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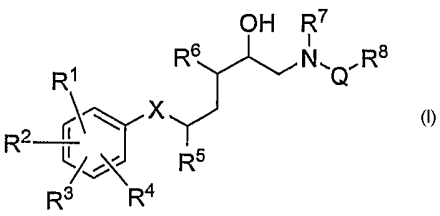
(54) Title: 1-ACYLAMINO-2-HYDROXY-3-AMINO-W-ARYLALKANES AS RENIN INHIBITORS



(I)

(57) Abstract: 1-Acylamino-2-hydroxy-3-amino-ω-arylalkanes of formula I. and the salts thereof, have renin-inhibiting properties and can be used as antihypertensive, medicinally active ingredients.

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1-ACYLAMINO-2-HYDROXY-3-AMINO-W-ARYLALKANES AS RENIN INHIBITORS

RELATED APPLICATIONS

This application claims priority from U.S. application 60/649,361, filed February 2, 2005, which is incorporated herein by reference.

BACKGROUND OF THE INVENTION

In the renin-angiotensin-aldosterone system (RAAS) the biologically active peptide angiotensin II (Ang II) is generated by a two-step mechanism. The highly specific aspartic protease renin cleaves angiotensinogen to angiotensin I (Ang I), which is then further processed to Ang II by the less specific angiotensin-converting enzyme (ACE). Ang II is known to work on at least two receptor subtypes called AT_1 and AT_2. Whereas AT_1 seems to transmit most of the known functions of Ang II, the role of AT_2 is still unknown.

Modulation of the RAAS represents a major advance in the treatment of cardiovascular diseases (Zaman, M. A. et al *Nature Reviews Drug Discovery* **2002**, *1*, 621-636). ACE inhibitors and AT_1 blockers have been accepted as treatments of hypertension (Waeber B. *et al.*, "The renin-angiotensin system: role in experimental and human hypertension", in Berkenhager W. H., Reid J. L. (eds): *Hypertension,* Amsterdam, Elsevier Science Publishing Co, **1996**, 489-519; Weber M. A., *Am. J. Hypertens.,* **1992**, *5*, 247S). In addition, ACE inhibitors are used for renal protection (Rosenberg M. E. *et al., Kidney International,* **1994**, *45*, 403; Breyer J. A. *et al., Kidney International,* **1994**, *45*, S156), in the prevention of congestive heart failure (Vaughan D. E. *et al., Cardiovasc. Res.,* **1994**, *28*, 159; Fouad-Tarazi F. *et al., Am. J. Med.,* **1988**, *84 (Suppl. 3A)*, 83) and myocardial infarction (Pfeffer M. A. *et al., N Engl. J: Med,* **1992**, *327*, 669).

Interest in the development of renin inhibitors stems from the specificity of renin (Kleinert H. D., *Cardiovasc. Drugs,* **1995**, *9*, 645). The only substrate known for renin is angiotensinogen, which can only be processed (under physiological conditions) by renin. In contrast, ACE can also cleave bradykinin besides Ang I and can be bypassed by chymase, a serine protease (Husain A., *J. Hypertens.,* **1993**, *11*, 1155). In patients, inhibition of ACE thus leads to bradykinin accumulation causing cough (5-20%) and potentially life-threatening angioneurotic edema (0.1-0.2%) (Israili Z. H. *et al., Annals of Internal Medicine,* **1992**, *117*, 234). Chymase is not inhibited by ACE inhibitors. Therefore, the formation of Ang II is still possible in patients treated with ACE inhibitors. Blockade of the ATI receptor (e.g., by losartan)

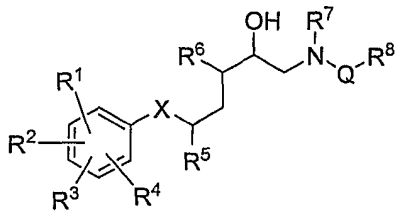
on the other hand overexposes other AT-receptor subtypes to Ang II, whose concentration is dramatically increased by the blockade of AT1 receptors. In summary, renin inhibitors are not only expected to be superior to ACE inhibitors and AT_1 blockers with regard to safety, but more importantly also with regard to their efficacy in blocking the RAAS.

Only limited clinical experience (Azizi M. *et al., J. Hypertens.,* **1994**, *12*, 419; Neutel J. M. *et al., Am. Heart,* **1991**, *122*, 1094) has been generated with renin inhibitors because their peptidomimetic character imparts insufficient oral activity (Kleinert H. D., *Cardiovasc. Drugs,* **1995**, *9*, 645). The clinical development of several compounds has been stopped because of this problem together with the high cost of goods. Only one compound has entered clinical trials (Rahuel J. *et al., Chem. Biol.,* **2000**, *7*, 493; Mealy N. E., *Drugs of the Future,* **2001**, *26*, 1139). Thus, metabolically stable, orally bioavailable and sufficiently soluble renin inhibitors that can be prepared on a large scale are not available. Recently, the first non-peptide renin inhibitors were described which show high *in vitro* activity (Oefner C. *et al., Chem. Biol.,* **1999**, *6*, 127; Patent Application WO 97/09311; Maerki H. P. *et al., Il Farmaco,* **2001**,*56*,21). The present invention relates to the unexpected identification of renin inhibitors of a non-peptidic nature and of low molecular weight. Orally active renin inhibitors which are active in indications beyond blood pressure regulation where the tissular renin-chymase system may be activated leading to pathophysiologically altered local functions such as renal, cardiac and vascular remodeling, atherosclerosis, and restenosis, are described.

All documents cited herein are incorporated by reference.

SUMMARY OF THE INVENTION

It has now been found that 1-acylamino-2-hydroxy-3-amino-ω-arylalkanes of formula **I**

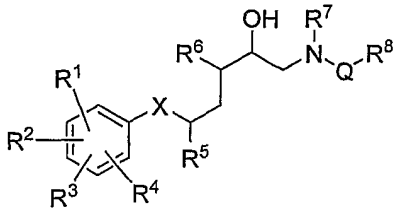


I

and the salts thereof have renin-inhibiting properties and can be used as antihypertensive, and renal, cardiac and vascular protecting medicinally active ingredients.

DETAILED DESCRIPTION

An embodiment of the invention is a compound of formula I



I

wherein

R^1 is hydrogen, halogen, hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, lower alkylthio-lower alkoxy, cyano-lower alkoxy, hydroxy-lower alkoxy, carboxy-lower alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, N-mono- or N,N-di-lower alkylcarbamoyl-lower alkoxy, or aryl;

R^2 is hydrogen, halogen, cyano, carbamoyl, lower alkyl, lower haloalkyl, cycloalkyl, halocycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-loweralkyl, cyano-lower alkyl, hydroxy-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, lower alkoxy-lower alkoxy-lower alkyl, lower haloalkoxy-lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, halocycloalkoxy-lower alkyl, hydroxy, lower alkanoyloxy-lower alkoxy, hydroxy-lower alkoxy, halo-(hydroxy)-lower alkoxy, lower alkanesulfonyl-(hydroxy)-lower alkoxy, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, lower alkanoylamino-lower alkyl, lower alkoxycarbonyl-amino-lower alkyl, aminocarbonylamino-lower alkyl, lower alkylaminocarbonylamino-lower alkyl, di(lower alkyl)aminocarbonylamino-lower alkyl, aminosulfonylamino-lower alkyl, lower alkylaminosulfonylamino-lower alkyl, di(lower alkyl)aminosulfonylamino-lower alkyl, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy, lower alkanoylamino-lower alkoxy, lower alkoxycarbonyl-amino-lower alkoxy, aminocarbonylamino-lower alkoxyl, lower alkylaminocarbonylamino-lower alkoxy, di(lower alkyl)aminocarbonylamino-lower alkoxy, aminosulfonylamino-lower alkoxy, lower alkylaminosulfonylamino-lower alkoxy, di(lower alkyl)aminosulfonylamino-lower alkoxy, oxo-lower alkoxy, lower alkoxy, lower haloalkoxy, cycloalkoxy, lower halocycloalkoxy, cycloalkyl-lower alkoxy, halocycloalkyl-lower alkoxy, lower alkenyloxy, cycloalkoxy-lower alkoxy, halocycloalkoxy-lower alkoxy, lower alkoxy-lower alkoxy, lower haloalkoxy-lower alkyl, lower alkoxy-lower alkenyl, lower alkenyloxy-lower alkoxy, lower alkoxy-lower alkenyloxy, lower alkenyloxy-lower alkyl, lower alkanoyl-lower alkoxy, lower alkylthio-lower alkoxy, lower alkanesulfonyl-lower alkoxy, lower alkylthio-(hydroxy)-lower alkoxy, aryl-lower alkoxy, optionally N-oxidized pyridyl-lower alkoxy, thiazolylthio-

lower alkoxy or thiazolinylthio-lower alkoxy, imidazolylthio-lower alkoxy, optionally N-oxidized pyridylthio-lower alkoxy, pyrimidinylthio-lower alkoxy, cyano-lower alkoxy, carboxy-lower alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, N-mono- or N,N-di-lower alkylcarbamoyl-lower alkoxy, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, carbamoyl-lower alkyl, or N-mono- or N,N-di-lower alkylcarbamoyl-lower alkyl;

R^3 is hydrogen, halogen, cyano, carbamoyl, lower alkyl, lower haloalkyl, lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, hydroxy-lower alkyl, lower alkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, optionally partially hydrogenated or N-oxidized pyridyl-lower alkyl, thiazolyl-thio-lower alkyl or thiazolinylthio-lower alkyl, imidazolylthio-lower alkyl, optionally N-oxidized pyridylthio-lower alkyl, pyrimidinylthio-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, lower alkanoyl-amino-lower alkyl, lower alkanesulfonylamino-lower alkyl, polyhalo-lower alkane-sulfonylamino-lower alkyl, pyrrolidino-lower alkyl, piperidino-lower alkyl, piperazino-lower alkyl, N'-lower alkylpiperazino-lower alkyl or N'-lower alkanoylpiperazino-lower alkyl, morpholino-lower alkyl, thiomorpholino-lower alkyl, S-oxothiomorpholino-lower alkyl or S,S-dioxothio-morpholino-lower alkyl, cyano-lower alkyl, carboxy-lower alkyl, lower alkoxy-carbonyl-lower alkyl, carbamoyl-lower alkyl, N-mono- or N,N-di-lower alkyl-carbamoyl-lower alkyl, cycloalkyl; phenyl or naphthyl that is unsubstituted or substituted with one to three groups independently selected from lower alkyl, lower alkoxy, hydroxy, lower alkylamino, di-lower alkylamino, halogen, trifluoromethyl, trifluoromethoxy, and cyano; hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, cycloalkoxy-lower alkoxy, hydoxy-lower alkoxy, aryl, lower haloalkoxy, lower alkylthio-lower alkoxy,lower haloalkylthio-lower alkoxy, lower alkanesulfonyl-lower alkoxy, lower haloalkanesulfonyl-lower alkoxy, optionally hydrogenated heteroaryl-lower alkoxy, heterocyclyl-lower alkoxy, optionally partially or fully hydrogenated heteroarylthio-lower alkoxy, such as thiazolylthio-lower alkoxy or thiazolinylthio-lower alkoxy, imidazolylthio-lower alkoxy, optionally N-oxidized pyridylthio-lower alkoxy, pyrimidinylthio-lower alkoxy, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy, lower alkanoylamino-lower alkoxy, lower alkanesulfonylamino-lower alkoxy, polyhalo-lower alkanesulfonylamino-lower alkoxy, pyrrolidino-lower alkoxy, piperidino-lower alkoxy, piperazino- lower alkoxy, N'-lower alkylpiperazino- lower alkoxy or N'-lower alkanoylpiperazino-lower alkoxy, morpholino-lower alkoxy, thiomorpholino- lower alkoxy, S-oxothiomorpholino- lower alkoxy or S,S-dioxothiomorpholino-lower alkoxy, cyano-lower alkoxy, carboxy-lower

alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, N-mono- or N,N-di-lower alkylcarbamoyl-lower alkoxy, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, carbamoyl-lower alkyl, or N-mono- or N,N-di-lower alkylcarbamoyl-lower alkyl; or

R^2 and R^3 taken together with the atoms through which they are attached form a fused dioxolane, dioxane, benzene or cyclohexene ring, wherein said ring is substituted with up to 2 substituents independently selected from lower alkyl and lower alkoxy-lower alkyl;

R^4 is hydrogen, lower alkyl, hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, or cycloalkyl-lower alkoxy; or

R^3 and R^4 taken together with the atoms through which they are attached form a fused dioxolane, dioxane, benzene or cyclohexene ring, wherein said ring is substituted with up to 2 substituents independently selected from lower alkyl and lower alkoxy-lower alkyl; provided that R^3 does not form a ring with R^2;

X is methylene or hydroxymethylene;

R^5 is lower alkyl, lower haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, lower haloalkyl-cycloalkyl, cycloalkyl-lower alkyl, aryl, aryl-lower alkyl, heterocyclyl, heterocyclyl-lower alkyl;

R^6 is amino, lower alkylamino, di-lower alkylamino, or lower alkanoylamino;

R^7 is hydrogen, lower alkyl, lower haloalkyl, cycloalkyl, lower alkoxy-lower alkyl, or lower haloalkoxy-lower alkyl;

Q is carbonyl, thiocarbonyl, or sulfonyl;

R^8 is lower alkyl, lower haloalkyl, C_8-C_{15}alkyl, C_8-C_{15}haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-loweralkyl, lower haloalkoxy-lower alkyl, cycloalkoxy-lower alkyl, cycloalkoxy-cycloalkyl, lower alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, lower alkylthio-cycloalkyl, lower haloalkylthio-cycloalkyl, lower alkanesulfonyl-cycloalkyl, lower haloalkanesulfonyl-cycloalkyl, aryl, aryl-lower alkyl, aryl-lower hydroxyalkyl, arylcycloalkyl, aryloxy-lower alkyl, aryloxy cycloalkyl, arylthio-lower alkyl, arylsulfonyl-

lower alkyl, arylthio-cycloalkyl, arylsulfonyl-cycloalkyl, lower alkanoyl-lower alkyl, hydroxy-lower alkyl, amino-lower alkyl, lower alkanoylamino-lower alkyl, N-mono-lower alkylamino-lower alkyl, N,N-di-lower alkylamino-lower alkyl, piperidino-lower alkyl, hydroxypiperidino-lower alkyl, lower alkoxypiperidino-lower alkyl, morpholino-lower alkyl, dimethylmorpholino-lower alkyl, thiomorpholino-lower alkyl, S,S-dioxothiomorpholino-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, carbamoyl-lower alkyl, N-mono- lower alkylcarbamoyl-lower alkyl, N,N-di-lower alkylcarbamoyl-lower alkyl, carboxy-(hydroxy)-lower alkyl, lower alkoxycarbonyl-(hydroxy)-lower alkyl, carbamoyl-(hydroxy)-lower alkyl, N-mono- lower alkylcarbamoyl-(hydroxy)-lower alkyl, N,N-di-lower alkylcarbamoyl-(hydroxy)-lower alkyl, 5- or 6-membered carboxycycloalkyl-lower alkyl, 5- or 6-membered lower alkoxycarbonyl-cycloalkyl-lower alkyl, 5- or 6-membered carbamoylcycloalkyl-lower alkyl, 5- or 6-membered N-mono-alkylcarbamoylcycloalkyl-lower alkyl, N,N-di-lower alkylcarbamoylcycloalkyl-lower alkyl, cyano-lower alkyl, sulfamoyl-lower alkyl, lower alkylsulfamoyl-lower alkyl, or di-lower alkylsulfamoyl-lower alkyl, imidazolyl-lower alkyl, oxopyrrolidinyl-lower alkyl, benzimidazolyl-lower alkyl, oxadiazolyl-lower alkyl, pyridyl-lower alkyl, oxopiperidinyl-lower alkyl or quinolinyl-lower alkyl, piperidin-4-yl-lower alkyl, or lower alkanoylpiperidin-4-yl-lower alkyl, wherein said aryl, imidazolyl, benzimidazolyl, oxadiazolyl, pyridyl, quinolinyl, aryloxy, arylthio and arylsulfonyl groups are optionally substituted with up to four groups independently selected from halo, cyano, nitro, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, optionally halogenated lower alkanesulfonyl, and lower alkoxycarbonyl;

or R^8 is OR^9 or NR^9R^{10}

R^9 is 1) hydrogen, lower alkyl, lower haloalkyl, lower alkenyl, $(C_8$-$C_{15})$alkyl, $(C_8$-$C_{15})$haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-loweralkyl, lower haloalkoxy-lower alkyl, cycloalkoxy-lower alkyl, cycloalkoxy-cycloalkyl, lower alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, lower alkylthio-cycloalkyl, lower haloalkylthio-cycloalkyl, lower alkanesulfonyl-cycloalkyl, lower haloalkanesulfonyl-cycloalkyl, aminocarbonyl-lower alkyl, lower alkyl-amonocarbonyl-lower alkyl, di(lower alkyl)-amonocarbonyl-lower alkyl, or 2) aryl, aryl-lower alkyl, aryloxy-lower alkyl, arylthio-lower alkyl, or arylsulfonyl-lower alkyl

wherein the aryl groups are optionally substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

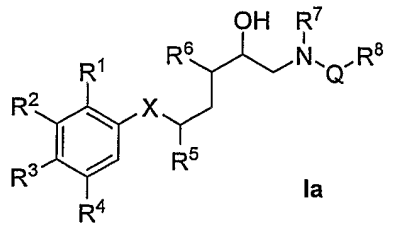
R^{10} is 1) hydrogen, lower alkyl, lower haloalkyl, $(C_8$-$C_{15})$alkyl, $(C_8$-$C_{15})$haloalkyl, cycloalkyl, halocycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, or 2) aryl or aryl-lower alkyl

wherein aryl is optionally substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

or R^9 and R^{10} taken together with the nitrogen to which they are attached form a 4-, 5-, 6- or 7-membered heterocyclic ring composed of carbon atoms and 0 or 1 N, O, or S atoms in addition to the nitrogen atom to which R^9 and R^{10} are attached, said ring atoms being substituted with the appropriate number of hydrogen atoms and optionally substituted with up to four groups independently selected from halogen, $(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, lower alkanoyl, lower alkoxycarbonyl, aryl, aryl-lower alkyl, and oxo, such that substitution of one oxo group on a carbon atom forms a carbonyl group and substitution of one or two oxo groups on sulfur forms sulfoxide or sulfone groups respectively; wherein the aryl and arylalkyl groups are substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

and the enantiomers, diastereomers, and salts thereof.

A preferred embodiment of the invention is a compound of the formula **Ia**



Ia

in which the substituents R^1-R^8, X, and Q are defined as above for **I** and the enantiomers, diastereomers, and salts thereof.

Another embodiment of the invention is a compound of formula **Ia**, wherein R^1 is hydrogen or aryl;

R^2 is hydrogen, lower alkyl, cycloalkyl-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, lower alkoxy-lower alkoxy, lower haloalkoxy-lower alkoxy, lower alkoxy-lower alkoxy-lower alkyl; cycloalkyl-lower alkoxy, phenyl-lower alkoxy that is unsubstituted or substituted by lower alkyl, lower alkoxy, hydroxy, halogen, nitro and/or by amino; optionally N-oxidized pyridyl-lower alkoxy, lower alkylthio-lower alkoxy, lower alkane-sulfonyl-lower alkoxy, lower alkanoyl-lower alkoxy, cyano-lower alkoxy, carboxy-lower alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, lower alkylcarbamoyl-lower alkoxy, or di-lower alkylcarbamoyl-lower alkoxy;

R^3 is hydrogen, halogen, cyano, lower alkyl, lower haloalkyl, aryl, hydroxy, lower alkoxy, or polyhalo-lower alkoxy; or

R^2 and R^3 taken together with the atoms through which they are attached form a fused dioxolane ring, wherein said ring is substituted with up to 2 substituents independently selected from lower alkyl and lower alkoxy-lower alkyl;

R^4 is hydrogen, lower alkoxy-lower alkoxy, lower alkoxy-lower alkyl, or cyloalkyl-lower alkoxy; or

R^3 and R^4 taken together with the atoms through which they are attached form a fused dioxolane ring, wherein said ring is substituted with up to 2 substituents independently selected from lower alkyl and lower alkoxy-lower alkyl; provided that R^3 does not form a ring with R^2;

X is methylene or hydroxymethylene;

R^5 is lower alkyl or cycloalkyl;

R^6 is amino, lower alkylamino, di-lower alkylamino, or lower alkanoylamino;

R^7 is hydrogen or methyl;

Q is carbonyl, thiocarbonyl, or sulfonyl;

R^8 is lower alkyl, lower haloalkyl, C_8-C_{15} alkyl, C_8-C_{15} haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, cycloalkoxy-lower alkyl, cycloalkoxy-cycloalkyl, lower alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, lower alkylthio-cycloalkyl, lower haloalkylthio-cycloalkyl, lower alkanesulfonyl-cycloalkyl, lower haloalkanesulfonyl-cycloalkyl, aryl, aryl-lower alkyl, aryl-lower hydroxyalkyl, arylcycloalkyl, aryloxy-lower alkyl, aryloxy cycloalkyl, arylthio-lower alkyl, arylsulfonyl-lower alkyl, arylthio-cycloalkyl, or arylsulfonyl-cycloalkyl wherein said aryl, aryloxy, arylthio and arylsulfonyl groups are optionally substituted with up to four groups independently selected from halo, cyano, nitro, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, optionally halogenated lower alkanesulfonyl, amino, lower alkylamino, di-lower allkylamino, and lower alkoxycarbonyl;

or R^8 is OR^9 or NR^9R^{10};

R^9 is selected from 1) hydrogen, lower alkyl, lower haloalkyl, lower alkenyl, (C_8-C_{15})alkyl, (C_8-C_{15})haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-loweralkyl, lower haloalkoxy-lower alkyl, cycloalkoxy-lower alkyl, cycloalkoxy-cycloalkyl, lower alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, lower alkylthio-cycloalkyl, lower haloalkylthio-cycloalkyl, lower alkanesulfonyl-cycloalkyl, lower haloalkanesulfonyl-cycloalkyl, aminocarbonyl-lower alkyl, lower alkyl-amonocarbonyl-lower alkyl, or di(lower alkyl)-amonocarbonyl-lower alkyl, or 2) aryl, aryl-lower alkyl, aryloxy-lower alkyl, arylthio-lower alkyl, or arylsulfonyl-lower alkyl

wherein aryl is optionally substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally

halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

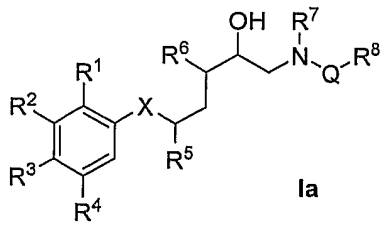
R^{10} is 1) hydrogen, lower alkyl, lower haloalkyl, (C_8-C_{15})alkyl, (C_8-C_{15})haloalkyl, cycloalkyl, halocycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, or lower haloalkanesulfonyl-lower alkyl, or 2) aryl or aryl-lower alkyl

wherein aryl is optionally substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

or R^9 and R^{10} taken together with the nitrogen to which they are attached form a 4-, 5-, 6- or 7-membered heterocyclic ring composed of carbon atoms and 0 or 1 N, O, or S atoms in addition to the nitrogen atom to which R^9 and R^{10} are attached, said ring atoms being substituted with the appropriate number of hydrogen atoms and optionally substituted with up to four groups independently selected from halogen, (C_1-C_6)alkyl, halo(C_1-C_6)alkyl , lower alkanoyl, lower alkoxycarbonyl, aryl, aryl-lower alkyl, and oxo, such that substitution of one oxo group on a carbon atom forms a carbonyl group and substitution of one or two oxo groups on sulfur forms sulfoxide or sulfone groups respectively; wherein the aryl and arylalkyl groups are substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

and the enantiomers, diastereomers, and salts thereof.

A preferred embodiment of the invention is a compound of the formula **Ia**



Ia

and the enantiomers, diastereomers, and salts thereof.

Another embodiment of the invention is a compound of formula Ia wherein

R^1 is hydrogen;

R^2 is $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkoxy, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, or cyloalkyl-lower alkoxy;

R^3 is fluoro, chloro, bromo, cyano, $(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$ haloalkyl, aryl, $(C_1$-$C_4)$alkoxy, or $(C_1$-$C_4)$haloalkoxy;

R^4 is hydrogen;

X is methylene;

R^5 is $(C_3$-$C_5)$alkyl;

R^6 is amino;

R^7 is hydrogen or methyl;

Q is carbonyl or sulfonyl;

R^8 is $(C_3$-$C_{11})$alkyl, $(C_3$-$C_{11})$haloalkyl, $(C_3$-$C_7)$cycloalkyl, $(C_3$-$C_{11})$cycloalkylalkyl, $(C_3$-$C_{11})$-alkoxyalkyl, aryl, aryl$(C_1$-$C_3)$alkyl, aryl$(C_3$-$C_6)$cycloalkyl, arylhydroxy$(C_1$-$C_3)$alkyl, aryloxy$(C_1$-$C_5)$alkyl, or aryloxy$(C_3$-$C_6)$cycloalkyl wherein aryl or aryloxy may be unsubstituted or substituted with one to three groups independently selected from halogen, cyano, $(C_1$-$C_3)$alkyl, halo$(C_1$-$C_3)$alkyl, $(C_1$-$C_3)$alkoxy, halo$(C_1$-$C_3)$alkoxy;

or R^8 is NR^9R^{10};

R^9 is 1) hydrogen, $(C_1$-$C_{10})$alkyl, $(C_3$-$C_7)$alkenyl, $(C_3$-$C_7)$cycloalkyl, $(C_3$-$C_6)$cycloalkyl$(C_1$-$C_5)$alkyl, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, or aminocarbonyl$(C_1$-$C_5)$alkyl, or 2) aryl or aryl$(C_1$-$C_4)$alkyl

wherein aryl is optionally substituted with up to 4 groups independently selected from fluorine, chlorine, cyano, $(C_1$-$C_3)$alkyl, halo$(C_1$-$C_3)$alkyl, $(C_1$-$C_3)$alkoxy, halo$(C_1$-$C_3)$alkoxy, and $(C_1$-$C_3)$alkanesulfonyl;

R^{10} is hydrogen, lower alkyl, or lower haloalkyl; or

R^8 and R^9 taken together are with the nitrogen to which they are attached form an azetidine, pyrrolidine, piperidine, azepine, piperazine, morpholine, or thiomorpholine ring said ring being optionally substituted with up to two groups independently

selected from halogen, (C_1-C_3)alkyl, halo(C_1-C_3)alkyl, and oxo, such that substitution of one oxo group on a carbon atom forms a carbonyl group and substitution of one or two oxo groups on sulfur forms sulfoxide or sulfone groups respectively;

and the enantiomers, diastereomers, and salts thereof.

Another embodiment of the invention is compounds of formula **Ia** wherein:

R^1 is hydrogen;

R^2 is 3-methoxypropoxy, 3-ethoxypropoxy, 4-methoxybutyl, or 2-(cyclopropyl)ethoxy;

R^3 is fluoro, chloro, bromo, cyano, methyl, ethyl, isopropyl or tert-butyl, trifluoromethyl, pentafluoroethyl, phenyl, methoxy, difluoromethoxy, or trifluoromethoxy;

R^4 is hydrogen;

X is methylene;

R^5 is branched (C_3-C_5)alkyl;

R^6 is amino;

R^7 is hydrogen;

Q is carbonyl or sulfonyl; and

R^8 is propyl, 2,2-dimethylpropyl, butyl, tert-butyl, n-pentyl, 2-methyl-2-butyl, hexyl, 2-hexyl, 2-methyl-2-pentyl, 2,2-dimethylpentyl, 3-heptyl, 2-methyl-2-hexyl, 2,4,4-trimethylpentyl, 2,2,2-trifluoroethyl, 3,3,3-trifluoropropyl, 4,4,4-trifluorobutyl, 1,1,1,3,3,3-hexafluoro-2-methyl-2-propyl, cyclohexyl, 1-methylcyclohexyl, 4-methylcyclohexyl, cyclopropylmethyl, cyclopentylmethyl, 1-cyclopentyl-1-pentyl, cyclohexylmethyl, 2-cyclohexyl-2-propyl, 2-cyclopropyl-1,1-dimethylethyl, 3-cyclopropyl-2-methyl-2-butyl, 3-methoxypropyl, 2-propoxy-2-propyl, phenyl, benzyl, 3-methyl-benzyl, 2-fluorobenzyl, 3-fluorobenzyl, 4-fluorobenzyl, 2,4-difluorobenzyl, 2,3-difluorobenzyl, 3,4-difluorobenzyl, 4-cyanobenzyl, 2-(trifluoromethyl)benzyl, 3-(trifluoromethyl)benzyl, 4-(trifluoro-methyl)benzyl, 4-(trifluoromethoxy)benzyl, phenethyl, 3-phenylpropyl, 2-phenyl-2-propyl, 3-(4-fluorophenyl)-3-pentyl, 1-phenyl-1-cyclopropyl, 1-(4-methylphenyl)-1-cyclopropyl, 1-(4-fluoro-phenyl)-1-cyclopropyl, 1-(4-methoxyphenyl)-1-cyclopropyl, 1-(2,4-dichlorophenyl)-1-cyclopropyl, 1-phenyl-1-

cyclopentyl, 1-phenyl-1-cyclohexyl, 1-(4-fluorophenyl)-1-cyclohexyl, 3-hydroxy-2-methyl-3-phenyl-2-propyl, 2-(4-cyanophenoxy)-2-propyl, or 2-(4-chlorophenoxy)-2-propyl;

or R^8 is NR^9R^{10};

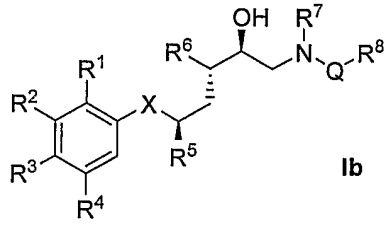
R^9 is hydrogen, butyl, isobutyl, t-butyl, pentyl, hexyl, 2,2-dimethyl-1-pentyl, 2-methyl-2-hexyl, 2,4,4-trimethyl-2-pentyl, allyl, 2-(cyclopropyl)ethyl, cyclohexylmethyl, 2-(cyclohexyl)methyl, cyclohexyl, 2-methoxyethyl, benzyl, 2-phenylethyl, 3-phenylpropyl, 3-(4-fluorophenyl)-2-methyl-2-propyl, 3-fluorophenyl, 3-(trifluoromethyl)phenyl, or 2-(aminocarbonyl)-2-methyl-1-propyl,

R^{10} is hydrogen, methyl, or isobutyl;

or R^9-R^{10} is $-(CH_2)_5-$ or $-(CH_2)_2O(CH_2)_2-$;

and the enantiomers, diastereomers, and salts thereof.

Especially effective are those compounds of formula **Ia** wherein at least one, two, or preferably all three of the asymmetric carbon atoms of the main chain have the stereochemical configuration shown in formula **Ib**



Ib

and the pharmaceutically acceptable salts thereof.

Preferred compounds of formulae **I**, **Ia**, and **Ib** are those wherein X is methylene and R^5 is isopropyl.

Especially preferred are the pharmaceutically acceptable salts of compounds of formulae **I**, **Ia**, and **Ib**.

Another embodiment of the invention is each of the following compounds and their enantiomers, diastereomers and salts:

Cpd. No.	Name
I-1	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)butyramide
I-2	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclopropylacetamide
I-3	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)pentanamide
I-4	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)pivalamide
I-5	N-((2S,3S,5S)-5-(3-(2-cyclopropylethoxy)benzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-6	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)hexanamide
I-7	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylbutanamide
I-8	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3,3-dimethylbutanamide
I-9	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-methoxybutanamide
I-10	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)benzamide
I-11	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3,3,3-trifluoropropanamide
I- 12	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclopentylacetamide
I-13	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)cyclohexanecarboxamide
I-14	N-((2S,3S,5S)-5-(3-(3-ethoxypropoxy)benzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-15	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)heptanamide
I-16	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylpentanamide
I-17	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methylhexanamide
I-18	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-phenylacetamide
I-19	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-6-methyl-1-(butanesulfonylamino)heptan-2-ol
I-20	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxyheptyl)-4,4,4-trifluorobutanamide
I-21	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclohexylacetamide
I-22	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(1-(4-fluorophenyl)-2-methylpropan-2-yl)urea
I-23	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-methylcyclohexanecarboxamide
I-24	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-methylcyclohexanecarboxamide
I-25	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-ethylbenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-26	N-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-ethylbenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-27	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-N-isopropylpentanamide
I-28	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-29	N-((2R,3R,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide

I-30	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3,3-dimethylhexanamide
I-31	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-ethylhexanamide
I-32	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methyl-2-propoxypropanamide
I-33	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-ethoxy-2,2-dimethylpropanamide
I-34	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-phenylpropanamide
I-35	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-m-tolylacetamide
I-36	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-6-methyl-1-(pentanesulfonylamino)heptan-2-ol
I-37	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(2-fluorophenyl)acetamide
I-38	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(3-fluorophenyl)acetamide
I-39	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)acetamide
I-40	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)acetamide
I-41	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-5,5,5-trifluoropentanamide
I-42	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-cyclopropyl-2,2-dimethylbutanamide
I-43	N-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)- 4-cyclopropyl-2,2-dimethylbutanamide
I-44	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-6-methyl-1-(benzenesulfonylamino)heptan-2-ol
I-45	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3,5,5-trimethylhexanamide
I-46	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-N,2,2-trimethylhexanamide
I-47	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-cyanophenyl)acetamide
I-48	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-phenylcyclopropanecarboxamide
I-49	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-phenylbutanamide
I-50	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methyl-2-phenylpropanamide
I-51	N-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methyl-2-phenylpropanamide
I-52	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclohexyl-2-methylpropanamide
I-53	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(3,4-difluorophenyl)acetamide
I-54	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(2,4-difluorophenyl)acetamide
I-55	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(2,3-difluorophenyl)acetamide
I-56	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-6-methyl-1-(benzylsulfonylamino)heptan-2-ol
I-57	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-p-tolylcyclopropanecarboxamide
I-58	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-isopropyl-N-butanesulfonylamino)-6-methylheptan-2-ol
I-59	(2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-isopropyl-N-butanesulfonylamino)-6-methylheptan-2-ol

I-60	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)-2-methylpropanamide
I-61	N-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)-2-methylpropanamide
I-62	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)-2-methylpropanamide
I-63	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclopentylhexanamide
I-64	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-phenylcyclopentanecarboxamide
I-65	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-phenylbenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-66	N-((2S,3S,5S)-5-(5-(3-methoxypropoxy)-2-phenylbenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-67	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-(4-methoxyphenyl)cyclopropanecarboxamide
I-68	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-bromobenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-69	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-hydroxy-2,2-dimethyl-3-phenylpropanamide
I-70	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-(4-chlorophenyl)cyclopropanecarboxamide
I-71	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-isopropyl-N-benzenesulfonylamino)-6-methylheptan-2-ol
I-72	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(2-(trifluoromethyl)phenyl)acetamide
I-73	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(3-(trifluoromethyl)phenyl)acetamide
I-74	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-(trifluoromethyl)phenyl)acetamide
I-75	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-phenylcyclohexanecarboxamide
I-76	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-cyanophenoxy)-2-methylpropanamide
I-77	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-bis(trifluoromethyl)propanamide
I-78	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-ethyl-2-(4-fluorophenyl)butanamide
I-79	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-isopropyl-N-benzylsulfonylamino)-6-methylheptan-2-ol
I-80	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-chlorophenoxy)-2-methylpropanamide
I-81	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-(trifluoromethoxy)phenyl)acetamide
I-82	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-(4-fluorophenyl)cyclohexanecarboxamide
I-83	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-(2,4-dichlorophenyl)cyclopropanecarboxamide
I-84	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)urea
I-85	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-butylurea
I-86	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-tert-butylurea
I-87	isobutyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptylcarbamate
I-88	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)piperidine-1-carboxamide
I-89	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-cyclopropylethyl)urea

I-90	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)morpholine-4-carboxamide
I-91	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylurea
I-92	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylurea
I-93	1-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylurea
I-94	pentyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptylcarbamate
I-95	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(3-methoxypropyl)urea
I-96	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-ethoxyethyl)urea
I-97	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-cyclohexylurea
I-98	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-hexylurea
I-99	3-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-methyl-1-pentylurea
I-100	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-methyl-3-pentylurea
I-101	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylthiourea
I-102	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-benzylurea
I-103	benzyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptylcarbamate
I-104	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(butylaminosulfonylamino)-6-methylheptan-2-ol
I-105	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(3-fluorophenyl)urea
I-106	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(cyclohexylmethyl)urea
I-107	3-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-cyclohexyl-1-methylurea
I-108	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-(butylaminosulfonyl)-N-isopropylamino)-6-methylheptan-2-ol
I-109	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2,2-dimethylpentyl)urea
I-110	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-methylhexan-2-yl)urea
I-111	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-carbamoyl-2-methylpropyl)urea
I-112	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-phenethylurea
I-113	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(pentylaminosulfonylamino)-6-methylheptan-2-ol
I-114	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-cyclohexylethyl)urea
I-115	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2,4,4-trimethylpentan-2-yl)urea
I-116	3-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1,1-diisobutylurea
I-117	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(3-phenylpropyl)urea
I-118	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-(allylaminosulfonyl)-N-isopropylamino)-6-methylheptan-2-ol
I-119	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(3-(trifluoromethyl)phenyl)urea and

I-120	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(1-(4-fluorophenyl)-2-methylpropan-2-yl)urea.

A preferred embodiment of the invention is each of the following compounds or their enantiomers, diastereomers, and pharmaceutically acceptable salts:

Cpd. No.	Name
I-6	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)hexanamide
I-16	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylpentanamide
I-17	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methylhexanamide
I-21	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclohexylacetamide
I-26	N-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-ethylbenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-28	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-28	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-31	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-ethylhexanamide
I-33	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-ethoxy-2,2-dimethylpropanamide
I-39	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)acetamide
I-40	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)acetamide
I-42	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-cyclopropyl-2,2-dimethylbutanamide
I-50	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methyl-2-phenylpropanamide
I-52	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclohexyl-2-methylpropanamide
I-60	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)-2-methylpropanamide

I-62	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)-2-methylpropanamide
I-64	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-phenylcyclopentanecarboxamide
I-74	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-(trifluoromethyl)phenyl)acetamide
I-75	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-phenylcyclohexanecarboxamide
I-78	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-ethyl-2-(4-fluorophenyl)butanamide
I-82	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-(4-fluorophenyl)cyclohexanecarboxamide
I-85	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-butylurea
I-91	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylurea
I-92	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylurea
I-98	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-hexylurea
I-99	3-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-methyl-1-pentylurea
I-109	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2,2-dimethylpentyl)urea
I-115	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2,4,4-trimethylpentan-2-yl)urea and
I-116	3-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1,1-diisobutylurea.

A more preferred embodiment of the invention is each of the following compounds or their enantiomers, diastereomers, and pharmaceutically acceptable salts:

Cpd. No.	Name
I-28	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide

I-42	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-cyclopropyl-2,2-dimethylbutanamide
I-50	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methyl-2-phenylpropanamide
I-52	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclohexyl-2-methylpropanamide and
I-62	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)-2-methylpropanamide.

Another embodiment of the invention is each of the following compounds and their enantiomers, diastereomers, and pharmaceutically acceptable salts:

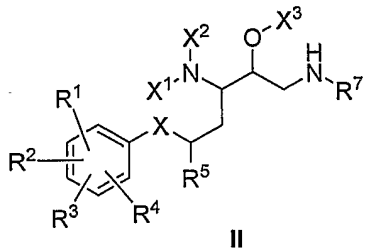
Cpd. No.	Name
I-6	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)hexanamide
I-17	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methylhexanamide
I-21	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclohexylacetamide
I-26	N-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-ethylbenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-31	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-ethylhexanamide
I-33	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-ethoxy-2,2-dimethylpropanamide
I-39	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)acetamide
I-40	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)acetamide
I-42	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-cyclopropyl-2,2-dimethylbutanamide
I-74	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-(trifluoromethyl)phenyl)acetamide
I-75	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-phenylcyclohexanecarboxamide

I-78	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-ethyl-2-(4-fluorophenyl)butanamide
I-82	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-(4-fluorophenyl)cyclohexanecarboxamide
I-85	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-butylurea
I-91	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylurea
I-92	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylurea
I-98	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-hexylurea
I-99	3-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-methyl-1-pentylurea
I-109	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2,2-dimethylpentyl)urea
I-115	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2,4,4-trimethylpentan-2-yl)urea and
I-116	3-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1,1-diisobutylurea.

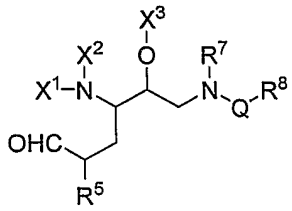
Another more preferred embodiment of the invention is each of the following compounds or their enantiomers, diastereomers, and pharmaceutically acceptable salts:

Cpd. No.	Name
I-42	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-cyclopropyl-2,2-dimethylbutanamide

Other embodiments of the invention are the intermediates used for the preparation of the compounds of the invention, especially the intermediates resulting in the preferred compounds of formula **I**, to processes for their preparation, and to their use as intermediates. This primarily relates to compounds of formulae **II** and **III**:



II



III

which are suitable as intermediates for the preparation of compounds of formula I.

Thus, another embodiment of the invention is a compound of formula II, wherein

R^1 is hydrogen, halogen, hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, lower alkylthio-lower alkoxy, cyano-lower alkoxy, hydroxy-lower alkoxy, carboxy-lower alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, N-mono- or N,N-di-lower alkylcarbamoyl-lower alkoxy, or aryl;

R^2 is hydrogen, halogen, cyano, carbamoyl, lower alkyl, lower haloalkyl, cycloalkyl, halocycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-loweralkyl, cyano-lower alkyl, hydroxy-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, lower alkoxy-lower alkoxy-lower alkyl, lower haloalkoxy-lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, halocycloalkoxy-lower alkyl, hydroxy, lower alkanoyloxy-lower alkoxy, hydroxy-lower alkoxy, halo-(hydroxy)-lower alkoxy, lower alkanesulfonyl-(hydroxy)-lower alkoxy, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, lower alkanoylamino-lower alkyl, lower alkoxycarbonyl-amino-lower alkyl, aminocarbonylamino-lower alkyl, lower alkylaminocarbonylamino-lower alkyl, di(lower alkyl)aminocarbonylamino-lower alkyl, aminosulfonylamino-lower alkyl, lower alkylaminosulfonylamino-lower alkyl, di(lower alkyl)aminosulfonylamino-lower alkyl, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy, lower alkanoylamino-lower alkoxy, lower alkoxycarbonyl-amino-lower alkoxy, aminocarbonylamino-lower alkoxyl, lower alkylaminocarbonylamino-lower alkoxy, di(lower alkyl)aminocarbonylamino-lower alkoxy, aminosulfonylamino-lower alkoxy, lower alkylaminosulfonylamino-lower alkoxy, di(lower alkyl)aminosulfonylamino-lower alkoxy, oxo-lower alkoxy, lower alkoxy, lower haloalkoxy, cycloalkoxy, lower halocycloalkoxy, cycloalkyl-lower alkoxy, halocycloalkyl-lower alkoxy, lower alkenyloxy, cycloalkoxy-lower alkoxy, halocycloalkoxy-lower alkoxy, lower alkoxy-lower alkoxy, lower haloalkoxy-lower alkyl, lower alkoxy-lower alkenyl, lower alkenyloxy-lower alkoxy, lower alkoxy-lower alkenyloxy, lower alkenyloxy-lower alkyl, lower alkanoyl-lower alkoxy, lower alkylthio-

lower alkoxy, lower alkanesulfonyl-lower alkoxy, lower alkylthio-(hydroxy)-lower alkoxy, aryl-lower alkoxy, optionally N-oxidized pyridyl-lower alkoxy, thiazolylthio-lower alkoxy or thiazolinylthio-lower alkoxy, imidazolylthio-lower alkoxy, optionally N-oxidized pyridylthio-lower alkoxy, pyrimidinylthio-lower alkoxy, cyano-lower alkoxy, carboxy-lower alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, N-mono- or N,N-di-lower alkylcarbamoyl-lower alkoxy, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, carbamoyl-lower alkyl, or N-mono- or N,N-di-lower alkylcarbamoyl-lower alkyl;

R^3 is hydrogen, halogen, cyano, carbamoyl, lower alkyl, lower haloalkyl, lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, hydroxy-lower alkyl, lower alkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, optionally partially hydrogenated or N-oxidized pyridyl-lower alkyl, thiazolyl-thio-lower alkyl or thiazolinylthio-lower alkyl, imidazolylthio-lower alkyl, optionally N-oxidized pyridylthio-lower alkyl, pyrimidinylthio-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, lower alkanoyl-amino-lower alkyl, lower alkanesulfonylamino-lower alkyl, polyhalo-lower alkane-sulfonylamino-lower alkyl, pyrrolidino-lower alkyl, piperidino-lower alkyl, piperazino-lower alkyl, N'-lower alkylpiperazino-lower alkyl or N'-lower alkanoylpiperazino-lower alkyl, morpholino-lower alkyl, thiomorpholino-lower alkyl, S-oxothiomorpholino-lower alkyl or S,S-dioxothio-morpholino-lower alkyl, cyano-lower alkyl, carboxy-lower alkyl, lower alkoxy-carbonyl-lower alkyl, carbamoyl-lower alkyl, N-mono- or N,N-di-lower alkyl-carbamoyl-lower alkyl, cycloalkyl; phenyl or naphthyl that is unsubstituted or substituted with one to three groups independently selected from lower alkyl, lower alkoxy, hydroxy, lower alkylamino, di-lower alkylamino, halogen, trifluoromethyl, trifluoromethoxy, and cyano; hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, cycloalkoxy-lower alkoxy, hydoxy-lower alkoxy, aryl, lower haloalkoxy, lower alkylthio-lower alkoxy,lower haloalkylthio-lower alkoxy, lower alkanesulfonyl-lower alkoxy, lower haloalkanesulfonyl-lower alkoxy, optionally hydrogenated heteroaryl-lower alkoxy, heterocyclyl-lower alkoxy, optionally partially or fully hydrogenated heteroarylthio-lower alkoxy, such as thiazolylthio-lower alkoxy or thiazolinylthio-lower alkoxy, imidazolylthio-lower alkoxy, optionally N-oxidized pyridylthio-lower alkoxy, pyrimidinylthio-lower alkoxy, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy, lower alkanoylamino-lower alkoxy, lower alkanesulfonylamino-lower alkoxy, polyhalo-lower alkanesulfonylamino-lower alkoxy, pyrrolidino-lower alkoxy, piperidino-lower alkoxy, piperazino- lower alkoxy, N'-lower alkylpiperazino- lower alkoxy or N'-lower alkanoylpiperazino-lower alkoxy,

morpholino-lower alkoxy, thiomorpholino- lower alkoxy, S-oxothiomorpholino- lower alkoxy or S,S-dioxothiomorpholino-lower alkoxy, cyano-lower alkoxy, carboxy-lower alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, N-mono- or N,N-di-lower alkylcarbamoyl-lower alkoxy, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, carbamoyl-lower alkyl, or N-mono- or N,N-di-lower alkylcarbamoyl-lower alkyl; or

R^2 and R^3 taken together with the atoms through which they are attached form a fused dioxolane, dioxane, benzene or cyclohexene ring, wherein said ring is substituted with up to 2 substituents independently selected from lower alkyl and lower alkoxy-lower alkyl;

R^4 is hydrogen, lower alkyl, hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, or cycloalkyl-lower alkoxy; or

R^3 and R^4 taken together with the atoms through which they are attached form a fused dioxolane, dioxane, benzene or cyclohexene ring, wherein said ring is substituted with up to 2 substituents independently selected from lower alkyl and lower alkoxy-lower alkyl; provided that R^3 does not form a ring with R^2;

X is methylene or hydroxymethylene;

R^5 is lower alkyl, lower haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, lower haloalkyl-cycloalkyl, cycloalkyl-lower alkyl, aryl, aryl-lower alkyl, heterocyclyl, heterocyclyl-lower alkyl;

R^6 is amino, lower alkylamino, di-lower alkylamino, or lower alkanoylamino;

R^7 is hydrogen, lower alkyl, lower haloalkyl, cycloalkyl, lower alkoxy-lower alkyl, or lower haloalkoxy-lower alkyl;

X^1 is an amino-protecting group;

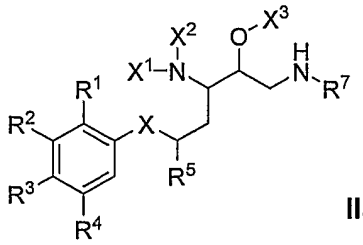
X^2 is hydrogen or together with X^3 is a bivalent protecting group;

X^3 is hydrogen or a hydroxy-protecting group;

and the enantiomers, diastereomers, and salts thereof;

and their use as intermediates for the preparation of medicinal active ingredients, especially of compounds of formula **I**.

