamide;

6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-N-[2-(3H-imidazol-4-yl)-ethyl]-nicotinamide;

6-{4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl}-N-(3-imidazol-1-yl-propyl)-nicotinamide;

N-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;

6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-N-(3-imidazol-1-yl-propyl)-nicotinamide;

N-(2-Ethylsulfanyl-ethyl)-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;

N-(1-Methyl-3-phenyl-propyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;

6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-phenethyl-nicotinamide;

N-Phenethyl-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;

N-(Tetrahydro-furan-2-ylmethyl)-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;

6-{4-[2-(4-Chlorophenyl)-propionyl]-piperazin-1-yl}-N-(tetrahydro-furan-2-ylmethyl)-nicotinamide;

N-(4-Phenyl-butyl)-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;

6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-(tetrahydro-furan-2-ylmethyl)-nicotinamide;

N-(Tetrahydro-furan-2-ylmethyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2-Phenyl-butyryl)-piperazin-1-yl]-N-(tetrahydro-furan-2-ylmethyl)-nicotinamide;

6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-[2-(3H-imidazol-4-yl)-ethyl]-nicotinamide;

N-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;

N-(3-Imidazol-1-yl-propyl)-6-[4-(2-o-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;

6-{4-[3-(3,4-Difluoro-phenyl)-propionyl]-piperazin-1-yl}-N-(3-imidazol-1-yl-propyl)-nicotinamide;

*N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(2-phenyl-butyryl)-piperazin-1-yl]-nicotinamide;

*N*-(3-Imidazol-1-yl-propyl)-6-[4-(2-p-tolyl-acetyl)-piperazin-1-yl]-nicotinamide;

6-[4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl]-*N*-(tetrahydrofuran-2-ylmethyl)-nicotinamide; and

6-[4-[2-(2-Chloro-6-fluoro-phenyl)-acetyl]-piperazin-1-yl]-*N*-[2-(3H-imidazol-4-yl)-ethyl]-nicotinamide .

37. The method of Claim 1 wherein the mammal is a human.

38. The method of Claim 37 wherein the disease or condition is a disease or condition related to serum levels of triglyceride, VLDL, HDL, LDL, total cholesterol or the process of reverse cholesterol transport.

39. The method of Claim 37 wherein the disease or condition is a disease or condition related to serum triglyceride levels.

40. The method of Claim 37 wherein the disease or condition is a disease or condition related to serum cholesterol levels.

41. The method of Claim 37 wherein the disease or condition is selected from the group consisting of Type II diabetes, impaired glucose tolerance, insulin resistance, hypertension, obesity, hypertriglyceridemia, low HDL, lipidemia, dyslipidemia, microalbuminemia, hyperuricaemia, hypercoagulability, hyperleptinaemia, metabolic syndrome and any combination of these.

42. The method of Claim 41 wherein the disease or condition is Type II diabetes.

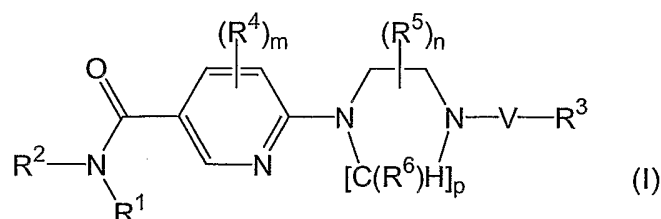
43. The method of Claim 41 wherein the disease or condition is obesity.

44. The method of Claim 41 wherein the disease or condition is dyslipidemia.



45. The method of Claim 41 wherein the disease or condition is metabolic syndrome.

46. A pharmaceutical composition comprising a pharmaceutically acceptable excipient or carrier and a therapeutically effective amount of a compound of formula (I):



wherein:

m is 1 to 3;

n is 1, 2, 3 or 4;

p is 2 or 3;

V is -C(O)- or -S(O)<sub>2</sub>-;

R<sup>1</sup> is hydrogen, alkyl, alkenyl, aryl, aralkyl, aralkenyl or cycloalkyl;

R<sup>2</sup> is selected from the group consisting of hydrogen, -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