Another embodiment of the invention is a compound of formula **IIa**



IIa

in which the substituents R^1-R^5, R^6, R^7, X and X^1-X^3 are as defined for formula **II**.

Another embodiment of the invention is a compound of formula **IIa**, wherein

R^1 is hydrogen or aryl;

R^2 is hydrogen, lower alkyl, cycloalkyl-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, lower alkoxy-lower alkoxy, lower haloalkoxy-lower alkoxy, lower alkoxy-lower alkoxy-lower alkyl; cycloalkyl-lower alkoxy, phenyl-lower alkoxy that is unsubstituted or substituted by lower alkyl, lower alkoxy, hydroxy, halogen, nitro and/or by amino; optionally N-oxidized pyridyl-lower alkoxy, lower alkylthio-lower alkoxy, lower alkane-sulfonyl-lower alkoxy, lower alkanoyl-lower alkoxy, cyano-lower alkoxy, carboxy-lower alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, lower alkylcarbamoyl-lower alkoxy, or di-lower alkylcarbamoyl-lower alkoxy;

R^3 is hydrogen, halogen, cyano, lower alkyl, lower haloalkyl, aryl, hydroxy, lower alkoxy, or polyhalo-lower alkoxy; or

R^2 and R^3 taken together with the atoms through which they are attached form a fused dioxolane ring, which is substituted with up to 2 substituents independently selected from lower alkyl and lower alkoxy-lower alkyl;

R^4 is hydrogen, lower alkoxy-lower alkoxy, lower alkoxy-lower alkyl, or cyloalkyl-lower alkoxy; or

R^3 and R^4 taken together with the atoms through which they are attached form a fused dioxolane ring which is substituted with up to 2 substituents independently selected from lower alkyl and lower alkoxy-lower alkyl; provided that R^3 does not form a ring with R^2;

X is methylene or hydroxymethylene;

R^5 is lower alkyl or cycloalkyl;

R^7 is hydrogen or methyl;

X^1 is lower alkoxycarbonyl, 2-(trialkylsily)ethoxycarbonyl, or α-phenyl- or α,α-diphenyl-lower alkoxycarbonyl that is unsubstituted or substituted by lower alkyl, lower alkoxy, nitro and/or by halogen, or is 2-halo-lower alkoxycarbonyl;

X^2 is hydrogen or together with X^3 is carbonyl or lower alkylidene;

X^3 is hydrogen, tri-lower alkylsilyl;

and the enantomers, diastereomers, and salts thereof.

Another embodiment of the invention is a compound formula **IIa** wherein

R^1 is hydrogen;

R^2 is $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkoxy, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, or cyloalkyl-lower alkoxy;

R^3 is fluoro, chloro, bromo, cyano, $(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$ haloalkyl, aryl, $(C_1$-$C_4)$alkoxy, or $(C_1$-$C_4)$haloalkoxy;

R^4 is hydrogen;

X is methylene;

R^5 is $(C_3$-$C_5)$alkyl;

R^7 is hydrogen;

X^1 is lower alkoxycarbonyl, or α-phenyl-lower alkoxycarbonyl that is unsubstituted or substituted by lower alkyl, lower alkoxy, nitro, and/or by halogen;

X^2 and X^3 are both hydrogen, or taken together are lower alkylidene;

and the enantiomers, diastereomers, and salts thereof.

Another embodiment of the invention is compounds of formula **IIa** wherein:

R^1 is hydrogen;

R^2 is 3-methoxypropoxy, 3-ethoxypropoxy, 4-methoxybutyl, or 2-(cyclopropyl)ethoxy;

R^3 is fluoro, chloro, bromo, cyano, methyl, ethyl, isopropyl or tert-butyl, trifluoromethyl, pentafluoroethyl, phenyl, methoxy, difluoromethoxy, or trifluoromethoxy;

R^4 is hydrogen;

X is methylene;

R^5 is branched (C_3-C_5)alkyl;

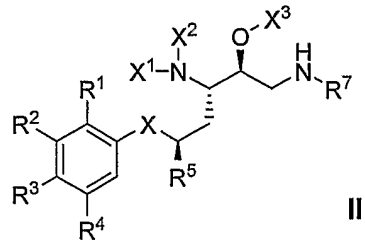
R^7 is hydrogen;

X^1 is lower alkoxycarbonyl, or α-phenyl-lower alkoxycarbonyl that is unsubstituted or substituted by lower alkyl, lower alkoxy, nitro, and/or by halogen;

X^2 and X^3 are both hydrogen, or taken together are lower alkylidene;

and the enantiomers, diastereomers, and salts thereof.

Another embodiment of the invention is a compound of formula **IIa** wherein at least one, for example one, two or preferably all, of the asymmetric carbon atoms of the main chain have the stereochemical configuration shown in formula **IIb**



IIb

the variables each being as defined for formula **IIa**, and the salts thereof.

Another embodiment of the invention is a compound of formula **IIb** wherein R^1 and R^4 is each hydrogen;

R^2 is 3-methoxypropoxy, 3-ethoxypropoxy, 4-methoxybutyl, or 2-(cyclopropyl)ethoxy;

R^3 is is fluoro, chloro, bromo, cyano, methyl, ethyl, isopropyl or tert-butyl, trifluoromethyl, pentafluoroethyl, phenyl, methoxy, difluoromethoxy, or trifluoromethoxy;

X is methylene;

R^5 is isopropyl;

R^7 is hydrogen;

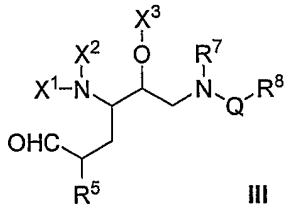
X^1 is tert-butoxycarbonyl; and

X^2 and X^3 are both hydrogen, or taken together are isopropylidene

and the salts thereof.

Preferred are compounds of formulae **II**, **IIa**, and **IIb** in the Examples and the salts thereof.

Another embodiment of the invention is compounds of formula **III**



III

wherein

R^5 is lower alkyl or cycloalkyl;

R^7 is hydrogen, lower alkyl, lower haloalkyl, cycloalkyl, lower alkoxy-lower alkyl, or lower lower haloalkoxy-lower alkyl

Q is carbonyl, thiocarbonyl, or sulfonyl;

R^8 is lower alkyl, lower haloalkyl, C_8-C_{15}alkyl, C_8-C_{15}haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-loweralkyl, lower haloalkoxy-lower alkyl, cycloalkoxy-lower alkyl, cycloalkoxy-cycloalkyl, lower alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, lower alkylthio-cycloalkyl, lower haloalkylthio-cycloalkyl, lower alkanesulfonyl-cycloalkyl, lower

haloalkanesulfonyl-cycloalkyl, aryl, aryl-lower alkyl, aryl-lower hydroxyalkyl, arylcycloalkyl, aryloxy-lower alkyl, aryloxy cycloalkyl, arylthio-lower alkyl, arylsulfonyl-lower alkyl, arylthio-cycloalkyl, arylsulfonyl-cycloalkyl, lower alkanoyl-lower alkyl, hydroxy-lower alkyl, amino-lower alkyl, lower alkanoylamino-lower alkyl, N-mono-lower alkylamino-lower alkyl, N,N-di-lower alkylamino-lower alkyl, piperidino-lower alkyl, hydroxypiperidino-lower alkyl, lower alkoxypiperidino-lower alkyl, morpholino-lower alkyl, dimethylmorpholino-lower alkyl, thiomorpholino-lower alkyl, S,S-dioxothiomorpholino-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, carbamoyl-lower alkyl, N-mono- lower alkylcarbamoyl-lower alkyl, N,N-di-lower alkylcarbamoyl-lower alkyl, carboxy-(hydroxy)-lower alkyl, lower alkoxycarbonyl-(hydroxy)-lower alkyl, carbamoyl-(hydroxy)-lower alkyl, N-mono- lower alkylcarbamoyl-(hydroxy)-lower alkyl, N,N-di-lower alkylcarbamoyl-(hydroxy)-lower alkyl, 5- or 6-membered carboxycycloalkyl-lower alkyl, 5- or 6-membered lower alkoxycarbonyl-cycloalkyl-lower alkyl, 5- or 6-membered carbamoylcycloalkyl-lower alkyl, 5- or 6-membered N-mono-alkylcarbamoylcycloalkyl-lower alkyl, N,N-di-lower alkylcarbamoylcycloalkyl-lower alkyl, cyano-lower alkyl, sulfamoyl-lower alkyl, lower alkylsulfamoyl-lower alkyl, or di-lower alkylsulfamoyl-lower alkyl, imidazolyl-lower alkyl, oxopyrrolidinyl-lower alkyl, benzimidazolyl-lower alkyl, oxadiazolyl-lower alkyl, pyridyl-lower alkyl, oxopiperidinyl-lower alkyl or quinolinyl-lower alkyl, piperidin-4-yl-lower alkyl, or lower alkanoylpiperidin-4-yl-lower alkyl, wherein said aryl, imidazolyl, benzimidazolyl, oxadiazolyl, pyridyl, quinolinyl, aryloxy, arylthio and arylsulfonyl groups are optionally substituted with up to four groups independently selected from halo, cyano, nitro, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, optionally halogenated lower alkanesulfonyl, and lower alkoxycarbonyl;

or R^8 is OR^9 or NR^9R^{10}

R^9 is 1) hydrogen, lower alkyl, lower haloalkyl, lower alkenyl, $(C_8$-$C_{15})$alkyl, $(C_8$-$C_{15})$haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-loweralkyl, lower haloalkoxy-lower alkyl, cycloalkoxy-lower alkyl, cycloalkoxy-cycloalkyl, lower alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, lower alkylthio-cycloalkyl, lower haloalkylthio-cycloalkyl, lower alkanesulfonyl-cycloalkyl, lower haloalkanesulfonyl-cycloalkyl, aminocarbonyl-lower alkyl, lower alkyl-amonocarbonyl-lower alkyl, or di(lower alkyl)-amonocarbonyl-lower

alkyl, or 2) aryl, aryl-lower alkyl, aryloxy-lower alkyl, arylthio-lower alkyl, or arylsulfonyl-lower alkyl

wherein aryl is optionally substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

R^{10} is 1) hydrogen, lower alkyl, lower haloalkyl, $(C_8$-$C_{15})$alkyl, $(C_8$-$C_{15})$haloalkyl, cycloalkyl, halocycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, or lower haloalkanesulfonyl-lower alkyl, or 2) aryl or aryl-lower alkyl

wherein aryl is optionally substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

or R^9 and R^{10} taken together with the nitrogen to which they are attached form a 4-, 5-, 6- or 7-membered heterocyclic ring composed of carbon atoms and 0 or 1 N, O, or S atoms in addition to the nitrogen atom to which R^9 and R^{10} are attached, said ring atoms being substituted with the appropriate number of hydrogen atoms and optionally substituted with up to four groups independently selected from halogen, $(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl , lower alkanoyl, lower alkoxycarbonyl, aryl, aryl-lower alkyl, and oxo, such that substitution of one oxo group on a carbon atom forms a carbonyl group and substitution of one or two oxo groups on sulfur forms sulfoxide or sulfone groups respectively; wherein the aryl and arylalkyl groups are substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

X^1 is an amino-protecting group;

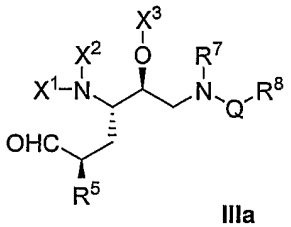
X^2 is hydrogen or together with X^3 is a bivalent protecting group;

X^3 is hydrogen or a hydroxy-protecting group;

and the enantiomers, diastereomers, and salts thereof;

and their use as intermediates for the preparation of medicinal active ingredients, especially of formula **I**.

Another embodiment of the invention is a compound of formula **III** in which at least one, two, or preferably all three of the asymmetric carbon atoms of the main chain have the stereochemical configuration shown in formula **IIIa**



IIIa

in which the substituents R^5, R^7, Q, R^8, X^1, X^2, and X^3 are as defined for formula **III** and the salts thereof.

Another embodiment of the invention is a compound of formula **IIIa**, wherein R^5 is lower alkyl or cycloalkyl;

R^7 is hydrogen or methyl;

Q is carbonyl or sulfonyl;

R^8 is lower alkyl, lower haloalkyl, C_8-C_{15} alkyl, C_8-C_{15} haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, cycloalkoxy-lower alkyl, cycloalkoxy-cycloalkyl, lower alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, lower alkylthio-cycloalkyl, lower haloalkylthio-cycloalkyl, lower alkanesulfonyl-cycloalkyl, lower haloalkanesulfonyl-cycloalkyl, aryl, aryl-lower alkyl, aryl-lower hydroxyalkyl, arylcycloalkyl, aryloxy-lower alkyl, aryloxy cycloalkyl, arylthio-lower alkyl, arylsulfonyl-lower alkyl, arylthio-cycloalkyl, or arylsulfonyl-cycloalkyl wherein said aryl, aryloxy, arylthio and arylsulfonyl groups are optionally substituted with up to four groups independently selected from halo, cyano, nitro, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, optionally halogenated lower alkanesulfonyl, and lower alkoxycarbonyl;

or R^8 is OR^9 or NR^9R^{10}

R^9 is 1) hydrogen, lower alkyl, lower haloalkyl, lower alkenyl, (C_8-C_{15})alkyl, (C_8-C_{15})haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-loweralkyl, lower haloalkoxy-lower alkyl, cycloalkoxy-lower alkyl, cycloalkoxy-cycloalkyl, lower alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, lower alkylthio-cycloalkyl, lower haloalkylthio-cycloalkyl, lower alkanesulfonyl-cycloalkyl, lower haloalkanesulfonyl-cycloalkyl, aminocarbonyl-lower alkyl, lower alkyl-amonocarbonyl-lower alkyl, or di(lower alkyl)-amonocarbonyl-lower alkyl, or 2) aryl, aryl-lower alkyl, aryloxy-lower alkyl, arylthio-lower alkyl, or arylsulfonyl-lower alkyl

wherein aryl is optionally substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

R^{10} is 1) hydrogen, lower alkyl, lower haloalkyl, (C_8-C_{15})alkyl, (C_8-C_{15})haloalkyl, cycloalkyl, halocycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, or lower haloalkanesulfonyl-lower alkyl, or 2) aryl or aryl-lower alkyl

wherein aryl is optionally substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

or R^9 and R^{10} taken together with the nitrogen to which they are attached form a 4-, 5-, 6- or 7-membered heterocyclic ring composed of carbon atoms and 0 or 1 N, O, or S atoms in addition to the nitrogen atom to which R^9 and R^{10} are attached, said ring atoms being substituted with the appropriate number of hydrogen atoms and optionally substituted with up to four groups independently selected from halogen, (C_1-C_6)alkyl, halo(C_1-C_6)alkyl, lower alkanoyl, lower alkoxycarbonyl, aryl, aryl-lower alkyl, and oxo, such that substitution of one oxo group on a carbon atom forms a carbonyl group and substitution of one or two oxo groups on sulfur forms sulfoxide or sulfone groups respectively; wherein the aryl and arylalkyl groups are substituted

with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

X^1 is lower alkoxycarbonyl, or α-phenyl- or α,α-diphenyl-lower alkoxycarbonyl that is unsubstituted or substituted by lower alkyl, lower alkoxy, nitro and/or by halogen, or is 2-halo-lower alkoxycarbonyl;

X^2 is hydrogen or together with X^3 is carbonyl or lower alkylidene;

X^3 is hydrogen, tri-lower alkylsilyl;

and the salts thereof.

Another embodiment of the invention is a compound formula **IIIa** wherein R^5 is $(C_3\text{-}C_5)$alkyl;

R^7 is hydrogen;

Q is carbonyl or sulfonyl;

R^8 is $(C_3\text{-}C_{11})$alkyl, $(C_3\text{-}C_{11})$haloalkyl, $(C_3\text{-}C_7)$cycloalkyl, $(C_3\text{-}C_{11})$cycloalkylalkyl, $(C_3\text{-}C_{11})$alkoxy-alkyl, aryl, aryl$(C_1\text{-}C_3)$alkyl, aryl$(C_3\text{-}C_6)$cycloalkyl, arylhydroxy$(C_1\text{-}C_3)$alkyl, aryloxy$(C_1\text{-}C_5)$alkyl, or aryloxy$(C_3\text{-}C_6)$cycloalkyl wherein aryl or aryloxy may be unsubstituted or substituted with one to three groups independently selected from halogen, cyano, $(C_1\text{-}C_3)$alkyl, halo$(C_1\text{-}C_3)$alkyl, $(C_1\text{-}C_3)$alkoxy, and halo$(C_1\text{-}C_3)$alkoxy;

or R^8 is NR^9R^{10};

R^9 is 1) hydrogen, $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_7)$alkenyl, $(C_3\text{-}C_7)$cycloalkyl, $(C_3\text{-}C_6)$cycloalkyl$(C_1\text{-}C_5)$alkyl, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl, or aminocarbonyl$(C_1\text{-}C_5)$alkyl, or 2) aryl or aryl$(C_1\text{-}C_4)$alkyl

wherein aryl is optionally substituted with up to 4 groups independently selected from fluorine, chlorine, cyano, $(C_1\text{-}C_3)$alkyl, halo$(C_1\text{-}C_3)$alkyl, $(C_1\text{-}C_3)$alkoxy, halo$(C_1\text{-}C_3)$alkoxy, and $(C_1\text{-}C_3)$alkanesulfonyl;

R^{10} is hydrogen, lower alkyl, or lower haloalkyl; or

R^8 and R^9 taken together are with the nitrogen to which they are attached form an azetidine, pyrrolidine, piperidine, azepine, piperazine, morpholine, or thiomorpholine ring said ring being optionally substituted with up to two groups independently

selected from halogen, (C_1-C_3)alkyl, halo(C_1-C_3)alkyl, and oxo, such that substitution of one oxo group on a carbon atom forms a carbonyl group and substitution of one or two oxo groups on sulfur forms sulfoxide or sulfone groups respectively;

X^1 is tert-butoxycarbonyl;

X^2 together with X^3 is isopropylidene;

and the salts thereof.

Another embodiment of the invention is a compound formula **IIIa** wherein R^5 is branched (C_3-C_5)alkyl;

R^7 is hydrogen;

Q is carbonyl or sulfonyl;

R^8 is propyl, 2,2-dimethylpropyl, butyl, tert-butyl, n-pentyl, 2-methyl-2-butyl, hexyl, 2-hexyl, 2-methyl-2-pentyl, 2,2-dimethylpentyl, 3-heptyl, 2-methyl-2-hexyl, 2,4,4-trimethylpentyl, 2,2,2-trifluoroethyl, 3,3,3-trifluoropropyl, 4,4,4-trifluorobutyl, 1,1,1,3,3,3-hexafluoro-2-methyl-2-propyl, cyclohexyl, 1-methylcyclohexyl, 4-methylcyclohexyl, cyclopropylmethyl, cyclopentylmethyl, 1-cyclopentyl-1-pentyl, cyclohexylmethyl, 2-cyclohexyl-2-propyl, 2-cyclopropyl-1,1-dimethylethyl, 3-cyclopropyl-2-methyl-2-butyl, 3-methoxypropyl, 2-propoxy-2-propyl, phenyl, benzyl, 3-methylbenzyl, 2-fluorobenzyl, 3-fluorobenzyl, 4-fluorobenzyl, 2,4-difluorobenzyl, 2,3-difluorobenzyl, 3,4-difluorobenzyl, 4-cyanobenzyl, 2-(trifluoromethyl)benzyl, 3-(trifluoromethyl)-benzyl, 4-(trifluoromethyl)benzyl, 4-(trifluoromethoxy)benzyl, phenethyl, 3-phenylpropyl, 2-phenyl-2-propyl, 3-(4-fluorophenyl)-3-pentyl, 1-phenyl-1-cyclopropyl, 1-(4-methylphenyl)-1-cyclopropyl, 1-(4-fluorophenyl)-1-cyclopropyl, 1-(4-methoxyphenyl)-1-cyclopropyl, 1-(2,4-dichlorophenyl)-1-cyclopropyl, 1-phenyl-1-cyclopentyl, 1-phenyl-1-cyclohexyl, 1-(4-fluorophenyl)-1-cyclohexyl, 3-hydroxy-2-methyl-3-phenyl-2-propyl, 2-(4-cyanophenoxy)-2-propyl or 2-(4-chlorophenoxy)-2-propyl;

or R^8 is NR^9R^{10};

R^9 is hydrogen, butyl, isobutyl, t-butyl, pentyl, hexyl, 2,2-dimethyl-1-pentyl, 2-methyl-2-hexyl, 2,4,4-trimethyl-2-pentyl, allyl, 2-(cyclopropyl)ethyl, cyclohexylmethyl, 2-(cyclohexyl)methyl, cyclohexyl, 2-methoxyethyl, benzyl, 2-phenylethyl, 3-

phenylpropyl, 3-(4-fluorophenyl)-2-methyl-2-propyl, 3-fluorophenyl, 3-(trifluoromethyl)phenyl, or 2-(aminocarbonyl)-2-methyl-1-propyl,

R^{10} is hydrogen, methyl, or isobutyl;

or R^9-R^{10} is $-(CH_2)_5-$ or $-(CH_2)_2O(CH_2)_2-$;

X^1 is tert-butoxycarbonyl;

X^2 together with X^3 is isopropylidene;

and the salts thereof;

Preferred are compounds of formulae **III** and **IIIa** in the Examples and the salts thereof.

The following terms are used herein.

Aryl and aryl in aryloxy, arylthio, arylsulfonyl, aryl-lower alkoxy, aryl-lower alkyl and the like are, for example, phenyl or naphthyl that is unsubstituted or mono-, di- or tri-substituted by optionally halogenated lower alkyl, optionally halogenated lower alkoxy, hydroxy, amino, lower alkylamino, di-lower alkylamino, halogen, cyano, carbamoyl, lower alkoxycarbonyl, trifluoromethoxy, and/or by trifluoromethyl.

Cycloalkoxy and cycloalkoxy in cycloalkoxy-lower alkoxy is, for example, 3- to 8-membered, preferably 3-, 5- or 6-membered, cycloalkoxy, such as cyclopropyloxy, cyclopentyloxy, cyclohexyloxy, also cyclobutyloxy, cycloheptyloxy, or cyclooctyloxy.

Cycloalkyl is, for example, 3- to 8-membered, preferably 3-, 5- or 6-membered, cycloalkyl, such as cyclopropyl, cyclopentyl, cyclohexyl, also cyclobutyl, cycloheptyl, or cyclooctyl.

Heterocyclyl is, for example, a 3- to 8-membered, preferably a 5- or 6-membered, saturated heterocycle, for example tetrahydrofuryl, tetrahydrothienyl, pyrrolidinyl, tetrahydropyranyl, tetrahydrothiopyranyl and piperidinyl.

Free or esterified or amidated carboxy-lower alkoxy is, for example, carboxy-lower alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, or N-mono- or N,N-di-lower alkylcarbamoyl-lower alkoxy.

Optionally lower alkanoylated, halogenated or sulfonylated hydroxy-lower alkoxy is, for example, lower alkanoyloxy-lower alkyl, hydroxy-lower alkoxy, halo-(hydroxy)-lower alkoxy, or lower alkanesulfonyl-(hydroxy)-lower alkoxy.

Optionally hydrogenated heteroaryl-lower alkoxy is, for example, optionally partially hydrogenated or N-oxidized pyridyl-lower alkoxy, thiazolyl-lower alkoxy, thiazolinyl-lower alkoxy or especially morpholino-lower alkoxy.

Optionally hydrogenated heteroarylthio-lower alkoxy is, for example, optionally partially or fully hydrogenated heteroarylthio-lower alkoxy, such as thiazolylthio-lower alkoxy, thiazolinylthio-lower alkoxy, imidazolylthio-lower alkoxy, imidazolinylthio-lower alkoxy optionally N-oxidized pyridlylthio-lower alkoxy, or pyrimidinylthio-lower alkoxy.

Free or esterified or amidated carboxy-lower alkyl is, for example, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, carbamoyl-lower alkyl, or N-mono- or N,N-di-lower alkylcarbamoyl-lower alkyl.

Optionally halogenated lower alkyl is, for example, lower alkyl, monohalo-lower alkyl or polyhalo-lower alkyl.

Optionally halogenated lower alkoxy is, for example, lower alkoxy, monohalo-lower alkoxy or polyhalo-lower alkoxy.

Optionally S-oxidized lower alkylthio-lower alkyl is, for example, lower alkylthio-lower alkyl, lower alkanesulfinyl-lower alkyl, or lower alkanesulfonyl-lower alkyl.

Optionally S-oxidized lower alkylthio-lower alkoxy is, for example, lower alkylthio-lower alkoxy, lower alkanesulfinyl-lower alkoxy or lower alkanesulfonyl-lower alkoxy.

Optionally hydrogenated heteroaryl-lower alkyl or optionally N-oxidized heteroaryl-lower alkyl is, for example, optionally partially hydrogenated or N-oxidized pyridyl-lower alkyl.

Optionally hydrogenated heteroarylthio-lower alkyl or optionally N-oxidized heteroarylthio-lower alkyl is, for example, thiazolylthio-lower alkyl or thiazolinylthio-lower alkyl, imidazolylthio-lower alkyl, optionally N-oxidized pyridylthio-lower alkyl, or pyrimidinylthio-lower alkyl.

Amino-lower alkyl that is unsubstituted or N-mono- or N,N-di-lower alkylated, N-lower alkanoylated or N-lower alkanesulfonylated or N,N-disubstituted by lower alkylene, by unsubstituted or N'-lower alkylated or N'-lower alkanoylated aza-lower alkylene, by oxa-lower alkylene or by optionally S-oxidized thia-lower alkylene is, for example, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, lower alkanoylamino-lower alkyl, lower alkanesulfonylamino-lower alkyl, polyhalo-lower alkanesulfonylamino-lower alkyl, pyrrolidino-lower alkyl, piperidino-lower alkyl, piperazino-, N'-lower alkylpiperazino- or N'-lower alkanoylpiperazino-

lower alkyl, morpholino-lower alkyl, thiomorpholino-, S-oxothiomorpholino-, or S,S-dioxothiomorpholino-lower alkyl.

Amino-lower alkoxy that is unsubstituted or N-mono- or N,N-di-lower alkylated, N-lower alkanoylated or N-lower alkanesulfonylated or N,N-disubstituted by lower alkylene, by unsubstituted or N'-lower alkylated amino-lower alkylene or lower alkanoylated-amino-lower alkylene, by oxa-lower alkylene or by optionally S-oxidized thia-lower alkylene is, for example, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy, lower alkanoylamino-lower alkoxy, lower alkanesulfonylamino-lower alkoxy, polyhalo-lower alkanesulfonylamino-lower alkoxy, pyrrolidino-lower alkoxy, piperidino-lower alkoxy, piperazino-, N'-lower alkylpiperazino- or N'-lower alkanoylpiperazino-lower alkoxy, morpholino-lower alkoxy, thiomorpholino-, S-oxothiomorpholino-, or S,S-dioxothio-morpholino-lower alkoxy.

Unsubstituted or N-mono- or N,N-di-lower alkylated or N-lower alkanoylated amino is, for example, amino, lower alkylamino, di-lower alkylamino, or lower alkanoylamino.

Free or aliphatically esterified or etherified hydroxy-lower alkyl is, for example, hydroxy-lower alkyl, lower alkanoyloxy-lower alkyl, lower alkoxy-lower alkyl, or lower alkenyloxy-lower alkyl.

Amino-lower alkyl that is unsubstituted or N-lower alkanoylated, N-mono- or N,N-di-lower alkylated or N,N-disubstituted by lower alkylene, by hydroxy-, lower alkoxy- or lower alkanoyloxy-lower alkylene, by unsubstituted or lower alkanoylated-amino-lower alkylene, by oxa-lower alkylene or by optionally S-oxidized thia-lower alkylene is, for example, amino-lower alkyl, lower alkanoylamino-lower alkyl, N-mono- or N,N-di-lower alkylamino-lower alkyl, optionally hydroxylated or lower alkoxylated piperidino-lower alkyl, such as piperidino-lower alkyl, hydroxypiperidino-lower alkyl or lower alkoxy-piperidino-lower alkyl, piperazino-, ω-lower alkylpiperazino- or N'-lower alkanoyl-piperazino-lower alkyl, unsubstituted or lower alkylated morpholino-lower alkyl, such as morpholino-lower alkyl or dimethylmorpholino-lower alkyl, or optionally S-oxidized thio-morpholino-lower alkyl, such as thiomorpholino-lower alkyl or S,S-dioxothiomorpholino-lower alkyl.

Free or esterified or amidated carboxy-(hydroxy)-lower alkyl is, for example, carboxy-(hydroxy)-lower alkyl, lower alkoxycarbonyl-(hydroxy)-lower alkyl or carbamoyl-(hydroxy)-lower alkyl.

Free or esterified or amidated carboxycycloalkyl-lower alkyl is, for example, 5- or 6-membered carboxycycloalkyl-lower alkyl, lower alkoxycarbonylcycloalkyl-

lower alkyl, carbamoylcycloalkyl-lower alkyl, or N-mono- or N,N-di-lower alkylcarbamoylcyclo-alkyl-lower alkyl.

Unsubstituted or N-mono- or N,N-di-lower alkylated sulfamoyl-lower alkyl is, for example, sulfamoyl-lower alkyl, lower alkylsulfamoyl-lower alkyl, or di-lower alkyl-sulfamoyl-lower alkyl.

Lower radicals and compounds are, for example, those having up to and including 7, preferably up to and including 4, carbon atoms.

5- or 6-Membered carboxycycloalkyl-lower alkyl, lower alkoxycarbonylcycloalkyl-lower alkyl, carbamoylcycloalkyl-lower alkyl, N-mono- or N,N-di-lower alkylcarbamoylcyclo-alkyl-lower alkyl is, for example, ω-(1-carboxycycloalkyl)-C_1-C_4 alkyl, ω-(1-lower alkoxycarbonylcycloalkyl)-C_1-C_4 alkyl, ω-(1-carbamoylcycloalkyl)-C_1-C_4 alkyl, ω-(1-lower alkylcarbamoylcycloalkyl)-C_1-C_4 alkyl, or ω-(1-di-lower alkylcarbamoylcycloalkyl)-C_1-C_4 alkyl, wherein cycloalkyl is, for example, cyclopentyl or cyclohexyl; lower alkoxycarbonyl is, for example, C_1-C_4 alkoxycarbonyl, such as methoxy- or ethoxycarbonyl; lower alkylcarbamoyl is, for example, C_1-C_4 alkylcarbamoyl, such as methylcarbamoyl; di-lower alkylcarbamoyl is, for example, di-C_1-C_4 alkylcarbamoyl, such as dimethylcarbamoyl; and lower alkyl is, for example, C_1-C_4 alkyl, such as methyl, ethyl, propyl, or butyl, especially (1-carboxycyclopentyl)methyl.

5- or 6-Membered cycloalkoxy-lower alkoxy is, for example, cyclopentyloxy-(C_1-C_4)alkoxy or cyclohexyloxy-(C_1-C_4)alkoxy, such as cyclopentyloxy-methoxy, cyclohexyloxy-methoxy, 2-cyclopentyloxy-ethoxy, 2-cyclohexyloxy-ethoxy, 2- or 3-cyclopentyloxy-propyloxy, 2- or 3-cyclohexyloxy-propyloxy, 4-cyclopentyloxy-butyloxy or 4-cyclohexyloxy-butyloxy, especially cyclopentyloxy-methoxy or cyclohexyloxy-methoxy.

5- or 6-Membered cycloalkoxy-lower alkyl is, for example, cyclopentyloxy-(C_1-C_4)alkyl or cyclohexyloxy-(C_1-C_4)alkyl, such as cyclopentyloxy-methyl, cyclohexyloxy-methyl, 2-cyclopentyloxy-ethyl, 2-cyclohexyloxy-ethyl, 2- or 3-cyclopentyloxy-propyl, 2- or 3-cyclohexyloxy-propyl, 2-cyclopentyloxy-2-methyl-propyl, 2-cyclohexyloxy-2-methyl-propyl, 2-cyclopentyloxy-2-ethyl-butyl, 2-cyclohexyloxy-2-ethyl-butyl, 4-cyclopentyloxy- butyl or 4-cyclohexyloxy-butyl, especially cyclopentyloxy-methyl or cyclohexyloxy-methyl.

Amino-lower alkoxy is, for example, amino-C_1-C_4 alkoxy, such as 2-aminoethoxy or 5-aminopentyloxy, also 3-aminopropyloxy or 4-aminobutyloxy.

Amino-lower alkyl is, for example, amino-C_1-C_4alkyl, such as 2-aminoethyl, 3-aminopropyl or 4-aminobutyl.

Carbamoyl-(hydroxy)-lower alkyl is, for example, carbamoyl-C_1-C_7 (hydroxy)alkyl, such as 1-carbamoyl-2-hydroxyethyl.

Carbamoyl-lower alkoxy is, for example, carbamoyl-C_1-C_4 alkoxy, such as carbamoylmethoxy, 2-carbamoylethoxy, 3-carbamoylpropyloxy, or 4-carbamoylbutyloxy, especially carbamoylmethoxy.

Carbamoyl-lower alkyl is, for example, carbamoyl-C_1-C_7 alkyl, such as carbamoylmethyl, 2-carbamoylethyl, 3-carbamoylpropyl, 2-(3-carbamoyl)propyl, 2-carbamoylpropyl, 3-(1-carbamoyl)propyl, 2-(2-carbamoyl)propyl, 2-(carbamoyl-2-methyl)propyl, 4-carbamoylbutyl, 1-carbamoylbutyl, 1-(1-carbamoyl-2-methyl)butyl, or 3-(4-carbamoyl-2-methyl)butyl.

Carboxy-(hydroxy)-lower alkyl is, for example, carboxy-C_1-C_7 (hydroxy)alkyl, such as 1 -carboxy-2-hydroxy-ethyl.

Carboxy-lower alkoxy is, for example, carboxy-C_1-C_4 alkoxy, such as carboxymethoxy, 2-carboxyethoxy, 2- or 3-carboxypropyloxy, or 4-carboxybutyloxy, especially carboxy-methoxy.

Carboxy-lower alkyl is, for example, carboxy-C_1-C_4 alkyl, such as carboxymethyl, 2-carboxyethyl, 2- or 3-carboxypropyl, 2-carboxy-2-methyl-propyl, 2-carboxy-2-ethyl-butyl, or 4-carboxybutyl, especially carboxymethyl.

Cyano-lower alkoxy is, for example, cyano-C_1-C_4 4 alkoxy, such as cyanomethoxy, 2-cyano-ethoxy, 2- or 3-cyanopropyloxy, or 4-cyanobutyloxy, especially cyanomethoxy.

Cyano-lower alkyl is, for example, cyano-C_1-C_4 alkyl, such as cyanomethyl, 2-cyanoethyl, 2- or 3-cyanopropyl, 2-cyano-2-methyl-propyl, 2-cyano-2-ethyl-butyl, or 4-cyanobutyl, especially cyanomethyl.

Di-(N-mono- or N,N-di-lower alkylcarbamoyl)-lower alkyl is, for example, di-(N-mono- or N,N-di-C_1-C_4 alkylcarbamoyl)-C_1-C_4 alkyl, such as 1,2-di-(N-mono- or N,N-di-C_1-C_4 alkylcarbamoyl)ethyl, or 1,3-di-(N-mono- or N,N-di- C_1-C_4 alkylcarbamoyl)propyl.

Dicarbamoyl-lower alkyl is, for example, dicarbamoyl-C_1-C_4 alkyl, such as 1,2-dicarbamoylethyl or 1,3-dicarbamoylpropyl.

Dimethylmorpholino-lower alkoxy can be N-oxidized and is, for example, 2,6-dimethylmorpholino- or 3,5-dimethylmorpholino-C_1-C_4 alkoxy, such as 2,6-dimethylmorpholino- or 3,5-dimethylmorpholino-methoxy, 2-(2,6-dimethylmorpholino- or 3,5-dimethylmorpholino)-ethoxy, 3-(2,6-dimethylmorpholino-or 3,5-dimethylmorpholino)-propyloxy, 2-(2,6-dimethylmorpholino- or 3,5-dimethylmorpholino-3-methyl)propyloxy, or 1- or 2-[4-(2,6-dimethylmorpholino- or 3,5-dimethylmorpholino)]-butyloxy.

Dimethylmorpholino-lower alkyl can be N-oxidized and is, for example, 2,6-dimethylmorpholino- or 3,5-dimethylmorpholino-C_1-C_4 alkyl, such as 2,6-dimethylmorpholino- or 3,5-dimethylmorpholino-methoxy, 2-(2,6-dimethylmorpholino- or 3,5-dimethylmorpholino)-ethoxy, 3-(2,6-dimethylmorpholino- or 3,5-dimethylmorpholino)-propyl, 2-(2,6-dimethylmorpholino- or 3,5-dimethylmorpholino-3-methyl)-propyl, or 1- or 2-[4-(2,6-dimethylmorpholino- or 3,5-dimethylmorpholino)]-butyl.

Di-lower alkylamino is, for example, di-C_1-C_4 alkylamino, such as dimethylamino, N-methyl-N-ethylamino, diethylamino, N-methyl-N-propylamino, or N-butyl-N-methylamino.

Di-lower alkylamino-lower alkoxy is, for example, N,N-di-C_1-C_4 alkylamino-C_1-C_4 alkoxy, such as 2-dimethylaminoethoxy, 3-dimethylaminopropyloxy, 4-dimethylaminobutyloxy, 2-diethylaminoethoxy, 2-(N-methyl-N-ethyl-amino)ethoxy, or 2-(N-butyl-N-methyl-amino)ethoxy.

Di-lower alkylamino-lower alkyl is, for example, N,N-di-C_1-C_4 alkylamino-C_1-C_4 alkyl, such as 2-dimethylaminoethyl, 3-dimethylaminopropyl, 4-dimethylaminobutyl, 2-diethylaminoethyl, 2-(N-methyl-N-ethyl-amino)ethyl, or 2-(N-butyl-N-methyl-amino)ethyl.

Di-lower alkylcarbamoyl-lower alkoxy is, for example, N,N-di-C_1-C_4 alkylcarbamoyl-C_1-C_4 alkoxy, such as methyl- or dimethyl-carbamoyl-C_1-C_4 alkoxy, such as N-methyl-, N-butyl- or N,N-dimethyl-carbamoylmethoxy, 2-(N-methylcarbamoyl)ethoxy, 2-(N-butylcarbamoyl)ethoxy, 2-(N,N-dimethylcarbamoyl)ethoxy, 3-(N-methylcarbamoyl)propyloxy, 3-(N-butylcarbamoyl)propyloxy, 3-(N,N-dimethylcarbamoyl)propyloxy or 4-(N-methylcarbamoyl)butyloxy, 4-(N-butylcarbamoyl)-butyloxy, or 4-(N,N-dimethylcarbamoyl)butyloxy, especially N-methyl-, N-butyl- or N,N-dimethyl-carbamoylmethoxy.

Di-lower alkylcarbamoyl-lower alkyl is, for example, N,N-di-C_1-C_4 alkylcarbamoyl-C_1-C_4 alkyl, such as 2-dimethylcarbamoylethyl, 3-dimethylcarbamoylpropyl, 2-dimethylcarbamoylpropyl, 2-(dimethylcarbamoyl-2-methyl)propyl, or 2-(1-dimethylcarbamoyl-3-methyl)butyl.

Di-lower alkylsulfamoyl-lower alkyl is, for example, N,N-di-C_1-C_4 alkylsulfamoyl-C_1-C_4 alkyl, N,N-dimethylsulfamoyl-C_1-C_4 alkyl, such as N,N-dimethylsulfamoylmethyl, 2-(N,N-dimethylcarbamoyl)ethyl, 3-(N,N-dimethylcarbamoyl)propyl, or 4-(N,N-dimethylcarbamoyl)butyl, especially N,N-dimethylcarbamoylmethyl.

Unsubstituted or N-lower alkanoylated piperidyl-lower alkyl is, for example, 1-C_1-C_7-lower alkanoylpiperidin-4-yl-C_1-C_4 alkyl, such as 1-acetylpiperidinylmethyl or 2-(1-acetyl-piperidinyl)ethyl.

Optionally partially hydrogenated pyridyl-lower alkoxy or N-oxidized pyridyl-lower alkoxy is, for example, optionally partially hydrogenated pyridyl-C_1-C_4 alkoxy or N-oxopyridyl-C_1-C_4 alkoxy, such as pyridyl-methoxy, dihydropyridyl-methoxy or N-oxopyridyl-methoxy, 2-(pyridyl)ethoxy, 2-(pyridyl)propyloxy, 3-(pyridyl)propyloxy, or 4-(pyridyl)butyloxy, especially (3-pyridyl)methoxy or (4-pyridyl)methoxy.

Optionally partially hydrogenated pyridyl-lower alkyl or N-oxidized pyridyl-lower alkyl is, for example, optionally partially hydrogenated pyridyl- C_1-C_4 alkyl or N-oxopyridyl-C_1-C_4 alkyl, such as pyridyl-methyl, dihydropyridyl-methyl, N-oxopyridyl-methyl, 2-(pyridyl)ethyl, 2-(pyridyl)propyl, 3-(pyridyl)propyl, or 4-(pyridyl)butyl, especially (3-pyridyl)methyl or (4-pyridyl)methyl.

Halo-(hydroxy)-lower alkoxy is, for example, halo-C_1-C_7 (hydroxy)alkoxy, especially halo-C_2-C_4 (hydroxy)alkoxy, such as 3-halo-, such as 3-chloro-2-hydroxy-propyloxy.

Hydroxy-lower alkoxy is, for example, hydroxy-C_2-C_7 alkoxy, especially hydroxy-C_2-C_4 alkoxy, such as 2-hydroxybutyloxy, 3-hydroxypropyloxy or 4-hydroxybutyloxy.

Hydroxy-lower alkyl is, for example, hydroxy- C_2-C_7 alkyl, especially hydroxy-C_2-C_4 alkyl, such as 2-hydroxyethyl, 3-hydroxypropyl or 4-hydroxybutyl.

Hydroxypiperidino-lower alkyl is, for example, 3- or 4-hydroxypiperidino-C_1-C_4 alkyl, such as 3- hydroxypiperidinomethyl, 4-hydroxypiperidinomethyl, 2-(3-hydroxypiperidino)ethyl, 2-(4-hydroxypiperidino)ethyl, 3-(3-hydroxypiperidino)propyl, 3-(4-hydroxypiperidino)propyl, 4-(3-hydroxypiperidino)butyl or 4-(4-hydroxypiperidino)butyl.

Imidazolyl-lower alkyl is, for example, imidazolyl-C_1-C_4 alkyl, such as imidazol-4-yl-methyl, 2-(imidazol-4-yl)ethyl, 3-(imidazol-4-yl)propyl, or 4-(imidazol-4-yl)butyl.

Imidazolyl-lower alkoxy is, for example, imidazolyl-C_1-C_4 alkoxy, such as imidazol-4-yl-methoxy, 2-(imidazol-4-yl)ethoxy, 3-(imidazol-4-yl)propyloxy, or 4-(imidazol-4-yl)butyloxy.

Morpholinocarbonyl-lower alkyl is, for example, morpholinocarbonyl-C_1-C_4 alkyl, such as 1-morpholinocarbonylethyl, 3-morpholinocarbonylpropyl, or 1-(morpholinocarbonyl-2-methyl)propyl.

Morpholino-lower alkyl can be N-oxidized and is, for example, N-oxomorpholino-C_1-C_4 alkyl, such as N-oxomorpholinomethyl, 2-(N-oxomorpholino)ethyl, 3-(N-oxomorpholino)propyl, or 4-(N-oxomorpholino)butyl.

Morpholino-lower alkoxy is, for example, morpholino-C_1-C_4 alkoxy, such as 1-morpholinoethoxy, 3-morpholinopropyloxy, or 1-(morpholino-2-methyl)propyloxy.

Morpholino-lower alkoxy can be N-oxidized and is, for example, N-oxomorpholino-C_1-C_4 alkoxy, such as N-oxomorpholinomethoxy, 2-(N-oxomorpholino)ethoxy, 3-(N-oxomorpholino)propyloxy, or 4-(N-oxomorpholino)butyloxy.

Lower alkanoyl is, for example, C_1-C_7 alkanoyl, especially C_2-C_6 alkanoyl, such as acetyl, propionyl, butyryl, isobutyryl or pivaloyl.

Lower alkanoylamino is, for example, N-C_1-C_7 alkanoylamino, such as acetylamino or pivaloylamino.

Lower alkanoylamino-lower alkyl is, for example, N-C_1-C_4 alkanoylamino-C_1-C_4 alkyl, such as 2-acetylaminoethyl.

Lower alkanoyl-lower alkoxy (oxo-lower alkoxy) carries the lower alkanoyl group in a position higher than the α-position and is, for example, C_1-C_7 alkanoyl-C_1-C_4 alkoxy, such as 4-acetoxy-butoxy.

Lower alkanoyloxy-lower alkyl carries the lower alkanoyloxy group in a position higher than the α-position and is, for example, C_1-C_7 alkanoyloxy-C_1-C_4 alkyl, such as 4-acetoxy-butyl.

Lower alkanesulfonyl-(hydroxy)-lower alkoxy is, for example, C_1-C_7 alkanesulfonyl-C_1-C_4 (hydroxy)alkoxy, such as 3-methanesulfonyl-2-hydroxy-propyloxy.

Lower alkanesulfonyl-lower alkoxy is, for example, C_1-C_7 alkanesulfonyl-C_1-C_4 alkoxy, such as methanesulfonylmethoxy or 3-methanesulfonyl-propyloxy.

Lower alkanesulfonylamino-lower alkoxy is, for example, C_1-C_7 alkanesulfonylamino-C_1-C_4 alkoxy, such as ethanesulfonylaminomethoxy, 2-ethanesulfonylaminoethoxy, 3-ethane-sulfonylaminopropyloxy, or 3-(1,1-dimethylethanesulfonylamino)propyloxy.

Lower alkanesulfonylamino-lower alkyl is, for example, C_1-C_7 alkanesulfonylamino-C_1-C_4 alkyl, such as ethanesulfonylaminomethyl, 2-ethanesulfonylaminoethyl, 3-ethanesulfonyl-aminopropyl, or 3-(1,1-dimethylethanesulfonylamino)propyl.

Lower alkanesulfonyl-lower alkyl is, for example, C_1-C_7 alkanesulfonyl-C_1-C_4 alkyl, such as ethanesulfonylmethyl, 2-ethanesulfonylethyl, 3-ethanesulfonylpropyl, or 3-(1,1-dimethyl-ethanesulfonyl)propyl.

Lower alkenyl is, for example, C_2-C_7 alkenyl, such as vinyl or allyl.

Lower alkenyloxy is, for example, C_2-C_7 alkenyloxy, such as allyloxy.

Lower alkenyloxy-lower alkoxy is, for example, C_3-C_7 alkenyloxy-C_1-C_4 alkoxy, such as allyloxymethoxy.

Lower alkenyloxy-lower alkyl is, for example, C_3-C_7 alkenyloxy-C_1-C_4 alkyl, such as allyloxymethyl.

Lower alkoxy is, for example, C_1-C_7 alkoxy, preferably C_1-C_5 alkoxy, such as methoxy, ethoxy, propyloxy, isopropyloxy, butyloxy, isobutyloxy, secondary butyloxy, tertiary butyloxy, pentyloxy, or a hexyloxy or heptyloxy group.

Lower alkoxycarbonyl is, for example, C_1-C_7 alkoxycarbonyl, preferably C_1-C_5 alkoxycarbonyl, such as methoxycarbonyl, ethoxycarbonyl, propyloxycarbonyl, isopropyloxycarbonyl, butyloxycarbonyl, isobutyloxycarbonyl, secondary butyloxycarbonyl, tertiary butyloxy, pentyloxycarbonyl, or a hexyloxycarbonyl or heptyloxycarbonyl group.

Lower alkoxycarbonyl-(hydroxy)-lower alkyl is, for example, C_1-C_4 alkoxycarbonyl-C_1-C_7 (hydroxy)alkyl, such as 1-methoxycarbonyl- or 1-ethoxycarbonyl-2-hydroxy-ethyl.

Lower alkoxycarbonylamino-lower alkoxy is, for example, C_1-C_7 alkoxycarbonylamino-C_2-C_7 alkoxy, preferably C_2-C_5 alkoxycarbonylamino-C_2-C_7 alkoxy, such as methoxycarbonylamino-C_2-C_7 alkoxy, ethoxycarbonylamino-C_2-C_7 alkoxy, propyloxycarbonylamino-C_2-C_7 alkoxy, isobutyloxycarbonylamino-C_2-C_7 alkoxy, butyloxycarbonylamino-C_2-C_7 alkoxy, isobutyloxycarbonylamino-C_2-C_7 alkoxy, secondary butyloxycarbonylamino-C_2-C_7 alkoxy or tertiary butyloxyamino-C_2-C_7 alkoxy, wherein C_2-C_7 alkoxy is, for example, methoxy, ethoxy, propyloxy, butyloxy, pentyloxy, or hexyloxy.

Lower alkoxycarbonylamino-lower alkyl is, for example, C_1-C_7 alkoxycarbonylamino-C_2-C_7 alkyl, preferably C_2-C_5 alkoxycarbonylamino-C_2-C_7 alkyl, such as methoxycarbonyl-C_2-C_7 alkyl, ethoxycarbonylamino-C_2-C_7 -alkyl, propyloxycarbonylamino-C_2-C_7 alkyl isopropyloxy-carbonylamino-C_2-C_7 alkyl, butyloxycarbonylamino-C_2-C_7 alkyl, isobutyloxycarbonylamino-C_2-C_7 alkyl, secondary butyloxycarbonylamino-C_2-C_7 alkyl, or tertiary butyloxyamino-C_2-C_7 alkyl, wherein C_2-C_7 alkyl is, for example, ethyl, propyl, butyl, pentyl, or hexyl.

Lower alkoxycarbonyl-lower alkoxy is, for example, C_1-C_4 alkoxycarbonyl-C_1-C_4 alkoxy, such as methoxycarbonyl- or ethoxycarbonyl-methoxy, 2-methoxycarbonyl- or 2-ethoxycarbonyl-ethoxy, 2- or 3-methoxycarbonyl- or 2- or 3-ethoxycarbonyl-propyloxy or 4-methoxycarbonyl- or 4-ethoxycarbonyl-butyloxy,

especially methoxycarbonyl- or ethoxycarbonyl-methoxy or 3-methoxycarbonyl- or 3-ethoxycarbonyl-propyloxy.

Lower alkoxycarbonyl-lower alkyl is, for example, C_1-C_4 alkoxycarbonyl-C_1-C_4 alkyl, such as methoxycarbonyl-methyl, ethoxycarbonyl-methyl, 2-methoxycarbonyl-ethyl, 2-ethoxycarbonyl-ethyl, 3-methoxycarbonyl-propyl, 3-ethoxycarbonyl-propyl or 4-ethoxycarbonyl-butyl.

Lower alkoxy-lower alkenyl is, for example, C_1-C_4 alkoxy-C_2-C_4 alkenyl, such as 4-methoxybut-2-enyl.

Lower alkoxy-lower alkoxy is, for example, C_1-C_4 alkoxy-C_2-C_4 alkoxy, such as 2-methoxy-, 2-ethoxy- or 2-propyloxy-ethoxy, 3-methoxy- or 3-ethoxy-propyloxy, or 4-methoxybutyloxy, especially 3-methoxypropyloxy or 4-methoxybutyloxy.

Lower alkoxy-lower alkoxy-lower alkyl is, for example, C_1-C_4 alkoxy-C_1-C_4 alkoxy-C_1-C_4 alkyl, such as 2-methoxy-, 2-ethoxy- or 2-propyloxy-ethoxymethyl, 2-(2-methoxy-, 2-ethoxy- or 2-propyloxy-ethoxy)ethyl, 3-(3-methoxy- or 3-ethoxy-propyloxy)propyl, or 4-(2-methoxybutyloxy)-butyl, especially 2-(3-methoxypropyloxy)ethyl or 2-(4-methoxybutyloxy)ethyl.

Lower alkoxy-lower alkyl is, for example, C_1-C_4 alkoxy-C_1-C_4 alkyl, such as ethoxymethyl, propyloxymethyl, butyloxymethyl, 2-methoxy-, 2-ethoxy- or 2-propyloxy-ethyl, 3-methoxy- or 3-ethoxy-propyl or 4-methoxybutyl, especially 3-methoxypropyl, or 4-methoxybutyl.

Piperidino-lower alkyl is, for example, piperidino- C_1-C_4 alkyl or hydroxypiperidino-C_1-C_4 alkyl, such as piperidinomethyl or 4-hydroxypiperidinomethyl.

Lower alkoxypiperidino-lower alkyl is, for example, C_1-C_4 alkoxypiperidino-C_1-C_4 alkyl, such as 4-(C_1-C_4 alkoxy)-piperidinomethyl, especially 4-methoxypiperidinomethyl.

Lower alkyl may be straight-chained or branched and/or bridged and is, for example, corresponding C_1-C_7 alkyl, such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, secondary butyl or tertiary butyl, or a pentyl, hexyl or heptyl group. Lower alkyl R^2 or $R^3$is especially C_2-C_7 alkyl; lower alkyl R^5 or R^7 is especially branched C_3-C_7 alkyl; and lower alkyl R^8 or R^3 is, for example, straight-chained, branched or bridged C_3-C_7 alkyl.

Lower alkylamino is, for example, C_1-C_4 alkylamino, such as methylamino, ethylamino, propylamino, butylamino, isobutylamino, secondary butylamino, or tertiary butylamino.

Lower alkylamino-lower alkoxy is, for example, C_1-C_4 alkylamino-C_1-C_4 alkoxy, such as propylaminomethoxy, 2-methylamino-, 2-ethylamino-, 2-propylamino-

or 2-butylamino-ethoxy, 3-ethylamino- or 3-propylamino-propyloxy or 4-methylaminobutoxy.

Lower alkylamino-lower alkyl is, for example, C_1-C_4 alkylamino-C_1-C_4 alkyl, such as propylaminomethyl, 2-methylamino-, 2-ethylamino-, 2-propylamino- or 2-butylamino-ethyl, 3-ethylamino- or 3-propylamino-propyl or 4-methylaminobutyl.

Lower alkylcarbamoyl-lower alkoxy is, for example, N- C_1-C_7 alkylcarbamoyl-C_1-C_4 alkoxy, such as methyl- or dimethyl-carbamoyl-C_1-C_4 alkoxy, e.g., methylcarbamoylmethoxy, 2-methylcarbamoylethoxy, or 3-methylcarbamoylpropyloxy.

Lower alkylenedioxy is, for example, methylenedioxy or ethylenedioxy, but can also be 1,3- or 1,2-propylenedioxy.

Lower alkylsulfamoyl-lower alkyl is, for example, N-C_1-C_7 alkylsulfamoyl-C_1-C_4 alkyl, such as N-methyl-, N-ethyl-, N-propyl- or N-butyl-sulfamoyl-C_1-C_4 alkyl, such as N-methyl-, N-ethyl-, N-propyl- or N-butyl-sulfamoylmethyl, 2-(N-methylsulfamoyl)ethyl, 2-(N-butylsulfamoyl)ethyl, 3-(N-methylsulfamoyl)propyl, 3-(N-butylsulfamoyl)propyl, or 4-(N-methylsulfamoyl)butyl, 4-(N-butylsulfamoyl)butyl or 4-(N,N-dimethylsulfamoyl)butyl, especially N-methyl-, N-butyl-, or N,N-dimethyl-sulfamoylmethyl.

Lower alkylthio-(hydroxy)-lower alkoxy is, for example, C_1-C_4 alkylthio-C_1-C_4 (hydroxy)alkoxy, such as 2-hydroxy-3-methylthiopropyloxy.

Lower alkylthio-lower alkoxy is, for example, C_1-C_4 alkylthio-C_1-C_4 alkoxy, such as methylthio-C_1-C_4 alkoxy, e.g. methylthiomethoxy, 2-methylthioethoxy, or 3-methylthiopropyloxy.

Lower alkylthio-lower alkyl is, for example, C_1-C_4 alkylthio-C_1-C_4 alkyl, such as methylthio-C_1-C_4 alkyl, e.g. methylthiomethyl, 2-methylthioethyl, or 3-methylthiopropyl.

N'-Lower alkanoylpiperazino-lower alkoxy is, for example, N'-lower alkanoylpiperazino-C_1-C_4 alkoxy, such as 4-acetylpiperazinomethoxy.

N'-Lower alkanoylpiperazino-lower alkyl is, for example, N'-C_2-C_7-lower alkanoyl-piperazino-C_1-C_4 alkyl, such as 4-acetylpiperazinomethyl.

N'-Lower alkylpiperazino-lower alkyl is, for example, N'-C_1-C_4 alkylpiperazino-C_1-C_4 alkyl, such as 4-methylpiperazinomethyl.

Oxo-lower alkoxy is, for example, oxo-C_1-C_4 alkoxy, such as 3,3-dimethyl-2-oxo-butyloxy.

Piperazino-lower alkyl is, for example, piperazino-C_1-C_4 alkyl, such as piperazinomethyl, 2-piperazinoethyl, or 3-piperazinopropyl.

Piperidino-lower alkoxy is, for example, piperidino-C_1-C_4 alkoxy, such as piperidinomethoxy, 2-piperidinoethoxy, or 3-piperidinopropyloxy.

Piperidino-lower alkyl is, for example, piperidino-C_1-C_4 alkyl, such as piperidinomethyl, 2-piperidinoethyl, or 3-piperidinopropyl.

Polyhalo-lower alkanesulfonylamino-lower alkoxy is, for example, trifluoro-C_1-C_7 alkanesulfonyl-C_1-C_4 alkoxy, such as trifluoromethanesulfonylaminobutyloxy.

Polyhalo-lower alkanesulfonylamino-lower alkyl is, for example, trifluoro-C_1-C_7 alkanesulfonyl-C_1-C_4 alkyl, such as trifluoromethanesulfonylaminobutyl.

Pyrimidinylthio-lower alkoxy is, for example, pyrimidinylthio-C_1-C_4 alkoxy, such as pyrimidinylthiomethoxy, 2-(pyrimidinylthio)ethoxy, or 3-(pyrimidinylthio)propyloxy.

Pyrrolidino-lower alkoxy is, for example, pyrrolidino-C_2-C_4 alkoxy, such as 2-pyrrolidinoethoxy, or 3-pyrrolidinopropyloxy.

Pyrrolidino-lower alkyl is, for example, pyrrolidino-C_1-C_4 alkyl, such as pyrrolidinomethyl, 2-pyrrolidinoethyl, or 3-pyrrolidinopropyl.

S,S-Dioxothiomorpholino-lower alkyl is, for example, S,S-dioxothiomorpholino-C_1-C_4 alkyl, such as S,S-dioxothiomorpholinomethyl or 2-(S,S-dioxo)thiomorpholinoethyl.

S-Oxothiomorpholino-lower alkyl is, for example, S-oxothiomorpholino-C_1-C_4 alkyl, such as S-oxothiomorpholinomethyl or 2-(S-oxo)thiomorpholinoethyl.

Sulfamoyl-lower alkyl is, for example, sulfamoyl-C_1-C_4 alkyl, such as sulfamoyl-C_1-C_4 alkyl, such as sulfamoylmethyl, 2-sulfamoylethyl, 3-sulfamoylpropyl, or 4-sulfamoylbutyl.

Thiazolinyl-lower alkoxy is, for example, thiazolinyl-C_1-C_4 alkoxy, such as thiazolinylmethoxy, 2-(thiazolinyl)ethoxy or 3-(thiazolinyl)propyloxy.

Thiazolinyl-lower alkyl is, for example, thiazolinyl-C_1-C_4 alkyl, such as thiazolinylmethyl, 2-(thiazolinyl)ethyl, or 3-(thiazolinyl)propyl.

Thiazolyl-lower alkoxy is, for example, thiazolyl-C_1-C_4 alkoxy, such as thiazolylmethoxy, 2-(thiazolyl)ethoxy, or 3-(thiazolyl)propyloxy.

Thiazolyl-lower alkyl is, for example, thiazolyl-C_1-C_4 alkyl, such as thiazolylmethyl, 2-(thiazolyl)ethyl, or 3-(thiazolyl)propyl.

Thiomorpholino-lower alkyl or S,S-dioxothiomorpholino-lower alkyl is, for example, thiomorpholino-C_1-C_4 alkyl, such as -methyl or -ethyl, or S,S-dioxothiomorpholino-C_1-C_4 alkyl, such as -methyl or -ethyl.

Depending on whether asymmetric carbon atoms are present, the compounds of the invention can be present as mixtures of isomers, especially as racemates, or in the form of pure isomers, especially optical antipodes.

Salts of compounds having salt-forming groups are especially acid addition salts, salts with bases or, where several salt-forming groups are present, can also be mixed salts or internal salts.

Salts are especially the pharmaceutically acceptable or non-toxic salts of compounds of formula I.

Such salts are formed, for example, by compounds of formula I having an acid group, for example a carboxy group or a sulfo group, and are, for example, salts thereof with suitable bases, such as non-toxic metal salts derived from metals of groups Ia, Ib, IIa and IIb of the Periodic Table of the Elements, for example alkali metal salts, especially lithium, sodium or potassium salts, or alkaline earth metal salts, for example magnesium or calcium salts, also zinc salts or ammonium salts, as well as salts formed with organic amines, such as unsubstituted or hydroxy-substituted mono-, di- or tri-alkylamines, especially mono-, di- or tri-lower alkylamines, or with quaternary ammonium bases, for example with methyl-, ethyl-, diethyl- or triethyl-amine, mono-, his- or tris-(2-hydroxy-lower alkyl)-amines, such as ethanol-, diethanol- or triethanol-amine, tris-(hydroxymethyl)-methylamine or 2-hydroxy-tert-butylamines, N,N-di-lower alkyl-N-(hydroxy-lower alkyl)-amines, such as N,N-dimethyl-N-(2-hydroxyethyl)-amine, or N-methyl-D-glucamine, or quaternary ammonium hydroxides, such as tetrabutylammonium hydroxide. The compounds of formula I having a basic group, for example an amino group, can form acid addition salts, for example with suitable inorganic acids, for example hydrohalic acids, such as hydrochloric acid or hydrobromic acid, or sulfuric acid with replacement of one or both protons, phosphoric acid with replacement of one or more protons, e.g., orthophosphoric acid or metaphosphoric acid, or pyrophosphoric acid with replacement of one or more protons, or with organic carboxylic, sulfonic, sulfo or phosphonic acids or N-substituted sulfamic acids, for example, acetic acid, propionic acid, glycolic acid, succinic acid, maleic acid, hydroxymaleic acid, methylmaleic acid, fumaric acid, malic acid, tartaric acid, gluconic acid, glucaric acid, glucuronic acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, salicylic acid, 4-aminosalicylic acid, 2-phenoxybenzoic acid, 2-acetoxybenzoic acid, embonic acid, nicotinic acid or isonicotinic acid, as well as with amino acids, such as the .alpha.-amino acids mentioned hereinbefore, and with methanesulfonic acid, ethanesulfonic acid, 2-hydroxyethanesulfonic acid, ethane-1,2-disulfonic acid, benzenesulfonic acid, 4-toluenesulfonic acid, naphthalene-2-sulfonic acid, 2- or 3-phosphoglycerate, glucose-6-phosphate, or N-cyclohexylsulfamic acid (forming cyclamates) or with other acidic organic compounds, such as ascorbic acid. Compounds of formula I having acid and basic groups can also form internal salts.

For isolation and purification purposes it is also possible to use pharmaceutically unacceptable salts.

Another embodiment of the invention is a pharmaceutical composition comprising an effective amount of compounds of formula **I**, **Ia**, or **Ib** and a pharmaceutically acceptable carrier therefor.

The compounds of the invention may be used, for example, in the preparation of pharmaceutical compositions that comprise an effective amount of the active ingredient together or in admixture with a significant amount of inorganic or organic, solid or liquid, pharmaceutically acceptable carriers.

The pharmaceutical compositions of the invention are compositions for enteral, such as nasal, rectal or oral, or parenteral, such as intramuscular or intravenous, administration to warm-blooded animals (mammals, especially human beings) that comprise an effective dose of the pharmacologically active ingredient alone or together with a pharmaceutically acceptable carrier. The dose of the active ingredient depends on the species of warm-blooded animal, body weight, age and individual condition, individual pharmacokinetic data, the disease to be treated, and the mode of administration.

The pharmaceutical compositions comprise from approximately 1% to approximately 95%, preferably from approximately 20% to approximately 90%, active ingredient. Pharmaceutical compositions according to the invention may be, for example, in unit dose form, such as in the form of ampoules, vials, suppositories, dragees, tablets, or capsules.

The pharmaceutical compositions of the invention are prepared in a manner known *per se*, for example by means of conventional dissolving, lyophilising, mixing, granulating, or confectioning processes.

Solutions of the active ingredient, and also suspensions, and especially isotonic aqueous solutions or suspensions, are preferably used, it being possible, for example in the case of lyophilised compositions that comprise the active ingredient alone or together with a carrier, for such solutions or suspensions to be made up prior to use. The pharmaceutical compositions may be sterilised and/or may comprise excipients, for example preservatives, stabilisers, wetting agents and/or emulsifiers, solubilisers, salts for regulating the osmotic pressure and/or buffers, and are prepared in a manner known *per se*, for example by means of conventional dissolving or lyophilising processes. The said solutions or suspensions may comprise conventional viscosity-increasing substances, such as sodium

carboxymethylcellulose, carboxymethylcellulose, dextran, polyvinylpyrrolidone, and gelatin.

Suspensions in oil comprise as the oil component the vegetable, synthetic or semi-synthetic oils customary for injection purposes, for example, liquid fatty acid esters that contain as the acid component a long-chained fatty acid having from 8 to 22, especially from 12 to 22, carbon atoms. Examples include lauric acid, tridecylic acid, myristic acid, pentadecylic acid, palmitic acid, margaric acid, stearic acid, arachidic acid, behenic acid or corresponding unsaturated acids, for example oleic acid, elaidic acid, erucic acid, brassidic acid or linoleic acid, if desired with the addition of antioxidants, for example vitamin E, β-carotene, or 3,5-di-tert-butyl-4-hydroxytoluene. The alcohol component of those fatty acid esters has a maximum of 6 carbon atoms and is a mono- or poly-hydric, for example a mono-, di- or tri-hydric, alcohol, for example methanol, ethanol, propanol, butanol or pentanol, or the isomers thereof, but especially glycol and glycerol. Examples of fatty acid esters include ethyl oleate, isopropyl myristate, isopropyl palmitate, polyoxyethylene glycerol trioleate, triglyceride of saturated fatty acids with a chain length of C_8-C_{12}, but especially vegetable oils, such as cottonseed oil, almond oil, olive oil, castor oil, sesame oil, soybean oil, and groundnut oil.

The injectable compositions are prepared in the customary manner under sterile conditions. The same applies to introducing the compositions into ampoules or vials and sealing the containers.

Pharmaceutical compositions for oral administration can be obtained by combining the active ingredient with solid carriers, if desired granulating a resulting mixture, and processing the mixture, if desired or necessary, after the addition of appropriate excipients, into tablets, dragee cores or capsules. They can also be incorporated into plastics carriers that allow the active ingredients to diffuse or be released in measured amounts.

Suitable carriers are especially fillers, such as sugars, for example lactose, saccharose, mannitol or sorbitol, cellulose preparations and/or calcium phosphates, for example tri-calcium phosphate or calcium hydrogen phosphate, and also binders, such as starch pastes using, for example, corn, wheat, rice or potato starch, gelatin, tragacanth, methylcellulose, hydroxypropylmethylcellulose, sodium carboxymethylcellulose and/or polyvinylpyrrolidone, and/or, if desired, disintegrators, such as the above-mentioned starches, also carboxy-methyl starch, crosslinked polyvinylpyrrolidone, agar, alginic acid or a salt thereof, such as sodium alginate. Excipients are especially flow conditioners and lubricants, for example silicic acid, talc, stearic acid or salts thereof, such as magnesium or calcium stearate, and/or

polyethylene glycol. Dragee cores are provided with suitable, optionally enteric, coatings, there being used, *inter alia*, concentrated sugar solutions which may comprise gum arabic, talc, polyvinylpyrrolidone, polyethylene glycol and/or titanium dioxide, or coating solutions in suitable organic solvents, or, for the preparation of enteric coatings, solutions of suitable cellulose preparations, such as ethylcellulose phthalate or hydroxypropylmethylcellulose phthalate. Capsules are dry-filled capsules made of gelatin and also soft, sealed capsules made of gelatin and a plasticiser, such as glycerol or sorbitol. The dry-filled capsules may comprise the active ingredient in the form of granules, for example with fillers, such as lactose, binders, such as starches, and/or glidants, such as talc or magnesium stearate, and if desired with stabilisers. In soft capsules the active ingredient is preferably dissolved or suspended in suitable oily excipients, such as fatty oils, paraffin oil or liquid polyethylene glycols, it likewise being possible for stabilisers and/or antibacterial agents to be added. Dyes or pigments may be added to the tablets or dragee coatings or to the capsule casings, for example for identification purposes or to indicate different doses of active ingredient.

The compositions of the invention are renin inhibitors. Said compositions contain compounds having a mean inhibition constant (IC_{50}) against renin of between about 50,000 nM to about 0.001 nM; preferably between about 100 nM to about 0.001 nM; and more preferably between about 10 nM to about 0.001 nM. The compositions of the invention may have additionally utility as inhibitors of other aspartic proteases including, but not limited to, HIV protease, plasmepsin and β-secretase.

The compositions of the invention reduce blood pressure. Said compositions include compounds having an IC_{50} for renin of between about 50,000 nM to about 0.001 nM; preferably between about 100 nM to about 0.001 nM; and more preferably between about 10 nM to about 0.001 nM.

The invention includes a therapeutic method for treating or ameliorating a renin mediated disorder in a subject in need thereof comprising administering to a subject in need thereof an effective amount of a compound of formula **I**, or the enantiomers, diastereomers, or salts thereof or composition thereof. Renin mediated disorders include hypertension, congestive heart failure, cardiac hypertrophy, cardiac fibrosis, cardiomyopathy post-infarction, complications resulting from diabetes, such as nephropathy, vasculopathy and neuropathy, diseases of the coronary vessels, post-surgical hypertension, restenosis following angioplasty, raised intra-ocular pressure, glaucoma, abnormal vascular growth, hyperaldosteronism, anxiety states,

and cognitive disorders (Fisher N.D.; Hollenberg N. K. *Expert Opin. Investig. Drugs.* **2001**, *10*, 417-26).

Administration methods include administering an effective amount (i.e., a therapeutically effective amount) of a compound or composition of the invention at different times during the course of therapy or concurrently in a combination form. The methods of the invention include all known therapeutic treatment regimens.

"Prodrug" means a pharmaceutically acceptable form of an effective derivative of a compound (or a salt thereof) of the invention, wherein the prodrug may be: 1) a relatively active precursor which converts *in vivo* to a compound of the invention; 2) a relatively inactive precursor which converts *in vivo* to a compound of the invention; or 3) a relatively less active component of the compound that contributes to therapeutic activity after becoming available *in vivo* (i.e., as a metabolite). See "Design of Prodrugs", ed. H. Bundgaard, Elsevier, 1985.

"Metabolite" means a pharmaceutically acceptable form of a metabolic derivative of a compound (or a salt thereof) of the invention, wherein the derivative is an active compound that contributes to therapeutic activity after becoming available *in vivo*.

"Effective amount" means that amount of active compound agent that elicits the desired biological response in a subject. Such response includes alleviation of the symptoms of the disease or disorder being treated. The effective amount of a compound of the invention in such a therapeutic method to be administered to warm-blooded animals, for example human beings, of, for example, approximately 70 kg body weight, especially the doses effective in the inhibition of the enzyme renin, in lowering blood pressure and/or in improving the symptoms of glaucoma, are from approximately 3 mg to approximately 3 g, preferably from approximately 10 mg to approximately 1 g, for example approximately from 20 mg to 200 mg, per person per day, divided preferably into 1 to 4 single doses which may, for example, be of the same size. Usually, children receive about half of the adult dose. The dose necessary for each individual can be monitored, for example by measuring the serum concentration of the active ingredient, and adjusted to an optimum level.

The invention includes the use of a compound of the invention for the preparation of a composition for treating or ameliorating a renin mediated chronic disorder or disease or infection in a subject in need thereof, wherein the composition comprises a mixture one or more compounds of the invention and an optional pharmaceutically acceptable carrier.

"Pharmaceutically acceptable carrier" means compounds and compositions that are of sufficient purity and quality for use in the formulation of a composition of the invention and that, when appropriately administered to an animal or human, do not produce an adverse reaction.

"Renin mediated disorder or disease" includes disorders or diseases associated with the elevated expression or overexpression of renin and conditions that accompany such diseases.

An embodiment of the invention includes administering a renin inhibiting compound of formula I or composition thereof in a combination therapy (see USP 5,821,232, USP 6,716,875, USP 5,663,188, Fossa, A. A.; DePasquale, M. J.; Ringer, L. J.; Winslow, R. L. "Synergistic effect on reduction in blood pressure with coadministration of a renin inhibitor or an angiotensin-converting enzyme inhibitor with an angiotensin II receptor antagonist" *Drug Development Research* **1994**, *33*(4), 422-8) with one or more additional agents for the treatment of hypertension including α-blockers, β-blockers, calcium channel blockers, diuretics, angiotensin converting enzyme (ACE) inhibitors, dual ACE and neutral endopeptidase (NEP) inhibitors, angiotensin-receptor blockers (ARBs), aldosterone synthase inhibitor, aldosterone-receptor antagonists, or endothelin receptor antagonist.

α-Blockers include doxazosin, prazosin, tamsulosin, and terazosin.

β-Blockers for combination therapy are selected from atenolol, bisoprol, metoprolol, acetutolol, esmolol, celiprolol, taliprolol, acebutolol, oxprenolol, pindolol, propanolol, bupranolol, penbutolol, mepindolol, carteolol, nadolol, carvedilol, and their pharmaceutically acceptable salts.

Calcium channel blockers include dihydropyridines (DHPs) and non-DHPs. The preferred DHPs are selected from the group consisting of amlodipine, felodipine, ryosidine, isradipine, lacidipine, nicardipine, nifedipine, nigulpidine, niludipine, nimodiphine, nisoldipine, nitrendipine, and nivaldipine and their pharmaceutically acceptable salts. Non-DHPs are selected from flunarizine, prenylamine, diltiazem, fendiline, gallopamil, mibefradil, anipamil, tiapamil, and verampimil and their pharmaceutically acceptable salts.

A diuretic is, for example, a thiazide derivative selected from amiloride, chlorothiazide, hydrochlorothiazide, methylchlorothiazide, and chlorothalidon.

ACE inhibitors include alacepril, benazepril, benazaprilat, captopril, ceronapril, cilazapril, delapril, enalapril, enalaprilat, fosinopril, lisinopril, moexipiril, moveltopril, perindopril, quinapril, quinaprilat, ramipril, ramiprilat, spirapril, temocapril,

trandolapril, and zofenopril. Preferred ACE inhibitors are benazepril, enalpril, lisinopril, and ramipril.

Dual ACE/NEP inhibitors are, for example, omapatrilat, fasidotril, and fasidotrilat.

Preferred ARBs include candesartan, eprosartan, irbesartan, losartan, olmesartan, tasosartan, telmisartan, and valsartan.

Preferred aldosterone synthase inhibitors are anastrozole, fadrozole, and exemestane.

Preferred aldosterone-receptor antagonists are spironolactone and eplerenone.

A preferred endothelin antagonist is, for example, bosentan, enrasentan, atrasentan, darusentan, sitaxentan, and tezosentan and their pharmaceutically acceptable salts.

Combination therapy includes co-administration of the compound of the invention and said other agent, sequential administration of the compound and the other agent, administration of a composition containing the compound and the other agent, or simultaneous administration of separate compositions containing of the compound and the other agent.

The compounds of the invention have enzyme-inhibiting properties. In particular, they inhibit the action of the natural enzyme renin. The latter passes from the kidneys into the blood where it effects the cleavage of angiotensinogen, releasing the decapeptide angiotensin I which is then cleaved in the blood, lungs, the kidneys and other organs by angiotensin converting enzyme to form the octapeptide angiotensin II. The octapeptide increases blood pressure both directly by binding to its receptor, causing arterial vasoconstriction, and indirectly by liberating from the adrenal glands the sodium-ion-retaining hormone aldosterone, accompanied by an increase in extracellular fluid volume. That increase can be attributed to the action of angiotensin II. Inhibitors of the enzymatic activity of renin bring about a reduction in the formation of angiotensin I. As a result a smaller amount of angiotensin II is produced. The reduced concentration of that active peptide hormone is the direct cause of the hypotensive effect of renin inhibitors.

The action of renin inhibitors *in vitro* is demonstrated experimentally by means of a test which measures the increase in fluorescence of an internally quenched peptide substrate. The sequence of this peptide corresponds to the

sequence of human angiotensinogen. The following test protocol is used: All reactions are carried out in a flat bottom white opaque microtiter plate. A 4 μL aliquot of 400 μM renin substrate (DABCYL-γ-Abu-Ile-His-Pro-Phe-His-Leu-Val-Ile-His-Thr-EDANS) in 192 μL assay buffer (50 mM BES, 150 mM NaCl, 0.25 mg/mL bovine serum albumin, pH7.0) is added to 4 μL of test compound in DMSO at various concentrations ranging from 10 μM to 1 nM final concentrations. Next, 100 μL of trypsin-activated recombinant human renin (final enzyme concentration of 0.2-2 nM) in assay buffer is added, and the solution is mixed by pipetting. The increase in fluorescence at 495 nm (excitation at 340 nm) is measured for 60-360 minutes at room temperature using a Perkin-Elmer Fusion microplate reader. The slope of a linear portion of the plot of fluorescence increase as a function of time is then determined, and the rate is used for calculating percent inhibition in relation to uninhibited control. The percent inhibition values are plotted as a function of inhibitor concentration, and the IC_{50} is determined from a fit of this data to a four parameter equation. The IC_{50} is defined as the concentration of a particular inhibitor that reduces the formation of product by 50% relative to a control sample containing no inhibitor. In the *in vitro* systems the compounds of the invention exhibit inhibiting activities at minimum concentrations of from approximately 5×10^{-5} M to approximately 10^{-12} M. Preferred compounds of the invention exhibit inhibiting activities at minimum concentrations of from approximately 5×10^{-8} M to approximately 10^{-12} M. More preferred compounds of the invention exhibit inhibiting activities at minimum concentrations of from approximately 10^{-8} M to approximately 10^{-12} M. (Wang G. T. et al. *Anal. Biochem.* **1993**, *210*, 351; Nakamura, N. et al. *J. Biochem. (Tokyo)* **1991**, *109*, 741; Murakami, K. et al. *Anal Biochem.* **1981**, *110*, 232).

The action of renin inhibitors *in vitro* in human plasma is demonstrated experimentally by the decrease in plasma renin activity (PRA) levels observed in the presence of the compounds. Incubations mixtures contained in the final volume of 250 μL 95.5 mM N,N-bis(2-hydroxyethyl)-2-aminoethanesulfonic acid, pH 7.0, 8 mM EDTA, 0.1 mM neomycin sulfate, 1 mg/mL sodium azide, 1 mM phenylmethanesulfonyl fluoride, 2% DMSO and 87.3% of pooled mixed-gender human plasma stabilized with EDTA. For plasma batches with low PRA (less than 1 ng/ml/hr) ~2 pM of recombinant human renin was added to achieve PRA of 3-4 ng/mL/hr. The cleavage of endogenous angiotensinogen in plasma was carried out at 37°C for 90 min and the product angiotensin I was measured by competitive radioimmunoassay using DiaSorin PRA kit. Uninhibited incubations containing 2%

DMSO and fully inhibited controls with 2 μM of isovaleryl-Phe-Nle-Sta-Ala-Sta-OH were used for deriving percent of inhibition for each concentration of inhibitors and fitting dose-response data into a four parametric model from which IC_{50} values, defined as concentrations of inhibitors at which 50% inhibition occurs, were determined.

The cardiac and systemic hemodynamic efficacy of selective renin inhibitors were evaluated *in vivo* in sodium-depleted, normotensive cynomolgus monkeys, in sodium-depleted, normotensive beagle dogs following a single oral and intravenous administration of the test compound. Arterial blood pressure was monitored by telemetry in freely moving, conscious animals.

Cynomolgus Monkey: Six male naïve cynomolgus monkeys weighing between 2.5 and 3.5 kg were used in the studies. At least 4 weeks before the experiment, the monkeys were anesthetized with ketamine hydrochloride (15 mg/kg, i.m.) and xylazine hydrochloride (0.7 mg/kg, i.m.), and were implanted into the abdominal cavity with a transmitter (Model #TL11M2-D70-PCT, Data Sciences, St. Paul, MN). The pressure catheter was inserted into the lower abdominal aorta *via* the femoral artery. The bipotential leads were placed in Lead II configuration. The animals were housed under constant temperature (19-25°C), humidity (>40%) and lighting conditions (12 h light and dark cycle), were fed once daily, and were allowed free access to water. The animals were sodium depleted by placing them on a low sodium diet (0.026%, Expanded Primate Diet 829552 MP-VENaCl (P), Special Diet Services, Ltd., UK) 7 days before the experiment and furosemide (3 mg/kg, intramuscularly i.m., Aventis Pharmaceuticals) was administered at -40 h and -16 h prior to administration of test compound.

For oral dosing, the renin inhibitors were formulated in 0.5% methylcellulose at dose levels of 10 and 30 mg/kg (5 mL/kg) by infant feeding tubes. For intravenous delivery, a silastic catheter was implanted into posterior vena cava *via* a femoral vein. The catheter was attached to the delivery pump *via* a tether system and a swivel joint. Test compound (dose levels of 0.1 to 10 mg/kg, formulated at 5% dextrose) was administered by continuous infusion (1.67 mL/kg/h) or by bolus injection (3.33 mL/kg in 2 min).

Arterial blood pressures (systolic, diastolic and mean) and body temperature were recorded continuously at 500 Hz and 50 Hz, respectively, using the Dataquest™ A.R.T. (Advanced Research Technology) software. Heart rate was derived from the phasic blood pressure tracing. During the recording period, the monkeys were kept in a separate room without human presence to avoid pressure

changes secondary to stress. All data were expressed as mean ± SEM. Effects of the renin inhibitors on blood pressure were assessed by ANOVA, taking into account the factors dose and time compared with the vehicle group.

Beagle Dogs: Non-naive Beagle dogs (2 per sex) weighing between 9 and 11 kg were used in the studies. Each animal was implanted subcutaneously with a telemetry transmitter (Data Sciences) and the blood pressure catheter was inserted into the left femoral artery. The electrocardiogram leads were also tunneled subcutaneously to the appropriate anatomical regions. The animals were housed under constant temperature and lighting conditions, were fed once daily, and were allowed free access to water. A sodium depleted state was produced by placing them on a low-sodium diet (<4 meq/day, a combination of canned Prescription Diet canine h/d, from Hill's Pet Products and dry pellets from Bio-Serv Inc., Frenchtown, NJ) beginning 10 days before the experiment, and furosemide (3 mg/kg i.m.; Aventis Pharmaceuticals) was administered at -40 and -16 hr prior to administration of test compound.

A renin inhibitor was orally administered by orogastric gavage to all overnight fasted anaimals at a dose level of 30 mg/kg (4 mL/kg formulated in 0.5% methylcellulose). Food was given 4 h postdose. In some experiments, the renin inhibitor was administered by bolus *i.v.* at increasing dose levels of 1, 3 and 6 mg/kg (2, 6 and 20 mg/mL formulated in sterile saline). Cardiovascular parameters were collected continuously at least 80 min predose and 3 h postdose, followed by every 10 min for 5 h and every 30 min for 16 h postdose. The Dataquest™ ART (version 2.2) software package from DSI (Data Sciences International) was used to collect telemetered cardiovascular data.

The efficacy of the renin inhibitors was also evaluated *in vivo* in double transgenic rats engineered to express human renin and human angiotensinogen (Bohlender J, Fukamizu A, Lippoldt A, Nomura T, Dietz R, Menard J, Murakami K, Luft FC, Ganten D. High human renin hypertension in transgenic rats. *Hypertension* **1997**, *29*, 428–434).

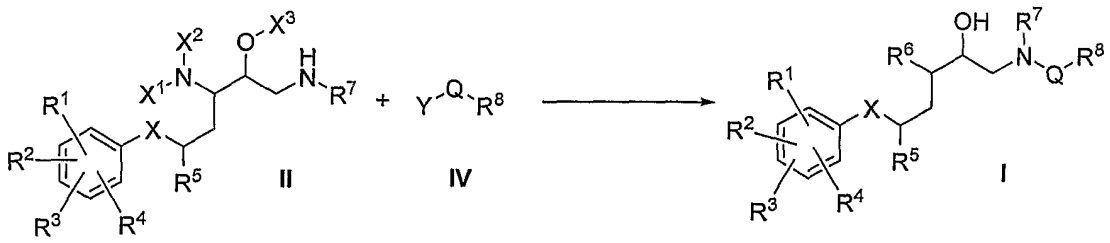
Experiments were conducted in 6-week-old double transgenic rats (dTGRs). The model has been described in detail earlier. Briefly, the human renin construct used to generate transgenic animals made up the entire genomic human renin gene (10 exons and 9 introns), with 3.0 kB of the 5'-promoter region and 1.2 kB of 3' additional sequences. The human angiotensinogen construct made up the entire human angiotensinogen gene (5 exons and 4 introns), with 1.3 kB of 5'-flanking and 2.4 kB of 3'-flanking sequences. The rats were purchased from RCC Ltd (Füllinsdorf,

Switzerland). Radio telemetry transmitters were surgically implanted at 4 weeks of age. The telemetry system provided 24-h recordings of systolic, mean, diastolic arterial pressure (SAP, MAP, DAP, respectively) and heart rate (HR). Beginning on day 42, animals were transferred to telemetry cages. A 24 h telemetry reading was obtained. Rats were then dosed orally on the following 4 consecutive days (days 43-46). The rats were monitored continuously and allowed free access to standard 0.3%-sodium rat chow and drinking water.

The compounds of the invention are useful for ameliorating or treating disorders or diseases in which decreasing the levels of renin products is effective in treating a disease state. In hypertension elevated levels of angiotensin I, the product of renin catalyzed cleavage of angioteninogen are present. Thus, the compounds of the invention can be used in the treatment of hypertension, congestive heart failure, cardiac hypertrophy, cardiac fibrosis, cardiomyopathy post-infarction, complications resulting from diabetes, such as nephropathy, vasculopathy and neuropathy, diseases of the coronary vessels, proteinuria, albumenuria, post-surgical hypertension, metabolic syndrome, obesity, restenosis following angioplasty, raised intra-ocular pressure, glaucoma, abnormal vascular growth, hyperaldosteronism, anxiety states, and cognitive disorders (Fisher N.D.; Hollenberg N. K. *Expert Opin. Investig. Drugs*. **2001**, *10*, 417-26).

The first process of the invention for the preparation of compounds of formula I wherein Q = C=O comprises

1) reacting a compound of formula **II** with a compound of formula **IV**



wherein

X^1 is lower alkyl, lower alkanoyl, or an amino-protecting group;

X^2 is H or together with X^3 is a bivalent protecting group;

X^3 is H or a hydroxy-protecting group; and

R^1, R^2, R^3, R^4, X, R^5, and R^7 in **II** are as defined for formula **I**,

R^8 in **IV** has one of the meanings given for formula **I**, Q is C=O and Y is either OH, Cl, F, Br, or OR^{11} such that OR^{11} is an activated ester, mixed or symmetrical anhydride linkage, or acyl carbonate to form an amide bond, and

2) removing any protecting groups present,

or, and if desired, converting the compound of formula **I** produced having at least one salt-forming group obtainable into its salt,

or converting an obtainable salt into the free compound or into a different salt and/or separating mixtures of isomers that may be obtainable.

Functional groups in starting materials which are prone to participate in undesired side reactions, especially amino, carboxy, hydroxy, and mercapto groups, can be protected by suitable conventional protecting groups which are customarily used in the synthesis of peptide compounds, and also in the synthesis of cephalosporins and penicillins as well as nucleic acid derivatives and sugars. Those protecting groups may already be present in the precursors and are intended to protect the functional groups in question against undesired secondary reactions, such as acylation, etherification, esterification, oxidation, solvolysis, etc. In certain cases the protecting groups can additionally cause the reactions to proceed selectively, for example stereoselectively. It is characteristic of protecting groups that they can be removed easily, i.e. without undesired secondary reactions taking place, for example by acid treatment, fluoride treatment, solvolysis, reduction, photolysis, and also enzymatically, for example under physiological conditions. Protecting groups may also be present in the end products. Compounds of formula **I** having protected functional groups may have greater metabolic stability or pharmacodynamic properties that are better in some other way than the corresponding compounds having free functional groups.

The protection of functional groups by such protecting groups, the protecting groups themselves, and the reactions for their removal are described, for example, in standard works such as T.W. Greene and P. G. M. Wuts "Protective Groups in Organic Synthesis" John Wiley & Sons, Inc., New York 1999.

In compounds of formula **II**, amino-protecting groups X^1 are, for example, acyl groups other than lower alkanoyl, also arylmethyl, lower alkylthio, 2-acyl-lower alk-1-enyl or silyl. The group X^1-N(X^2)- can also be in the form of an azido group.

Acyl groups other than lower alkanoyl are, for example, halo-lower alkanoyl, for example 2-haloacetyl, such as 2-chloro-, 2-bromo-, 2-iodo-, 2,2,2-trifluoro- or 2,2,2-trichloro-acetyl, unsubstituted or substituted, for example halo-, lower alkoxy- or nitro-substituted, benzoyl, for example benzoyl, 4-chlorobenzoyl, 4-methoxybenzoyl or 4-nitrobenzoyl, or lower alkoxycarbonyl that is branched in the 1-position of the lower alkyl radical or suitably substituted in the 1- or 2-position, for example tertiary lower alkoxycarbonyl, such as tert-butoxycarbonyl, arylmethoxy-carbonyl having one or two aryl radicals which are phenyl that is unsubstituted or mono- or poly-substituted, for example, by lower alkyl, for example tertiary lower alkyl, such as tertiary butyl, lower alkoxy, such as methoxy, hydroxy, halogen, such as chlorine, and/or by nitro, for example benzyloxycarbonyl, unsubstituted or substituted benzyloxycarbonyl, such as 4-nitrobenzyl-oxycarbonyl, diphenylmethoxycarbonyl, fluorenylmethoxycarbonyl or substituted diphenylmethoxycarbonyl, such as di(4-methoxyphenyl)methoxycarbonyl, aroylmethoxycarbonyl wherein the aroyl group is preferably benzoyl that is unsubstituted or substituted, for example, by halogen, such as bromine, for example phenacyloxycarbonyl, 2-halo-lower alkoxycarbonyl, for example 2,2,2-trichloroethoxycarbonyl, 2-bromoethoxycarbonyl or 2-iodo-ethoxycarbonyl, 2-(tri-substituted silyl)-lower alkoxycarbonyl, for example 2-tri-lower alkylsilyl-lower alkoxycarbonyl, for example 2-trimethylsilylethoxycarbonyl or 2-(di-n-butyl-methyl-silyl)-ethoxycarbonyl, or triarylsilyl-lower alkoxycarbonyl, for example 2-triphenylsilylethoxycarbonyl.

In a 2-acyl-lower alk-1-enyl radical that can be used as an amino-protecting group, acyl is, for example, the corresponding radical of a lower alkanecarboxylic acid, of a benzoic acid that is unsubstituted or substituted, for example, by lower alkyl, such as methyl or tertiary butyl, lower alkoxy, such as methoxy, halogen, such as chlorine, and/or by nitro, or especially of a carbonic acid semiester, such as a carbonic acid lower alkyl semiester. Corresponding protecting groups are especially 1-lower alkanoyl-prop-1-en-2-yl, for example 1-acetyl-prop-1-en-2-yl, or lower alkoxycarbonyl-prop-1-en-2-yl, for example 1-ethoxy-carbonyl-prop-1-en-2-yl.

Silylamino groups are, for example, tri-lower alkylsilylamino groups, for example trimethylsilylamino, triisopropylamino and t-butyldimethylsilylamino.

An amino group can also be protected by conversion into the protonated form; suitable corresponding anions are especially those of strong inorganic acids, such as sulfuric acid, phosphoric acid or hydrohalic acids, for example the chlorine or bromine anion, or of organic sulfonic acids, such as p-toluenesulfonic acid.

Preferred amino-protecting groups X^1 are acyl radicals of carbonic acid semiesters, such as lower alkoxycarbonyl, especially tert-butyloxycarbonyl or fluorenylmethoxycarbonyl, unsubstituted or lower alkyl-, lower alkoxy-, nitro- and/or halo-substituted ά-phenyl- or .ά,ά-diphenyl-lower alkoxycarbonyl, such as benzyloxycarbonyl, p-nitrobenzyloxy-carbonyl or diphenylmethoxycarbonyl, or 2-halo-lower alkoxycarbonyl, e.g., 2,2,2-trichloroethoxycarbonyl, or 2-(trialkylsyl)ethoxycarbonyl e.g. 2-(trimethylsilyl)ethoxycarbonyl, also trityl or formyl.