R<sup>3</sup> is selected from the group consisting of hydrogen, -R<sup>9</sup>-OR<sup>8</sup>, -R<sup>9</sup>-N(R<sup>8</sup>)<sub>2</sub>, alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

each R<sup>4</sup> is independently hydrogen, alkyl, alkenyl, halo, haloalkyl, aryl or -R<sup>9</sup>-OR<sup>8</sup>;

each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl;

or one R<sup>5</sup> and one R<sup>6</sup> may together form an straight or branched alkylene bridge;

each R<sup>7</sup> is independently a straight or branched alkylene or alkenylene chain;

each R<sup>8</sup> is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocylalkyl, heteroaryl or heteroarylalkyl;

each R<sup>9</sup> is independently a direct bond or a straight or branched alkylene or alkenylene chain; and

R<sup>10</sup> is alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocylalkyl, heteroaryl or heteroarylalkyl;

as a single stereoisomer, a mixture of stereoisomers, or a racemic mixture thereof of stereoisomers;

or as a pharmaceutically acceptable salt, prodrug, solvate or polymorph thereof.

47. The pharmaceutical composition of Claim 46 wherein the therapeutically effective amount of the compound of formula (I) is an amount effective to modulate a lipid level in a mammal when administered to the mammal.

48. The pharmaceutical composition of Claim 47 wherein the lipid is triglyceride.

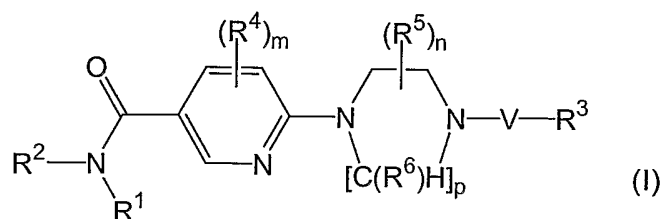
49. The pharmaceutical composition of Claim 47 wherein the lipid is cholesterol.

50. The pharmaceutical composition of Claim 46 wherein the therapeutically effective amount of the compound of formula (I) is an amount effective to modulate HDL-cholesterol levels when administered to a mammal.

51. A method for treating a patient for, or protecting a patient from developing, a disease or condition mediated by stearoyl-CoA desaturase (SCD), which method comprises administering to a patient afflicted with such disease or condition, or at risk of developing such disease or condition, a therapeutically effective amount of a

compound that inhibits activity of SCD in a patient when administered thereto.

52. A compound of formula (I):



wherein:

m is 1, 2 or 3;

n is 1, 2, 3 or 4;

p is 2, 3 or 4;

V is -C(O)-, -S(O)- or -S(O)<sub>2</sub>-;

R<sup>1</sup> is hydrogen, alkyl, alkenyl, aryl, aralkyl, aralkenyl or cycloalkyl;

R<sup>2</sup> is selected from the group consisting of hydrogen, -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

R<sup>3</sup> is selected from the group consisting of cycloalkyl substituted by one or more substituents independently selected from the group consisting of alkyl, alkenyl, halo, haloalkyl, haloalkenyl, cyano, nitro, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -R<sup>9</sup>-OR<sup>8</sup>, -R<sup>9</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>9</sup>-C(O)R<sup>8</sup>, -R<sup>9</sup>-C(O)OR<sup>8</sup>, -R<sup>9</sup>-C(O)N(R<sup>8</sup>)<sub>2</sub>, -R<sup>9</sup>-N(R<sup>8</sup>)C(O)OR<sup>10</sup>, -R<sup>9</sup>-N(R<sup>8</sup>)C(O)R<sup>10</sup>, -R<sup>9</sup>-N(R<sup>8</sup>)(S(O)<sub>t</sub>R<sup>10</sup>) (where t is 1 or 2), -R<sup>9</sup>-S(O)<sub>t</sub>OR<sup>10</sup> (where t is 1 or 2), -R<sup>9</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), and -R<sup>9</sup>-S(O)<sub>t</sub>N(R<sup>8</sup>)<sub>2</sub> (where t is 1 or 2);

each R<sup>4</sup> is independently hydrogen, alkyl, alkenyl, halo, haloalkyl, aryl, cyano, nitro, -R<sup>9</sup>-OR<sup>8</sup>, -R<sup>9</sup>-N(R<sup>8</sup>)<sub>2</sub> or -S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2);

each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl;

or one R<sup>5</sup> and one R<sup>6</sup> may together form an straight or branched

alkylene bridge;

each R<sup>7</sup> is independently a straight or branched alkylene or alkenylene chain;

each R<sup>8</sup> is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl or heteroarylalkyl;

each R<sup>9</sup> is independently a direct bond or a straight or branched alkylene or alkenylene chain; and