Hydroxy-protecting groups X^3 are, for example, acyl groups, for example lower alkanoyl that is substituted by halogen, such as chlorine, for example 2,2-dichloroacetyl, or especially acyl radicals of a carbonic acid semiester mentioned for protected amino groups. A preferred hydroxy-protecting group is, for example, 2,2,2-trichloroethoxycarbonyl, 4-nitrobenzyloxy-carbonyl, diphenylmethoxycarbonyl or trityl. A further suitable hydroxy-protecting group X_3 is tri-lower alkylsilyl, for example trimethylsilyl, triisopropylsilyl or dimethyl-tert-butylsilyl, a readily removable etherifying group, for example an alkyl group, such as tertiary lower alkyl, for example tertiary butyl, an oxa- or a thia-aliphatic or -cycloaliphatic, especially 2-oxa- or 2-thia-aliphatic or -cycloaliphatic, hydrocarbon radical, for example 1-lower alkoxy-lower alkyl or 1-lower alkylthio-lower alkyl, for example methoxymethyl, 1-methoxyethyl, 1-ethoxyethyl, methylthiomethyl, 1-methylthioethyl or 1-ethylthioethyl, or 2-oxa- or 2-thia-cycloalkyl having from 5 to 7 ring atoms, for example 2-tetrahydrofuryl or 2-tetrahydropyranyl, or a corresponding thia analogue, and also 1-phenyl-lower alkyl, for example benzyl, diphenylmethyl or trityl, wherein the phenyl radicals can be substituted, for example, by halogen, for example chlorine, lower alkoxy, for example methoxy, and/or by nitro.

Bivalent protecting groups formed by X^2 and X^3 together are, for example, methylene groups substituted by one or two alkyl radicals and are accordingly unsubstituted or substituted alkylidene, such as lower alkylidene, for example isopropylidene, cycloalkylidene, such as cyclohexylidene, also carbonyl or benzylidene; or dialkylsilyl groups, such dimethylsilyl.

In compounds of formula **IV**, Y is a reactively etherified or esterified hydroxy, and is, for example, in the form of an activated ester or anhydride. The reactive acid derivatives can also be formed *in situ*.

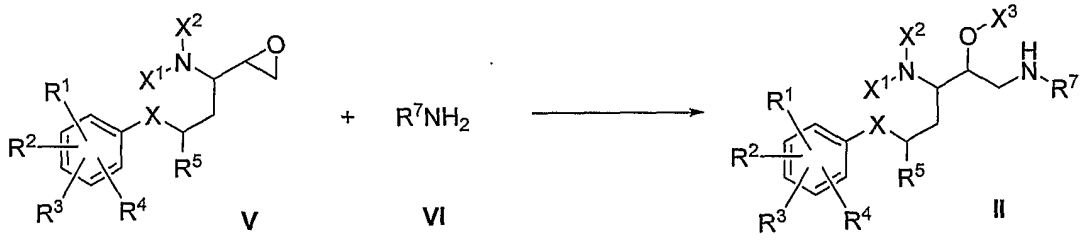
Such activated esters of compounds of formula **IV** are especially esters unsaturated at the linking carbon atom of the esterifying radical, for example of the vinyl ester type, such as vinyl esters (obtainable, for example, by transesterification of a corresponding ester with vinyl acetate; activated vinyl ester method), carbamoyl

esters (obtainable, for example, by treatment of the corresponding acid with an isoxazolium reagent; 1,2-oxazolium or Woodward method), or 1-lower alkoxyvinyl esters (obtainable, for example, by treatment of the corresponding acid with a lower alkoxyacetylene; ethoxyacetylene method), or esters of the amidino type, such as N,N'-disubstituted amidino esters (obtainable, for example, by treatment of the corresponding acid with a suitable N,N'-disubstituted carbodiimide, for example N,N'-dicyclohexylcarbodiimide; carbodiimide method), or N,N-disubstituted amidino esters (obtainable, for example, by treatment of the corresponding acid with an N,N-disubstituted cyanamide; cyanamide method), suitable aryl esters, especially phenyl esters suitably substituted by electron-attracting substituents (obtainable, for example, by treatment of the corresponding acid with a suitably substituted phenol, for example 4-nitrophenol, 4-methylsulfonylphenol, 2,4,5-trichlorophenol, 2,3,4,5,6-pentachlorophenol or 4-phenyldiazophenol, in the presence of a condensation agent, such as N,N'-dicyclohexylcarbodiimide; activated aryl esters method), cyanomethyl esters (obtainable, for example, by treatment of the corresponding acid with chloroacetonitrile in the presence of a base; cyanomethyl esters method), thioesters, especially unsubstituted or substituted, for example nitro-substituted, phenylthio esters (obtainable, for example, by treatment of the corresponding acid with unsubstituted or substituted, for example nitro-substituted, thiophenols, inter alia by the anhydride or carbodiimide method; activated thiol esters method), or especially amino or amido esters (obtainable, for example, by treatment of the corresponding acid with an N-hydroxyamino or N-hydroxyamido compound, for example N-hydroxysuccinimide, N-hydroxypiperidine, N-hydroxyphthalimide, N-hydroxy-5-norbornene-2,3-dicarboxylic acid imide, 1-hydroxybenzotriazole or 3-hydroxy-3,4-dihydro-1,2,3-benzotriazin-4-one, for example by the anhydride or carbodiimide method; activated N-hydroxy esters method). Internal esters, for example .gamma.-lactones, can also be used.

Anhydrides of acids of formula **IV** may be symmetric or preferably mixed anhydrides of those acids, for example anhydrides with inorganic acids, such as acid halides, especially acid chlorides (obtainable, for example, by treatment of the corresponding acid with thionyl chloride, phosphorus pentachloride or oxalyl chloride; acid chloride method), azides (obtainable, for example, from a corresponding acid ester *via* the corresponding hydrazide and treatment thereof with nitrous acid; azide method), anhydrides with carbonic acid semiesters, for example carbonic acid lower alkyl semiesters (obtainable, for example, by treatment of the corresponding acid with chloroformic acid lower alkyl esters or with a 1-lower alkoxycarbonyl-2-lower alkoxy-1,2-dihydroquinoline; mixed O-alkyl-carbonic acid anhydrides method), or

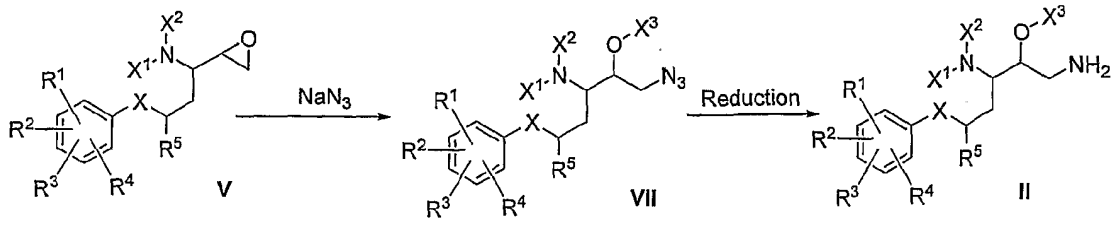
anhydrides with dihalogenated, especially dichlorinated, phosphoric acid (obtainable, for example, by treatment of the corresponding acid with phosphorus oxychloride; phosphorus oxychloride method), anhydrides with other phosphoric acid derivatives (for example those obtainable with phenyl-N-phenylphosphoramidochloridate) or with phosphorous acid derivatives, or anhydrides with organic acids, such as mixed anhydrides with organic carboxylic acids (obtainable, for example, by treatment of the corresponding acid with an unsubstituted or substituted lower alkane- or phenyl-lower alkane-carboxylic acid halide, for example phenylacetic acid chloride, pivalic acid chloride or trifluoroacetic acid chloride; mixed carboxylic acid anhydrides method) or with organic sulfonic acids (obtainable, for example, by treatment of a salt, such as an alkali metal salt, of the corresponding acid with a suitable organic sulfonic acid halide, such as a lower alkane- or aryl-, for example methane- or p-toluene-sulfonic acid chloride; mixed sulfonic acid anhydrides method) and symmetric anhydrides (obtainable, for example, by condensation of the corresponding acid in the presence of a carbodiimide).

Amine compounds of formula **II** can be prepared, for example, by reacting an epoxide compound of formula **V** with an amine of formula **VI**:

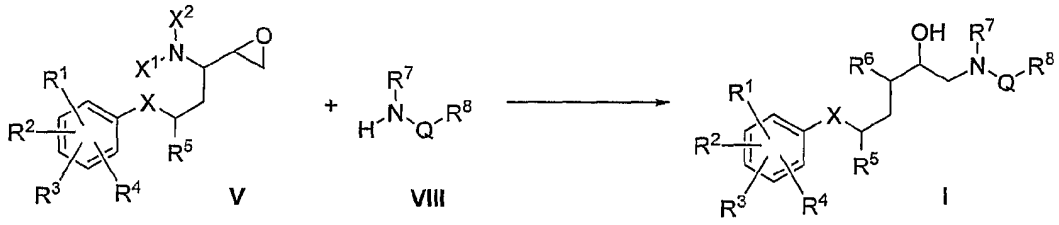


where R^7 is defined as in formula **I**; followed by appropriate protecting group manipulation.

Amine compounds of formula **II** wherein R^7 = H can also be prepared by reduction of azide compounds of formula **VII** using hydrogen gas in the presence of a transition metal catalyst, for example Raney nickel or platinum or palladium catalysts, for example platinum or palladium on active carbon, or with triphenylphosphine in an aqueous-organic solvent mixture (Staudinger reduction). Azide compounds **VII** can be prepared by reacting by reacting an epoxide compound of formula **V** with nucleophilic azide source such as sodium azide in an organic solvent such as DMF or acetonitrile:

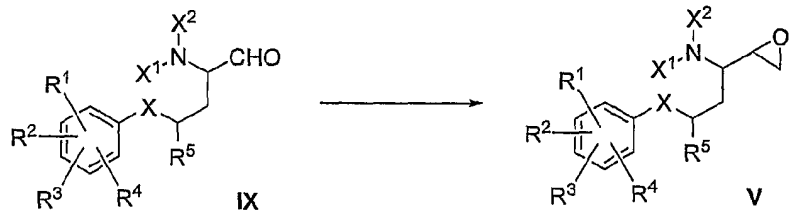


In a second process of the invention, compounds of formula **I** wherein Q is SO_2 are prepared, for example, by 1) treatment of epoxide compounds of formula **V** with compounds of formula **VIII** wherein Q = SO_2, followed by 2) protecting group removal:

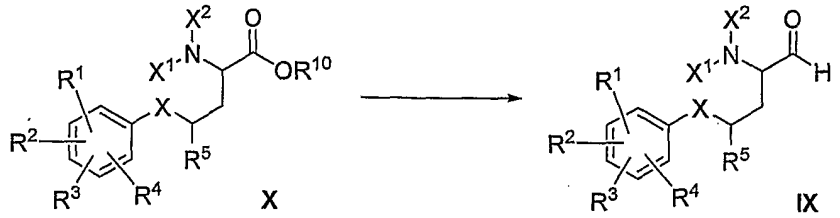


In a third process of the invention, compounds of formula **I** wherein Q = S are prepared, for example, by treatment of optionally protected compounds of formula **I** in which Q = O with P_2S_5 or Lawesson's reagent, followed by protecting group removal.

Epoxide compounds of formula **V** can, in turn, be prepared in a number of ways including, for example, by reacting with aldehyde compounds of formula **IX** with trimethylsulfoxonium Iodide or trimethylsulfonium iodide (J. Aube "Epoxidation and Related Processes" Chapter 3.2 in Volume 1 of "Comprehensive Organic Synthesis" Edited by B. M. Trost, I. Fleming and Stuart L. Schreiber, Pergamon Press New York, 1992).



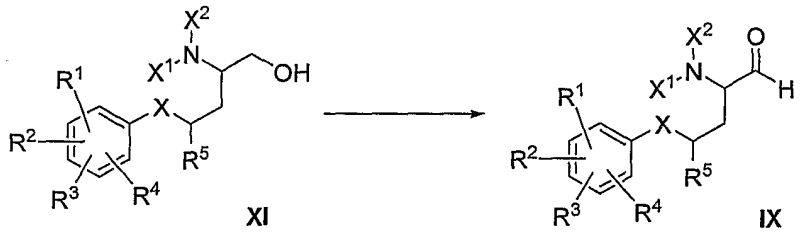
Compounds of formula **IX** can be prepared from compounds of formula **X**, wherein R^{10} is lower alkyl or aryl-lower alkyl, in a number of ways. For example, compounds of formula **X** can be converted to compounds of formula **IX**:



X IX

by direct reduction from ester to aldehyde using specialized reagents and conditions known to minimize over-reduction (I. T. Harrison and S. Harrison "Compendium of Organic Synthetic Methods" Section 53, pp 152-153, John Wiley and Sons, New York 1971). One method of carrying out this transformation is by treatment with diisobutyl aluminum hydride in an organic solvent at lowered temperatures. The synthesis of compounds of Formula **IX** is described in U.S. Patent 5,559,111 at columns 25-26.

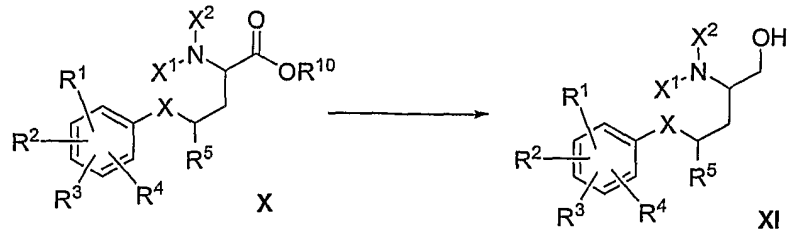
Alternately, compounds of formula **IX** can be prepared from alcohol compounds of formula **XI**:



XI IX

using one of several oxidation protocols which are designed to minimize overoxidation (I. T. Harrison and S. Harrison "Compendium of Organic Synthetic Methods" Section 48, pp 137-143, John Wiley and Sons, New York 1971). Such oxidation protocols include oxalyl chloride/ dimethyl sulfoxide (Swern oxidation), (1,1,1-triacetoxy)-1,1-dihydro-1,2-dihydro-1,2-benziodoxol-3(1H)-one (Dess-Martin periodinane), sulfur trioxide/pyridine or tetrapropylammonium perruthenate (TPAP).

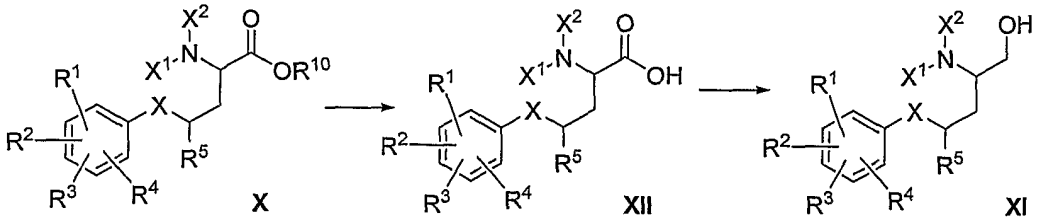
Alcohol compounds of formula **XI** are prepared from ester compounds of formula **X** by a variety of reducing agents (I. T. Harrison and S. Harrison "Compendium of Organic Synthetic Methods" Section 38, pp 87-91, John Wiley and Sons, New York 1971) including, for example, lithium aluminum hydride.



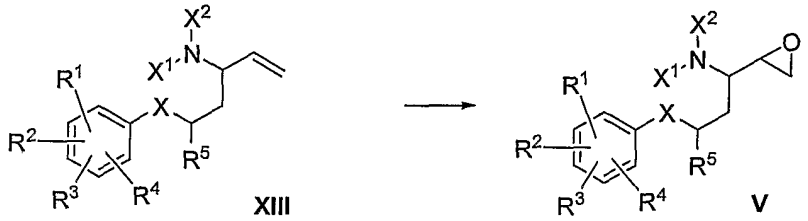
X XI

As another example, compounds of formula **X** can be hydrolyzed to carboxylic acid compounds of formula **XII** (I. T. Harrison and S. Harrison

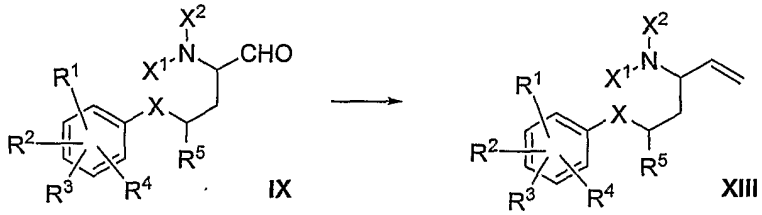
"Compendium of Organic Synthetic Methods" Section 23, pp 42-46, John Wiley and Sons, New York 1971). Compounds of formula **XII** can be converted to alcohol compounds of formula **XI** using a wide variety of reducing agents and conditions (I. T. Harrison and S. Harrison "Compendium of Organic Synthetic Methods" Section 32, pp 76-78, John Wiley and Sons, New York 1971).



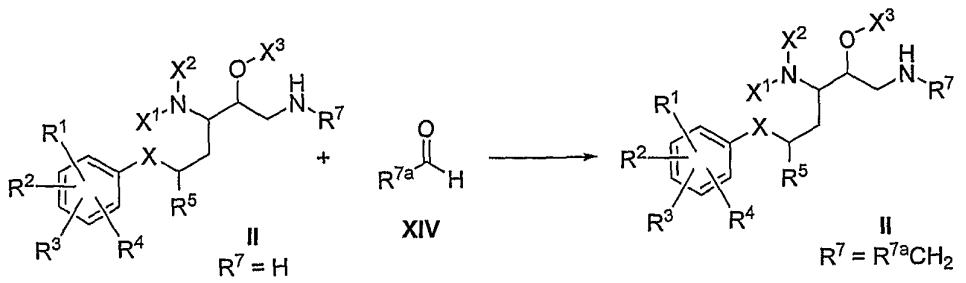
Alternately, epoxide compounds of formula **V** can be prepared from alkene compounds of formula **XIII** by epoxidation of the alkene with for example mCPBA, monoperphthalic acid, peracetic acid, dimethyldioxirane, H_2O_2/benzonitrile.



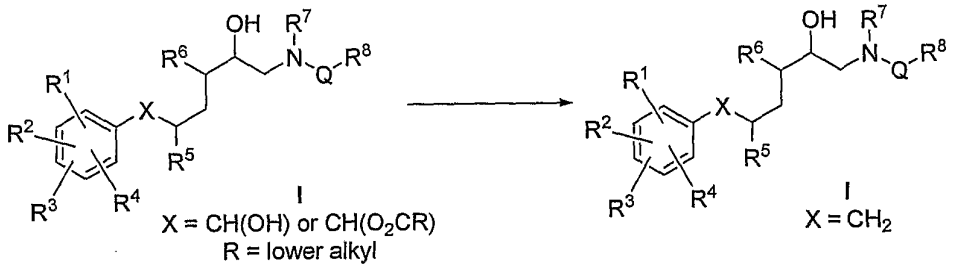
Alkene compounds of formula **XIII** are prepared from aldehyde compounds of formula **IX** utilizing the Wittig reaction or the Tebbe reagent.



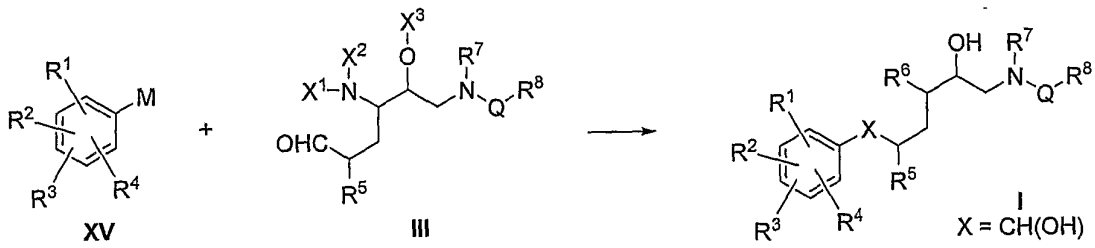
Compounds of formula **II** in which R^7 is a lower alkyl, certain lower haloalkyl groups, lower cycloalkyl, certain lower alkoxyalkyl groups or certain lower lower haloalkoxy-lower alkyl groups are prepared by reductive alkylation of primary amines of formula **II** wherein R^7 = H with aldehydes of formula **XIV** wherein R^{7a} is the lower homolg of R^7 (E. W. Baxter and A. B. Reitz "Reductive aminations of carbonyl compounds with borohydride and borane reducing agents" in Organic Reactions Volume 59 pp 1-714, Edited by L. E. Overman, John Wiley and Sons, New York, 2002).



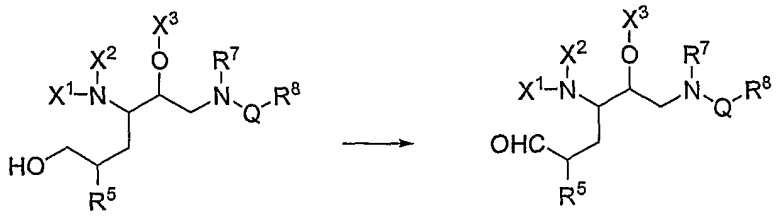
In a fourth process of the invention, compounds of formula I wherein X = CH_2 are prepared by 1) hydrogenolysis or deoxygenation of optionally protected compounds of formula I wherein X = CH(OH), or an ester thereof such as an acetate, using for example hydrogen gas and a transition metal catalyst, for example Raney nickel or platinum or palladium catalysts, for example platinum or palladium on active carbon; followed by 2) protecting group removal:



In a fifth process of the invention, compounds of formula I wherein X = CH(OH) are prepared by addition of organometallic compounds of formula XV wherein M is for example Li, MgCl, MgBr or MgI to aldehyde compounds of formula III:

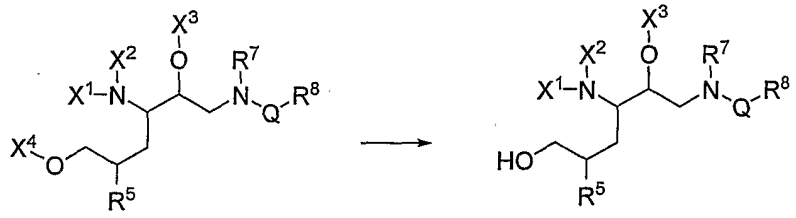


Aldehyde compounds of formula III are prepared by oxidation of alcohols of formula XVI using, for example, oxalyl chloride/ dimethyl sulfoxide (Swern oxidation), (1,1,1-triacetoxy)-1,1-dihydro-1,2-dihydro-1,2-benziodoxol-3(1H)-one (Dess-Martin periodinane), sulfur trioxide/pyridine or tetrapropylammonium perruthenate (TPAP).



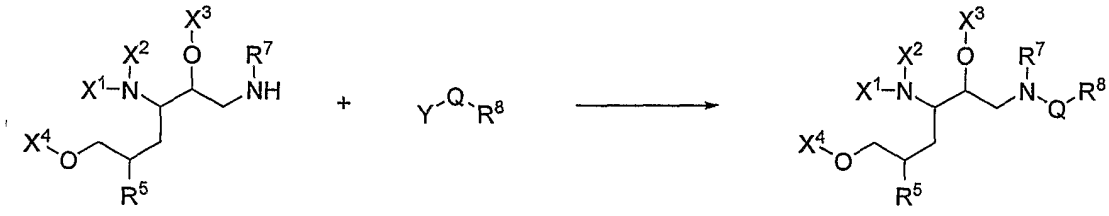
XVI III

Alcohols of formula **XVI** are obtained from protected alcohols of formula **XVII** wherein X^4 is an alcohol protecting group that can be removed selectively in the presence of the protecting groups X^1, X^2 and X^3, for example a benzyl group or a trialkylsilyl ether.



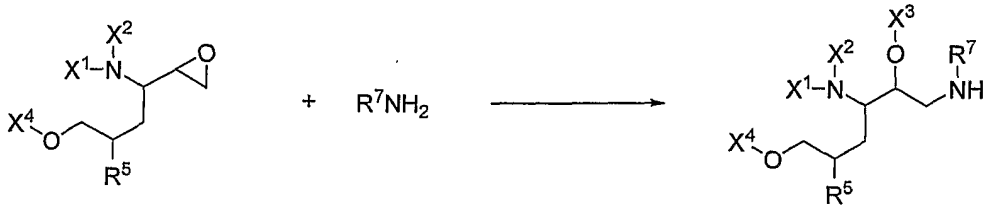
XVII XVI

Compounds of formula **XVII** wherein Q is C=O are prepared from amines of formula **XVIII** by coupling with a carboxylic acid derivative of formula **IV** wherein Q is C=O:



XVIII IV XVII

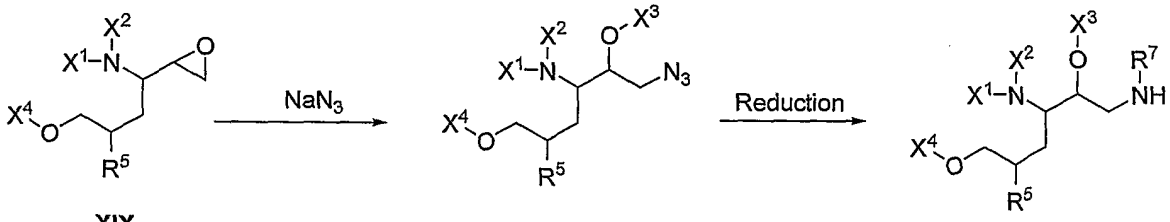
Compounds of formula **XVIII** are prepared by opening epoxides of formula **XIX** with amines of formula **VI**:



XIX VI XVIII

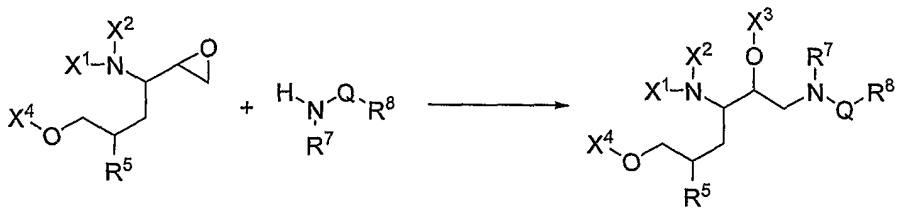
Amine compounds of formula **XVIII** wherein R^7 = H can also be prepared by reduction of azide compounds of formula **XX** using hydrogen gas in the presence of a transition metal catalyst, for example Raney nickel or platinum or palladium catalysts, for example platinum or palladium on active carbon, or with

triphenylphosphine in the a mixed aqueous-organic solvent (Staudinger reduction). Azide compounds **XX** can be prepared by reacting by reacting an epoxide compound of formula **XIX** with nucleophillic azide source such as sodium azide in an organic solvent such as DMF or acetonitrile:



XIX **XX** **XVIII**

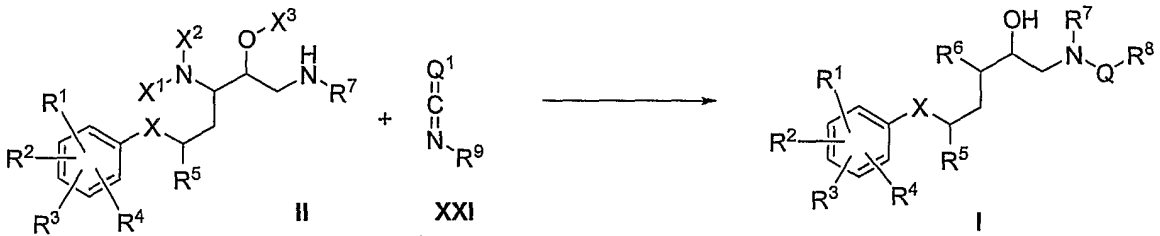
Compounds of formula **XVII** wherein Q = SO_2 are prepared, for example, by treatment of epoxide compounds of formula **XIX** with compounds of formula **VIII** wherein Q = SO_2, followed by protecting group removal:



XIX **VIII** **XVII**

Epoxides of formula **XIX** are prepared by appropriate adaptations of the various procedures described above for the preparation of epoxides of formula **V**.

A sixth process of the invention for the preparation of compounds of formula **I** wherein Q is C=O or C=S and R^{10} is hydrogen comprises 1) reacting a amine compound of formula **II** with an isocyanate or isothiocyanate of formula **XXI**:



II **XXI**

Q^1 = O or S

I

Q = O, S

$R^8 = NR^9R^{10}$

R^{10} = H

and 2) removing any protecting groups present.

In each of the processes mentioned above, the starting compounds may also be used in the form of salts, provided that the reaction conditions allow it.

A free amino group present in a compound of formula I obtainable in accordance with the process can be acylated or alkylated, for example to introduce a radical R^6 other than hydrogen. The acylation, sulfonylation and the alkylation can be carried out in accordance with one of the methods mentioned for protecting groups or according to known processes.

Furthermore, a free hydroxy group present in a compound of formula I obtainable in accordance with the process, for example as a constituent of the radical R^8, can be acylated. The acylation can be carried out with acylating reagents in accordance with one of the methods mentioned for protecting groups or according to known processes.

In compounds of formula I in which R^1, R^2, R^3, and/or R^4 are hydroxy it is also possible to replace hydroxy by one of the etherified hydroxy groups mentioned under formula I by reacting the corresponding compound of formula I wherein R^1, R^2, R^3, and/or R^4 is hydroxy in customary manner, for example in the presence of a basic condensation agent, with a compound of the formula(e) R'^1-Y, R'^2-Y, R'^3-Y, and/or R'^4-Y, wherein R'^1 is lower alkyl or free or esterified or amidated carboxy-lower alkyl, R'^2 is lower alkyl, lower alkoxy-lower alkyl, lower alkoxy-lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, optionally lower alkanoylated, halogenated or sulfonylated hydroxy-lower alkyl, oxo-lower alkyl, lower alkyl, lower alkenyl, cycloalkoxy-lower alkyl, lower alkoxy-lower alkyl, lower alkoxy-lower alkenyl, lower alkenyloxy-lower alkyl, lower alkenyloxy-lower alkyl, lower alkenyloxy-lower alkyl, lower alkanoyl-lower alkyl, optionally S-oxidized lower alkyl-thio-lower alkyl, lower alkylthio-(hydroxy)-lower alkyl, aryl-lower alkyl, optionally hydrogenated heteroaryl-lower alkyl, optionally hydrogenated heteroarylthio-lower alkyl, cyano-lower alkyl or free or esterified or amidated carboxy-lower alkyl, R'^3 is lower alkyl, lower alkoxy-lower alkyl, hydroxy-lower alkyl, aryl-lower alkyl, halogenated lower alkyl, cyano-lower alkyl or free or esterified or amidated carboxy-lower alkyl, and R'^4 is lower alkyl, and Y is reactive esterified hydroxy, especially hydroxy esterified by a mineral acid, by sulfuric acid or by an organic sulfonic acid, such as halogen, preferably chlorine, bromine or iodine, lower alkanesulfonyloxy or unsubstituted or substituted benzenesulfonyloxy, especially methane-, ethane-, benzene-, p-toluene- or p-bromobenzene-sulfonyl. The reaction is preferably carried out in the presence of a basic condensation agent, such as an alkali metal carbonate, for example potassium carbonate, in an inert solvent, such as a lower alkanol, such as methanol, ethanol, butanol, tert-butanol or especially amyl alcohol, advantageously at elevated temperature, for example in a

temperature range of approximately from 40-140°C, if necessary with removal of the resulting water of reaction by distillation, for example by azeotropic distillation.

It is also possible for salts of compounds of formula I obtainable in accordance with the process to be converted in a manner known *per se* into the free compounds, for example by treatment with a base, such as an alkali metal hydroxide, a metal carbonate or metal hydrogen carbonate, or ammonia, or another of the salt-forming bases mentioned at the beginning, or with an acid, such as a mineral acid, for example with hydrochloric acid, or another of the salt-forming acids mentioned at the beginning.

Resulting salts can be converted into different salts in a manner known *per se*: acid addition salts, for example, by treatment with a suitable metal salt, such as a sodium, barium or silver salt, of a different acid in a suitable solvent in which an inorganic salt being formed is insoluble and is therefore eliminated from the reaction equilibrium, and basic salts by freeing of the free acid and conversion into a salt again.

The compounds of formula I, including their salts, may also be obtained in the form of hydrates or may include the solvent used for crystallization.

As a result of the close relationship between the novel compounds in free form and in the form of their salts, any reference herein to the free compounds and their salts is to be understood as including also the corresponding salts and free compounds, respectively, as appropriate and expedient.

Stereoisomeric mixtures, i.e., mixtures of diastereoisomers and/or enantiomers, such as racemic mixtures, can be separated into the corresponding isomers in a manner known *per se* by suitable separating processes. For example, mixtures of diastereoisomers can be separated into the individual diastereoisomers by fractional crystallization, chromatography, solvent partition, etc. Racemates can be separated from one another, after conversion of the optical antipodes into diastereoisomers, for example by reaction with optically active compounds, for example optically active acids or bases, by chromatography on column materials charged with optically active compounds or by enzymatic methods, for example by selective reaction of only one of the two enantiomers. This separation can be carried out either at the stage of one of the starting materials or with the compounds of formula I themselves.

In a compound of formula I the configuration at individual chirality centers can be selectively reversed. For example, the configuration of asymmetric carbon atoms that carry nucleophilic substituents, such as amino or hydroxy, can be reversed by second order nucleophilic substitution, optionally after conversion of the bonded

nucleophilic substituent into a suitable nucleofugal leaving group and reaction with a reagent introducing the original substituent, or the configuration at carbon atoms having hydroxy groups can be reversed by oxidation and reduction, analogously to patent application EP 236,734.

Another embodiment of the invention is those forms of the process in which a compound obtainable as an intermediate at any stage is used as a starting material and the remaining steps are carried out or the process is interrupted at any stage, or a starting material is formed under the reaction conditions or is used in the form of a reactive derivative or salt, or a compound obtained in accordance with the process of the invention is formed under the process conditions and further processed *in situ*. It is preferable to use those starting materials which result in the compounds described above.

Representative compounds of the invention can be synthesized in accordance with the general synthetic schemes described above and are illustrated in the examples that follow. The methods for preparing the various starting materials used in the schemes and examples are well within the knowledge of persons skilled in the art

The following abbreviations have the indicated meanings:

aq	aqueous
Boc	tert-butoxy carbonyl or t-butoxy carbonyl
$(Boc)_2O$	di-*tert*-butyl dicarbonate
brine	saturated aqueous sodium chloride
CH_2Cl_2	methylene chloride
CH_3CN or MeCN	acetonitrile
Cpd	compound
d	day
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DMAP	4-(dimethylamino)pyridine
DMF	N,N-dimethyl formamide
DMSO	Dimethyl sulfoxide
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone
EDC.HCl	1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride
eq, equiv	equivalents
Et	ethyl
EtOAc	ethyl acetate
Fmoc	1-[[(9H-fluoren-9-ylmethoxy)carbonyl]oxy]-
Fmoc-OSu	1-[[(9H-fluoren-9-ylmethoxy)carbonyl]oxy]-2,5-pyrrolidinedione
h, hr	hour
HBTU	O-benzotriazol-1-yl-N,N,N',N'-tetramethyluronium

	hexafluorophosphate
HOBt	1-hydroxybenzotriazole
KHMDS	potassium hexamethyldisilazane
LAH or $LiALH_4$	lithium aluminum hydride
LHMDS	lithium hexamethyldisilazane
Me	methyl
MeOH	methanol
MsCl	methanesulfonyl chloride
min	minute
MS	mass spectrum
NaH	sodium hydride
$NaHCO_3$	sodium bicarbonate
NaN_3	sodium azide
NaOH	sodium hydroxide
Na_2SO_4	sodium sulfate
$Pd_2(dba)_3$	tris(dibenzylideneacetone)dipalladium(0)
Ph or PH	phenyl
RT/rt/r.t.	room temperature
satd	saturated
$SOCl_2$	thionyl chloride
TEA	triethylamine or Et_3N
Teoc	1-[2-(trimethylsilyl)ethoxycarbonyloxy]-
Teoc-OSu	1-[2-(trimethylsilyl)ethoxycarbonyloxy]pyrrolidin-2,5-dione
TFA	trifluoroacetic acid
THF	tetrahydrofuran
tlc	thin layer chromatography
TMSCl	chlorotrimethylsilane or trimethylsilyl chloride
t_R	retention time

Analytical Methods

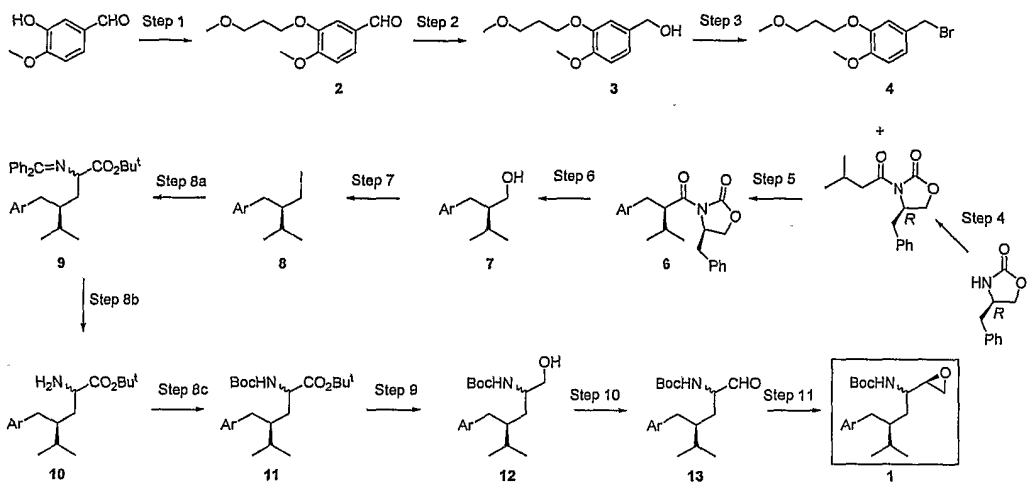
LC-MS (3 min)

Column: Chromolith SpeedRod, RP-18e, 50 x 4.6 mm; Mobil phase: A: 0.01%TFA/water, B: 0.01%TFA/CH_3CN; Flow rate: 1 mL/min; Gradient:

Time (min)	A%	B%
0.0	90	10
2.0	10	90
2.4	10	90
2.5	90	10
3.0	90	10

EXAMPLE 1

tert-Butyl (3S)-3-(3-(3-methoxypropoxy)-4-methoxybenzyl)-4-methyl-1-(oxiran-2-yl)pentylcarbamate



Step 1

To a mixture of 3-hydroxy-4-methoxy-benzaldehyde (26.60 g, 0.175 mol, 1.0 equiv), triphenylphosphine (60.80 g, 1.3 equiv), and 3-methoxy-1-propanol (16.00 g, 1.0 equiv) in THF (100 mL) and toluene (300 mL) was added a solution of DIAD (47.0 g, 1.3 equiv) in toluene (100 mL) dropwise. The resulting mixture was evacuated and then stirred for 24 h at room temperature. The reaction mixture was concentrated *in vacuo*. The crude product was carried on to the next step without further purification. An analytical sample of 4-methoxy-3-(3-methoxy-propoxy)-benzaldehyde (**2**) was obtained by chromatography (33% to 50% ethyl acetate in hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.84 (s, 1H), 7.46-7.42 (m, 2H), 6.97 (d, *J* = 8.4 Hz, 1H), 4.18 (t, *J* = 6.4 Hz, 2H), 3.95 (s, 3H), 3.57 (t, *J* = 6.2 Hz, 2H), 3.35 (s, 3H), 2.13 (p, *J* = 6.3 Hz, 2H).

Step 2

A mixture of crude 4-methoxy-3-(3-methoxy-propoxy)-benzaldehyde (**2**) and ethanol (300 mL) was treated with a suspension of $NaBH_4$ (15.0 g) and ethanol (150 mL). The resulting mixture was stirred overnight at room temperature. The reaction mixture was concentrated *in vacuo*. The residue was treated with 10% Na_2CO_3 and extracted three times with CH_2Cl_2. The organic phase was dried over Na_2SO_4,

filtered and concentrated *in vacuo*. The residue was filtered through silica gel column (33% to 75% ethyl acetate in hexanes) to give the crude 4-methoxy-3-(3-methoxy-propoxy)-benzyl alcohol **(3)**. An analytical sample was obtained by further chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.95-6.83 (m, 3H), 4.60 (s, 2H), 4.12 (t, *J* = 6.4 Hz, 2H), 3.85 (s, 3H), 3.57 (t, *J* = 6.2 Hz, 2H), 3.34 (s, 3H), 2.10 (p, *J* = 6.3 Hz, 2H), 1.75 (br s, 1H).

Step 3

To a 2-L round bottom flask of crude 4-methoxy-3-(3-methoxy-propoxy)-benzyl alcohol **(3)** was added Et_2O (400 mL) and pyridine (0.26 mL). The flask was evacuated and refilled with N_2. PBr_3 (20.93 g) was then added slowly to the stirred solution at room temperature. After 3 h, the reaction mixture was quenched with satd aq $NaHCO_3$ and extracted three times with ethyl acetate. The organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo*. A mixture of the crude product in Et_2O (100 mL) and hexane (400 mL) was vigorously stirred for 0.5 h. The mixture was filtered and the solid collected was washed with hexane. The filtrate was concentrated *in vacuo* to leave a residue which was purified on silica gel chromatography (25% to 33% ethyl acetate in hexanes) to afford 4-methoxy-3-(3-methoxy-propoxy)-benzyl bromide **(4)**. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.96-6.93 (m, 2H), 6.81 (d, J = 8.8 Hz, 1H), 4.49 (s, 2H), 4.12 (t, *J* = 6.4 Hz, 2H), 3.86 (s, 3H), 3.57 (t, *J* = 6.2 Hz, 2H), 3.36 (s, 3H), 2.11 (p, *J* = 6.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 149.6, 148.5, 130.2, 121.6, 113.8, 111.4, 69.2, 66.0, 58.7, 56.0, 34.4, 29.5.

Step 4

A 250-mL round bottom flask was charged with (*R*)-(+)-4-benzyl-2-oxazolidinone (7.520 g, 42.4 mmol, 1.0 equiv) and THF (100 mL). The flask was evacuated and refilled with N_2. The mixture was cooled with a dry ice-acetone bath and 1.6 M *n*-BuLi in hexanes (30 mL, 48 mmol, 1.13 equiv) was added slowly. After 0.5 h, isovaleroyl chloride (5.5 mL, 45.1 mmol, 1.06 equiv) was added. After 10 min, the dry ice-acetone bath was removed and replaced with an ice bath. After an additional 2.5 h, the reaction mixture was quenched with 10% aq Na_2CO_3 (65 mL) and vigorously stirred for 3 h. The mixture was extracted three times with ethyl acetate. The organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (25% to 33% ethyl acetate in hexanes) to afford (4*R*)-benzyl-3-(3-methyl-butyryl)-2-oxazolidinone (**5**) (10.5308 g, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.36-7.21 (m, 5H), 4.71-4.65

(m, 1H), 4.22-4.11 (m, 2H), 3.31 (dd, *J* = 13.3, 3.4 Hz, 1H), 2.89 (dd, *J* = 16.1, 6.7 Hz, 1H), 2.78 (dd, *J* = 16.3, 7.2 Hz, 1H), 2.75 (dd, *J* = 13.2, 9.7 Hz, 1H), 2.27-2.17 (m, 1H), 1.02 (d, *J* = 6.7 Hz, 3H), 1.00 (d, *J* = 6.7 Hz, 3H).

Step 5

To a 250-mL round bottom flask of compound (4*R*)-benzyl-3-(3-methyl-butyryl)-2-oxazolidinone (**5**) (5.500 g, 21.0 mmol) was added THF (60 mL). The flask was evacuated and refilled with N_2. The mixture was cooled with a dry ice-acetone bath and 1.0M LiHMDS in THF (23.5 mL, 23.5 mmol) was added dropwise. After 0.5 h, a solution of 4-methoxy-3-(3-methoxy-propoxy)-benzyl bromide (**4**) (5.8043 g, 20.1 mmol) in THF (30 mL) was added slowly *via* cannula. The resulting mixture was allowed to slowly warm to room temperature while stirring overnight. The mixture was quenched with satd aq NH_4Cl and extracted three times with ethyl acetate. The organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (25% to 33% ethyl acetate in hexanes) to afford (R)-3-((R)-2-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-methylbutanoyl)-4-benzyloxazolidin-2-one (**6**) (8.349 g, 84%). LC-MS (3 min) t_R = 2.05 min *m/z* 492 ($M+Na^+$), 470 ($M+H^+$), 293, 261; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.24-7.20 (m, 3H), 6.93-6.91 (m, 2H), 6.85 (d, *J* = 1.8 Hz, 1H), 6.77 (dd, *J* = 8.2, 1.8 Hz, 1H), 6.73 (d, *J* = 8.2 Hz, 1H), 4.63-4.57 (m, 1H), 4.28-4.23 (m, 1H), 4.09-4.03 (m, 3H), 3.96 (dd, *J* = 8.9, 2.5 Hz, 1H), 3.78 (s, 3H), 3.55-3.49 (m, 2H), 3.31 (s, 3H), 2.97-2.80 (m, 3H), 2.19 (dd, *J* = 13.5, 9.4 Hz, 1H), 2.11-1.97 (m, 3H), 1.06 (d, *J* = 7.0 Hz, 3H), 1.03 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 175.9, 153.0, 148.2, 147.8, 135.2, 131.9, 129.3, 128.8, 127.1, 121.4, 114.1, 111.4, 69.4, 65.9, 65.3, 58.6, 56.0, 55.0, 50.1, 37.3, 35.4, 31.4, 29.5, 20.7, 19.5.

Step 6

To a 100-mL round bottom flask of (R)-3-((R)-2-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-methylbutanoyl)-4-benzyloxazolidin-2-one (**6**) (2.1475 g, 4.57 mmol) was added Et_2O (50 mL) and H_2O (0.18 mL). The flask was evacuated and refilled with N_2. The mixture was cooled with an ice bath and 2.0 M $LiBH_4$ in THF (5.5 mL, 11.0 mmol) was added dropwise. After 10 min, the cooling bath was removed and the mixture was stirred for an additional 0.5 h. The mixture was then cooled with an ice bath, quenched with 1 *N* aq NaOH (20 mL) and extracted three times with CH_2Cl_2. The organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (33% to 50% ethyl acetate in hexanes) to afford (R)-2-(3-(3-methoxypropoxy)-4-

methoxybenzyl)-3-methylbutan-1-ol (**7**) (0.7894 g, 58%). LC-MS (3 min) t_R = 1.60 min *m/z* 319 (MNa^+), 297 (MH^+), 209; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.80-6.71 (m, 3H), 4.10 (t, *J* = 6.6 Hz, 2H), 3.84 (s, 3H), 3.59-3.55 (m, 4H), 3.36 (s, 3H), 2.65 (dd, *J* = 13.8, 5.6 Hz, 1H), 2.45 (dd, *J* = 13.8, 9.4 Hz, 1H), 2.10 (p, *J* = 6.3 Hz, 2H), 1.88-1.80 (m, 1H), 1.66-1.59 (m, 1H), 1.41 (br s, 1H), 0.97 (d, *J* = 7.0 Hz, 3H), 0.96 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 148.2, 147.5, 133.9, 121.1, 114.0, 111.6, 69.3, 65.9, 63.0, 58.7, 56.0, 48.8, 34.1, 29.5, 27.9, 19.7, 19.5.

Step 7

A 100 mL round bottom flask was charged with triphenylphosphine (1.3055 g, 4.98 mmol, 1.2 equiv) and CH_2Cl_2 (20 mL). Imidazole (0.5590 g, 8.21 mmol, 2.0 equiv) and iodine (1.4547 g, 5.73 mmol, 1.4 equiv) were added. The flask was evacuated and refilled with N_2. A solution of (R)-2-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-methylbutan-1-ol (**7**) (1.1992 g, 4.04 mmol, 1.0 equiv) in CH_2Cl_2 (20 mL) was added to the resulting suspension *via* cannula. After 3 h, the solvents were removed *in vacuo*. The residue was purified by chromatography on silica gel (25% to 33% ethyl acetate in hexanes) to give 2-(3-methoxypropoxy)-4-((R)-2-(iodomethyl)-3-methylbutyl)-1-methoxybenzene (**8**) (1.4742 g, 90%). LC-MS (3 min) t_R = 2.33 min, *m/z* 407 (MH^+), 375, 177; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.80-6.73 (m, 3H), 4.11 (t, *J* = 6.4 Hz, 2H), 3.84 (s, 3H), 3.58 (t, J = 6.2 Hz, 2H), 3.36 (s, 3H), 3.21 (dd, *J* = 10.0, 4.7 Hz, 1H), 3.09 (dd, *J* = 10.0, 4.4 Hz, 1H), 2.77 (dd, *J* = 13.9, 4.8 Hz, 1H), 2.34 (dd, *J* = 13.8, 9.7 Hz, 1H), 2.11 (p, *J* = 6.3 Hz, 2H), 1.75-1.65 (m, 1H), 1.16-1.10 (m, 1H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 148.2, 147.7, 132.9, 121.1, 114.0, 111.7, 69.3, 65.9, 58.7, 56.0, 47.6, 36.6, 30.5, 29.5, 19.8, 19.5, 14.5.

Step 8

A flame dried 100-mL round bottom flask was charged with *N*-(diphenylmethylene)glycine *tert*-butyl ester (0.6625 g, 2.24 mmol, 1.25 equiv), THF (10 mL) and HMPA (1 mL). The flask was evacuated and refilled with N_2. The mixture was cooled with a dry ice-acetone bath and 1.0 M LiHMDS in THF (2.5 mL, 2.5 mmol) was added dropwise. After 15 min, a solution of 2-(3-methoxypropoxy)-4-((R)-2-(iodomethyl)-3-methylbutyl)-1-methoxybenzene (**8**) (0.7301 g, 1.80 mmol, 1.0 equiv) in THF (10 mL) was added slowly *via* cannula. The resulting mixture was allowed to slowly warm to room temperature while stirring overnight. The mixture was quenched with saturated brine and extracted three times with ethyl acetate. The organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford

crude (4S)-tert-butyl 4-(3-(3-methoxypropoxy)-4-methoxybenzyl)-2-(diphenylmethyleneamino)-5-methylhexanoate (**9**) which was used without further purification.

A mixture of crude alkylation product **9**, THF (30 mL) and 1 *M* aq citric acid (35 mL) was vigorously stirred overnight. The solvent was removed *in vacuo*. The aqueous phase was carefully treated with Na_2CO_3 (6.5 g) and extracted three times with CH_2Cl_2. The organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude (4S)-tert-butyl 4-(3-(3-methoxypropoxy)-4-methoxybenzyl)-2-amino-5-methylhexanoate (**10**) was stirred overnight with Boc_2O (1.5 g, mmol) in CH_2Cl_2. The solvent was removed *in vacuo* and the residue was purified on silica gel chromatography (20% to 33% ethyl acetate in hexanes) to give 0.6581 g (72%) of tert-butyl (3S)-1-(tert-butoxycarbonyl)-3-(3-(3-methoxypropoxy)-4-ethylbenzyl)-4-methylpentyl-carbamate (**11**). LC-MS (3 min) t_R = 2.36 *m/z* 532 ($M+Na^+$), 410, 354; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.79-6.65 (m, 3H), 4.90 (d, *J* = 8.5 Hz, 1H), 4.22 (q, *J* = 7.9 Hz, 1H), 4.09 (t, *J* = 6.3 Hz, 2H), 3.82 (s, 3H), 3.57 (t, *J* = 6.3 Hz, 2H), 3.35 (s, 3H), 2.58 (dd, *J* = 13.6, 6.6 Hz, 1H), 2.45 (dd, *J* = 13.3, 8.1 Hz, 1H), 2.13-2.06 (m, 2H), 1.78-1.73 (m, 1H), 1.65 (br s, 1H), 1.52-1.47 (m, 2H), 1.44 (s, 9H), 1.43 (s, 9H), 0.86 (d, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 172.3, 155.3, 148.0, 147.3, 133.7, 121.1, 114.1, 111.4, 81.3, 79.2, 69.2, 65.7, 58.4, 55.8, 52.2, 41.9, 36.1, 33.4, 29.4, 28.1, 27.8, 27.3, 19.3, 18.3, 18.2, 17.3.

Step 9

To a -78°C solution of tert-butyl (3S)-1-(tert-butoxycarbonyl)-3-(3-(3-methoxypropoxy)-4-ethylbenzyl)-4-methylpentylcarbamate (**11**) (0.7012 g, 1.38 mmol) in THF (15 mL) was added 1.0 M diisobutylaluminum hydride in hexanes (8 mL, 8.0mmol) dropwise. The mixture was allowed to slowly warm to room temperature while stirring overnight. The reaction mixture was carefully quenched with MeOH (9 mL). After 1 h, the mixture was diluted with saturated Rochelle's salt and extracted three times with ethyl acetate. The organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (50% ethyl acetate in hexanes) to give tert-butyl (4S)-4-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-hydroxy-5-methylhexan-2-ylcarbamate (**12**) (0.5049 g, 83%).

Step 10

To a 100-mL round bottom flask of tert-butyl (4S)-4-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-hydroxy-5-methylhexan-2-ylcarbamate **12** (0.5049 g, 1.15 mmol, 1.0 equiv) were added DMSO (5 mL) and triethylamine (2 mL). The flask was cooled with an ice bath. A mixture of pyridine-sulphur trioxide complex (1.85 g, 10 equiv) in dry DMSO (5 mL) was added. After 0.5 h, the ice bath was removed. The reaction mixture was allowed to stir at room temperature for an additional 0.5 h. The mixture was poured into ice water and extracted three times with ethyl acetate. The combined organic phase was washed with 10% aq citric acid, sat'd aq $NaHCO_3$ and brine, dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by chromatography on silica gel (20% to 50% ethyl acetate in hexanes) to afford tert-butyl (3S)-3-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-formyl-4-methylpentylcarbamate (**13**) (0.4909 g, 98%).

Step 11

A flame-dried 100-mL round bottom flask was charged with 60% sodium hydride in oil (0.247 g, 6.17 mmol) and trimethyloxosulfonium iodide (1.356 g, 6.16 mmol). The flask was evacuated and refilled with N_2. Dry DMSO (8 mL) was added. The mixture was stirred at room temperature for 1 h. When H_2 evolution had ceased, the resulting solution was clear.

A second 100-mL round bottom flask was charged with tert-butyl (3S)-3-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-formyl-4-methylpentylcarbamate (**13**) (0.4602 g, 1.05 mmol) and 6 mL of THF (6 mL). The flask was evacuated and refilled with N_2 and an aliquot of the ylid solution prepared above (2 mL, 1.5 mmol, 1.5 equiv) was added by syringe. The resulting mixture was stirred for 1 h at room temperature. The reaction mixture was quenched with brine and extracted three times with ethyl acetate. The organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (33% ethyl acetate in hexanes) to afford tert-butyl (3S)-3-(3-(3-methoxypropoxy)-4-methoxybenzyl)-4-methyl-1-(oxiran-2-yl)pentylcarbamate (**1**) (0.250 g, 53%) as a mixture of four isomers, of which tert-butyl (1S,3S)-3-(3-(3-methoxypropoxy)-4-methoxybenzyl)-4-methyl-1-((R)-oxiran-2-yl)pentylcarbamate was the major isomer.

EXAMPLE 2

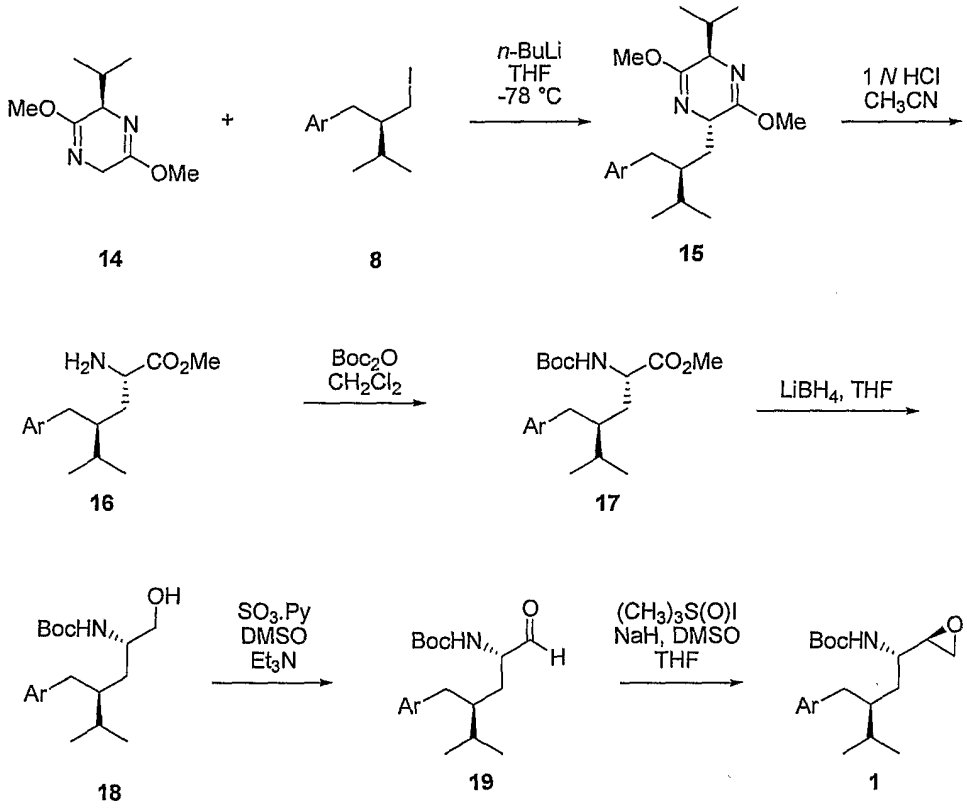
Halides

The following halides were prepared following the procedures of Example 1 Steps 5, 6, and 7:

1-(((S)-2-(bromomethyl)-3-methylbutoxy)methyl)benzene (chloromethyl benzyl ether was used in Step 5 in place of 4-methoxy-3-(3-methoxy-propoxy)-benzyl bromide) 1-((3-((R)-2-(bromomethyl)-3-methylbutyl)phenoxy)methyl)benzene (3-benzyloxybenzyl bromide was used in Step 5 in place of 4-methoxy-3-(3-methoxy-propoxy)-benzyl bromide).

EXAMPLE 3

Tert-butyl (1S,3S)-3-(3-(3-methoxypropoxy)-4-methoxybenzyl)-4-methyl-1-((R)-oxiran-2-yl)pentylcarbamate



Ar = 4-methoxy-3-(3-methoxypropoxy)phenyl

Step 1

A flame-dried 100-mL round bottom flask was charged with (*R*)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine (**14**) (2.4080 g, 13.07 mmol) and THF (20 mL), and evacuated and refilled with N_2. The mixture was cooled with a dry ice-acetone bath and 2.5 M *n*-BuLi in hexanes (5.2 mL, 13.00 mmol) was added dropwise over 15 min. After an additional 0.5 h, a solution of 2-(3-methoxypropoxy)-4-((R)-2-(iodomethyl)-3-methylbutyl)-1-methoxybenzene (**8**) (3.3023 g, 8.13 mmol, 0.62 equiv) from Example 1 Step 7 in THF (20 mL) was added dropwise *via* cannula over

10 min. The reaction mixture was allowed to stir at -78°C for 16 h and quenched with brine (20 mL) at -78°C. After warming to room temperature, the mixture was extracted three times with ethyl acetate. The organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude (2S,5R)-2-((S)-2-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-methylbutyl)-2,5-dihydro-5-isopropyl-3,6-dimethoxypyrazine (**15**) (4.85 g, 80%) was carried on to the next step without further purification. LC-MS (3 min) t_R = 2.41 min *m/z* 463 ($M+H^+$).

Step 2

A mixture of crude (2S,5R)-2-((S)-2-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-methylbutyl)-2,5-dihydro-5-isopropyl-3,6-dimethoxypyrazine (**15**) (4.85 g, 10.49 mmol) in acetonitrile (100 mL) and 1 *N* aq HCl (100 mL, 100 mmol) was vigorously stirred at room temperature for 3 h. The solvent was removed *in vacuo*. The aqueous phase was cooled with an ice bath, carefully treated with Na_2CO_3 (7.06 g, 66.6 mmol) and extracted three times with CH_2Cl_2. The organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford (2S,4S)-methyl 4-(3-(3-methoxypropoxy)-4-methoxybenzyl)-2-amino-5-methylhexanoate (**16**) (4.58 g) which was carried on to the next step without further purification.

Step 3

A mixture of (2S,4S)-methyl 4-(3-(3-methoxypropoxy)-4-methoxybenzyl)-2-amino-5-methylhexanoate (**16**) (4.58 g, 12.46 mmol) and Boc_2O (7.33 g, 33.58 mmol, 2.57 equiv) in CH_2Cl_2 (100 mL) was stirred at room temperature for 14 h. The solvent was removed *in vacuo* and the residue was purified by chromatography on silica gel (20% to 33% ethyl acetate in hexanes) to give tert-butyl (1S,3S)-1-(methoxycarbonyl)-3-(3-(3-methoxypropoxy)-4-methoxybenzyl)-4-methylpentylcarbamate (**17**) (3.3224 g, 87% from 2-(3-methoxypropoxy)-4-((R)-2-(iodomethyl)-3-methylbutyl)-1-methoxybenzene). R_f = 0.29 (30% ethyl acetate in hexanes); LC-MS (3 min) t_R = 2.07 min in 3 min chromatography, *m/z* 490 (MNa^+), 368; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.77-6.67 (m, 3H), 4.89 (d, *J* = 8.8 Hz, 1H), 4.36 (q, *J* = 7.7 Hz, 1H), 4.10 (t, *J* = 6.4 Hz, 2H), 3.83 (s, 3H), 3.71 (s, 3H), 3.57 (t, *J* = 6.2 Hz, 2H), 3.35 (s, 3H), 2.64 (dd, *J* = 13.8, 5.3 Hz, 1H), 2.43 (dd, *J* = 13.6, 8.6 Hz, 1H), 2.09 (p, *J* = 6.3 Hz, 2H), 1.74-1.53 (m, 4H), 1.44 (s, 9H), 0.83 (d, *J* = 6.5 Hz, 3H), 0.82 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 173.9, 155.5, 148.2, 147.5, 133.6, 121.3, 114.2, 111.5, 79.8, 69.4, 65.9, 58.6, 56.0, 52.2, 51.8, 41.9, 36.5, 33.2, 31.6, 29.6, 28.3, 27.7, 22.6, 20.0, 17.0, 14.1.

Step 4

To a solution of tert-butyl (1S,3S)-1-(methoxycarbonyl)-3-(3-(3-methoxypropoxy)-4-methoxybenzyl)-4-methylpentylcarbamate (**17**) (3.2926 g, 7.04 mmol) in THF (50 mL) was slowly added 2.0 M LiBH4 in THF (11 mL, 22 mmol, 3 equiv). The mixture was allowed to stir at room temperature for 15 h. The reaction mixture was diluted with ethyl acetate (60 mL) and carefully quenched with 1 *N* aq HCl (60 mL). After the emulsion disappeared, the organic layer was separated. The aqueous layer was extracted three times with ethyl acetate. The combined organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (50% to 66% ethyl acetate in hexanes) to afford tert-butyl (2S,4S)-4-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-hydroxy-5-methylhexan-2-ylcarbamate (**18**) (3.1192 g, 100%). LC-MS (3 min) t_R = 1.82 min *m/z* 462 ($M+Na^+$), 340; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.78-6.67 (m, 3H), 4.56 (br s, 1H), 4.10 (t, *J* = 6.6 Hz, 2H), 3.83 (s, 3H), 3.64 (br s, 1H), 3.57 (t, *J* = 6.3 Hz, 2H), 3.45-3.41 (m, 1H), 3.35 (s, 3H), 2.48 (d, *J* = 7.3 Hz, 2H), 2.09 (p, *J* = 6.4 Hz, 2H), 1.99 (br s, 2H), 1.77-1.69 (m, 1H), 1.58-1.52 (m, 1H), 1.47-1.40 (m, 1H), 1.44 (s, 9H), 1.27-1.21 (m, 1H), 0.88 (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 156.4, 148.2, 147.5, 134.0, 121.2, 114.3, 111.5, 79.4, 69.4, 66.0, 60.4, 58.6, 56.0, 50.9, 42.3, 36.9, 31.4, 29.5, 28.3, 21.0, 19.7, 17.7, 14.2.

Step 5

To a 250-mL round bottom flask of tert-butyl (2S,4S)-4-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-hydroxy-5-methylhexan-2-ylcarbamate (**18**) (3.0542 g, 6.95 mmol, 1.0 equiv) was added DMSO (25 mL) and triethylamine (10 mL). The flask was cooled with an ice bath. A mixture of pyridine-sulphur trioxide complex (11.6 g, 72.9 mmol, 10.5 equiv) and dry DMSO (25 mL) was added. After 0.5 h, the ice bath was removed. The reaction mixture was allowed to stir at room temperature for an additional 0.5 h. The mixture was poured into ice water and extracted three times with ethyl acetate. The combined organic phase was washed with 10% aq citric acid, satd aq $NaHCO_3$, brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude tert-butyl (1S,3S)-3-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-formyl-4-methylpentyl-carbamate (**19**) (3.2205 g, 100%) was carried on to the next step without further purification. R_f = 0.27 (30% ethyl acetate in hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.51 (s, 1H), 6.78-6.68 (m, 3H), 4.91 (d, *J* = 7.6 Hz, 1H), 4.14-4.08 (m, 3H), 3.83 (s, 3H), 3.57 (t, *J* = 6.2 Hz, 2H), 3.35 (s, 3H), 2.62-2.47 (m, 2H), 2.14-2.05 (m, 2H), 1.78-1.58 (m, 4H), 1.44 (s, 9H), 0.87 (d, *J* = 6.8 Hz, 3H), 0.84 (d, *J* = 6.8 Hz, 3H).

Step 5

A flame-dried 250-mL round bottom flask was charged with 60% sodium hydride in oil (1.4483 g, 36.2 mmol) and trimethyloxosulfonium iodide (8.0500 g, 36.5 mmol). The flask was evacuated, refilled with N_2 and dry DMSO (50 mL) was added. The mixture was stirred at room temperature for 1 h. When H_2 evolution had ceased, the resulting ylid solution was clear.

A second 250-mL round bottom flask was charged with crude tert-butyl (1S,3S)-3-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-formyl-4-methylpentylcarbamate (**19**) (3.2205 g, 6.97 mmol) and THF (30 mL). The flask was evacuated and refilled with N_2. An aliquot of the ylid solution prepared above (14.5 mL, 10.5 mmol, 1.5 equiv) was added through a syringe. The resulting mixture was stirred for 1 h at room temperature. The reaction mixture was quenched with brine and extracted three times with ethyl acetate. The organic phase was dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (33% ethyl acetate in hexanes) to afford tert-butyl (1S,3S)-3-(3-(3-methoxypropoxy)-4-methoxybenzyl)-4-methyl-1-((R)-oxiran-2-yl)pentylcarbamate (**1**) (1.4458 g, 46%). R_f = 0.30 (30% ethyl acetate in hexanes); LC-MS (3 min) t_R = 2.06 min *m/z* 474 ($M+Na^+$), 396; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.79-6.66 (m, 3H), 4.31 (d, *J* = 9.7 Hz, 1H), 4.14-4.07 (m, 2H), 3.97 (br s, 1H), 3.83 (s, 3H), 3.59-3.55 (m, 2H), 3.35 (s, 3H), 2.93 (br s, 1H), 2.72-2.66 (m, 2H), 2.57 (dd, *J* = 4.8, 2.8 Hz, 1H), 2.41 (dd, *J* = 13.5, 9.1 Hz, 1H), 2.13-2.06 (m, 2H), 1.74-1.49 (m, 3H), 1.43 (s, 9H), 1.37-1.30 (m, 1H), 0.88-0.82 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 155.7, 148.1, 147.4, 133.8, 121.2, 114.2, 111.4, 79.2, 69.3, 65.8, 58.6, 55.9, 54.1, 53.8, 47.2, 44.3, 42.0, 36.9, 33.3, 29.5, 28.2, 20.2, 19.3, 17.9, 16.8.

EXAMPLE 4

Epoxides

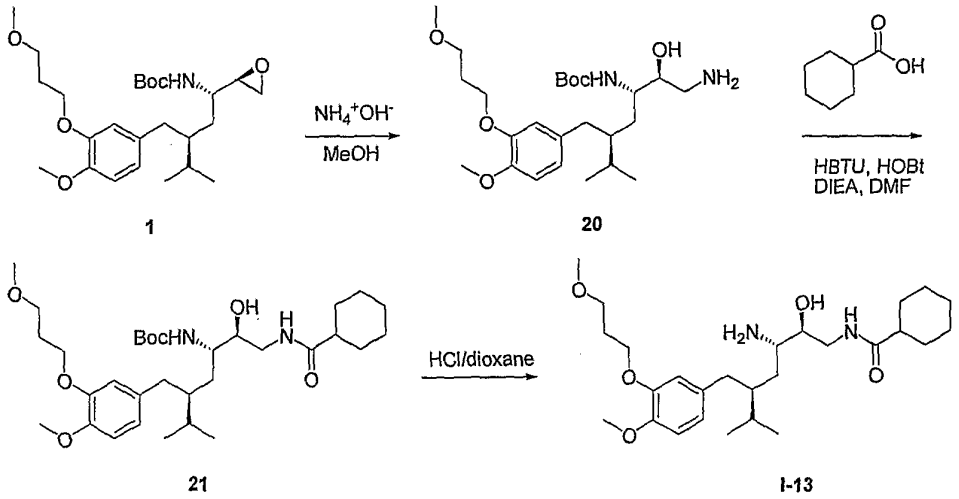
The following epoxides were prepared by following the procedures of Example 2:

tert-butyl (1S,3S)-3-((benzyloxy)methyl)-4-methyl-1-((R)-oxiran-2-yl)pentylcarbamate, by using 1-(((S)-2-(bromomethyl)-3-methylbutoxy)methyl)benzene in place of 2-(3-methoxypropoxy)-4-((R)-2-(iodomethyl)-3-methylbutyl)-1-methoxybenzene in Step 1.

tert-butyl (1S,3S)-3-(3-(benzyloxy)benzyl)-4-methyl-1-((R)-oxiran-2-yl)pentylcarbamate, by using 1-((3-((R)-2-(bromomethyl)-3-methylbutyl)phenoxy)methyl)benzene in place of 2-(3-methoxypropoxy)-4-((R)-2-(iodomethyl)-3-methylbutyl)-1-methoxybenzene in Step 1.

EXAMPLE 5

N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)cyclohexanecarboxamide (I-13)



1 20 21 I-13

Step 1

To a solution of *tert*-butyl (1S,3S)-3-(3-(3-methoxypropoxy)-4-methoxybenzyl)-4-methyl-1-((R)-oxiran-2-yl)pentylcarbamate (**1**) (0.50 g, 1.11 mmol) in methanol (10 mL) was added ammonium hydroxide solution (10 mL, excess). The resulting clear solution was stirred overnight at room temperature. The solvent was removed to dryness to give crude *tert*-butyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-amino-2-hydroxy-6-methylheptan-3-ylcarbamate (**20**) (0.52 g, quant.), which was used for next step without purification. MS *m/z* 469 (M+1).

Step 2

To a solution of *tert*-butyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-amino-2-hydroxy-6-methylheptan-3-ylcarbamate (**20**) (20.1 mg, 0.043mmol) in DMF (0.4 mL) was added diisopropylethylamine (0.1 mL), followed by cyclohexanecarboxylic acid (6.1 mg, 0.047 mmol), O-benzotriazol-1-yl-N,N,N',N'-tetramethyluronium hexafluorophosphate (17.9 mg, 0.047 mmol), and HOBt (6.3 mg, 0.047 mmol). The resulting mixture was stirred at room temperature until the reaction was complete (2-3 h) and purified by preparative HPLC to give tert-butyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-

(cyclohexanecarbonyl)amino-2-hydroxy-6-methylheptan-3-ylcarbamate (**21**) (12.2 mg, 49%). MS *m/z* 579 (M+1).

Step 3

tert-Butyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-(cyclohexane-carbonyl)amino-2-hydroxy-6-methylheptan-3-ylcarbamate (**21**) (12.2 mg, 0.021 mmol) was treated with 4 M HCl in dioxane (2 mL, 8 mmol) at room temperature for 1 hr. The solvent was removed *in vacuo* to give N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)cyclohexanecarboxamide (**I-13**) as the HCl salt in quantitative yield. ^{1}H NMR (CD_3OD) δ (ppm): 6.88-6.73 (m, 3H), 4.05 (t, *J* = 6.4 Hz, 2 H), 3.80 (s, 3 H), 3.75-3.66 (m, 1 H), 3.58 (t, *J* = 6.4 Hz, 2 H), 3.35 (s, 3 H), 3.26-3.22 (m, 1 H), 3.10-3.05 (m, 1 H), 2.87-2.82 (m, 1 H), 2.62 (dd, *J* = 13.6, 6.4 Hz, 1 H), 2.39 (d, *J* = 13.6, 8.0 Hz, 1 H), 2.22-2.16 (m, 1 H), 2.02 (m, 2 H), 1.76-1.68 (m, 7 H), 1.62-1.60 (m, 1 H), 1.43-1.26 (m, 6 H), 0.96-0.89 (m, 6 H); MS *m/z* 479 (M+1).

EXAMPLE 6

The following compounds of formula I were prepared using the procedures of Example 5 Steps 2 and 3, replacing the cyclohexanecarboxylic acid used in Step 2 with other carboxylic acids and in some cases using alternative amide forming coupling reagents well known in the art such as EDC·HCl in place HBTU:

Cpd. No.	Name
I-1	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)butyramide
I-2	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclopropylacetamide
I-3	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)pentanamide
I-4	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)pivalamide
I-6	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)hexanamide
I-7	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylbutanamide
I-8	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3,3-dimethylbutanamide
I-9	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-methoxybutanamide
I-10	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)benzamide
I-11	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3,3,3-trifluoropropanamide
I-12	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclopentylacetamide
I-15	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-

	methylheptyl)heptanamide
I-16	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylpentanamide
I-17	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methylhexanamide
I-18	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-phenylacetamide
I-20	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxyheptyl)-4,4,4-trifluorobutanamide
I-21	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclohexylacetamide
I-22	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(1-(4-fluorophenyl)-2-methylpropan-2-yl)urea
I-23	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-methylcyclohexanecarboxamide
I-24	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-methylcyclohexanecarboxamide
I-28	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-29	N-((2R,3R,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-30	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3,3-dimethylhexanamide
I-31	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-ethylhexanamide
I-32	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methyl-2-propoxypropanamide
I-33	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-ethoxy-2,2-dimethylpropanamide
I-34	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-phenylpropanamide
I-35	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-m-tolylacetamide
I-37	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(2-fluorophenyl)acetamide
I-38	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(3-fluorophenyl)acetamide
I-39	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)acetamide
I-40	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)acetamide
I-41	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-5,5,5-trifluoropentanamide
I-42	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-cyclopropyl-2,2-dimethylbutanamide
I-43	N-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-cyclopropyl-2,2-dimethylbutanamide
I-45	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3,5,5-trimethylhexanamide
I-47	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-cyanophenyl)acetamide
I-48	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-phenylcyclopropanecarboxamide
I-49	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-phenylbutanamide
I-50	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methyl-2-phenylpropanamide
I-51	N-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methyl-2-phenylpropanamide
I-52	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclohexyl-2-methylpropanamide
I-53	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(3,4-difluorophenyl)acetamide
I-54	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(2,4-difluorophenyl)acetamide
I-55	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(2,3-difluorophenyl)acetamide

I-57	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-p-tolylcyclopropanecarboxamide
I-60	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)-2-methylpropanamide
I-61	N-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)-2-methylpropanamide
I-62	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)-2-methylpropanamide
I-63	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclopentylhexanamide
I-64	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-phenylcyclopentanecarboxamide
I-67	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-(4-methoxyphenyl)cyclopropanecarboxamide
I-69	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-hydroxy-2,2-dimethyl-3-phenylpropanamide
I-70	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-(4-chlorophenyl)cyclopropanecarboxamide
I-72	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(2-(trifluoromethyl)phenyl)acetamide
I-73	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(3-(trifluoromethyl)phenyl)acetamide
I-74	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-(trifluoromethyl)phenyl)acetamide
I-75	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-phenylcyclohexanecarboxamide
I-76	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-cyanophenoxy)-2-methylpropanamide
I-77	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-bis(trifluoromethyl)propanamide
I-78	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-ethyl-2-(4-fluorophenyl)butanamide
I-80	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-chlorophenoxy)-2-methylpropanamide
I-81	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-(trifluoromethoxy)phenyl)acetamide
I-82	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-(4-fluorophenyl)cyclohexanecarboxamide
I-83	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-(2,4-dichlorophenyl)cyclopropanecarboxamide.

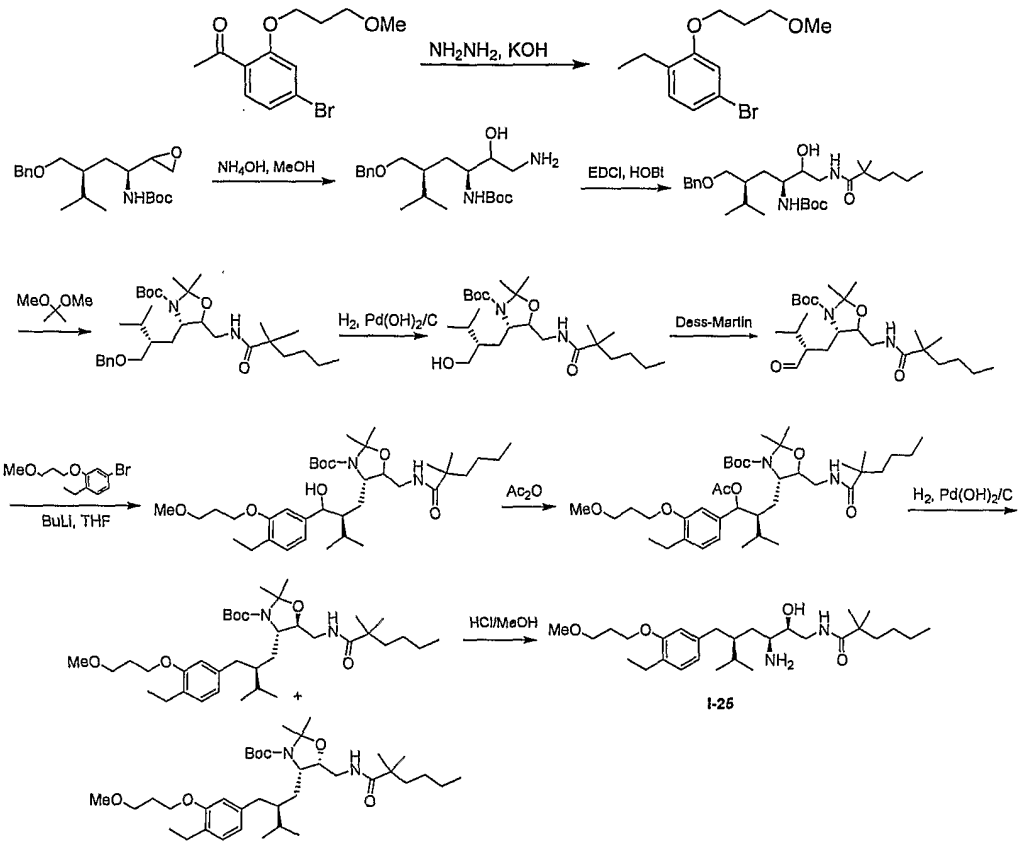
EXAMPLE 7

The following compounds of formula I were prepared by following the procedures of Example 5, replacing the ammonium hydroxide in Step 1 with methylamine or isopropylamine, and substituting the cyclohexanecarboxylic acid used in Step 2 with 2,2-dimethylhexanoic acid or pentanoic acid:

Cpd. No.	Name
I-46	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-N,2,2-trimethylhexanamide
I-27	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-N-isopropylpentanamide.

EXAMPLE 8

N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-ethylbenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide (**I-25**)



Step 1

A mixture of 1-[4-bromo-2-(3-methoxy-propoxy)-phenyl]-ethanone (6.0 g, 21.0 mmol), KOH (4.7 g, 84 mmol) and NH_2NH_2 (2.7 g, 86 mmol) in 2-(2-hydroxy-ethoxy)-ethanol (50 mL) was stirred at 195°C overnight. The resulting mixture was cooled to 0°C and 5 % aq HCl was added until the mixture had pH = 1-2. The aqueous layer was extracted with ethylacetate (2x). The combined organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography to afford 4-bromo-1-ethyl-2-(3-(methoxy)propoxy)benzene (5.0 g, 87%). MS m/z 273 ($M+H^+$)

Step 2

To a room temperature solution of tert-butyl (1S,3S)-3-((benzyloxy)methyl)-4-methyl-1-(oxiran-2-yl)pentylcarbamate (182 mg, 0.50 mmol) in MeOH (1.5 mL) was added 28% aq NH_4OH(3 mL). The resulting clear solution was stirred at room temperature overnight. The solvent and excess ammonia was removed to give tert-

butyl (3S,5S)-1-amino-5-((benzyloxy)-methyl)-2-hydroxy-6-methylheptan-3-ylcarbamate (180 mg, 0.47 mmol, 94% yield). ^{1}H NMR (400MHz, CD_3OD) δ 7.40-7.20 (m, 5H), 4.45 (s, 1H), 3.60 (m, 2H), 3.45 (d, J=7.2 Hz, 2H), 2.65-2.35 (m, 2H), 1.80 (m, 1H), 1.70-1.20 (m, 3H), 1.45 (s, 9H), 1.00-0.70 (m, 6H); MS *m/z* 381 ($M+H^+$).

Step 3

To a solution of tert-butyl (3S,5S)-1-amino-5-((benzyloxy)methyl)-2-hydroxy-6-methylheptan-3-ylcarbamate (380 mg, 1.0 mmol) in dry CH_2Cl_2 (15 mL) were successively added 2,2-dimethyl-hexanoic acid (158 mg, 1.1 mmol), diisopropylethylamine (645 mg, 5.0 mmol), HOBt (270 mg, 2.0 mmol), and EDC.HCl (384 mg, 2.0 mmol) at 0°C. After stirred at 0°C for 15 min, the reaction solution was washed with water and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography to afford N-((3S,5S)-3-(tert-butoxycarbonyl)amino-5-((benzyloxy)methyl)-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide (240 mg, 47%) of acceptable purity based on LC-MS. MS *m/z* 507 ($M+H^+$).

Step 4

A solution of N-((3S,5S)-3-(tert-butoxycarbonyl)amino-5-((benzyloxy)methyl)-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide (506 mg, 1.0 mmol) in acetone (8 mL) was cooled to 0°C. 2,2-dimethoxy-propane (832 mg, 8.0 mmol) was added followed by $BF_3.Et_2O$ (0.1 mL). The solution was stirred at 0°C for 30 min and at room temperature for 2 h. Triethylamine (0.5 mL) was added, the mixture was diluted with water and acetone was removed *in vacuo*. The aqueous layer was extracted with ethyl acetate and the organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography to afford (4S)-tert-butyl 5-((2,2-dimethylhexanamido)methyl)-4-((S)-2-((benzyloxy)methyl)-3-methylbutyl)-2,2-dimethyloxazolidine-3-carboxylate (379 mg, 0.69 mmol, 69.0% yield) of acceptable purity based on LC-MS. MS *m/z* 547 ($M+H^+$).

Step 5

A mixture of (4S)-tert-butyl 5-((2,2-dimethylhexanamido)methyl)-4-((S)-2-((benzyloxy)methyl)-3-methylbutyl)-2,2-dimethyloxazolidine-3-carboxylate (546 mg, 1.0 mmol) and 20% $Pd(OH)_2/C$ (55 mg) in MeOH (10 mL) was hydrogenated at room temperature for 2 h. The mixture was filtered and the filtrate was concentrated *in vacuo* to give (4S)-tert-butyl 5-((2,2-dimethylhexanamido)methyl)-4-((S)-2-

(hydroxymethyl)-3-methylbutyl)-2,2-dimethyloxazolidine-3-carboxylate (380 mg, 83%). ^{1}H NMR (400MHz, $CDCl_3$) δ 6.04 (brs, 1H), 4.10-3.80 (m, 1H), 3.70-3.35 (m, 2H), 3.20 (m, 1H), 2.87 (m, 2H), 1.50 (m, 13H), 1.40-1.15 (m, 3H), 1.15 (s, 6H), 1.00-0.75 (m, 9H); MS *m/z* 457 ($M+H^+$).

Step 6

To a solution of (4S)-tert-butyl 5-((2,2-dimethylhexanamido)methyl)-4-((S)-2-(hydroxymethyl)-3-methylbutyl)-2,2-dimethyloxazolidine-3-carboxylate (456 mg, 1.0 mmol) in dry CH_2Cl_2 (20 mL), was added Dess-Martin periodinane (636 mg, 1.5 mmol). The mixture was stirred at room temperature for 5 h and filtered. The filtrate was concentrated *in vacuo* to give (4S)-tert-butyl 5-((2,2-dimethylhexanamido)methyl)-4-((S)-2-formyl-3-methylbutyl)-2,2-dimethyloxazolidine-3-carboxylate (410 mg, 0.90 mmol, 90% yield) of acceptable purity based on LC-MS. MS (E/Z): 455 ($M+H^+$).

Step 7

A solution of 4-bromo-1-ethyl-2-(3-methoxy-propoxy)-benzene (1.09 g, 4.0 mmol) in anhydrous THF (15 mL) was added dropwise a stirred solution of 2.5 M *n*-BuLi in hexanes (1.60 mL, 4.0 mmol) at -78°C. The mixture was stirred for 1 h at -78°C. A solution of (4S)-tert-butyl 5-((2,2-dimethylhexanamido)methyl)-4-((S)-2-formyl-3-methylbutyl)-2,2-dimethyloxazolidine-3-carboxylate (227 mg, 0.50 mmol) in anhydrous THF (2.0 mL) was added dropwise at -78°C. The mixture was stirred for 2 h at -78°C, and the temperature was raised from at -78°C to room temperature during 2 h. After stirring for 18 h at room temperature, the reaction was quenched by addition of 10% aq NH_4Cl solution (10 mL). The product was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography to provide (4S)-tert-butyl 5-((2,2-dimethylhexanamido)methyl)-4-((S)-2-((3-(3-methoxypropoxy)-4-ethylphenyl)(hydroxy)methyl)-3-methylbutyl)-2,2-dimethyloxazolidine-3-carboxylate (97 mg, 30%) with acceptable purity based on LC-MS. MS *m/z* 649 ($M+H^+$).

Step 8

To a solution of (4S)-tert-butyl 5-((2,2-dimethylhexanamido)methyl)-4-((S)-2-((3-(3-methoxypropoxy)-4-ethylphenyl)(hydroxy)methyl)-3-methylbutyl)-2,2-dimethyloxazolidine-3-carboxylate (95 mg, 0.15 mmol) in dry CH_2Cl_2 (5 mL) was added acetic anhydride (0.5 mL) and pyridine (0.15 mL). The resulting solution was

stirred at room temperature overnight. The solvent was removed *in vacuo* and the residue was purified by preparative tlc to afford (4S)-tert-butyl 5-((2,2-dimethylhexanamido)methyl)-4-((S)-2-((3-(3-methoxypropoxy)-4-ethylphenyl)-(acetoxy)methyl)-3-methylbutyl)-2,2-dimethyloxazolidine-3-carboxylate (68 mg, 67%) with acceptable purity based on LC-MS. MS *m/z* 691 ($M+H^+$).

Step 9

The mixture of (4S)-tert-butyl 5-((2,2-dimethylhexanamido)methyl)-4-((S)-2-((3-(3-methoxypropoxy)-4-ethylphenyl)(acetoxy)methyl)-3-methylbutyl)-2,2-dimethyloxazolidine-3-carboxylate (67 mg, 0.1 mmol) and 20% $Pd(OH)_2/C$ (20 mg) in MeOH (4 mL) was hydrogenated at room temperature and 1 atm for 2 h. The mixture was filtered and the filtrate was concentrated *in vacuo* to leave a residue which was purified by preparative tlc to afford (4S,5S)-tert-butyl 5-((2,2-dimethylhexanamido)methyl)-4-((S)-2-(3-(3-methoxypropoxy)-4-ethylbenzyl)-3-methylbutyl)-2,2-dimethyloxazolidine-3-carboxylate (19 mg, 0.03mmol) and (4S,5R)-tert-butyl 5-((2,2-dimethylhexanamido)methyl)-4-((S)-2-(3-(3-methoxypropoxy)-4-ethylbenzyl)-3-methylbutyl)-2,2-dimethyloxazolidine-3-carboxylate (24 mg, 0.04mmol). MS *m/z* 633 ($M+H^+$).

Step 10

A solution of (4S,5S)-tert-butyl 5-((2,2-dimethylhexanamido)methyl)-4-((S)-2-(3-(3-methoxypropoxy)-4-ethylbenzyl)-3-methylbutyl)-2,2-dimethyloxazolidine-3-carboxylate (19 mg, 0.03 mmol) in 2*N* HCl-MeOH (3.0 mL) was stirred at 40°C for 2 h. The solvent was removed *in vacuo* to afford N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-ethylbenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide (**I-25**) (8.4 mg, 0.017mmol, 56.7% yield) as its HCl salt. ^1H NMR (400MHz, CD_3OD) δ 7.03 (d, J=8.0 Hz, 1H), 6.70 (m, 2H), 4.05 (t, J=6.0 Hz, 2H), 3.75 (brs, 1H), 3.60 (t, J=6.0 Hz, 2H), 3.37 (m, 1H), 3.35 (S, 3H), 3.28 (m, 1H), 3.00 (m, 1H), 2.60 (m, 3H), 2.43 (m, 1H), 2.05 (m, 2H), 1.90-1.65 (m, 4H), 1.55-1.20 (m, 9H), 1.15 (s, 6H), 0.96 (d, J=6.8Hz, 3H), 0.95-0.70 (m, 6H); MS *m/z* 493 ($M+H^+$).

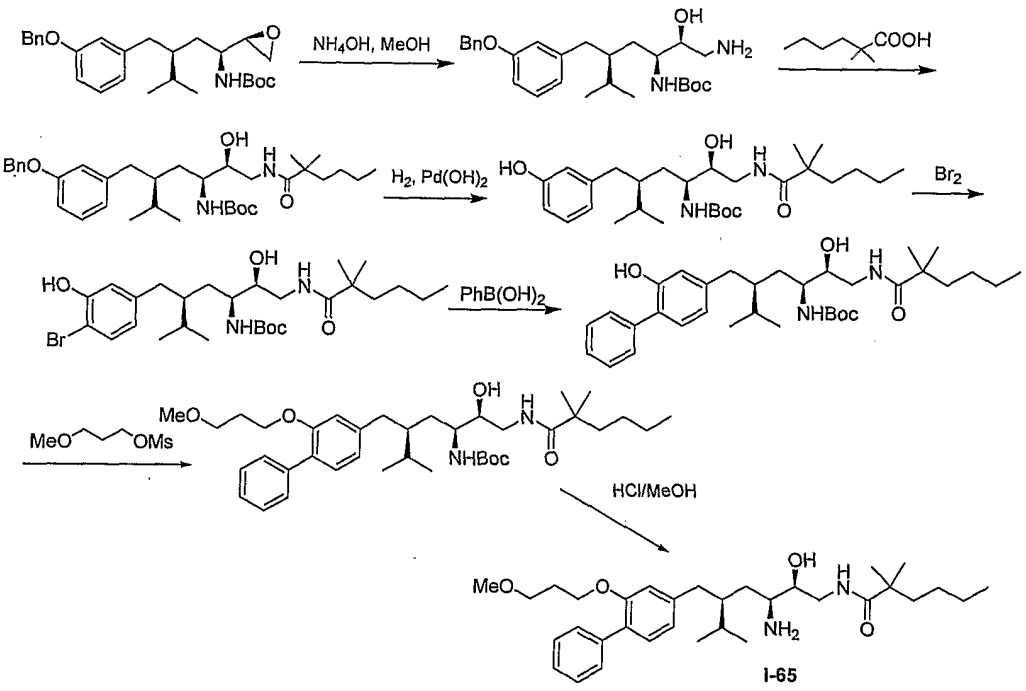
EXAMPLE 9

Treatment of (4S,5R)-tert-butyl 5-((2,2-dimethylhexanamido)methyl)-4-((S)-2-(3-(3-methoxypropoxy)-4-ethylbenzyl)-3-methylbutyl)-2,2-dimethyloxazolidine-3-carboxylate according to the procedure of Example 8 Step 10 afforded N-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-ethylbenzyl)-3-amino-2-hydroxy-6-

methylheptyl)-2,2-dimethylhexanamide (**I-26**) as its HCl salt. ^{1}H NMR (400MHz, CD_3OD) δ 7.03 (m, 1H), 6.70 (m, 2H), 4.05 (t, J=6.0 Hz, 2H), 3.70 (m, 1H), 3.60 (t, J=6.0 Hz, 2H), 3.38 (m, 1H), 3.35 (S, 3H), 3.20 (m, 1H), 3.00 (m, 1H), 2.60 (m, 3H), 2.43 (m, 1H), 2.05 (m, 2H), 1.90-1.65 (m, 3H), 1.63 (m, 1H), 1.55-1.20 (m, 10H), 1.15 (s, 6H), 0.96 (d, J=6.8Hz, 3H), 0.95-0.80 (m, 6H) (m, 9H); MS *m/z* 493 ($M+H^+$)

EXAMPLE 10

N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-phenylbenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide (**I-65**)



Step 1

To a solution of tert-butyl (1S,3S)-3-(3-(benzyloxy)benzyl)-4-methyl-1-((R)-oxiran-2-yl)pentylcarbamate (1.1 g, 2.5 mmol) in MeOH (10 mL) at room temperature was added 28% aq NH_4OH (15 mL). The resulting clear solution was stirred at room temperature overnight. Solvent and excess ammonia were removed in vacuo to provide tert-butyl (2S,3S,5S)-5-(3-(benzyloxy)--benzyl)-1-amino-2-hydroxy-6-methylheptan-3-ylcarbamate (1.15 g, 100%). ^{1}H NMR (400MHz, CD_3OD) δ 7.45-7.25 (m, 5H), 7.10 (m, 1H), 6.85-6.70 (m, 3H), 5.05 (s, 2H), 3.75-3.45 (m, 2H), 2.80-2.60 (m, 3H), 2.35 (m, 1H), 1.80-1.50 (m, 3H), 1.45 (s, 9H), 1.00-0.70 (m, 6H); MS *m/z* 457 ($M+H^+$).

Step 2

To a solution tert-butyl (2S,3S,5S)-5-(3-(benzyloxy)benzyl)-1-amino-2-hydroxy-6-methylheptan-3-ylcarbamate (1.14 g, 2.5 mmol) in dry CH_2Cl_2 (20 mL) were successively added 2,2-dimethyl-hexanoic acid (395 mg, 2.75 mmol), diisopropylethylamine (1.61 g, 12.5 mmol), HOBt (675 mg, 5.0 mmol), and EDC.HCl (960 mg, 5.0 mmol) at 0°C. After addition, the reaction mixture was stirred at at 0°C for 15 min and allowed to warm to room temperature for 1 h. The reaction solution was washed with water and brine, dried over Na_2SO_4, filtered and concentrated in *vacuo*. The residue was purified by chromatography on silica gel to afford N-((2S,3S,5S)-5-(3-benzyloxybenzyl)-3-(tert-butoxycarbonyl)amino-2-hydroxy-6-methylheptyl)-2,2-dimethyl-hexanamide (700 mg, 48%). ^{1}H NMR (400MHz, $CDCl_3$) δ 7.45-7.25 (m, 5H), 7.10 (m, 1H), 6.80-6.70 (m, 3H), 5.05 (s, 2H), 4.75 (m, 1H), 3.80-3.50 (m, 3H), 3.30-3.00 (m, 2H), 2.80 (m, 1H), 2.60-2.50 (m, 1H), 1.80-1.50 (m, 3H), 1.45 (s, 9H), 1.50 0.72 (m, 21H); MS *m/z* 583 ($M+H^+$).