R<sup>10</sup> is alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl or heteroarylalkyl;

as a single stereoisomer, a mixture of stereoisomers, a racemic mixture thereof of stereoisomers, or as a tautomer;

or as a pharmaceutically acceptable salt, prodrug, solvate or polymorph thereof.

53. The compound of Claim 52 wherein R<sup>3</sup> is cyclopropyl substituted by optionally substituted aryl or optionally substituted heteroaryl.

54. The compound of Claim 53 wherein:

m is 1 or 2;

n is 1 or 2;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of hydrogen, -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0, 1 or 2), alkyl, alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclalkyl, optionally substituted heterocyclalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

each R<sup>4</sup> is independently hydrogen, alkyl, alkenyl, halo, haloalkyl, aryl or -R<sup>9</sup>-OR<sup>8</sup>;

each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, alkenyl, halo, haloalkyl or aryl;

each R<sup>7</sup> is independently a straight or branched alkylene or alkenylene chain;

each R<sup>8</sup> is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl;

R<sup>9</sup> is a direct bond or a straight or branched alkylene chain; and

R<sup>10</sup> is alkyl, aryl or aralkyl.

55. The compound of Claim 54 wherein:

m is 1 or 2;

n is 1 or 2;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl and optionally substituted heteroarylalkenyl;

each R<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl; and

each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl.

56. The compound of Claim 55 wherein:

m is 1;

n is 1;

p is 2;

V is -C(O)-;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is optionally substituted aralkyl, optionally substituted heteroarylalkyl, or optionally substituted heterocyclylalkyl;

R<sup>3</sup> is cyclopropyl substituted by phenyl;

R<sup>4</sup> is hydrogen, alkyl, halo or haloalkyl;

R<sup>5</sup> is hydrogen, oxo, alkyl, halo or haloalkyl; and

each R<sup>6</sup> is hydrogen.

57. The compound of Claim 56 selected from the group consisting of

the following:

6-[4-(2-Phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-*N*-(3-phenyl-propyl)-nicotinamide;

*N*-(4-Phenyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

*N*-(1-Methyl-3-phenyl-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide

*N*-Phenethyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;

6-[4-(2-Phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-*N*-(tetrahydrofuran-2-ylmethyl)-nicotinamide;

*N*-[2-(3H-Imidazol-4-yl)-ethyl]-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide and

*N*-(3-Imidazol-1-yl-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide

58. The compound of Claim 54 wherein:

*m* is 1 or 2;

*n* is 1 or 2;

*p* is 2;

*V* is -C(O)-;

*R*<sup>1</sup> is hydrogen or alkyl;

*R*<sup>2</sup> is selected from the group consisting of -*R*<sup>7</sup>-OR<sup>8</sup>, -*R*<sup>7</sup>-N(*R*<sup>8</sup>)<sub>2</sub>, -*R*<sup>7</sup>-S(O)<sub>*t*</sub>*R*<sup>10</sup> (where *t* is 0, 1 or 2), alkyl, alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl or optionally substituted cycloalkylalkenyl;

each *R*<sup>4</sup> is independently hydrogen, alkyl, halo, or haloalkyl;

each *R*<sup>5</sup> and *R*<sup>6</sup> is independently hydrogen, oxo, alkyl, halo or haloalkyl;

each *R*<sup>7</sup> is a straight or branched alkylene chain;

each *R*<sup>8</sup> is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl and aralkyl; and

*R*<sup>10</sup> is alkyl, aryl or aralkyl.