Step 3

A solution of N-((2S,3S,5S)-5-(3-benzyloxybenzyl)-3-(tert-butoxycarbonyl)amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide (582 mg, 1.0 mmol) and 20% $Pd(OH)_2/C$ (60 mg) in MeOH (10 mL) was hydrogenated at room temperature for 2 h. The mixture was filtered and the filtrate was concentrated in vacuo to give N-((2S,3S,5S)-5-(3-hydroxybenzyl)-3-(tert-butoxycarbonyl)amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide (410 mg, 83%). ^{1}H NMR (400MHz, $CDCl_3$) δ 7.10 (m, 1H), 7.00 (s, 1H), 6.68 (m, 2H), 4.80 (d, J=7.2 Hz, 1H), 3.55 (m, 3H), 2.90 (m, 1H), 2.60-2.35 (m, 2H), 1.69 (m, 1H), 1.75-1.50 (m, 3H), 1.45 (s, 9H), 1.60-1.20 (m, 9H), 1.15 (s, 6H), 0.86 (m, 9H); MS *m/z* 493 ($M+H^+$).

Step 4

To a solution of N-((2S,3S,5S)-5-(3-hydroxybenzyl)-3-(tert-butoxycarbonyl)amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide (492 mg, 1.0 mmol) in anhydrous THF (15 mL) was added $NaHCO_3$ (170 mg). The solution was cooled to -78°C and a solution of Br_2 (192 mg, 1.2 mmol) in anhydrous THF (2 mL) was added dropwise. The mixture was stirred for 2 h at -78°C, and the temperature was raised from -78°C to room temperature over 2 h. After stirring for 18 h at room temperature, the reaction was quenched by addition of aqueous $NaHSO_3$ and the mixture was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over $MgSO_4$, and evaporated. The residue was

purified by column chromatography to give N-((2S,3S,5S)-5-(3-hydroxy-4-bromobenzyl)-3-(tert-butoxycarbonyl)amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide (277 mg, 49%). ^{1}H NMR (400MHz, $CDCl_3$) δ 7.32 (d, J=8.4 Hz, 1H), 7.10 (d, J=2.4 Hz, 1H), 6.77 (brt, 1H), 6.65 (dd, J=8.4 & 2.4 Hz, 1H), 4.35 (d, J=9.2 Hz, 1H), 3.75-3.55 (m, 4H), 2.85 (m, 1H), 2.75 (m, 1H), 1.80-1.65 (m, 2H), 1.55-1.45 (m, 2H), 1.45 (s, 9H), 1.40 -1.20 (m, 4H), 1.15 (s, 6H), 1.00-0.70 (m, 6H); MS *m/z* 571 ($M+H^+$).

Step 5

To a mixture of N-((2S,3S,5S)-5-(3-hydroxy-4-bromobenzyl)-3-(tert-butoxycarbonyl)-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide (285 mg, 0.50 mmol) in toluene (1.0 mL) and 2 M aqueous sodium carbonate (0.9 mL) under nitrogen were successively added $PhB(OH)_2$ (67 mg, 0.55 mmol) and tetrakis-(triphenylphosphine) palladium (17.5 mg, 0.015 mmol). The mixture was heated under reflux for 4 h and cooled. The mixture was partitioned between water and ether; the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by preparative HPLC to give N-((2S,3S,5S)-5-(3-hydroxy-4-phenylbenzyl)-3-(tert-butoxycarbonyl)amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide (116 mg, 40%). MS *m/z* 569 ($M+H^+$).

Step 6

To a solution of N-((2S,3S,5S)-5-(3-hydroxy-4-phenylbenzyl)-3-(tert-butoxycarbonyl)-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide (284 mg, 0.50 mmol) in acetonitrile (5 mL) were added 3-methoxypropyl methanesulfonate (168 mg, 1.0 mmol) and K_2CO_3 (345 mg, 2.5 mmol). The mixture was refluxed for 15 h and the solvent was removed. The residue was diluted with water and extracted with ethyl acetate. The combined organic phase was washed by brine, and dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by preparative HPLC to give N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-phenylbenzyl)-3-(tert-butoxycarbonyl)amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide (180 mg, 56%). MS *m/z* 641 ($M+H^+$).

Step 7

A solution of N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-phenylbenzyl)-3-(tert-butoxy-carbonyl)amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide (32 mg, 0.05 mmol) in 2 N HCl-MeOH (2.0 mL, 4 mmol) was stirred at 40°C for 2 h. The

solvent was removed *in vacuo* and the residue was purified by preparative HPLC to afford N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-phenylbenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide (**I-65**) as its trifluoroacetic acid salt (16 mg, 60%). ^{1}H NMR (400MHz, $CDCl_3$) δ 7.45 (m, 1H), 7.38 (m, 1H), 7.30 (m, 3H), 7.10 (d, J=8.4 Hz, 1H), 6.80 (m, 1H), 6.50 (brs, 1H), 4.10 (t, J=6.4Hz, 2H), 3.61 (t, J=6.0Hz, 2H), 3.48 (m ,1H), 3.40 (s, 3H), 3.38 (m, 1H), 3.25 (m, 1H), 2.62 (m, 2H), 2.10 (m, 2H), 1.48 (m, 4H), 1.28 (m, 2H), 1.17 (s, 6H), 1.17 (m, 2H), 0.87 (m, 4H), 0.71 (d, J=7.2 Hz, 3H), 0.60 (d, J=7.2Hz, 3H); MS *m/z* 541 ($M+H^+$). Isomeric N-((2S,3S,5S)-5-(5-(3-methoxypropoxy)-2-phenylbenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide (**I-66**) was isolated as a minor product.

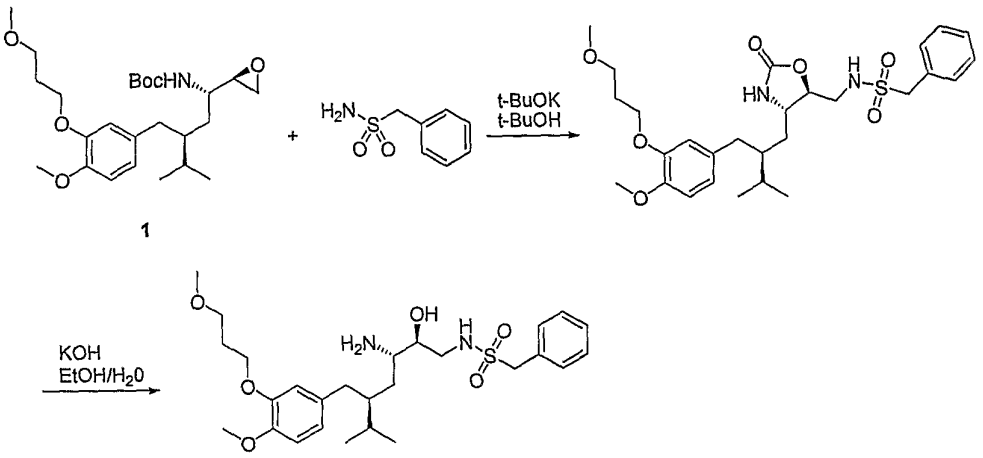
EXAMPLE 11

The following compounds of formula I were prepared by following the procedures of Example 10

Cpd. No.	Name
I-5	N-((2S,3S,5S)-5-(3-(2-cyclopropylethoxy)benzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide - *by treatment of the product of Step 3 with 2-(cyclopropyl)ethyl methanesulfonate according to the conditions of Step 6 and deprotection by the method of Step 7.*
I-14	N-((2S,3S,5S)-5-(3-(3-ethoxypropoxy)benzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide - *by treatment of the product of Step 3 with 3-(ethoxy)propyl methanesulfonate according to the conditions of Step 6 and deprotection by the method of Step 7.*
I-68	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-bromobenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide - *by treatment of the product of Step 4 with 3-methoxypropyl methanesulfonate according to the conditions of Step 6 and deprotection by the method of Step 7.*

EXAMPLE 12

(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-(phenylmethylsulfonylamino)-3-amino-6-methylheptan-2-ol (**I-56**)



1

Step 1

The mixture of tert-butyl (1S,3S)-3-(3-(3-methoxypropoxy)-4-methoxybenzyl)-4-methyl-1-((R)-oxiran-2-yl)pentylcarbamate (**1**) (22.0 mg, 0.047 mmol) and phenylmethanesulfonamide (80.5 mg, 0.47 mmol) was dissolved in 1 M KO*t*-Bu in *t*-BuOH (2 mL, 2 mmol). The resulting solution was heated in a CEM microwave synthesizer at 70°C for 15 min, and the completion of reaction was confirmed by LC-MS. The mixture neutralized by addition of 6 N HCl and preparative HPLC gave (4S,5S)-4-((S)-2-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-methylbutyl)-5-((phenylmethanesulfonyl)aminomethyl)oxazolidin-2-one (3.3 mg, 13 %) as a clear oil. ^{1}H NMR (CD_3OD) δ (ppm): 7.39 (s, 5 H), 6.78 (dd, *J* = 8.0, 6.4 Hz, 1 H), 6.71 (s, 1 H), 6.65 (d, *J* = 8.0 Hz, 1 H), 5.98, 5.83 (two s, 1 H), 5.48, 5.32 (t, *J* = 8.0 Hz, 1 H), 4.28 (d, *J* = 3.2 Hz, 2 H), 4.09 (t, *J* = 6.4 Hz, 2 H), 3.98, 3.84 (two m, 1 H), 3.83 (s, 3 H), 3.58 (t, *J* = 6.4 Hz, 2 H), 3.61-3.57 (m, 1 H), 3.52-3.49 (m, 2 H), 3.35, 3.34 (two s, 3 H), 3.00-2.85 (m, 2 H), 2.65-2.54 (m, 1 H), 2.35-2.29 (m, 1 H), 2.08 (m, 2 H), 1.73-1.68 (m, 1 H), 1.54-1.44 (m, 2 H), 1.38-1.30 (m, 1 H), 0.94-0.84 (m, 6 H); MS: $[M+H]^+$ = 549.

Step 2

To a solution of (4S,5S)-4-((S)-2-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-methylbutyl)-5-((phenylmethanesulfonyl)aminomethyl)oxazolidin-2-one (3.3 mg, 0.006 mmol) in ethanol (0.7 mL) and water (0.33 mL) was added solid KOH (1 pellet, excess). The resulting solution was heated at 100°C for 10 min in a CEM microwave apparatus. Reaction completion was confirmed by LC-MS, and the solution was acidified with 6 N HCl to neutral, and HPLC give (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-(phenylmethylsulfonylamino)-3-amino-6-methylheptan-2-ol (**I-56**) as its trifluoroacetic acid salt. ^{1}H NMR (CD_3OD) δ (ppm):

7.43-7.37 (m, 5 H), 6.86-6.73 (m, 3 H), 4.36 (d, *J* = 4.4 Hz, 2 H), 4.05 (t, *J* = 6.0 Hz, 2 H), 3.79 (s, 3 H), 3.66, 3.50 (two m, 1 H), 3.57 (t, *J* = 6.4 Hz, 2 H), 3.33 (s, 3 H), 3.25, 3.14 (two m, 1 H), 3.01-2.88 (m, 2 H), 2.64-2.38 (m, 2 H), 2.04-1.96 (m, 2 H), 1.83-1.69 (m, 2 H), 1.60, 1.30 (two m, 1 H), 1.53 (t, *J* = 6.8 Hz, 1 H), 0.95-0.86 (m, 6 H); MS *m/z* 523 (M+1).

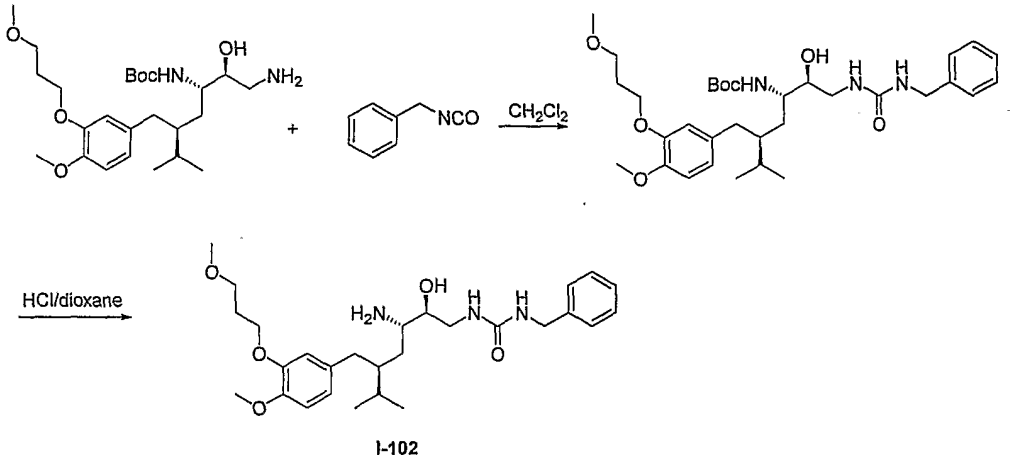
EXAMPLE 13

The following compounds of formula **I** were prepared by following the procedures of Example 12:

Cpd. No.	Name
I-19	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-6-methyl-1-(butanesulfonylamino)heptan-2-ol
I-36	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-6-methyl-1-(pentanesulfonylamino)heptan-2-ol
I-44	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-6-methyl-1-(benzenesulfonylamino)heptan-2-ol
I-58	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-isopropyl-N-butanesulfonylamino)-6-methylheptan-2-ol
I-59	(2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-isopropyl-N-butanesulfonylamino)-6-methylheptan-2-ol
I-71	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-isopropyl-N-benzenesulfonylamino)-6-methylheptan-2-ol
I-79	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-isopropyl-N-benzylsulfonylamino)-6-methylheptan-2-ol.

EXAMPLE 14

1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-benzylurea **(I-102)**



I-102

Step 1

To a solution of tert-butyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-amino-2-hydroxy-6-methylheptan-3-ylcarbamate **2** (20.1 mg, 0.043 mmol) in acetonitrile (1 mL) was added benzyl isocyanate (5.8 mg, 0.43 mmol). The resulting solution was stirred at room temperature overnight and purified directly by preparative HPLC to give 1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-(tert-butoxycarbonylamino)-2-hydroxy-6-methylheptyl)-3-benzylurea (16.3 mg, 63%). MS m/z 602 $[M+H]^+$.

Step 2

1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-(tert-butoxycarbonylamino)-2-hydroxy-6-methylheptyl)-3-benzylurea (16.3 mg, 0.027 mmol) was treated with 4 M HCl in dioxane (2 mL, 8 mmol) at room temperature for 1 h. The solvent was removed *in vacuo* to give 1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-benzylurea (**I-102**) as its HCl salt in quantitative yield. ^{1}H NMR (CD_3OD) δ 7.27-7.25 (m, 4 H), 7.20 (m, 1 H), 6.86-6.72 (m, 3 H), 4.30 (m, 2 H), 4.04 (t, *J* = 6.4 Hz, 2 H), 3.80 (s, 3 H), 3.57 (t, *J* = 6.4 Hz, 3 H), 3.31 (s, 3 H), 3.28 (m, 1 H), 3.12 (m, 1 H), 2.99-2.92 (m, 1 H), 2.61 (dd, *J* = 13.6, 6.4 Hz, 1 H), 2.42 (d, *J* = 13.6, 8.0 Hz, 1 H), 2.05-1.98 (m, 2 H), 1.87-1.70 (m, 3 H), 1.60 (m, 1 H), 0.97-0.88 (m, 6 H); MS m/z 502 $[M+H]^+$.

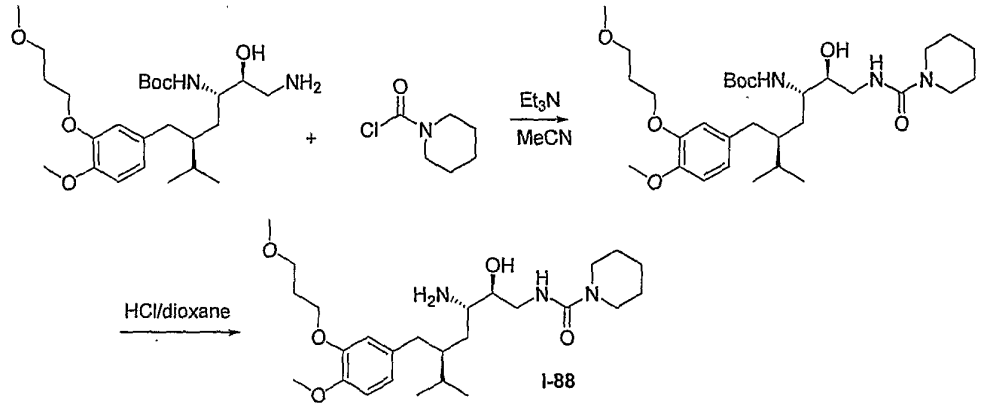
EXAMPLE 15

The following compounds of formula I were prepared by the procedures of Example 14, substituting the appropriate isocyanate in Step 1:

I-85	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-butylurea
I-86	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-tert-butylurea
I-89	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-cyclopropylethyl)urea
I-91	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylurea
I-92	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylurea
I-93	1-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylurea
I-95	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(3-methoxypropyl)urea
I-96	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-ethoxyethyl)urea
I-97	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-cyclohexylurea
I-98	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-hexylurea
I-100	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-methyl-3-pentylurea
I-105	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(3-fluorophenyl)urea
I-106	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(cyclohexylmethyl)urea
I-108	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-(butylaminosulfonyl)-N-isopropylamino)-6-methylheptan-2-ol
I-109	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2,2-dimethylpentyl)urea
I-110	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-methylhexan-2-yl)urea
I-112	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-phenethylurea
I-114	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-cyclohexylethyl)urea
I-115	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2,4,4-trimethylpentan-2-yl)urea
I-117	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(3-phenylpropyl)urea
I-119	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(3-(trifluoromethyl)phenyl)urea
I-120	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(1-(4-fluorophenyl)-2-methylpropan-2-yl)urea.

EXAMPLE 16

N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)piperidine-1-carboxamide (I-88)



Step 1

To a solution of *tert*-butyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-amino-2-hydroxy-6-methylheptan-3-ylcarbamate (20 mg, 0.043 mmol) in MeCN (0.4 mL) and Et_3N (0.1 mL), piperidine-1-carbonyl chloride (6.5 µL, 0.051 *mmol*) was added in one portion at room temperature. The resulting solution was stirred at room temperature until no starting remained (~ 30 min), and purified by preparative HPLC to afford N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-(tert-butoxycarbonylamino)-2-hydroxy-6-methylheptyl)piperidine-1-carboxamide (18.5 mg, 76%). MS *m/z* 580 $[M+H]^+$.

Step 2

N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-(tert-butoxycarbonylamino)-2-hydroxy-6-methylheptyl)piperidine-1-carboxamide (18.5 mg, 0.032 mmol) was dissolved in 4 M HCl in dioxane (2 mL, 8 mmol) and stirred at room temperature for 1 h. The solvent was removed *in vacuo* to give N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)piperidine-1-carboxamide (**I-88**) as its HCl salt in quantitative yield. ^1H NMR (CD_3OD) δ 0.9 (m), 1.5-1.8 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.92 (m), 3.36 (s)m 3.38 (m), 3.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m). MS m/z 480 $[M+H]^+$.

EXAMPLE 17

The following compounds of Formula I were prepared by the procedure of Example 16 substituting the appropriate carbamoyl chloride in Step 1:

I-90 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)morpholine-4-carboxamide

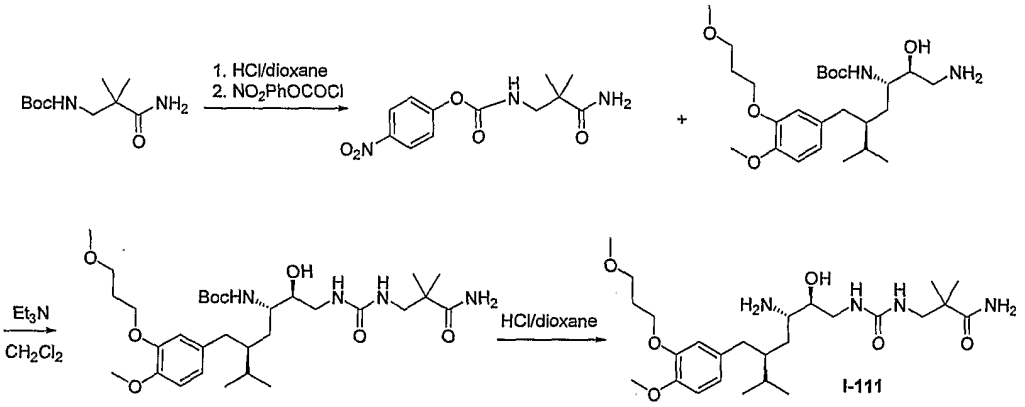
I-99 3-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-methyl-1-pentylurea

I-107 3-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-cyclohexyl-1-methylurea

I-116 3-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1,1-diisobutylurea.

EXAMPLE 18

1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-carbamoyl-2-methylpropyl)urea (**I-111**)



Step 1

tert-Butyl 2-carbamoyl-2-methylpropylcarbamate (**1**) (1.01 g, 4.67 mmol) was dissolved in 4 M HCl in dioxane (10 mL, 40 mmol) at room temperature and stirred for 3 h. Removal of solvent afforded 2-(aminomethyl)-2-methylpropanamide as its HCl salt. This material was stirred with CH_2Cl_2 (10 mL) and pyridine (1.11 g, 14.0 mmol) was added, followed by 4-nitrophenyl chloroformate (1.07 g, 5.14 mmol). The resulting solution was stirred at room temperature for 30 min, diluted with CH_2Cl_2 (10 mL), washed with 1 N aq HCl (10 mL) and satd aq $NaHCO_3$ (10 mL), dried over Na_2SO_4, and concentrated to give 4-nitrophenyl 2-carbamoyl-2-methylpropyl-carbamate as a solid (1.54 g, quantitative) which was used for next in the next step without further purification. MS m/z 282 $[M+H]^+$.

Step 2

To a solution of *tert*-butyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-amino-2-hydroxy-6-methylheptan-3-ylcarbamate (21.6 mg, 0.046

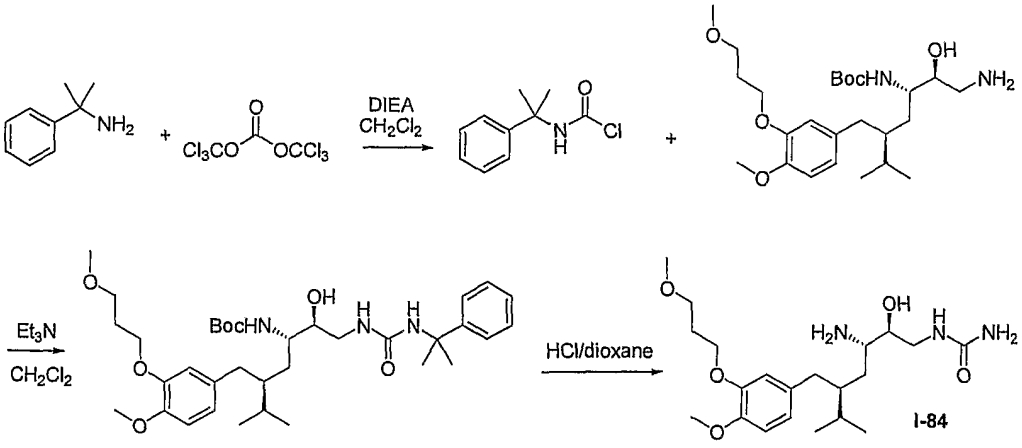
mmol) in CH_2Cl_2 (0.5 mL) and Et_3N (0.1 mL), 4-nitrophenyl 2-carbamoyl-2-methylpropyl carbamate (13.0 mg, 0.046 mmol) was added. The resulting solution was stirred at room temperature until no starting material remained (~ 30 min), and HPLC purification gave 1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-carbamoyl-2-methylpropyl)urea (3.3 mg, 9 %). MS m/z 611 $[M+H]^+$.

Step 3

1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-carbamoyl-2-methylpropyl)urea (3.3 mg mg, 0.005 mmol) was treated with HCl/dioxane (4 M, 1 mL) at room temperature for 1 hr. Solvent was removed *in vacuo* to give 1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-carbamoyl-2-methylpropyl)urea (**I-111**) as its HCl salt in quantitative yield. ^1H NMR (CD_3OD) δ 0.9 (m), 1.16 (s), 1.60 (m), 0.7 (m), 2.02 (m), 2.40 (m), 2.60 (m), 3.24 (m), 3.36 (s), 3.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m). MS m/z 511 $[M+H]^+$.

EXAMPLE 19

1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)urea (**I-84**)



Step 1

To the solution of 2-phenylpropan-2-amine (62.0 mg, 0.44 mmol) in CH_2Cl_2 (1.0 mL), diisopropylethylamine (0.38 mL, 2.2 mmol) was added followed by bis(trichloromethyl) carbonate (66.6 mg, 0.22 mmol). The resulting solution was

stirred at room temperature for 30 min, diluted with CH_2Cl_2 (5 mL), washed with 1 N aq HCl (2 mL), satd aq $NaHCO_3$ (2 mL), brine (2 mL), dried over Na_2SO_4, and evaporated under reduced pressure to give (2-phenylpropan-2-yl)carbamic chloride, which was used in the next step without purification, MS m/z 198 $[M+H]^+$.

Step 2

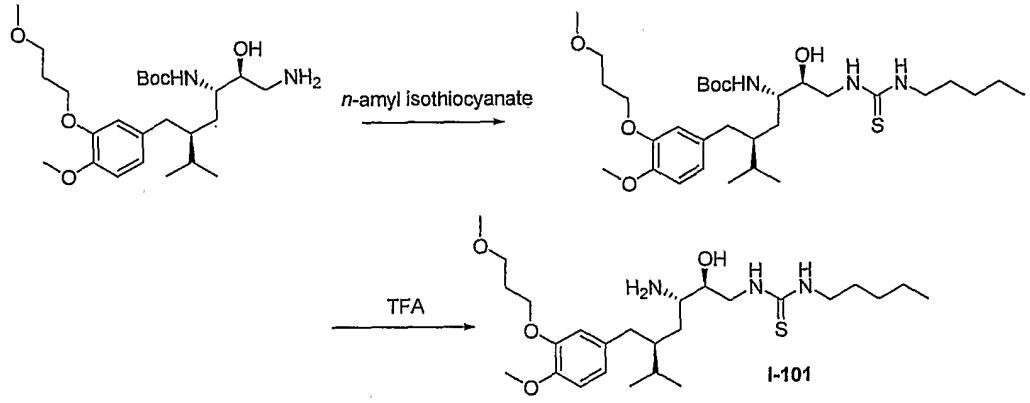
To a solution of *tert*-butyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-amino-2-hydroxy-6-methylheptan-3-ylcarbamate (20.6 mg, 0.044 mmol) in CH_2Cl_2 (0.5 mL) and Et_3N (0.1 mL), was added (2-phenylpropan-2-yl)carbamic chloride (8.7 mg, 0.044 mmol). The resulting solution was stirred at room temperature until no starting material remained (~ 30 min), and purified by preparative HPLC to give 1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-(*tert*-butoxycarbonylamino)-2-hydroxy-6-methylheptyl)urea (21.4 mg, 77 %). MS m/z 630 $[M+H]^+$.

Step 3

1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-(*tert*-butoxycarbonylamino)-2-hydroxy-6-methylheptyl)urea (21.4 mg, 0.034 mmol) was dissolved in 4 M HCl in dioxane (2 mL, 8 mmol) and stirred at room temperature for 1 h. The crude product was submitted to preparative HPLC to afford 1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)urea (**I-84**) as its trifluoroacetic acid salt. ^1H NMR ($CDCl_3$) δ 0.9 (m), 1.4-1.8 (m), 2.04 (m), 2.24 (m), 2.68 (m), 3.02 (m), 3.16 (m), 3.36 (s), 3.60 (t), 3.80 (s), 4.06 (t), 6.74 (m), 6.78 (m), 7.5 (br). MS m/z 412 $[M+H]^+$.

EXAMPLE 20

1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylthiourea (**I-101**)



Step 1

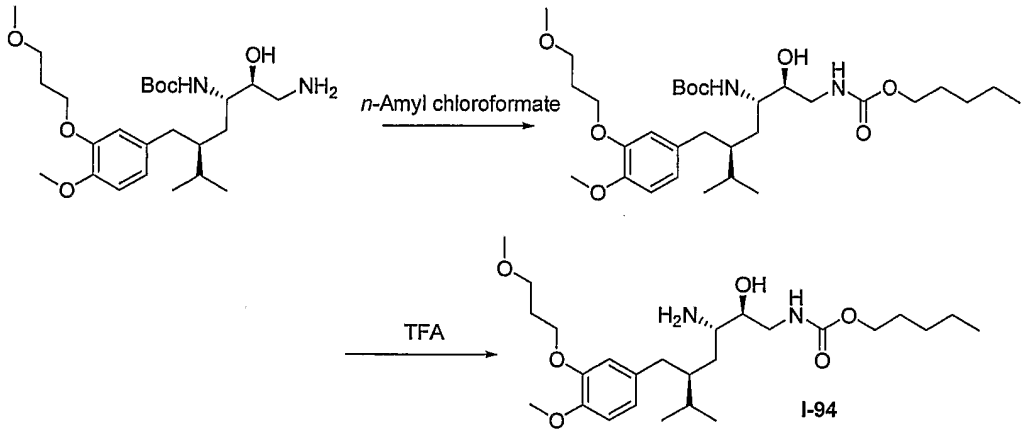
A mixture of tert-butyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-amino-2-hydroxy-6-methylheptan-3-ylcarbamate (68.4 mg, 0.146 mmol, 1.0 equiv) and *n*-amyl isothiocyanate (90.4 mg, 0.70 mmol, 4.8 equiv) in CH_2Cl_2 (3 mL) was stirred at room temperature for 23 h. The solvent was removed *in vacuo* and the residue was purified by reversed-phase preparative HPLC (Phenomenex® Luna 5μ C18(2) 100A, 150 × 10.00 mm, 5 micron, 10% →65% CH_3CN/H_2O, 0.1% CF_3COOH over 3 min and then 65% →90% CH_3CN/H_2O, 0.1% CF_3COOH over 22 min, flow rate 8 mL/min) to afford 1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-(tert-butoxycarbonylamino)-2-hydroxy-6-methylheptyl)-3-pentylthiourea (48.2 mg, 55%). LC-MS (3 min) t_R = 2.14 min *m/z* 598 $[M+H]^+$.

Step 2

A solution of 1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-(tert-butoxycarbonylamino)-2-hydroxy-6-methylheptyl)-3-pentylthiourea (48.2 mg) in trifluoroacetic acid (2 mL) and CH_2Cl_2 (3 mL) was stirred at room temperature for 3 h. The solvents were removed *in vacuo*, the residue was purified by reversed-phase HPLC (XTerra® Prep MS C_{18} OBD™ Column, 5 μm, 19 × 50 mm, 10% →90% CH_3CN/H_2O, 0.1% CF_3COOH over 8 min, flow rate 20 mL/min) to give *N*-[(2*S*,3*S*,5*S*)-5-[3-(3-methoxypropoxy)-4-methoxybenzyl]-3-amino-2-hydroxy-6-methylheptyl]-*N'*-pentylthiourea (**I-101**) as its trifluoroacetate salt. LC-MS (3 min) t_R = 1.43 min *m/z* 498 $[M+H]^+$; ^1H NMR (400 MHz, CD_3OD) δ 6.72-6.58 (m, 3H), 3.92 (t, *J* = 6.3 Hz, 2H), 3.70 (br s, 1H), 3.65 (s, 3H), 3.60 (br s, 1H), 3.44 (t, *J* = 6.2 Hz, 2H), 3.30-3.22 (m, 2H), 3.20 (s, 3H), 2.97-2.85 (m, 2H), 2.49 (dd, *J* = 13.6, 6.3 Hz, 1H), 2.25 (dd, *J* = 13.5, 7.6 Hz, 1H), 1.88 (p, *J* = 6.3

EXAMPLE 21

Pentyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptylcarbamate (I-94)



Step 1

To a solution of tert-butyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-amino-2-hydroxy-6-methylheptan-3-ylcarbamate (67.3 mg, 0.144 mmol, 1.0 equiv) and triethylamine (0.15 mL, 1.08 mmol, 7.5 equiv) in CH_2Cl_2 (3 mL) was added *n*-amyl chloroformate (30 mg, 0.20 mmol, 1.4 equiv). The resulting mixture was stirred at room temperature for 6 h. After the solvents were removed *in vacuo*, the residue was purified by reversed-phase HPLC (Phenomenex® Luna 5μ C18(2) 100A, 150 × 10.00 mm, 5 micron, 10% →65% CH_3CN/H_2O, 0.1% CF_3COOH over 3 min and then 65% →90% CH_3CN/H_2O, 0.1% CF_3COOH over 22 min, flow rate 8 mL/min) to afford 0.0206 g (25%) of pentyl (2*S*,3*S*,5*S*)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-(*tert*-butoxycarbonylamino)-2-hydroxy-6-methylheptylcarbamate. LC-MS (3 min) t_R = 2.18 min *m/z* 605 $[M+Na]^+$, 483 $[M-Boc]^+$; ^1H NMR (400 MHz, $CDCl_3$) δ 6.77-6.67 (m, 3H), 5.42 (br s, 1H), 4.71 (br d, *J* = 9.4 Hz, 1H), 4.10 (t, *J* = 6.5 Hz, 2H), 4.03 (t, *J* = 6.6 Hz, 2H), 3.88 (br s, 1H), 3.83 (s, 3H), 3.62-3.55 (m, 4H), 3.35 (s, 3H), 3.30 (br s, 1H), 3.06-3.02 (m, 1H), 2.53 (dd, *J* = 13.6, 6.0 Hz, 1H), 2.42 (dd, *J* = 13.5, 8.5 Hz, 1H), 2.08 (p, *J* = 6.4 Hz, 2H), 1.44 (s, 9H), 1.69-1.19 (m, 10H), 0.90-0.83 (m, 9H).

Step 2

A mixture of pentyl (2*S*,3*S*,5*S*)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-(*tert*-butoxycarbonylamino)-2-hydroxy-6-methylheptylcarbamate (20.6 mg, 0.0353

mmol), trifluoroacetic acid (2 mL) and CH_2Cl_2 (2 mL) was stirred at room temperature for 4 h. After the solvents were removed *in vacuo*, the residue was purified by reversed-phase HPLC (XTerra® Prep MS C_{18} OBD™ Column, 5 μm, 19 × 5 mm, 10% →90% CH_3CN/H_2O, 0.1% CF_3COOH over 8 min, flow rate 20 mL/min) to give 0.0175 g (83%) of pentyl (2*S*,3*S*,5*S*)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptylcarbamate (**I-94**) as its trifluoroacetate salt. LC-MS (3 min) t_R = 1.45 min *m/z* 483 $[M+H]^+$; ^1H NMR (400 MHz, CD_3OD) δ 6.74 (d, *J* = 8.2 Hz, 1H), 6.68 (d, *J* = 1.8 Hz, 1H), 6.62 (dd, *J* = 8.2, 2.0 Hz, 1H), 3.95-3.89 (m, 4H), 3.67 (s, 3H), 3.48-3.40 (m, 3H), 3.22 (s, 3H), 3.08 (dd, *J* = 14.4, 6.5 Hz, 1H), 2.94 (dd, *J* = 14.4, 6.2 Hz, 1H), 2.82-2.78 (m, 1H), 2.50 (dd, *J* = 13.6, 6.3 Hz, 1H), 2.28 (dd, *J* = 13.6, 7.8 Hz, 1H), 1.90 (p, *J* = 6.2 Hz, 2H), 1.62-1.58 (m, 2H), 1.50-1.45 (m, 4H) 1.22-1.19 (m, 4H), 0.84-0.77 (m, 9H).

EXAMPLE 22

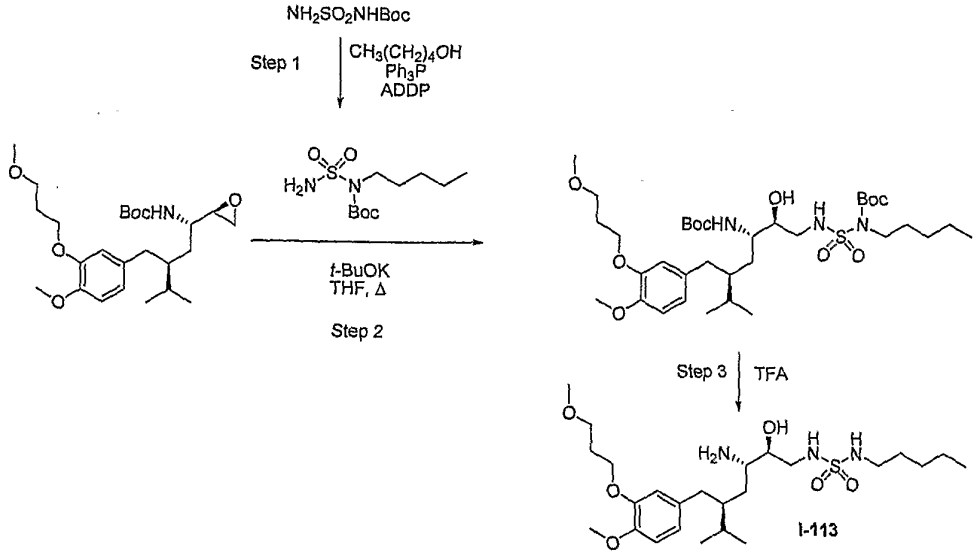
The following compunds of Formula I were prepared by the procedure of Example 21 substituting the appropriate chloroformate in Step 1

I-87 isobutyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptylcarbamate

I-103 benzyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptylcarbamate.

EXAMPLE 23

(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-6-methyl-1-(pentylaminosulfonylamino)-heptan-2-ol (**I-113**)



Step 1

To a stirred mixture of 1-pentanol (0.43 g, 4.88 mmol, 1.0 equiv), *N-tert*-butoxycarbonyl-sulfamide {prepared from chlorosulfonyl isocyanate according to Y. Nishino et al., *Organic Process Research & Development* **2003**, *7*, 649-654} (1.02 g, 5.18 mmol, 1.06 equiv), triphenylphosphine (1.76 g, 6.71 mmol, 1.37 equiv) and ethyl acetate (5 mL) was added 1,1'-(azodicarbonyl)dipiperidine (ADDP) (1.55 g, 6.14 mmol, 1.26 equiv). The reaction mixture was stirred at room temperature for 14 h. After the solvents were removed *in vacuo*, the residue was purified by chromatography on silica gel (10% to 20% ethyl acetate in hexanes) to afford N-aminosulfonyl-*tert*-butyl pentylcarbamate (0.849 g, 65%). LC-MS (3 min) t_R = 1.74 min *m/z* 251 $[M\text{-}CH_3]^+$, 210 $[M\text{-}C_4H_8]^+$; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.29 (br s, 2H), 3.68-3.64 (m, 2H), 1.69-1.61 (m, 2H), 1.53 (s, 9H), 1.37-1.24 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.5, 84.1, 47.6, 29.0, 28.4, 27.9, 22.1, 14.0.

Step 2

A mixture of N-aminosulfonyl-*tert*-butyl pentylcarbamate (0.207 g, 0.77 mmol) and 1 M KOt-Bu in THF (0.75 mL, 0.75 mmol) in THF (4 mL) was heated at 65°C for 2.5 h. A solution of *tert*-butyl (1S,3S)-3-(3-(3-methoxypropoxy)-4-methoxybenzyl)-4-methyl-1-((R)-oxiran-2-yl)pentylcarbamate (0.0349 g, 0.077 mmol) in THF (3 mL) was added and then the solvents were removed *in vacuo*. The neat residue was heated at 65°C for 9 h and purified by chromatography on silica gel (20% to 50% ethyl acetate in hexanes) to afford (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-

methoxybenzyl)-3-(*tert*-butoxycarbonylamino)-6-methyl-1-(N-pentyl-N-(*tert*-butoxycarbonyl)aminosulfonylamino)-heptan-2-ol (0.0289 g, 52%). LC-MS (3 min) t_R = 2.42 min *m/z* 740 $[M+Na]^+$, 618 $[M-Boc]^+$, 518 $[M-2Boc]^+$.

Step 3

A mixture of (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-(tert-butoxycarbonylamino)-6-methyl-1-(N-pentyl-N-(tert-butoxycarbonyl)aminosulfonylamino)-heptan-2-ol (27.5 mg), trifluoroacetic acid (3 mL) and CH_2Cl_2 (3 mL) was stirred at room temperature for 2 h. After the solvents were removed *in vacuo*, the residue was purified by reversed-phase HPLC (Phenomenex® Luna 5μ C18(2) 100A, 150 × 10.00 mm, 5 micron, 10% →90% CH_3CN/H_2O, 0.1% CF_3COOH over 14 min, flow rate 8 mL/min) to give (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-6-methyl-1-(pentylaminosulfonylamino)-heptan-2-ol (**I-113**) as its trifluoroacetate salt. LC-MS (3 min) t_R = 1.37 *m/z* 518 $[M+H]^+$; ^1H NMR (400 MHz, CD_3OD) δ 6.76-6.62 (m, 3H), 3.94 (t, *J* = 6.2 Hz, 2H), 3.68 (s, 3H), 3.55-3.50 (m, 1H), 3.47 (t, *J* = 6.2 Hz, 2H), 3.23 (s, 3H), 3.08-3.03 (m, 1H), 2.91-2.81 (m, 4H), 2.55-2.31 (m, 2H), 1.94-1.87 (m, 2H), 1.74-1.40 (m, 6H), 1.25-1.21 (m, 4 H), 0.85-0.77 (m, 9H).

EXAMPLE 24

The following compunds of Formula I were prepared by the procedure of Example 23:

I-104 (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(butylaminosulfonylamino)-6-methylheptan-2-ol

I-118 (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-(allylaminosulfonyl)-N-isopropylamino)-6-methylheptan-2-ol.