59. The compound of Claim 58 wherein:

*m* is 1;

*n* is 1;

*p* is 2;

V is -C(O)-;  
 R<sup>1</sup> is hydrogen or alkyl;  
 R<sup>2</sup> is selected from the group consisting of alkyl, -R<sup>7</sup>-OR<sup>8</sup>, -R<sup>7</sup>-N(R<sup>8</sup>)<sub>2</sub>, or -R<sup>7</sup>-S(O)<sub>t</sub>R<sup>10</sup> (where t is 0);  
 R<sup>3</sup> is cyclopropyl substituted by phenyl;  
 R<sup>4</sup> is hydrogen;  
 R<sup>5</sup> is hydrogen;  
 each R<sup>6</sup> is hydrogen;  
 R<sup>7</sup> is a straight or branched alkylene chain;  
 R<sup>8</sup> is hydrogen or alkyl; and  
 R<sup>10</sup> is alkyl, aryl or aralkyl.

60. The compound of Claim 59 selected from the group consisting of the following:

*N*-(3-Ethoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide  
*N*-(2-Ethylsulfanyl-ethyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(1,3-Dimethylbutyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Methyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Methoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Butoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-Pentyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Dimethylamino-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(3-Isopropoxy-propyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-(1-Methyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-nicotinamide;  
*N*-Butyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-

nicotinamide;

*N*-Hexyl-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-

nicotinamide; and

*N*-(2-Methyl-butyl)-6-[4-(2-phenyl-cyclopropanecarbonyl)-piperazin-1-yl]-

nicotinamide.

61. A method for treating a mammal having a disease or condition alleviated by the inhibition of stearyl-CoA desaturase (SCD) activity, which method comprises administering to a mammal in need thereof a therapeutically effective amount of a compound that inhibits the activity of SCD in the mammal.