The following are compounds of the invention:

Table of Compounds

Cpd. No.	LC-MS (3 min) t_R (min)	Mass Observed	^1H NMR solvent	Selected ^1H NMR resonances
I-1	1.24	439	CD_3OD	0.9 (m), 1.2-1.9 (m), 2.02 (m), 2.18 (m), 2.40 (m), 2.64 (m), 2.82 (m), 3.08 (m), 3.36 (s), 3.60 (t), 3.62 (m), 3.80 (m), 4.06 (t), 6.7-6.9 (m)
I-2	1.24	451	CD_3OD	0.2 (m), 0.52 (m), 0.9 (m), 1.3-1.9 (m), 2.02 (m), 1.10 (m), 2.40 (m), 2.62 (m), 2.86 (m), 3.12 (m), 3.36 (s), 3.60 (t), 3.80 (t), 4.06 (t), 6.7-6.9 (m)

I-3	1.25	453	$CDCl_3$	6.79-6.66 (m, 3H), 6.13 (br s, 1H), 4.10 (t, *J* = 6.4 Hz, 2H), 3.83 (s, 3H), 3.58 (t, *J* = 6.0 Hz, 2H), 3.54-1.48 (m, 1H), 3.36 (s, 3H), 3.31-3.23 (m, 1H), 3.13-3.02 (m, 2H), 2.71-2.37 (m, 5H), 2.20-2.06 (m, 5H), 1.78-1.55 (m, 4H), 1.38-1.28 (m, 4H), 0.92-0.85 (m, 9H)
I-4	1.29	453	CD_3OD	0.92 (m), 1.18 (s), 1.6 (m), 2.02 (m), 2.40 (m), 2.62 (m), 3.34 (s), 3.58 (t), 3.80 (s), 4.04 (t), 6.76 (m), 6.80 (d), 6.84 (m)
I-5		461	CD_3OD	0.12(m,2H),0.48(m,2H),1.15(s,6H),4.02(t,2H),6.75(m,3H),7.17(t,1H)
I-6	1.37	467	CD_3OD	0.9 (m), 1.32 (m), 1.6-1.8 (m), 2.02 (m), 2.20 (t), 2.40 (m), 2.62 (m), 2.84 (m), 3.10 (m), 3.36 (s), 3.38 (m), 3.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-7	1.35	467	CD_3OD	0.8-1.0 (m), 1.14 (s), 1.4-1.9 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.90 (m), 3.10 (m), 3.36 (s), 3.40 (m), 3.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-8	1.35	467	CD_3OD	0.9 (m), 1.00 (s), 1.6-1.8 (m), 2.02 (m), 2.04 (m), 2.40 (m), 2.62 (m), 2.84 (m), 3.06 (m), 3.36 (s), 3.38 (m), 3.58 (m), 3.60 (t), 3.80 (s), 4.04 (t), 6.7-6.9 (m)
I-9	1.16	469	CD_3OD	0.9 (m), 1.4-1.9 (m), 2.02 (m), 2.24 (m), 2.40 (m), 2.62 (m), 2.80 (m), 3.08 (m), 3.26 (m), 3.36 (s), 3.40 (t), 3.60 (t), 3.80 (s), 4.04 (t), 6.7-6.9 (m)
I-10	1.30	473	CD_3OD	0.9 (m), 1.30 (m), 1.66 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.98 (m), 3.26 (m), 3.36 (s), 3.58 (t), 3.60 (m), 3.68 (m), 3.76 (s), 4.04 (t), 6.7-6.9 (m), 7.48 (dd), 7.58 (dd), 7.84 (d)
I-11	1.26	479	CD_3OD	0.9 (m), 1.4-1.9 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.82 (m), 3.0-3.3 (m), 3.36 (s), 3.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I- 12	1.38	479	CD_3OD	0.9 (m), 1.1-1.9 (m), 2.02 (m), 2.20 (m), 2.40 (m), 2.62 (m), 2.84 (m), 3.08 (m), 3.36 (s), 3.60 (t), 3.7 (m), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-13	1.36	479	CD_3OD	0.9 (m), 1.2-1.5 (m), 1.6-1.85 (m), 2.02 (m), 2.20 (m), 2.40 (m), 2.60 (m), 2.84 (m), 3.06 (m), 3.36 (s), 3.38 (m), 3.60 (t), 3.70 (m), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-14		479	CD_3OD	1.12(s,6H),3.60(m,2H),4.02(m,2H),6.73(m,3H),7.17(t,1H)
I-15	1.45	481	CD_3OD	0.9 (m), 1.30 (m), 1.6-1.9 (m), 2.02 (m), 2.20 (t), 2.40 (m), 2.62 (m), 2.84 (m), 3.10 (m), 3.36 (s), 3.38 (m), 3.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-16	1.43	481	CD_3OD	0.9 (m), 1.16 (s), 1.20 (m), 1.4-1.9 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.92 (m), 3.14 (m), 3.36 (s), 3.40 (m), 3.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-17	1.48	481	CD_3OD	0.80-1.00 (m), 1.10 (m), 1.30 (m), 1.60 (m), 1.70 (m), 2.00 (m), 2.30 (m), 2.40 (m), 2.60 (m), 3.00 (m), 3.10 (m), 3.30 (s), 3.40 (m), 3.60 (m), 3.80 (s), 4.05 (t), 6.70-7.00 (m)
I-18	1.33	487	CD_3OD	0.9 (m), 1.3-1.9 (m), 2.02 (m), 2.30 (m), 2.56 (m), 2.78 (m), 3.14 (m), 3.36 (s), 3.38 (m), 3.50 (s), 3.60 (t), 3.68 (m), 3.80 (s), 4.06 (t), 6.7-6.9 (m), 7.2 (m), 7.3 (m)
I-19	1.3	489		ND
I-20	1.32	493	CD_3OD	0.9 (m), 2.03 (q), 3.36 (s), 3.60 (t), 3.80 (s), 4.08 (t), 6.7-6.9 (m)
I-21	1.45	493	CD_3OD	0.9 (m), 1.1-1.8 (m), 2.04 (m), 2.40 (m), 2.60 (m), 2.84 (m), 3.06 (m), 3.38 (s), 3.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-22		493	CD_3OD	0.02 (m, 2H), 0.48 (m, 2H), 0.60 (m, 1H), 1.20 (s, 6H), 4.06 (t, 2H)
I-23	1.44	493	CD_3OD	0.9 (m), 1.12 (s), 1.2-1.8 (m), 1.98 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.98 (m), 3.14 (m), 3.36 (s), 3.42 (m), 3.60 (t), 3.64 (m), 3.80 (s), 4.04 (t), 6.7-6.9 (m)
I-24	1.48	493	CD_3OD	0.9 (m), 1.3-1.8 (m), 2.02 (m), 2.12 (m), 2.40 (m), 2.60 (m), 2.84 (m), 3.08 (m), 3.36 (s), 3.38 (m), 3.58 (m), 3.60 (t), 3.80 (s), 4.04 (t), 6.7-6.9 (m)
I-25		493	CD_3OD	1.16(s,6H),3.60(t,2H),4.05(t,2H),6.68(s,1H),7.02(d,2H)
I-26		493	CD_3OD	1.16(s,6H),3.60(t,2H),4.05(t,2H),6.68(s,1H),6.72(d,1H),7.02(d,1H)
I-27	1.37	495	$CDCl_3$	6.80-6.66 (m, 3H), 4.14-3.95 (m, 3H), 3.83 (s, 3H), 3.61-3.50 (m, 3H), 3.35 (s, 3H), 2.80-1.22 (m, 18H), 1.08-0.81 (m, 15H)
I-28		495	CD_3OD	1.15(s, 6H), 1.20(m, 2H), 1.28(m,2H), 2.02(m, 2H), 3.58(m,2H), 4.05(t, 2H)
I-29	1.51	495	CD_3OD	
I-30		495	CD_3OD	0.92 (t, 3H), 0.97 (s, 6H), 1.30 (m, 4H), 2.05 (m, 4H), 3.56 (t, 2H), 4.06 (m, 2H)
I-31	1.53	495	CD_3OD	0.80-1.00 (m), 1.20 (m), 1.50 (m), 1.60 (m), 1.70 (m), 2.00 (m), 2.10 (m), 2.40 (m), 2.60 (m), 3.00 (m), 3.10 (m), 3.30 (s), 3.40 (m), 3.60 (m), 3.80 (s), 4.05 (t), 6.70-7.00 (m)
I-32	1.40	497	CD_3OD	0.9 (m), 1.38 (s), 1.5-1.8 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.94 (m),

				3.20 (m), 3.36 (s), 3.38 (t), 3.60 (t), 3.64 (m), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-33	1.36	497	CD_3OD	0.9 (m), 1.16 (st), 1.4-1.8 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.94 (m), 3.18 (m), 3.36 (s), 3.40 (m), 3.50 (q), 3.60 (t), 3.64 (m), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-34	1.40	501	CD_3OD	0.9 (m), 1.3-1.9 (m), 2.02 (m), 2.40 (m), 2.50 (m), 2.60 (m), 2.78 (m), 2.90 (m), 3.06 (m), 3.38 (s), 3.56 (m), 3.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m), 7.2 (m)
I-35	1.40	501	DMSO-d_6	1.58 (m), 2.08 (m), 2.3-2.5 (m), 2.74 (m), 3.02 (s), 3.16 (m), 3.72 (m), 3.92 (m), 4.02 (s), 4.20 (s), 4.26 (t), 4.32 (m), 4.46 (m), 4.50 (s), 4.76 (t), 7.4-7.9 (m), 8.6 (br)
I-36	1.40	503	CD_3OD	0.9 (m), 1.40 (m), 1.5-1.9 (m), 2.02 (m), 2.44 (m), 2.60 (m), 3.08 (m), 3.24 (m) 3.36 (s), 3.58 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-37	1.34	505	DMSO-d_6	1.58 (m), 2.0-2.5 (m), 2.72 (m), 3.18 (m), 3.72 (m), 3.92 (m), 4.00 (s), 4.26 (t), 4.30 (s), 4.44 (m), 4.50 (s), 4.78 (t), 4.80 (br), 7.4-7.6 (m), 7.88 (dd), 8.1 (m), 8.6 (br)
I-38	1.36	505	CD_3OD	0,9 (m), 1.38 (m), 1.5-1.8 (m), 2.02 (m), 2.30 (m), 2.54 (m), 2.78 (m), 3.14 (m), 3.36 (s), 3.38 (m), 3.54 (s), 3.60 (t), 3.70 (m), 3.80 (s), 4.06 (t), 6.7-7.0 (m), 7.08 (m), 7.26 (m)
I-39	1.35	505	CD_3OD	0.9 (m), 1.3-1.8 (m), 2.02 (m), 2.36 (m), 2.44 (m), 2.84 (m), 3.16 (m), 3.36 (s), 3.38 (m), 3.48 (s), 3.56 (t), 3.58 (m), 3.78 (s), 4.04 (t), 6.7-6.9 (m), 7.04 (m), 7.34 (m)
I-40	1.35	505	CD_3OD	0.9 (m), 1.3-1.8 (m), 2.02 (m), 2.36 (m), 2.44 (m), 2.84 (m), 3.16 (m), 3.36 (s), 3.38 (m), 3.48 (s), 3.56 (t), 3.58 (m), 3.78 (s), 4.04 (t), 6.7-6.9 (m), 7.04 (m), 7.34 (m)
I-41	1.33	507	CD_3OD	0.9 (m), 1.4-1.9 (m), 2.02 (m), 2.20 (m), 2.26 (m), 2.40 (m), 2.64 (m), 2.78 (m), 3.08 (m), 3.36 (s), 3.38 (m), 3.58 (m), 3.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-42	1.53	507	CD_3OD	0.02 (m), 0.4 (m), 0.64 (m), 0.9 (m), 1.16 (m), 1.18 (s), 1.7 (m), 2.04 (m), 2.44 (m), 2.64 (m), 3.96 (m), 316 (m), 3.36 (m), 3.38 (s), 3.62 (t), 3.76 (m), 3.84 (s), 4.10 (t), 6.78-6.90 (m)
I-43		507	CD_3OD	0.00(m,2H), 0.39(m, 2H), 0.60(m,1H), 0.89(d, 3H), 0.96(d, 3H), 3.35(s, 3H), 3.82(s, 3H)
I-44	1.33	509	CD_3OD	0.9 (m), 1.34 (m), 1.6-1.9 (m), 2.02 (m), 2.42 (m), 2.60 (m), 2.88 (m), 3.20 (m), 3.36 (s), 3.60 (mt), 3.80 (s), 4.08 (t), 6.7-6.9 (m), 7.26 (m), 7.88 (d)
I-45	1.55	509	CD_3OD	0.9 (m), 1.1-1.9 (m), 2.02 (m), 2.20 (m), 2.40 (m), 2.62 (m), 2.84 (m), 3.08 (m), 3.36 (s), 3.58 (t), 3.7 (m), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-46	1.32	509	CD_3OD	0.9 (m), 1.06 (s), 1.2-1.9 (m), 2.02 (m), 2.28 (m), 2.66 (m), 2.76 (s), 3.24 (m), 3.36 (s), 3.60 (t), 3.70 (m), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-47	1.26	512	CD_3OD	0.9 (m), 1.3-1.8 (m), 2.02 (m), 2.26 (m), 2.52 (m), 2.78 (m), 3.16 (m), 3.36 (s), 3.38 (m), 3.60 (mt), 3.80 (s), 4.04 (t), 6.74 (m), 6.86 (m), 7.44 (m), 7.60 (m)
I-48	1.43	513	CD_3OD	0.9 (m), 1.08 (m), 1.4-1.8 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.82 (m), 3.06 (m), 3.26 (m), 3.36 (s), 3.52 (m), 3.60 (t), 3.80 (s), 4.04 (t), 6.7-6.9 (m), 7.38 (m)
I-49	1.42	515	CD_3OD	0.9 (m), 1.6-2.0 (m), 2.02 (m), 2.24 (t), 2.40 (m), 2.62 (m), 2.82 (m), 3.08 (m), 3.36 (s), 3.38 (m), 3.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m), 7.18 (m), 7.24 (m)
I-50	1.42	515	CD_3OD	0.9 (m), 1.4-1.8 (m), 2.02 (m), 2.36 (m), 2.56 (m), 2.84 (m), 3.08 (m), 3.34 (s), 3.36 (m), 3.58 (m), 3.60 (t), 3.80 (s), 4.04 (t), 6.7-6.9 (m), 7.20 (m), 7.36 (m)
I-51		515	$CDCl_3$	0.83(d, 3H), 0.90(d, 3H), 1.50(s, 6H), 3.31(S, 3H), 3.80(s, 3H)
I-52	1.62	522	CD_3OD	0.80-1.00 (m), 1.1 (s), 1.50-1.80 (m),1.85 (m) 2.00 (m), 2.40 (m), 2.60 (m), 2.90 (m), 3.10 (m), 3.30 (s), 3.60 (m), 3.80 (s), 4.05 (t), 6.60-6.80 (m)
I-53	1.40	523	CD_3OD	0.9 (m), 1.4-1.8 (m), 2.02 (m), 2.32 (m), 2.58 (m), 2.80 (m), 3.18 (m), 3.36 (s), 3.38 (m), 3.52 (s), 3.60 (t), 3.70 (m), 3.80 (s), 4.04 (t), 6.7-6.9 (m), 7.02-7.26 (m)
I-54	1.40	523	CD_3OD	0.9 (m), 1.3-1.9 (m), 2.02 (m), 2.38 (m), 2.58 (m), 2.84 (m), 3.18 (m), 3.36 (s), 3.38 (m), 3.60 (ts), 3.70 (m), 3.80 (s), 4.06 (t), 6.7-6.9 (m), 7.38 (m)
I-55	1.41	523	CD_3OD	0.9 (m), 1.4-1.8 (m), 2.02 (m), 2.38 (m), 2.58 (m), 2.84 (m), 3.18 (m), 3.36 (s), 3.38 (m), 3.60 (ts), 3.70 (m), 3.80 (s), 4.04 (t), 6.7-6.9 (m), 7.10 (m)
I-56	1.36	523	CD_3OD	0.9 (m), 1.34 (m), 1.5-1.9 (m), 2.00 (m), 2.42 (m), 2.60 (m), 2.96

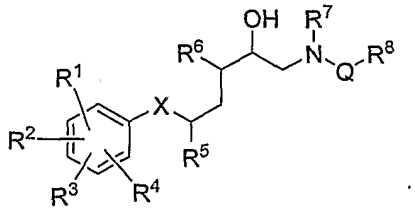
				(m), 3.14 (m), 3.36 (s), 3.50, 3.64 (m), 3.58 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m), 7.40 (m)
I-57	1.49	527	CD_3OD	0.9 (m), 1.04 (m), 1.3-1.8 (m), 2.02 (m), 2.32 (s), 2.40 (m), 2.60 (m), 2.84 (m), 3.08 (m), 3.26 (m), 3.36 (s), 3.60 (t), 3.64 (m), 3.80 (s), 4.04 (t), 6.7-6.9 (m), 7.1-7.3 (m)
I-58	1.47	531	$CDCl_3$	6.78-6.66 (m, 3H), 4.09 (t, *J* = 6.4 Hz, 2H), 4.03-3.96 (m, 1H), 3.83 (s, 3H), 3.57 (t, *J* = 6.0 Hz, 2H), 3.43-3.39 (m, 1H), 3.35 (s, 3H), 3.13 (d, *J* = 6.4 Hz, 2H), 2.97-2.92 (m, 2H), 2.73-1.17 (m, 20H), 0.96-0.86 (m, 9H)
I-59	1.45	531	$CDCl_3$	6.78-6.68 (m, 3H), 4.11-3.95 (m, 3H), 3.83 (s, 3H), 3.59-3.55 (m, 3H), 3.36 (s, 3H), 3.19-1.32 (m, 18H), 1.21-1.16 (m, 6H), 0.97-0.87 (m, 9H)
I-60	1.45	533	CD_3OD	0.9 (m), 1.3-1.8 (m), 1.74 (s), 2.02 (m), 2.36 (m), 2.58 (m), 2.82 (m), 3.36 (s), 3.38 (m), 3.58 (t), 3.64 (m), 3.80 (s), 4.04 (t), 6.74 (dd), 6.78 (s), 6.84 (d), 7.02 (m), 7.38 (m)
I-61		533	$CDCl_3$	0.84(d, 3H), 0.92(d,3H), 1.50(s, 6H), 3.35(s, 3H), 3.84(s,3H)
I-62		533	$CDCl_3$	0.85(d, 3H), 0.90(d,3H), 1.51(s, 6H), 3.32(s, 3H), 3.80(s,3H)
I-63	1.67	544	CD_3OD	0.80-1.00 (m), 1.10-1.40 (m), 1.40-1.80 (m),1.85 (m) 2.00 (m), 2.40 (m), 2.60 (m), 3.00 (m), 3.10 (m), 3.30 (s), 3.40 (m), 3.60 (m), 3.80 (s), 4.05 (t), 6.70-7.00 (m)
I-64	1.56	541	CD_3OD	0.86 (m), 1.5-1.8 (m), 1.98 (m), 2.02 (m), 2.24 (m), 2.48 (m), 2.70 (m), 3.04 (m), 3.36 (m), 3.38 (m), 3.60 (t), 3.80 (s), 4.06 (t), 6.7 (m), 6.84 (d), 7.18 (m), 7.24 (m), 7.38 (d)
I-65		541	CD_3OD	1.18(s,6H),3.60(m,2H),4.10(m,2H),6.79(m,2H),7.10(d,1H),7.22(m,2H),7.38(m,2H),7.50(d,1H)
I-66		541	CD_3OD	1.18(s,6H),3.60(m,2H),4.07(m,2H),6.84(m,2H),7.10(d,1H),7.30(m,1H),7.38(m,2H),7.45(m,2H)
I-67	1.44	543	CD_3OD	0.9 (m), 1.08 (m), 1.4-1.8 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.82 (m), 3.06 (m), 3.26 (m), 3.36 (s), 3.52 (m), 3.60 (t), 3.78 (s), 3.80 (s), 4.06 (t), 6.78 (m), 6.90 (m), 7.28 (m)
I-68		543	CD_3OD	1.16(s,6H),3.56(t,2H),4.03(t,2H),6.74(d,1H),6.85(s,1H),7.42(d,1H)
I-69	1.38	545	CD_3OD	0.9 (m), 1.08 (s), 1.3-1.9 (m), 2.02 (m), 2.40 (m), 2.60 (m), 3.36 (s), 3.58 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m), 7.3 (m)
I-70	1.53	547	CD_3OD	0.9 (m), 1.08 (m), 1.4-1.8 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.82 (m), 3.06 (m), 3.26 (m), 3.36 (s), 3.52 (m), 3.60 (t), 3.80 (s), 4.04 (t), 6.7-6.9 (m), 7.38 (m)
I-71	1.45	551	$CDCl_3$	7.84-7.79 (m, 2H), 7.60-7.48 (m, 3H), 6.79-6.68 (m, 3H), 4.11-4.00 (m, 3H), 3.82 (s, 3H), 3.63-3.52 (m, 3H), 3.33 (s, 3H), 3.23-1.22 (m, 12H), 1.05-0.86 (m, 12H)
I-72	1.45	555	CD_3OD	0.9 (m), 1.4-1.9 (m), 2.02 (m), 2.40 (m), 2.58 (m), 2.86 (m), 3.16 (m), 3.36 (s), 3.38 (m), 3.60 (t), 3.70 (m), 3.78 (s), 3.80 (s), 4.06 (t), 6.7-6.9 (m), 7.44 (m), 7.58 (dd), 7.66 (d)
I-73	1.50	555	CD_3OD	0.9 (m), 1.4-1.8 (m), 2.02 (m), 2.32 (m), 2.58 (m), 2.80 (m), 3.18 (m), 3.36 (s), 3.38 (m), 3.60 (ts), 3.70 (m), 3.80 (s), 4.04 (t), 6.7-6.9 (m), 7.44-7.64 (m)
I-74	1.50	555	CD_3OD	0.9 (m), 1.4-1.8 (m), 2.02 (m), 2.34 (m), 2.56 (m), 2.80 (m), 3.16 (m), 3.36 (s), 3.38 (m), 3.60 (t), 3.62 (s), 3.70 (m), 3.80 (s), 4.06 (t), 6.7-6.9 (m), 7.50 (d), 7.58 (d)
I-75	1.60	555	CD_3OD	0.82 (d), 0.88 (d),1.3-1.7 (m), 1.82 (m), 2.02 (m), 2.24 (m), 2.40 (m), 2.76 (m), 3.08 (m), 3.36 (s), 3.38 (m), 3.60 (t), 3.70 (m), 3.80 (s), 4.06 (t), 6.70 (dd), 6.74 (d), 6.84 (d), 7.18 (dd), 7.26 (dd), 7.40 (d)
I-76	1.38	556	CD_3OD	0.9 (m), 1.58 (s), 1.7 (m), 2.02 (m), 2.38 (m), 2.58 (m), 2.88 (m), 3.16 (m), 3.36 (s), 3.38 (m), 3.60 (t), 3.80 (s), 4.04 (t), 6.7-6.9 (m), 7.02 (d), 7.64 (d)
I-77	1.49	561	CD_3OD	0.9 (m), 1.4-1.9 (m), 1.72 (s), 2.02 (m), 2.40 (m), 2.60 (m), 2.94 (m), 3.20 (m), 3.36 (s), 3.56 (m), 3.60 (t), 3.62 (m), 3.80 (s), 4.06 (t), .6.7-6.9 (m)
I-78	1.56	561	CD_3OD	0.76 (m), 0.9 (m), 1.4-1.8 (m), 2.0 (m), 2.36 (m), 2.56 (m), 2.84 (m), 3.06 (m), 3.36 (s), 3.38 (m), 3.56 (m), 3.58 (t), 3.80 (s), 4.04 (t), 6.74 (dd), 6.76 (d), 6.84 (d), 7.02 (m), 7.28 (m)
I-79	1.44	565	$CDCl_3$	7.44-7.33 (m, 5H), 6.79-6.66 (m, 3H), 4.35-4.22 (m, 2H), 4.11-4.07 (m, 2H), 3.83 and 3.82 (s, 3H), 3.74-3.65 (m, 1H), 3.57 (t, *J* = 6.0 Hz, 2H), 3.35 (s, 3H), 3.37-3.31 (m, 1H), 3.08-2.97 (m, 2H), 2.74-1.21 (m), 1.08 (d, *J* = 7.2 Hz, 3H), 1.06 (d, *J* = 7.2 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 6H)
I-80	1.60	565	CD_3OD	0.9 (m), 1.48 (s), 1.4-1.8 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.96 (m), 3.22 (m), 3.36 (s), 3.40 (m), 3.58 (t), 3.70 (m), 3.80 (s), 4.06 (m),

				6.76 (d), 6.80 (s), 6.86 (d), 6.96 (d), 7.26 (d)
I-81	1.55	571	CD_3OD	0.9 (m), 1.3-1.9 (m), 2.02 (m), 2.36 (m), 2.58 (m), 2.80 (m), 3.16 (m), 3.36 (s), 3.38 (m), 3.60 (ts), 3.70 (m), 3.80 (s), 4.06 (t), 6.7-6.9 (m), 7.18 (m), 7.40 (m)
I-82	1.63	573	CD_3OD	0.82 (d), 0.88 (d),1.3-1.7 (m), 1.80 (m), 2.02 (m), 2.24 (m), 2.40 (m), 2.52 (m), 2.76 (m), 3.10 (m), 3.36 (s), 3.38 (m), 3.60 (t), 3.66 (m), 3.80 (s), 4.06 (t), 6.70 (dd), 6.74 (d), 6.84 (d), 7.02 (m), 7.42 (m)
I-83	1.57	582	CD_3OD	0.9 (m), 1.12 (m), 1.4-1.8 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.98 (m), 3.04 (m), 3.36 (s), 3.38 (m), 3.56 (m), 3.60 (t), 3.80 (s), 4.04 (t), 6.76 (m), 6.86 (m), 7.38-7.50 (m)
I-84	1.09	412	$CDCl_3$	0.9 (m), 1.4-1.8 (m), 2.04 (m), 2.24 (m), 2.68 (m), 3.02 (m), 3.16 (m), 3.36 (s), 3.60 (t), 3.80 (s), 4.06 (t), 6.74 (m), 6.78 (m), 7.5 (br)
I-85	1.25	468	$CDCl_3$	6.80-6.68 (m, 3H), 4.97 (br s, 2H), 4.11-4.06 (m, 2H), 3.82 (s, 3H), 3.60-3.55 (m, 2H), 3.35 (s, 3H), 3.40-1.24 (m, 20H), 0.92-0.84 (m, 9H)
I-86	1.28	468	CD_3OD	6.77-6.62 (m, 3H), 3.96-3.92 (m, 2H), 3.69 (s, 3H), 3.54-3.50 (m, 1H), 3.47 (t, J = 6.2 Hz, 2H), 3.43-3.39 (m, 1H), 3.23 (s, 3H), 3.15-2.82 (m, 3H), 2.55-2.24 (m, 2H), 1.91 (p, J = 6.2 Hz, 2H), 1.72-1.56 (m, 2H), 1.48 (tm, J = 7.0 Hz, 1H), 1.18 and 1.17 (s, 9H), 0.87-0.78 (m, 6H)
I-87	1.36	469	CD_3OD	6.73 (d, J = 7.9 Hz, 1H), 6.67 (d, J = 2.0 Hz, 1H), 6.61 (dd, J = 8.0, 1.9 Hz, 1H), 3.93 (t, J = 6.3 Hz, 2H), 3.70 (d, J = 6.5 Hz, 2H), 3.67 (s, 3H), 3.47-3.39 (m, 3H), 3.22 (s, 3H), 3.09 (dd, J = 14.4, 6.5 Hz, 1H), 2.93 (dd, J = 14.4, 6.5 Hz, 1H), 2.82-2.78 (m, 1H), 2.50 (dd, J = 13.5, 6.2 Hz, 1H), 2.27 (dd, J = 13.6, 8.1 Hz, 1H), 1.90 (p, J = 6.3 Hz, 2H), 1.81-1.71 (m, 1H), 1.62-1.57 (m, 2H), 1.48-1.44 (m, 2H), 0.82 (d, J = 6.7 Hz, 6H), 0.79 (d, J = 7.0 Hz, 6H)
I-88	1.29	480	CD_3OD	0.9 (m), 1.5-1.8 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.92 (m), 3.36 (s)m 3.38 (m), 3.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-89	1.30	480	CD_3OD	0.02 (m), 0.42 (m), 0.84 (m), 0,9 (m), 1.38 (m), 1.60 (m), 1.7 (m), 2.02 (m), 2.40 (m), 2.60 (m), 3.0 (m), 3.36 (s), 3.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-90	1.14	482	CD_3OD	0.9 (m), 1.60 (m), 1.7 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.9 (m), 3.18 (m), 3.36 (s), 3.36 (m), 3.60 (t), 3.62 (m), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-91	1.38	482	CD_3OD	0.9 (m), 1.30 (m), 1.44 (m), 1.60 (m), 1.76 (m), 2.02 (m), 2.42 (m), 2.60 (m), 2.98 (m), 3.12 (t), 3.26 (m), 3.36 (s), 3.60 (t), 3.80 (s) 4.06 (t), 6.7-6.9 (m)
I-92	1.37	482	CD_3OD	0.9 (m), 1.30 (m), 1.46 (m), 1.60 (m), 1.74 (m), 2.02 (m), 2.42 (m), 2.62 (m), 2.94 (m), 3.08 (t, m), 3.26 (m), 3.36 (s), 3.56 (m), 3.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-93	1.38	482	CD_3OD	0.9 (m), 1.3-1.5 (m), 1.6-1.9 (m), 2.02 (m), 2.40 (m), 2.60 (m), 3.0 (m), 3.08 (t), 3.22 (m), 3.36 (s), 3.60 (t), 3.66 (m), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-94	1.45	483	CD_3OD	6.74 (d, J = 8.2 Hz, 1H), 6.68 (d, J = 1.8 Hz, 1H), 6.62 (dd, J = 8.2, 2.0 Hz, 1H), 3.95-3.89 (m, 4H), 3.67 (s, 3H), 3.48-3.40 (m, 3H), 3.22 (s, 3H), 3.08 (dd, J = 14.4, 6.5 Hz, 1H), 2.94 (dd, J = 14.4, 6.2 Hz, 1H), 2.82-2.78 (m, 1H), 2.50 (dd, J = 13.6, 6.3 Hz, 1H), 2.28 (dd, J = 13.6, 7.8 Hz, 1H), 1.90 (p, J = 6.2 Hz, 2H), 1.62-1.58 (m, 2H), 1.50-1.45 (m, 4H) 1.22-1.19 (m, 4H), 0.84-0.77 (m, 9H)
I-95	1.17	484	CD_3OD	0.9 (m), 1.4-1.8 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.94 (m), 3.06 (m), 3.18 (t), 3.24 (m), 3.30 (s), 3.36 (s), 3.40 (t), 3.56 (m), 3.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-96	1.20	484	CD_3OD	0.9 (m), 1.18 (t), 1.4-1.8 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.92 (m), 3.06 (m), 3.26 (m), 3.36 (s), 3.46 (m), 3.60 (t), 3.80 (s), 4.04 (t), 6.7-6.9 (m)
I-97	1.41	494	CD_3OD	0.9 (m), 1.1-1.4 (m), 1.6-1.9 (m), 2.02 (m), 2.42 (m), 2.60 (m), 3.02 (m), 3.10 (m), 3.24 (m), 3.36 (s), 3.42 (m), 3.60 (t), 3.70 (m), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-98	1.47	496	CD_3OD	0.9 (m), 1.30 (m), 1.44 (m), 1.60 (m), 1.76 (m), 2.02 (m), 2.42 (m), 2.60 (m), 2.98 (m), 3.12 (t), 3.24 (m), 3.36 (s), 3.60 (t), 3.80 (s) 4.04 (t), 6.7-6.9 (m)
I-99		496	CD_3OD	1.31 (m, 4H), 1.49 (m,2H), 2.39 (m, 1H), 2.60 (m, 1H), 2.86 (s, 3H), 3.59 (t, 2H), 4.05 (t, 2H)
I-100	1.44	496	CD_3OD	0.9 (m), 1.2-1.8 (m), 2.02 (m), 2,40 (m), 2.64 (m), 2.84 (s), 2.98 (m), 3.12 (t), 3.36 (s), 3.54 (m), 3.60 (t), 3.63 (m), 3.80 (s), 4.06 (t), 6.7-6.9 (m)

I-101	1.43	498	CD_3OD	6.72-6.58 (m, 3H), 3.92 (t, *J* = 6.4 Hz, 2H), 3.70 (br s, 1H), 3.65 (s, 3H), 3.60 (br s, 1H), 3.44 (t, *J* = 6.2 Hz, 2H), 3.30-3.22 (m, 2H), 3.20 (s, 3H), 2.89-2.85 (m, 1H), 2.49 (dd, *J* = 13.6, 6.4 Hz, 1H), 2.25 (dd, *J* = 13.6, 7.6 Hz, 1H), 1.88 (p, *J* = 6.3 Hz, 2H), 1.62-1.37 (m, 5H), 1.21-1.13 (m, 4H), 0.82-0.74 (m, 9H)
I-102	1.29	502	CD_3OD	0.9 (m), 1.40 (m), 1.60 (m), 1.7 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.96 (m), 3.12 (m), 3.28 (m), 3.36 (s), 3.60 (t), 3.80 (s), 4.06 (t), 4.30 (m), 6.7-6.9 (m), 7.20 (m), 7.26 (m)
I-103	1.42	503	CD_3OD	7.25-7.16 (m, 5H), 6.75-6.60 (m, 3H), 4.99 (s, 2H), 3.94 (t, J = 6.3 Hz, 2H), 3.67 (s, 3H), 3.48-3.40 (m, 3H), 3.22 (s, 3H), 3.15-2.76 (m, 4H), 2.53-2.45 (m, 1H), 2.30-2.24 (m, 1H), 1.94-1.86 (m, 2H), 1.62-1.58 (m, 2H), 1.48 (t, J = 6.6 Hz, 1H), 0.84-0.78 (m, 6H)
I-104	1.32	504	CD_3OD	6.77-6.64 (m, 3H), 3.96 (t, J = 6.4 Hz, 2H), 3.69 (s, 3H), 3.48 (t, J = 6.2 Hz, 2H), 3.24 (s, 3H), 3.16-3.14 (m, 1H), 2.92-2.82 (m, 4H), 2.56-2.32 (m, 2H), 1.95-1.89 (m, 2H), 1.75-1.63 (m, 3H), 1.51-1.23 (m, 6H), 0.86-0.79 (m, 9H)
I-105	1.47	506	CD_3OD	0.9 (m), 1.4-1.9 (m), 2.00 (m), 2.42 (m), 2.62 (m), 3.0 (m), 3.18 (m), 3.26 (m), 3.36 (s), 3.60 (t), 3.62 (m), 3.78 (s), 4.04 (t), 6.66-6.82 (m), 7.00 (d), 7.22 (dd), 7.40 (dd)
I-106	1.44	508	CD_3OD	0.9 (m), 1.1-1.5 (m), 1.6-1.8 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.96 (d), 2.98 (m), 3.12 (m), 3.22 (m), 3.36 (s), 3.60 (t), 3.64 (m), 3.80 (s), 4.06 (m), 6.7-6.9 (m)
I-107	1.44	508	CD_3OD	0.9 (m), 1.1-1.8 (m), 2.02 (m), 2.40 (m), 2.60 (m), 2.72 (s), 2.88, 2.98 (m), 3.14 (m), 3.36 (sm), 3.60 (t), 3.80 (s), 3.92 (m), 4.04 (t), 6.7-6.9 (m), 7.38 (m)
I-108	1.44	510	$CDCl_3$	6.78-6.65 (m, 3H), 6.20 (br s, 1H), 4.26-4.19 (m, 1H), 4.08 (t, *J* = 6.6 Hz, 2H), 3.82 (s, 3H), 3.56 (t, *J* = 6.2 Hz, 2H), 3.35 (s, 3H), 3.31-3.27 (m, 1H), 3.22-3.11 (m, 3H), 2.67-2.34 (m, 3H), 2.09 (p, *J* = 6.3 Hz, 2H), 1.77-1.27 (m, 9H), 1.10-1.07 (m, 6H), 0.92-0.86 (m, 9H)
I-109		510	$CDCl_3$	0.84 (s, 6H), 1.18 (m, 2H), 1.27 (m, 2H), 2.00 (m, 2H), 2.95 (dd, 2H),
I-110		510	CD_3OD	0.91 (m, 8H), 1.25 (s, 6H), 2.02 (m, 2H)
I-111	1.09	511	CD_3OD	0.9 (m), 1.16 (s), 1.60 (m), 0.7 (m), 2.02 (m), 2.40 (m), 2.60 (m), 3.24 (m), 3.36 (s), 3.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-112	1.37	516	CD_3OD	0.9 (m), 1.6-1.8 (m), 2.02 (m), 2.42 (m), 2.62 (m), 2.78 (t), 2.94 (m), 3.12 (m), 3.26 (m), 3.36 (s), 3.58 (t), 3.80 (s), 4.04 (t), 6.7-6.9 (m), 7.2-7.3 (m)
I-113	1.37	518	CD_3OD	6.76-6.62 (m, 3H), 3.94 (t, *J* = 6.2 Hz, 2H), 3.68 (s, 3H), 3.55-3.50 (m, 1H), 3.47 (t, *J* = 6.2 Hz, 2H), 3.23 (s, 3H), 3.08-3.03 (m, 1H), 2.91-2.81 (m, 4H), 2.55-2.31 (m, 2H), 1.94-1.87 (m, 2H), 1.74-1.40 (6H), 1.25-1.21 (m, 4 H), 0.85-0.77 (m, 9H)
I-114	1.58	522	CD_3OD	0.92 (m), 1.2 (m), 1.6 (m), 2.02 (m), 2.40 (m), 2.60 (m), 3.36 (s), 3.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-115	1.55	524	CD_3OD	0.9 (m), 1.00 (s), 1.34 (s), 1.6-1.8 (m), 2.02 (m), 2.40 (m), 2.60 (m), 3.06 (m), 3.22 (m), 3.36 (s), 3.56 (m), 3.60 (t), 3.80 (s), 4.04 (t), 6.7-6.9 (m)
I-116	1.62	524	CD_3OD	0.9 (m), 1.4-1.9 (m), 1.98 (m), 2.02 (m), 2.40 (m), 2.60 (m), 3.10 (m), 3.36 (s), 2.60 (t), 3.80 (s), 4.06 (t), 6.7-6.9 (m)
I-117	1.45	530	CD_3OD	0.9 (m), 1.6-1.8 (m), 2.02 (m), 2.42 (m), 2.62 (mt), 2.96 (m), 3.14 (t), 3.24 (m), 3.36 (s), 3.58 (m), 3.60 (t), 3.80 (s), 4.04 (t), 6.7-6.9 (m), 7.1-7.3 (m)
I-118	1.33	530	$CDCl_3$	6.79-6.68 (m, 3H), 5.92-5.81 (m, 1H), 5.28-5.14 (m, 2H), 4.09 (t, *J* = 6.6 Hz, 2H), 4.03 (p, *J* = 6.7 Hz, 1H), 3.83 (s, 3H), 3.65-3.61 (m, 2H), 3.57 (t, *J* = 6.2 Hz, 2H), 3.45-3.40 (m, 1H), 3.35 (s, 3H), 3.25-3.06 (m, 2H), 2.53 (dd, *J* = 14.0, 7.2 Hz, 1H), 2.43 (dd, *J* = 13.8, 7.4 Hz, 1H), 2.09 (p, *J* = 6.3 Hz, 2H), 1.79-1.31 (m, 3H), 1.22-1.17 (m, 6H), 0.89-0.86 (m, 6H)
I-119	1.55	556	CD_3OD	0.9 (m), 1.4-1.9 (m), 2.00 (m), 2.42 (m), 2.62 (m), 3.0 (m), 3.20 (m), 3.26 (m), 3.36 (s), 3.58 (t), 3.62 (m), 3.76 (s), 4.04 (t), 6.7-6.9 (m), 7.24 (d), 7.42 (dd), 7.52 (d), 7.92 (d)
I-120	1.53	562	CD_3OD	0.9 (m), 1.22 (s), 1.24 (s), 1.4-1.8 (m), 2.00 (m), 2.42 (m), 2.60 (m), 3.02 (m), 3.06 (m), 3.36 (s), 3.60 (t), 3.80 (s), 4.02 (t), 6.76 (m), 6.84 (d), 6.94 (m), 7.14 (m).

WHAT IS CLAIMED IS

1. A a compound of formula I



I

wherein

R^1 is hydrogen, halogen, hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, lower alkylthio-lower alkoxy, cyano-lower alkoxy, hydroxy-lower alkoxy, carboxy-lower alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, N-mono- or N,N-di-lower alkylcarbamoyl-lower alkoxy, or aryl;

R^2 is hydrogen, halogen, cyano, carbamoyl, lower alkyl, lower haloalkyl, cycloalkyl, halocycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-loweralkyl, cyano-lower alkyl, hydroxy-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, lower alkoxy-lower alkoxy-lower alkyl, lower haloalkoxy-lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, halocycloalkoxy-lower alkyl, hydroxy, lower alkanoyloxy-lower alkoxy, hydroxy-lower alkoxy, halo-(hydroxy)-lower alkoxy, lower alkanesulfonyl-(hydroxy)-lower alkoxy, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, lower alkanoylamino-lower alkyl, lower alkoxycarbonyl-amino-lower alkyl, aminocarbonylamino-lower alkyl, lower alkylaminocarbonylamino-lower alkyl, di(lower alkyl)aminocarbonylamino-lower alkyl, aminosulfonylamino-lower alkyl, lower alkylaminosulfonylamino-lower alkyl, di(lower alkyl)aminosulfonylamino-lower alkyl, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy, lower alkanoylamino-lower alkoxy, lower alkoxycarbonyl-amino-lower alkoxy, aminocarbonylamino-lower alkoxyl, lower alkylaminocarbonylamino-lower alkoxy, di(lower alkyl)aminocarbonylamino-lower alkoxy, aminosulfonylamino-lower alkoxy, lower alkylaminosulfonylamino-lower alkoxy, di(lower alkyl)aminosulfonylamino-lower alkoxy, oxo-lower alkoxy, lower alkoxy, lower haloalkoxy, cycloalkoxy, lower halocycloalkoxy, cycloalkyl-lower alkoxy, halocycloalkyl-lower alkoxy, lower alkenyloxy, cycloalkoxy-lower alkoxy, halocycloalkoxy-lower alkoxy, lower alkoxy-lower alkoxy, lower haloalkoxy-lower alkyl, lower alkoxy-lower alkenyl, lower alkenyloxy-lower alkoxy, lower alkoxy-lower alkenyloxy, lower alkenyloxy-lower alkyl, lower alkanoyl-lower alkoxy, lower alkylthio-lower alkoxy, lower alkanesulfonyl-lower alkoxy, lower alkylthio-(hydroxy)-lower alkoxy, aryl-lower alkoxy, optionally N-oxidized pyridyl-lower alkoxy, thiazolylthio-

lower alkoxy or thiazolinylthio-lower alkoxy, imidazolylthio-lower alkoxy, optionally N-oxidized pyridylthio-lower alkoxy, pyrimidinylthio-lower alkoxy, cyano-lower alkoxy, carboxy-lower alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, N-mono- or N,N-di-lower alkylcarbamoyl-lower alkoxy, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, carbamoyl-lower alkyl, or N-mono- or N,N-di-lower alkylcarbamoyl-lower alkyl;

R^3 is hydrogen, halogen, cyano, carbamoyl, lower alkyl, lower haloalkyl, lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, hydroxy-lower alkyl, lower alkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, optionally partially hydrogenated or N-oxidized pyridyl-lower alkyl, thiazolyl-thio-lower alkyl or thiazolinylthio-lower alkyl, imidazolylthio-lower alkyl, optionally N-oxidized pyridylthio-lower alkyl, pyrimidinylthio-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, lower alkanoyl-amino-lower alkyl, lower alkanesulfonylamino-lower alkyl, polyhalo-lower alkane-sulfonylamino-lower alkyl, pyrrolidino-lower alkyl, piperidino-lower alkyl, piperazino-lower alkyl, N'-lower alkylpiperazino-lower alkyl or N'-lower alkanoylpiperazino-lower alkyl, morpholino-lower alkyl, thiomorpholino-lower alkyl, S-oxothiomorpholino-lower alkyl or S,S-dioxothio-morpholino-lower alkyl, cyano-lower alkyl, carboxy-lower alkyl, lower alkoxy-carbonyl-lower alkyl, carbamoyl-lower alkyl, N-mono- or N,N-di-lower alkyl-carbamoyl-lower alkyl, cycloalkyl; phenyl or naphthyl that is unsubstituted or substituted with one to three groups independently selected from lower alkyl, lower alkoxy, hydroxy, lower alkylamino, di-lower alkylamino, halogen, trifluoromethyl, trifluoromethoxy, and cyano; hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, cycloalkoxy-lower alkoxy, hydoxy-lower alkoxy, aryl, lower haloalkoxy, lower alkylthio-lower alkoxy,lower haloalkylthio-lower alkoxy, lower alkanesulfonyl-lower alkoxy, lower haloalkanesulfonyl-lower alkoxy, optionally hydrogenated heteroaryl-lower alkoxy, heterocyclyl-lower alkoxy, optionally partially or fully hydrogenated heteroarylthio-lower alkoxy, such as thiazolylthio-lower alkoxy or thiazolinylthio-lower alkoxy, imidazolylthio-lower alkoxy, optionally N-oxidized pyridylthio-lower alkoxy, pyrimidinylthio-lower alkoxy, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy, lower alkanoylamino-lower alkoxy, lower alkanesulfonylamino-lower alkoxy, polyhalo-lower alkanesulfonylamino-lower alkoxy, pyrrolidino-lower alkoxy, piperidino-lower alkoxy, piperazino- lower alkoxy, N'-lower alkylpiperazino- lower alkoxy or N'-lower alkanoylpiperazino-lower alkoxy, morpholino-lower alkoxy, thiomorpholino- lower alkoxy, S-oxothiomorpholino- lower alkoxy or S,S-dioxothiomorpholino-lower alkoxy, cyano-lower alkoxy, carboxy-lower

alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, N-mono- or N,N-di-lower alkylcarbamoyl-lower alkoxy, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, carbamoyl-lower alkyl, or N-mono- or N,N-di-lower alkylcarbamoyl-lower alkyl; or

R^2 and R^3 taken together with the atoms through which they are attached form a fused dioxolane, dioxane, benzene or cyclohexene ring, wherein said ring is substituted with up to 2 substituents independently selected from lower alkyl and lower alkoxy-lower alkyl;

R^4 is hydrogen, lower alkyl, hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, or cycloalkyl-lower alkoxy; or

R^3 and R^4 taken together with the atoms through which they are attached form a fused dioxolane, dioxane, benzene or cyclohexene ring, wherein said ring is substituted with up to 2 substituents independently selected from lower alkyl and lower alkoxy-lower alkyl; provided that R^3 does not form a ring with R^2;

X is methylene or hydroxymethylene;

R^5 is lower alkyl, lower haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, lower haloalkyl-cycloalkyl, cycloalkyl-lower alkyl, aryl, aryl-lower alkyl, heterocyclyl, heterocyclyl-lower alkyl;

R^6 is amino, lower alkylamino, di-lower alkylamino, or lower alkanoylamino;

R^7 is hydrogen, lower alkyl, lower haloalkyl, cycloalkyl, lower alkoxy-lower alkyl, or lower haloalkoxy-lower alkyl;

Q is carbonyl, thiocarbonyl, or sulfonyl;

R^8 is lower alkyl, lower haloalkyl, C_8-C_{15}alkyl, C_8-C_{15}haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-loweralkyl, lower haloalkoxy-lower alkyl, cycloalkoxy-lower alkyl, cycloalkoxy-cycloalkyl, lower alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, lower alkylthio-cycloalkyl, lower haloalkylthio-cycloalkyl, lower alkanesulfonyl-cycloalkyl, lower haloalkanesulfonyl-cycloalkyl, aryl, aryl-lower alkyl, aryl-lower hydroxyalkyl, arylcycloalkyl, aryloxy-lower alkyl, aryloxy cycloalkyl, arylthio-lower alkyl, arylsulfonyl-

lower alkyl, arylthio-cycloalkyl, arylsulfonyl-cycloalkyl, lower alkanoyl-lower alkyl, hydroxy-lower alkyl, amino-lower alkyl, lower alkanoylamino-lower alkyl, N-mono-lower alkylamino-lower alkyl, N,N-di-lower alkylamino-lower alkyl, piperidino-lower alkyl, hydroxypiperidino-lower alkyl, lower alkoxypiperidino-lower alkyl, morpholino-lower alkyl, dimethylmorpholino-lower alkyl, thiomorpholino-lower alkyl, S,S-dioxothiomorpholino-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, carbamoyl-lower alkyl, N-mono- lower alkylcarbamoyl-lower alkyl, N,N-di-lower alkylcarbamoyl-lower alkyl, carboxy-(hydroxy)-lower alkyl, lower alkoxycarbonyl-(hydroxy)-lower alkyl, carbamoyl-(hydroxy)-lower alkyl, N-mono- lower alkylcarbamoyl-(hydroxy)-lower alkyl, N,N-di-lower alkylcarbamoyl-(hydroxy)-lower alkyl, 5- or 6-membered carboxycycloalkyl-lower alkyl, 5- or 6-membered lower alkoxycarbonyl-cycloalkyl-lower alkyl, 5- or 6-membered carbamoylcycloalkyl-lower alkyl, 5- or 6-membered N-mono-alkylcarbamoylcycloalkyl-lower alkyl, N,N-di-lower alkylcarbamoylcycloalkyl-lower alkyl, cyano-lower alkyl, sulfamoyl-lower alkyl, lower alkylsulfamoyl-lower alkyl, or di-lower alkylsulfamoyl-lower alkyl, imidazolyl-lower alkyl, oxopyrrolidinyl-lower alkyl, benzimidazolyl-lower alkyl, oxadiazolyl-lower alkyl, pyridyl-lower alkyl, oxopiperidinyl-lower alkyl or quinolinyl-lower alkyl, piperidin-4-yl-lower alkyl, or lower alkanoylpiperidin-4-yl-lower alkyl, wherein said aryl, imidazolyl, benzimidazolyl, oxadiazolyl, pyridyl, quinolinyl, aryloxy, arylthio and arylsulfonyl groups are optionally substituted with up to four groups independently selected from halo, cyano, nitro, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, optionally halogenated lower alkanesulfonyl, and lower alkoxycarbonyl;

or R^8 is OR^9 or NR^9R^{10}

R^9 is 1) hydrogen, lower alkyl, lower haloalkyl, lower alkenyl, (C_8-C_{15})alkyl, (C_8-C_{15})haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-loweralkyl, lower haloalkoxy-lower alkyl, cycloalkoxy-lower alkyl, cycloalkoxy-cycloalkyl, lower alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, lower alkylthio-cycloalkyl, lower haloalkylthio-cycloalkyl, lower alkanesulfonyl-cycloalkyl, lower haloalkanesulfonyl-cycloalkyl, aminocarbonyl-lower alkyl, lower alkyl-amonocarbonyl-lower alkyl, di(lower alkyl)-amonocarbonyl-lower alkyl, or 2) aryl, aryl-lower alkyl, aryloxy-lower alkyl, arylthio-lower alkyl, or arylsulfonyl-lower alkyl

wherein the aryl groups are optionally substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

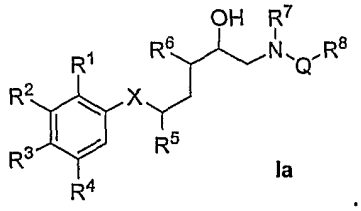
R^{10} is 1) hydrogen, lower alkyl, lower haloalkyl, $(C_8$-$C_{15})$alkyl, $(C_8$-$C_{15})$haloalkyl, cycloalkyl, halocycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, or 2) aryl or aryl-lower alkyl

wherein aryl is optionally substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

or R^9 and R^{10} taken together with the nitrogen to which they are attached form a 4-, 5-, 6- or 7-membered heterocyclic ring composed of carbon atoms and 0 or 1 N, O, or S atoms in addition to the nitrogen atom to which R^9 and R^{10} are attached, said ring atoms being substituted with the appropriate number of hydrogen atoms and optionally substituted with up to four groups independently selected from halogen, $(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, lower alkanoyl, lower alkoxycarbonyl, aryl, aryl-lower alkyl, and oxo, such that substitution of one oxo group on a carbon atom forms a carbonyl group and substitution of one or two oxo groups on sulfur forms sulfoxide or sulfone groups respectively; wherein the aryl and arylalkyl groups are substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

and the enantiomers, diastereomers, and salts thereof.