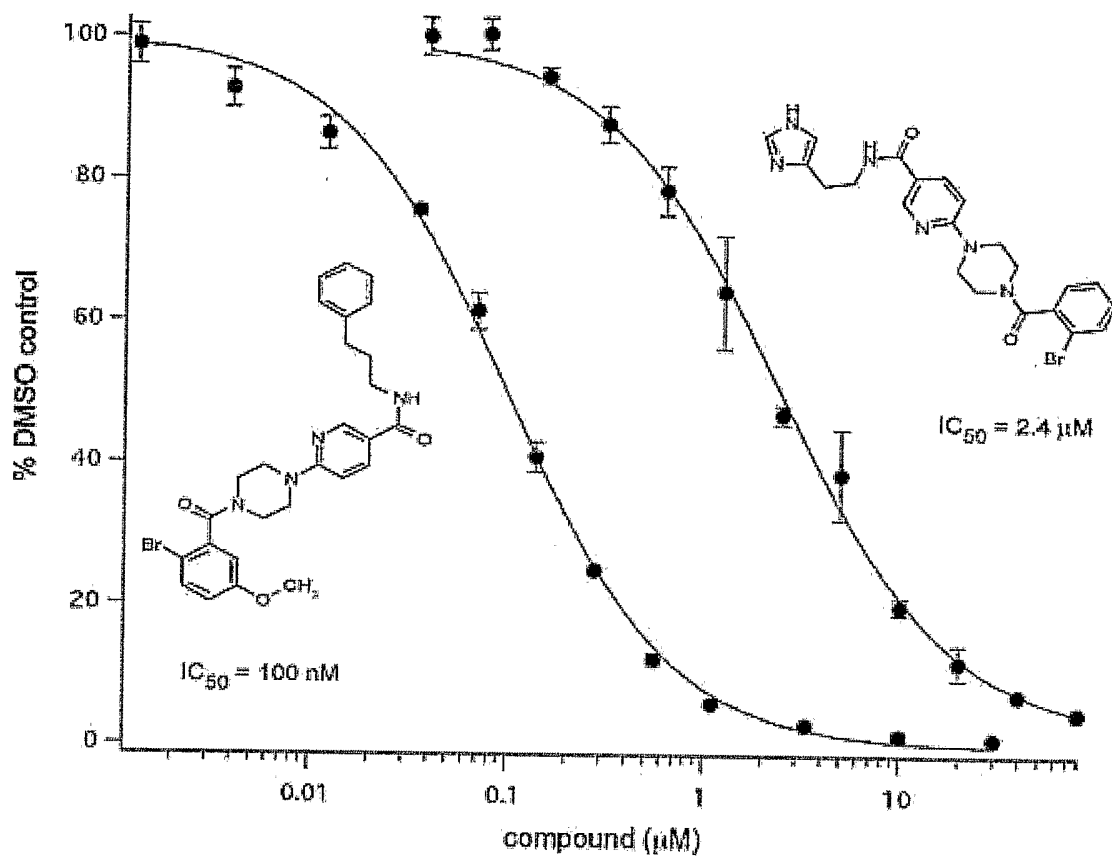


FIGURE 1

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2004/021792

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 A61K31/496 C07D401/00 A61P43/00 A61P3/04 A61P3/06  
A61P3/10

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

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A61K C07D

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

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

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

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 01/25203 A (TREGA BIOSCIENCES, INC) 12 April 2001 (2001-04-12)</p> <p>page 56, line 18 - page 57, line 27; claims; examples 1,3,4</p>	<p>1, 9, 10, 16-18, 20, 21, 37-41, 46-54, 58, 61</p>
E	<p>EP 1 452 525 A (NIPPON SHINYAKU CO., LTD) 1 September 2004 (2004-09-01)</p> <p>page 11, paragraph 51 - paragraph 52; examples 1, 21-27, 38-46, 50, 51, 53-62 -/--</p>	<p>1, 23-25, 27, 28, 37-41, 46-51, 61</p>

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

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- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

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- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

9 March 2005

Date of mailing of the international search report

18/03/2005

Name and mailing address of the ISA

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Authorized officer

Hoff, P

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/021792

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	& WO 03/037862 A (NIPPON SHINYAKU) 8 May 2003 (2003-05-08)	1,23-25, 27,28, 37-41, 46-51,61
X	----- WO 02/10154 A (ELI LILLY AND COMPANY; HERRON, DAVID, KENT; JOSEPH, SAJAN; MARQUART, A) 7 February 2002 (2002-02-07) page 1, line 1 - line 26; examples P29,P31,70	1,2,6,7, 37,41, 46-51,61
X	----- WO 03/043636 A (F. HOFFMANN-LA ROCHE AG) 30 May 2003 (2003-05-30)  page 5, line 9 - line 25; example 36	1,2,6,7, 37-40, 46-51,61
X	----- EP 1 396 487 A (YAMANOUCHI PHARMACEUTICAL CO. LTD) 10 March 2004 (2004-03-10)  page 10, paragraph 59 - paragraph 60; example 72	1,23, 37-40, 46-51,61
X	----- WO 03/050088 A (ELI LILLY AND COMPANY; HERRON, DAVID, KENT; JOSEPH, SAJAN; MARQUART, A) 19 June 2003 (2003-06-19) page 1, line 1 - line 27; examples 9,11	1,37-41, 46-51,61
X	----- EP 1 156 045 A (NIPPON SHINYAKU CO., LTD) 21 November 2001 (2001-11-21) page 8, paragraph 48; example 144	1,37-40, 46-51,61
X	----- EP 1 035 115 A (F. HOFFMANN-LA ROCHE AG) 13 September 2000 (2000-09-13) page 4, paragraph 9; examples 43,59	1,37, 46-51,61
X	----- WO 2004/010927 A (WISCONSIN ALUMNI RESEARCH FOUNDATION) 5 February 2004 (2004-02-05) page 3, paragraph 8 - paragraph 9; claims	51,61
X	----- WO 01/62954 A (XENON GENETICS, INC; WISCONSIN ALUMNI RESEARCH FOUNDATION; UNIVERSITY) 30 August 2001 (2001-08-30) page 18, line 6 - page 22, line 9; claims 32,38-48	51,61
X	----- DATABASE REGISTRY STN; Chemical Library 24 April 2003 (2003-04-24), XP002317630 RN: 504430-63-1	52
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Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE REGISTRY STN; Chemical Library 14 October 2001 (2001-10-14), XP002317631 RN: 362000-30-4 -----	52

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2004/021792

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

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

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 1-45,51,61 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

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

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

### Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/021792

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