2. A compound of claim 1 of the formula **Ia**



Ia

3. A compound of claim 2, wherein

R^1 is hydrogen or aryl;

R^2 is hydrogen, lower alkyl, cycloalkyl-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, lower alkoxy-lower alkoxy, lower haloalkoxy-lower alkoxy, lower alkoxy-lower alkoxy-lower alkyl; cycloalkyl-lower alkoxy, phenyl-lower alkoxy that is unsubstituted or substituted by lower alkyl, lower alkoxy, hydroxy, halogen, nitro and/or by amino; optionally N-oxidized pyridyl-lower alkoxy, lower alkylthio-lower alkoxy, lower alkane-sulfonyl-lower alkoxy, lower alkanoyl-lower alkoxy, cyano-lower alkoxy, carboxy-lower alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, lower alkylcarbamoyl-lower alkoxy, or di-lower alkylcarbamoyl-lower alkoxy;

R^3 is hydrogen, halogen, cyano, lower alkyl, lower haloalkyl, aryl, hydroxy, lower alkoxy, or polyhalo-lower alkoxy; or

R^2 and R^3 taken together with the atoms through which they are attached form a fused dioxolane ring, wherein said ring is substituted with up to 2 substituents independently selected from lower alkyl and lower alkoxy-lower alkyl;

R^4 is hydrogen, lower alkoxy-lower alkoxy, lower alkoxy-lower alkyl, or cyloalkyl-lower alkoxy; or

R^3 and R^4 taken together with the atoms through which they are attached form a fused dioxolane ring, wherein said ring is substituted with up to 2 substituents independently selected from lower alkyl and lower alkoxy-lower alkyl; provided that R^3 does not form a ring with R^2;

X is methylene or hydroxymethylene;

R^5 is lower alkyl or cycloalkyl;

R^6 is amino, lower alkylamino, di-lower alkylamino, or lower alkanoylamino;

R^7 is hydrogen or methyl;

Q is carbonyl, thiocarbonyl, or sulfonyl;

R^8 is lower alkyl, lower haloalkyl, C_8-C_{15} alkyl, C_8-C_{15} haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, cycloalkoxy-lower alkyl, cycloalkoxy-cycloalkyl, lower alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, lower alkylthio-cycloalkyl, lower haloalkylthio-cycloalkyl, lower alkanesulfonyl-cycloalkyl, lower haloalkanesulfonyl-cycloalkyl, aryl, aryl-lower alkyl, aryl-lower hydroxyalkyl, arylcycloalkyl, aryloxy-lower alkyl, aryloxy cycloalkyl, arylthio-lower alkyl, arylsulfonyl-lower alkyl, arylthio-cycloalkyl, or arylsulfonyl-cycloalkyl wherein said aryl, aryloxy, arylthio and arylsulfonyl groups are optionally substituted with up to four groups independently selected from halo, cyano, nitro, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, optionally halogenated lower alkanesulfonyl, amino, lower alkylamino, di-lower allkylamino, and lower alkoxycarbonyl;

or R^8 is OR^9 or NR^9R^{10};

R^9 is selected from 1) hydrogen, lower alkyl, lower haloalkyl, lower alkenyl, (C_8-C_{15})alkyl, (C_8-C_{15})haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-loweralkyl, lower haloalkoxy-lower alkyl, cycloalkoxy-lower alkyl, cycloalkoxy-cycloalkyl, lower alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, lower alkylthio-cycloalkyl, lower haloalkylthio-cycloalkyl, lower alkanesulfonyl-cycloalkyl, lower haloalkanesulfonyl-cycloalkyl, aminocarbonyl-lower alkyl, lower alkyl-amonocarbonyl-lower alkyl, or di(lower alkyl)-amonocarbonyl-lower alkyl, or 2) aryl, aryl-lower alkyl, aryloxy-lower alkyl, arylthio-lower alkyl, or arylsulfonyl-lower alkyl

wherein aryl is optionally substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

R^{10} is 1) hydrogen, lower alkyl, lower haloalkyl, (C_8-C_{15})alkyl, (C_8-C_{15})haloalkyl, cycloalkyl, halocycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, alkylthio-lower alkyl, lower

haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, or lower haloalkanesulfonyl-lower alkyl, or 2) aryl or aryl-lower alkyl wherein aryl is optionally substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

or R^9 and R^{10} taken together with the nitrogen to which they are attached form a 4-, 5-, 6- or 7-membered heterocyclic ring composed of carbon atoms and 0 or 1 N, O, or S atoms in addition to the nitrogen atom to which R^9 and R^{10} are attached, said ring atoms being substituted with the appropriate number of hydrogen atoms and optionally substituted with up to four groups independently selected from halogen, $(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl , lower alkanoyl, lower alkoxycarbonyl, aryl, aryl-lower alkyl, and oxo, such that substitution of one oxo group on a carbon atom forms a carbonyl group and substitution of one or two oxo groups on sulfur forms sulfoxide or sulfone groups respectively; wherein the aryl and arylalkyl groups are substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;
and the enantiomers, diastereomers, and salts thereof.

4. A compound of claim 3, wherein

R^1 is hydrogen;

R^2 is $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkoxy, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, or cyloalkyl-lower alkoxy;

R^3 is fluoro, chloro, bromo, cyano, $(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$ haloalkyl, aryl, $(C_1$-$C_4)$alkoxy, or $(C_1$-$C_4)$haloalkoxy;

R^4 is hydrogen;

X is methylene;

R^5 is $(C_3$-$C_5)$alkyl;

R^6 is amino;

R^7 is hydrogen or methyl;

Q is carbonyl or sulfonyl;

R^8 is $(C_3$-$C_{11})$alkyl, $(C_3$-$C_{11})$haloalkyl, $(C_3$-$C_7)$cycloalkyl, $(C_3$-$C_{11})$cycloalkylalkyl, $(C_3$-$C_{11})$-alkoxyalkyl, aryl, aryl$(C_1$-$C_3)$alkyl, aryl$(C_3$-$C_6)$cycloalkyl, arylhydroxy$(C_1$-$C_3)$alkyl, aryloxy$(C_1$-$C_5)$alkyl, or aryloxy$(C_3$-$C_6)$cycloalkyl wherein aryl or aryloxy may be unsubstituted or substituted with one to three groups independently selected from halogen, cyano, $(C_1$-$C_3)$alkyl, halo$(C_1$-$C_3)$alkyl, $(C_1$-$C_3)$alkoxy, halo$(C_1$-$C_3)$alkoxy;

or R^8 is NR^9R^{10};

R^9 is 1) hydrogen, $(C_1$-$C_{10})$alkyl, $(C_3$-$C_7)$alkenyl, $(C_3$-$C_7)$cycloalkyl, $(C_3$-$C_6)$cycloalkyl$(C_1$-$C_5)$alkyl, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, or aminocarbonyl$(C_1$-$C_5)$alkyl, or

2) aryl or aryl$(C_1$-$C_4)$alkyl

wherein aryl is optionally substituted with up to 4 groups independently selected from fluorine, chlorine, cyano, $(C_1$-$C_3)$alkyl, halo$(C_1$-$C_3)$alkyl, $(C_1$-$C_3)$alkoxy, halo$(C_1$-$C_3)$alkoxy, and $(C_1$-$C_3)$alkanesulfonyl;

R^{10} is hydrogen, lower alkyl, or lower haloalkyl; or

R^8 and R^9 taken together are with the nitrogen to which they are attached form an azetidine, pyrrolidine, piperidine, azepine, piperazine, morpholine, or thiomorpholine ring said ring being optionally substituted with up to two groups independently selected from halogen, $(C_1$-$C_3)$alkyl, halo$(C_1$-$C_3)$alkyl, and oxo, such that substitution of one oxo group on a carbon atom forms a carbonyl group and substitution of one or two oxo groups on sulfur forms sulfoxide or sulfone groups respectively;

and the enantiomers, diastereomers, and salts thereof.

5. A compound of claim 3,wherein:

R^1 is hydrogen;

R^2 is 3-methoxypropoxy, 3-ethoxypropoxy, 4-methoxybutyl, or 2-(cyclopropyl)ethoxy;

R^3 is fluoro, chloro, bromo, cyano, methyl, ethyl, isopropyl or tert-butyl, trifluoromethyl, pentafluoroethyl, phenyl, methoxy, difluoromethoxy, or trifluoromethoxy;

R^4 is hydrogen;

X is methylene;

R^5 is branched (C_3-C_5)alkyl;

R^6 is amino;

R^7 is hydrogen;

Q is carbonyl or sulfonyl; and

R^8 is propyl, 2,2-dimethylpropyl, butyl, tert-butyl, n-pentyl, 2-methyl-2-butyl, hexyl, 2-hexyl, 2-methyl-2-pentyl, 2,2-dimethylpentyl, 3-heptyl, 2-methyl-2-hexyl, 2,4,4-trimethylpentyl, 2,2,2-trifluoroethyl, 3,3,3-trifluoropropyl, 4,4,4-trifluorobutyl, 1,1,1,3,3,3-hexafluoro-2-methyl-2-propyl, cyclohexyl, 1-methylcyclohexyl, 4-methylcyclohexyl, cyclopropylmethyl, cyclopentylmethyl, 1-cyclopentyl-1-pentyl, cyclohexylmethyl, 2-cyclohexyl-2-propyl, 2-cyclopropyl-1,1-dimethylethyl, 3-cyclopropyl-2-methyl-2-butyl, 3-methoxypropyl, 2-propoxy-2-propyl, phenyl, benzyl, 3-methyl-benzyl, 2-fluorobenzyl, 3-fluorobenzyl, 4-fluorobenzyl, 2,4-difluorobenzyl, 2,3-difluorobenzyl, 3,4-difluorobenzyl, 4-cyanobenzyl, 2-(trifluoromethyl)benzyl, 3-(trifluoromethyl)benzyl, 4-(trifluoro-methyl)benzyl, 4-(trifluoromethoxy)benzyl, phenethyl, 3-phenylpropyl, 2-phenyl-2-propyl, 3-(4-fluorophenyl)-3-pentyl, 1-phenyl-1-cyclopropyl, 1-(4-methylphenyl)-1-cyclopropyl, 1-(4-fluoro-phenyl)-1-cyclopropyl, 1-(4-methoxyphenyl)-1-cyclopropyl, 1-(2,4-dichlorophenyl)-1-cyclopropyl, 1-phenyl-1-cyclopentyl, 1-phenyl-1-cyclohexyl, 1-(4-fluorophenyl)-1-cyclohexyl, 3-hydroxy-2-methyl-3-phenyl-2-propyl, 2-(4-cyanophenoxy)-2-propyl, or 2-(4-chlorophenoxy)-2-propyl;

or R^8 is NR^9R^{10};

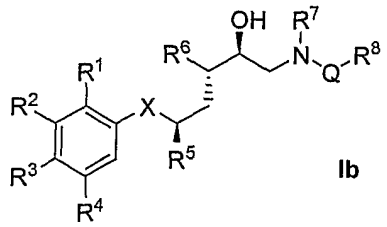
R^9 is hydrogen, butyl, isobutyl, t-butyl, pentyl, hexyl, 2,2-dimethyl-1-pentyl, 2-methyl-2-hexyl, 2,4,4-trimethyl-2-pentyl, allyl, 2-(cyclopropyl)ethyl, cyclohexylmethyl, 2-(cyclohexyl)methyl, cyclohexyl, 2-methoxyethyl, benzyl, 2-phenylethyl, 3-phenylpropyl, 3-(4-fluorophenyl)-2-methyl-2-propyl, 3-fluorophenyl, 3-(trifluoromethyl)phenyl, or 2-(aminocarbonyl)-2-methyl-1-propyl,

R^{10} is hydrogen, methyl, or isobutyl;

or R^9-R^{10} is $-(CH_2)_5-$ or $-(CH_2)_2O(CH_2)_2-$;

and the enantiomers, diastereomers, and salts thereof.

6. A compound of claim 3, wherein at least one, two, or preferably all three of the asymmetric carbon atoms of the main chain have the stereochemical configuration shown in formula **Ib**



Ib

and the pharmaceutically acceptable salts thereof.

7. A compound of claim1, wherein X is methylene and R^5 is isopropyl.

8. A compound of claim 3, wherein X is methylene and R^5 is isopropyl.

9. A compound of claim 6, wherein R^5 is isopropyl.

10. A compound of claim 1 which is:

Cpd. No.	Name
I-1	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)butyramide
I-2	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclopropylacetamide
I-3	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)pentanamide
I-4	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)pivalamide
I-5	N-((2S,3S,5S)-5-(3-(2-cyclopropylethoxy)benzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-6	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)hexanamide
I-7	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylbutanamide
I-8	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3,3-dimethylbutanamide
I-9	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-methoxybutanamide
I-10	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)benzamide
I-11	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3,3,3-trifluoropropanamide
I- 12	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclopentylacetamide
I-13	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)cyclohexanecarboxamide
I-14	N-((2S,3S,5S)-5-(3-(3-ethoxypropoxy)benzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-15	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)heptanamide

I-16 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylpentanamide

I-17 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methylhexanamide

I-18 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-phenylacetamide

I-19 (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-6-methyl-1-(butanesulfonylamino)heptan-2-ol

I-20 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxyheptyl)-4,4,4-trifluorobutanamide

I-21 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclohexylacetamide

I-22 1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(1-(4-fluorophenyl)-2-methylpropan-2-yl)urea

I-23 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-methylcyclohexanecarboxamide

I-24 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-methylcyclohexanecarboxamide

I-25 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-ethylbenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide

I-26 N-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-ethylbenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide

I-27 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-N-isopropylpentanamide

I-28 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide

I-29 N-((2R,3R,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide

I-30 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3,3-dimethylhexanamide

I-31 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-ethylhexanamide

I-32 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methyl-2-propoxypropanamide

I-33 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-ethoxy-2,2-dimethylpropanamide

I-34 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-phenylpropanamide

I-35 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-m-tolylacetamide

I-36 (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-6-methyl-1-(pentanesulfonylamino)heptan-2-ol

I-37 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(2-fluorophenyl)acetamide

I-38 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(3-fluorophenyl)acetamide

I-39 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)acetamide

I-40 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)acetamide

I-41 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-5,5,5-trifluoropentanamide

I-42 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-cyclopropyl-2,2-dimethylbutanamide

I-43 N-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)- 4-cyclopropyl-2,2-dimethylbutanamide

I-44 (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-6-methyl-1-(benzenesulfonylamino)heptan-2-ol

I-45 N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3,5,5-trimethylhexanamide

I-46	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-N,2,2-trimethylhexanamide
I-47	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-cyanophenyl)acetamide
I-48	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-phenylcyclopropanecarboxamide
I-49	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-phenylbutanamide
I-50	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methyl-2-phenylpropanamide
I-51	N-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methyl-2-phenylpropanamide
I-52	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclohexyl-2-methylpropanamide
I-53	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(3,4-difluorophenyl)acetamide
I-54	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(2,4-difluorophenyl)acetamide
I-55	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(2,3-difluorophenyl)acetamide
I-56	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-6-methyl-1-(benzylsulfonylamino)heptan-2-ol
I-57	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-p-tolylcyclopropanecarboxamide
I-58	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-isopropyl-N-butanesulfonylamino)-6-methylheptan-2-ol
I-59	(2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-isopropyl-N-butanesulfonylamino)-6-methylheptan-2-ol
I-60	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)-2-methylpropanamide
I-61	N-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)-2-methylpropanamide
I-62	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)-2-methylpropanamide
I-63	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclopentylhexanamide
I-64	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-phenylcyclopentanecarboxamide
I-65	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-phenylbenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-66	N-((2S,3S,5S)-5-(5-(3-methoxypropoxy)-2-phenylbenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-67	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-(4-methoxyphenyl)cyclopropanecarboxamide
I-68	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-bromobenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-69	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-hydroxy-2,2-dimethyl-3-phenylpropanamide
I-70	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-(4-chlorophenyl)cyclopropanecarboxamide
I-71	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-isopropyl-N-benzenesulfonylamino)-6-methylheptan-2-ol
I-72	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(2-(trifluoromethyl)phenyl)acetamide
I-73	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(3-(trifluoromethyl)phenyl)acetamide
I-74	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-(trifluoromethyl)phenyl)acetamide
I-75	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-phenylcyclohexanecarboxamide

I-76	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-cyanophenoxy)-2-methylpropanamide
I-77	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-bis(trifluoromethyl)propanamide
I-78	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-ethyl-2-(4-fluorophenyl)butanamide
I-79	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-isopropyl-N-benzylsulfonylamino)-6-methylheptan-2-ol
I-80	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-chlorophenoxy)-2-methylpropanamide
I-81	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-(trifluoromethoxy)phenyl)acetamide
I-82	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-(4-fluorophenyl)cyclohexanecarboxamide
I-83	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-(2,4-dichlorophenyl)cyclopropanecarboxamide
I-84	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)urea
I-85	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-butylurea
I-86	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-tert-butylurea
I-87	isobutyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptylcarbamate
I-88	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)piperidine-1-carboxamide
I-89	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-cyclopropylethyl)urea
I-90	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)morpholine-4-carboxamide
I-91	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylurea
I-92	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylurea
I-93	1-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylurea
I-94	pentyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptylcarbamate
I-95	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(3-methoxypropyl)urea
I-96	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-ethoxyethyl)urea
I-97	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-cyclohexylurea
I-98	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-hexylurea
I-99	3-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-methyl-1-pentylurea
I-100	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-methyl-3-pentylurea
I-101	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylthiourea
I-102	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-benzylurea
I-103	benzyl (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptylcarbamate
I-104	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(butylaminosulfonylamino)-6-methylheptan-2-ol
I-105	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(3-fluorophenyl)urea

I-106	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(cyclohexylmethyl)urea
I-107	3-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-cyclohexyl-1-methylurea
I-108	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-(butylaminosulfonyl)-N-isopropylamino)-6-methylheptan-2-ol
I-109	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2,2-dimethylpentyl)urea
I-110	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-methylhexan-2-yl)urea
I-111	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-carbamoyl-2-methylpropyl)urea
I-112	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-phenethylurea
I-113	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(pentylaminosulfonylamino)-6-methylheptan-2-ol
I-114	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2-cyclohexylethyl)urea
I-115	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2,4,4-trimethylpentan-2-yl)urea
I-116	3-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1,1-diisobutylurea
I-117	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(3-phenylpropyl)urea
I-118	(2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-1-(N-(allylaminosulfonyl)-N-isopropylamino)-6-methylheptan-2-ol
I-119	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(3-(trifluoromethyl)phenyl)urea or
I-120	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(1-(4-fluorophenyl)-2-methylpropan-2-yl)urea

and their enantiomers, diastereomers and salts.

11. A compound of claim 1 which is:

Cpd. No.	Name
I-28	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-42	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-cyclopropyl-2,2-dimethylbutanamide
I-50	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methyl-2-phenylpropanamide
I-52	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclohexyl-2-methylpropanamide or
I-62	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)-2-methylpropanamide

and their enantiomers, diastereomers and salts.

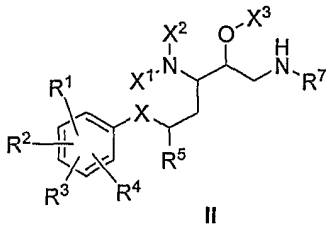
12. A compound of claim 1 which is:

Cpd. No.	Name
I-6	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)hexanamide
I-17	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-methylhexanamide
I-21	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-cyclohexylacetamide
I-26	N-((2R,3S,5S)-5-(3-(3-methoxypropoxy)-4-ethylbenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2,2-dimethylhexanamide
I-31	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-ethylhexanamide
I-33	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-ethoxy-2,2-dimethylpropanamide
I-39	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)acetamide
I-40	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-fluorophenyl)acetamide
I-42	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-cyclopropyl-2,2-dimethylbutanamide
I-74	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-(4-(trifluoromethyl)phenyl)acetamide
I-75	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-phenylcyclohexanecarboxamide
I-78	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-2-ethyl-2-(4-fluorophenyl)butanamide
I-82	N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-(4-fluorophenyl)cyclohexanecarboxamide
I-85	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-butylurea
I-91	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylurea
I-92	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-pentylurea
I-98	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-hexylurea
I-99	3-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1-methyl-1-pentylurea
I-109	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2,2-dimethylpentyl)urea
I-115	1-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-3-(2,4,4-trimethylpentan-2-yl)urea or
I-116	3-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-1,1-diisobutylurea

and their enantiomers, diastereomers and salts.

13. A compound of claim 1 which is:
N-((2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-3-amino-2-hydroxy-6-methylheptyl)-4-cyclopropyl-2,2-dimethylbutanamide and its enantiomers, diastereomers and salts.

14. A compound of formula **II**:



II

wherein

R^1 is hydrogen, halogen, hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, lower alkylthio-lower alkoxy, cyano-lower alkoxy, hydroxy-lower alkoxy, carboxy-lower alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, N-mono- or N,N-di-lower alkylcarbamoyl-lower alkoxy, or aryl;

R^2 is hydrogen, halogen, cyano, carbamoyl, lower alkyl, lower haloalkyl, cycloalkyl, halocycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-loweralkyl, cyano-lower alkyl, hydroxy-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, lower alkoxy-lower alkoxy-lower alkyl, lower haloalkoxy-lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, halocycloalkoxy-lower alkyl, hydroxy, lower alkanoyloxy-lower alkoxy, hydroxy-lower alkoxy, halo-(hydroxy)-lower alkoxy, lower alkanesulfonyl-(hydroxy)-lower alkoxy, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, lower alkanoylamino-lower alkyl, lower alkoxycarbonyl-amino-lower alkyl, aminocarbonylamino-lower alkyl, lower alkylaminocarbonylamino-lower alkyl, di(lower alkyl)aminocarbonylamino-lower alkyl, aminosulfonylamino-lower alkyl, lower alkylaminosulfonylamino-lower alkyl, di(lower alkyl)aminosulfonylamino-lower alkyl, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy, lower alkanoylamino-lower alkoxy, lower alkoxycarbonyl-amino-lower alkoxy, aminocarbonylamino-lower alkoxyl, lower alkylaminocarbonylamino-lower alkoxy, di(lower alkyl)aminocarbonylamino-lower alkoxy, aminosulfonylamino-lower alkoxy, lower alkylaminosulfonylamino-lower alkoxy, di(lower alkyl)aminosulfonylamino-lower alkoxy, oxo-lower alkoxy, lower alkoxy, lower haloalkoxy, cycloalkoxy, lower halocycloalkoxy, cycloalkyl-lower alkoxy, halocycloalkyl-lower alkoxy, lower alkenyloxy, cycloalkoxy-lower alkoxy, halocycloalkoxy-lower alkoxy, lower alkoxy-lower alkoxy, lower haloalkoxy-lower

alkyl, lower alkoxy-lower alkenyl, lower alkenyloxy-lower alkoxy, lower alkoxy-lower alkenyloxy, lower alkenyloxy-lower alkyl, lower alkanoyl-lower alkoxy, lower alkylthio-lower alkoxy, lower alkanesulfonyl-lower alkoxy, lower alkylthio-(hydroxy)-lower alkoxy, aryl-lower alkoxy, optionally N-oxidized pyridyl-lower alkoxy, thiazolylthio-lower alkoxy or thiazolinylthio-lower alkoxy, imidazolylthio-lower alkoxy, optionally N-oxidized pyridylthio-lower alkoxy, pyrimidinylthio-lower alkoxy, cyano-lower alkoxy, carboxy-lower alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, N-mono- or N,N-di-lower alkylcarbamoyl-lower alkoxy, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, carbamoyl-lower alkyl, or N-mono- or N,N-di-lower alkylcarbamoyl-lower alkyl;

R^3 is hydrogen, halogen, cyano, carbamoyl, lower alkyl, lower haloalkyl, lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, hydroxy-lower alkyl, lower alkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, optionally partially hydrogenated or N-oxidized pyridyl-lower alkyl, thiazolyl-thio-lower alkyl or thiazolinylthio-lower alkyl, imidazolylthio-lower alkyl, optionally N-oxidized pyridylthio-lower alkyl, pyrimidinylthio-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, lower alkanoyl-amino-lower alkyl, lower alkanesulfonylamino-lower alkyl, polyhalo-lower alkane-sulfonylamino-lower alkyl, pyrrolidino-lower alkyl, piperidino-lower alkyl, piperazino-lower alkyl, N'-lower alkylpiperazino-lower alkyl or N'-lower alkanoylpiperazino-lower alkyl, morpholino-lower alkyl, thiomorpholino-lower alkyl, S-oxothiomorpholino-lower alkyl or S,S-dioxothio-morpholino-lower alkyl, cyano-lower alkyl, carboxy-lower alkyl, lower alkoxy-carbonyl-lower alkyl, carbamoyl-lower alkyl, N-mono- or N,N-di-lower alkyl-carbamoyl-lower alkyl, cycloalkyl; phenyl or naphthyl that is unsubstituted or substituted with one to three groups independently selected from lower alkyl, lower alkoxy, hydroxy, lower alkylamino, di-lower alkylamino, halogen, trifluoromethyl, trifluoromethoxy, and cyano; hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, cycloalkoxy-lower alkoxy, hydoxy-lower alkoxy, aryl, lower haloalkoxy, lower alkylthio-lower alkoxy,lower haloalkylthio-lower alkoxy, lower alkanesulfonyl-lower alkoxy, lower haloalkanesulfonyl-lower alkoxy, optionally hydrogenated heteroaryl-lower alkoxy, heterocyclyl-lower alkoxy, optionally partially or fully hydrogenated heteroarylthio-lower alkoxy, such as thiazolylthio-lower alkoxy or thiazolinylthio-lower alkoxy, imidazolylthio-lower alkoxy, optionally N-oxidized pyridylthio-lower alkoxy, pyrimidinylthio-lower alkoxy, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy, lower alkanoylamino-lower alkoxy, lower alkanesulfonylamino-lower alkoxy, polyhalo-lower alkanesulfonylamino-lower alkoxy,

pyrrolidino-lower alkoxy, piperidino-lower alkoxy, piperazino- lower alkoxy, N'-lower alkylpiperazino- lower alkoxy or N'-lower alkanoylpiperazino-lower alkoxy, morpholino-lower alkoxy, thiomorpholino- lower alkoxy, S-oxothiomorpholino- lower alkoxy or S,S-dioxothiomorpholino-lower alkoxy, cyano-lower alkoxy, carboxy-lower alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, N-mono- or N,N-di-lower alkylcarbamoyl-lower alkoxy, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, carbamoyl-lower alkyl, or N-mono- or N,N-di-lower alkylcarbamoyl-lower alkyl; or

R^2 and R^3 taken together with the atoms through which they are attached form a fused dioxolane, dioxane, benzene or cyclohexene ring, wherein said ring is substituted with up to 2 substituents independently selected from lower alkyl and lower alkoxy-lower alkyl;

R^4 is hydrogen, lower alkyl, hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, or cycloalkyl-lower alkoxy; or

R^3 and R^4 taken together with the atoms through which they are attached form a fused dioxolane, dioxane, benzene or cyclohexene ring, wherein said ring is substituted with up to 2 substituents independently selected from lower alkyl and lower alkoxy-lower alkyl; provided that R^3 does not form a ring with R^2;

X is methylene or hydroxymethylene;

R^5 is lower alkyl, lower haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, lower haloalkyl-cycloalkyl, cycloalkyl-lower alkyl, aryl, aryl-lower alkyl, heterocyclyl, heterocyclyl-lower alkyl;

R^6 is amino, lower alkylamino, di-lower alkylamino, or lower alkanoylamino;

R^7 is hydrogen, lower alkyl, lower haloalkyl, cycloalkyl, lower alkoxy-lower alkyl, or lower haloalkoxy-lower alkyl;

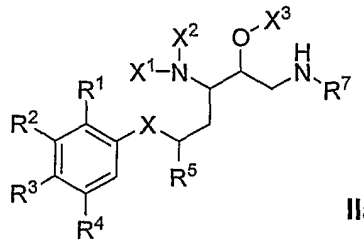
X^1 is an amino-protecting group;

X^2 is hydrogen or together with X^3 is a bivalent protecting group;

X^3 is hydrogen or a hydroxy-protecting group;

and the enantiomers, diastereomers, and salts thereof.

15. A compound of claim 14 of the formula **IIa**



IIa

16. A compound of claim 15, wherein

R^1 is hydrogen or aryl;

R^2 is hydrogen, lower alkyl, cycloalkyl-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, lower alkoxy-lower alkoxy, lower haloalkoxy-lower alkoxy, lower alkoxy-lower alkoxy-lower alkyl; cycloalkyl-lower alkoxy, phenyl-lower alkoxy that is unsubstituted or substituted by lower alkyl, lower alkoxy, hydroxy, halogen, nitro and/or by amino; optionally N-oxidized pyridyl-lower alkoxy, lower alkylthio-lower alkoxy, lower alkane-sulfonyl-lower alkoxy, lower alkanoyl-lower alkoxy, cyano-lower alkoxy, carboxy-lower alkoxy, lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, lower alkylcarbamoyl-lower alkoxy, or di-lower alkylcarbamoyl-lower alkoxy;

R^3 is hydrogen, halogen, cyano, lower alkyl, lower haloalkyl, aryl, hydroxy, lower alkoxy, or polyhalo-lower alkoxy; or

R^2 and R^3 taken together with the atoms through which they are attached form a fused dioxolane ring, which is substituted with up to 2 substituents independently selected from lower alkyl and lower alkoxy-lower alkyl;

R^4 is hydrogen, lower alkoxy-lower alkoxy, lower alkoxy-lower alkyl, or cyloalkyl-lower alkoxy; or

R^3 and R^4 taken together with the atoms through which they are attached form a fused dioxolane ring which is substituted with up to 2 substituents independently selected from lower alkyl and lower alkoxy-lower alkyl; provided that R^3 does not form a ring with R^2;

X is methylene or hydroxymethylene;

R^5 is lower alkyl or cycloalkyl;

R^7 is hydrogen or methyl;

X^1 is lower alkoxycarbonyl, 2-(trialkylsily)ethoxycarbonyl, or α-phenyl- or α,α-diphenyl-lower alkoxycarbonyl that is unsubstituted or substituted by lower alkyl, lower alkoxy, nitro and/or by halogen, or is 2-halo-lower alkoxycarbonyl;

X^2 is hydrogen or together with X^3 is carbonyl or lower alkylidene;

X^3 is hydrogen, tri-lower alkylsilyl;

and the enantomers, diastereomers, and salts thereof.

17. A compound of claim 16, wherein

R^1 is hydrogen;

R^2 is $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkoxy, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, or cyloalkyl-lower alkoxy;

R^3 is fluoro, chloro, bromo, cyano, $(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$ haloalkyl, aryl, $(C_1$-$C_4)$alkoxy, or $(C_1$-$C_4)$haloalkoxy;

R^4 is hydrogen;

X is methylene;

R^5 is $(C_3$-$C_5)$alkyl;

R^7 is hydrogen;

X^1 is lower alkoxycarbonyl, or α-phenyl-lower alkoxycarbonyl that is unsubstituted or substituted by lower alkyl, lower alkoxy, nitro, and/or by halogen;

X^2 and X^3 are both hydrogen, or taken together are lower alkylidene;

and the enantiomers, diastereomers, and salts thereof.

18. A compound of claim 17, wherein

R^1 is hydrogen;

R^2 is 3-methoxypropoxy, 3-ethoxypropoxy, 4-methoxybutyl, or 2-(cyclopropyl)ethoxy;

R^3 is fluoro, chloro, bromo, cyano, methyl, ethyl, isopropyl or tert-butyl, trifluoromethyl, pentafluoroethyl, phenyl, methoxy, difluoromethoxy, or trifluoromethoxy;

R^4 is hydrogen;

X is methylene;

R^5 is branched (C_3-C_5)alkyl;

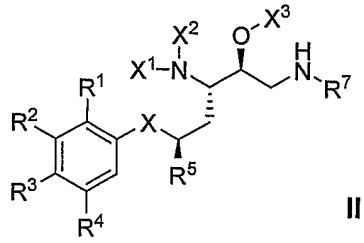
R^7 is hydrogen;

X^1 is lower alkoxycarbonyl, or α-phenyl-lower alkoxycarbonyl that is unsubstituted or substituted by lower alkyl, lower alkoxy, nitro, and/or by halogen;

X^2 and X^3 are both hydrogen, or taken together are lower alkylidene;

and the enantiomers, diastereomers, and salts thereof.

19. A compound of claim 15, wherein at least one, preferably all, of the asymmetric carbon atoms of the main chain have the stereochemical configuration shown in formula **IIb**



IIb

and the salts thereof.

20. A compound of claim 19, wherein

R^1 and R^4 is each hydrogen;

R^2 is 3-methoxypropoxy, 3-ethoxypropoxy, 4-methoxybutyl, or 2-(cyclopropyl)ethoxy;

R^3 is is fluoro, chloro, bromo, cyano, methyl, ethyl, isopropyl or tert-butyl, trifluoromethyl, pentafluoroethyl, phenyl, methoxy, difluoromethoxy, or trifluoromethoxy;

X is methylene;

R^5 is isopropyl;

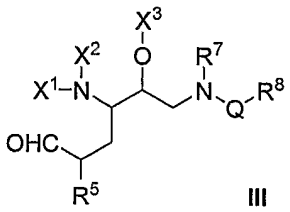
R^7 is hydrogen;

X^1 is tert-butoxycarbonyl; and

X^2 and X^3 are both hydrogen, or taken together are isopropylidene

and the salts thereof.

21. A compound of formula **III**



III

wherein

R^5 is lower alkyl or cycloalkyl;

R^7 is hydrogen, lower alkyl, lower haloalkyl, cycloalkyl, lower alkoxy-lower alkyl, or lower lower haloalkoxy-lower alkyl

Q is carbonyl, thiocarbonyl, or sulfonyl;

R^8 is lower alkyl, lower haloalkyl, C_8-C_{15}alkyl, C_8-C_{15}haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-loweralkyl, lower haloalkoxy-lower alkyl, cycloalkoxy-lower alkyl, cycloalkoxy-cycloalkyl, lower alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, lower alkylthio-cycloalkyl, lower haloalkylthio-cycloalkyl, lower alkanesulfonyl-cycloalkyl, lower haloalkanesulfonyl-cycloalkyl, aryl, aryl-lower alkyl, aryl-lower hydroxyalkyl, arylcycloalkyl, aryloxy-lower alkyl, aryloxy cycloalkyl, arylthio-lower alkyl, arylsulfonyl-lower alkyl, arylthio-cycloalkyl, arylsulfonyl-cycloalkyl, lower alkanoyl-lower alkyl, hydroxy-lower alkyl, amino-lower alkyl, lower alkanoylamino-lower alkyl, N-mono-lower alkylamino-lower alkyl, N,N-di-lower alkylamino-lower alkyl, piperidino-lower alkyl, hydroxypiperidino-lower alkyl, lower alkoxypiperidino-lower alkyl, morpholino-lower alkyl, dimethylmorpholino-lower alkyl, thiomorpholino-lower alkyl, S,S-dioxothiomorpholino-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower

alkyl, carbamoyl-lower alkyl, N-mono- lower alkylcarbamoyl-lower alkyl, N,N-di-lower alkylcarbamoyl-lower alkyl, carboxy-(hydroxy)-lower alkyl, lower alkoxycarbonyl-(hydroxy)-lower alkyl, carbamoyl-(hydroxy)-lower alkyl, N-mono- lower alkylcarbamoyl-(hydroxy)-lower alkyl, N,N-di-lower alkylcarbamoyl-(hydroxy)-lower alkyl, 5- or 6-membered carboxycycloalkyl-lower alkyl, 5- or 6-membered lower alkoxycarbonyl-cycloalkyl-lower alkyl, 5- or 6-membered carbamoylcycloalkyl-lower alkyl, 5- or 6-membered N-mono-alkylcarbamoylcycloalkyl-lower alkyl, N,N-di-lower alkylcarbamoylcycloalkyl-lower alkyl, cyano-lower alkyl, sulfamoyl-lower alkyl, lower alkylsulfamoyl-lower alkyl, or di-lower alkylsulfamoyl-lower alkyl, imidazolyl-lower alkyl, oxopyrrolidinyl-lower alkyl, benzimidazolyl-lower alkyl, oxadiazolyl-lower alkyl, pyridyl-lower alkyl, oxopiperidinyl-lower alkyl or quinolinyl-lower alkyl, piperidin-4-yl-lower alkyl, or lower alkanoylpiperidin-4-yl-lower alkyl, wherein said aryl, imidazolyl, benzimidazolyl, oxadiazolyl, pyridyl, quinolinyl, aryloxy, arylthio and arylsulfonyl groups are optionally substituted with up to four groups independently selected from halo, cyano, nitro, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, optionally halogenated lower alkanesulfonyl, and lower alkoxycarbonyl;

or R^8 is OR^9 or NR^9R^{10}

R^9 is 1) hydrogen, lower alkyl, lower haloalkyl, lower alkenyl, $(C_8$-$C_{15})$alkyl, $(C_8$-$C_{15})$haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-loweralkyl, lower haloalkoxy-lower alkyl, cycloalkoxy-lower alkyl, cycloalkoxy-cycloalkyl, lower alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, lower alkylthio-cycloalkyl, lower haloalkylthio-cycloalkyl, lower alkanesulfonyl-cycloalkyl, lower haloalkanesulfonyl-cycloalkyl, aminocarbonyl-lower alkyl, lower alkyl-amonocarbonyl-lower alkyl, or di(lower alkyl)-amonocarbonyl-lower alkyl, or 2) aryl, aryl-lower alkyl, aryloxy-lower alkyl, arylthio-lower alkyl, or arylsulfonyl-lower alkyl

wherein aryl is optionally substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

R^{10} is 1) hydrogen, lower alkyl, lower haloalkyl, (C_8-C_{15})alkyl, (C_8-C_{15})haloalkyl, cycloalkyl, halocycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, or lower haloalkanesulfonyl-lower alkyl, or 2) aryl or aryl-lower alkyl

wherein aryl is optionally substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

or R^9 and R^{10} taken together with the nitrogen to which they are attached form a 4-, 5-, 6- or 7-membered heterocyclic ring composed of carbon atoms and 0 or 1 N, O, or S atoms in addition to the nitrogen atom to which R^9 and R^{10} are attached, said ring atoms being substituted with the appropriate number of hydrogen atoms and optionally substituted with up to four groups independently selected from halogen, (C_1-C_6)alkyl, halo(C_1-C_6)alkyl , lower alkanoyl, lower alkoxycarbonyl, aryl, aryl-lower alkyl, and oxo, such that substitution of one oxo group on a carbon atom forms a carbonyl group and substitution of one or two oxo groups on sulfur forms sulfoxide or sulfone groups respectively; wherein the aryl and arylalkyl groups are substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

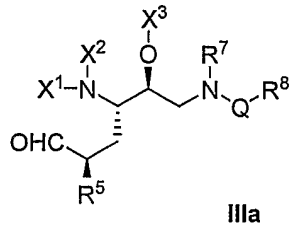
X^1 is an amino-protecting group;

X^2 is hydrogen or together with X^3 is a bivalent protecting group;

X^3 is hydrogen or a hydroxy-protecting group;

and the enantiomers, diastereomers, and salts thereof;

22. A compound of claim 20 in which at least one, preferably all three, of the asymmetric carbon atoms of the main chain have the stereochemical configuration shown in formula **IIIa**



IIIa

and the salts thereof.

23. A compound of claim 22, wherein

R^5 is lower alkyl or cycloalkyl;

R^7 is hydrogen or methyl;

Q is carbonyl or sulfonyl;

R^8 is lower alkyl, lower haloalkyl, C_8-C_{15} alkyl, C_8-C_{15} haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, cycloalkoxy-lower alkyl, cycloalkoxy-cycloalkyl, lower alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, lower alkylthio-cycloalkyl, lower haloalkylthio-cycloalkyl, lower alkanesulfonyl-cycloalkyl, lower haloalkanesulfonyl-cycloalkyl, aryl, aryl-lower alkyl, aryl-lower hydroxyalkyl, arylcycloalkyl, aryloxy-lower alkyl, aryloxy cycloalkyl, arylthio-lower alkyl, arylsulfonyl-lower alkyl, arylthio-cycloalkyl, or arylsulfonyl-cycloalkyl wherein said aryl, aryloxy, arylthio and arylsulfonyl groups are optionally substituted with up to four groups independently selected from halo, cyano, nitro, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, optionally halogenated lower alkanesulfonyl, and lower alkoxycarbonyl;

or R^8 is OR^9 or NR^9R^{10}

R^9 is 1) hydrogen, lower alkyl, lower haloalkyl, lower alkenyl, (C_8-C_{15})alkyl, (C_8-C_{15})haloalkyl, cycloalkyl, halocycloalkyl, lower alkyl-cycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-loweralkyl, lower haloalkoxy-lower alkyl, cycloalkoxy-lower alkyl, cycloalkoxy-cycloalkyl, lower alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, lower haloalkanesulfonyl-lower alkyl, lower alkylthio-cycloalkyl, lower haloalkylthio-cycloalkyl, lower alkanesulfonyl-cycloalkyl, lower haloalkanesulfonyl-cycloalkyl, aminocarbonyl-lower alkyl, lower alkyl-amonocarbonyl-lower alkyl, or di(lower alkyl)-amonocarbonyl-lower

alkyl, or 2) aryl, aryl-lower alkyl, aryloxy-lower alkyl, arylthio-lower alkyl, or arylsulfonyl-lower alkyl

wherein aryl is optionally substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

R^{10} is 1) hydrogen, lower alkyl, lower haloalkyl, $(C_8$-$C_{15})$alkyl, $(C_8$-$C_{15})$haloalkyl, cycloalkyl, halocycloalkyl, cycloalkyl-lower alkyl, halocycloalkyl-lower alkyl, lower alkoxy-lower alkyl, lower haloalkoxy-lower alkyl, alkylthio-lower alkyl, lower haloalkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, or lower haloalkanesulfonyl-lower alkyl, or 2) aryl or aryl-lower alkyl

wherein aryl is optionally substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

or R^9 and R^{10} taken together with the nitrogen to which they are attached form a 4-, 5-, 6- or 7-membered heterocyclic ring composed of carbon atoms and 0 or 1 N, O, or S atoms in addition to the nitrogen atom to which R^9 and R^{10} are attached, said ring atoms being substituted with the appropriate number of hydrogen atoms and optionally substituted with up to four groups independently selected from halogen, $(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, lower alkanoyl, lower alkoxycarbonyl, aryl, aryl-lower alkyl, and oxo, such that substitution of one oxo group on a carbon atom forms a carbonyl group and substitution of one or two oxo groups on sulfur forms sulfoxide or sulfone groups respectively; wherein the aryl and arylalkyl groups are substituted with up to four groups independently selected from halo, cyano, optionally halogenated lower alkyl, optionally halogenated lower alkoxy, optionally halogenated lower alkylthio, and optionally halogenated lower alkanesulfonyl;

X^1 is lower alkoxycarbonyl, or α-phenyl- or α,α-diphenyl-lower alkoxycarbonyl that is unsubstituted or substituted by lower alkyl, lower alkoxy, nitro and/or by halogen, or is 2-halo-lower alkoxycarbonyl;

X^2 is hydrogen or together with X^3 is carbonyl or lower alkylidene;

X^3 is hydrogen, tri-lower alkylsilyl;

and the salts thereof.

24. A compound of claim 22, wherein

R^5 is $(C_3\text{-}C_5)$alkyl;

R^7 is hydrogen;

Q is carbonyl or sulfonyl;

R^8 is $(C_3\text{-}C_{11})$alkyl, $(C_3\text{-}C_{11})$haloalkyl, $(C_3\text{-}C_7)$cycloalkyl, $(C_3\text{-}C_{11})$cycloalkylalkyl, $(C_3\text{-}C_{11})$alkoxy-alkyl, aryl, aryl$(C_1\text{-}C_3)$alkyl, aryl$(C_3\text{-}C_6)$cycloalkyl, arylhydroxy$(C_1\text{-}C_3)$alkyl, aryloxy$(C_1\text{-}C_5)$alkyl, or aryloxy$(C_3\text{-}C_6)$cycloalkyl wherein aryl or aryloxy may be unsubstituted or substituted with one to three groups independently selected from halogen, cyano, $(C_1\text{-}C_3)$alkyl, halo$(C_1\text{-}C_3)$alkyl, $(C_1\text{-}C_3)$alkoxy, and halo$(C_1\text{-}C_3)$alkoxy;

or R^8 is NR^9R^{10};

R^9 is 1) hydrogen, $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_7)$alkenyl, $(C_3\text{-}C_7)$cycloalkyl, $(C_3\text{-}C_6)$cycloalkyl$(C_1\text{-}C_5)$alkyl, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl, or aminocarbonyl$(C_1\text{-}C_5)$alkyl, or 2) aryl or aryl$(C_1\text{-}C_4)$alkyl

wherein aryl is optionally substituted with up to 4 groups independently selected from fluorine, chlorine, cyano, $(C_1\text{-}C_3)$alkyl, halo$(C_1\text{-}C_3)$alkyl, $(C_1\text{-}C_3)$alkoxy, halo$(C_1\text{-}C_3)$alkoxy, and $(C_1\text{-}C_3)$alkanesulfonyl;

R^{10} is hydrogen, lower alkyl, or lower haloalkyl; or

R^8 and R^9 taken together are with the nitrogen to which they are attached form an azetidine, pyrrolidine, piperidine, azepine, piperazine, morpholine, or thiomorpholine ring said ring being optionally substituted with up to two groups independently selected from halogen, $(C_1\text{-}C_3)$alkyl, halo$(C_1\text{-}C_3)$alkyl, and oxo, such that substitution of one oxo group on a carbon atom forms a carbonyl group and substitution of one or two oxo groups on sulfur forms sulfoxide or sulfone groups respectively;

X^1 is tert-butoxycarbonyl;

X^2 together with X^3 is isopropylidene;

and the salts thereof.

25. A compound of claim 22, wherein

R^5 is branched $(C_3$-$C_5)$alkyl;

R^7 is hydrogen;

Q is carbonyl or sulfonyl;

R^8 is propyl, 2,2-dimethylpropyl, butyl, tert-butyl, n-pentyl, 2-methyl-2-butyl, hexyl, 2-hexyl, 2-methyl-2-pentyl, 2,2-dimethylpentyl, 3-heptyl, 2-methyl-2-hexyl, 2,4,4-trimethylpentyl, 2,2,2-trifluoroethyl, 3,3,3-trifluoropropyl, 4,4,4-trifluorobutyl, 1,1,1,3,3,3-hexafluoro-2-methyl-2-propyl, cyclohexyl, 1-methylcyclohexyl, 4-methylcyclohexyl, cyclopropylmethyl, cyclopentylmethyl, 1-cyclopentyl-1-pentyl, cyclohexylmethyl, 2-cyclohexyl-2-propyl, 2-cyclopropyl-1,1-dimethylethyl, 3-cyclopropyl-2-methyl-2-butyl, 3-methoxypropyl, 2-propoxy-2-propyl, phenyl, benzyl, 3-methylbenzyl, 2-fluorobenzyl, 3-fluorobenzyl, 4-fluorobenzyl, 2,4-difluorobenzyl, 2,3-difluorobenzyl, 3,4-difluorobenzyl, 4-cyanobenzyl, 2-(trifluoromethyl)benzyl, 3-(trifluoromethyl)-benzyl, 4-(trifluoromethyl)benzyl, 4-(trifluoromethoxy)benzyl, phenethyl, 3-phenylpropyl, 2-phenyl-2-propyl, 3-(4-fluorophenyl)-3-pentyl, 1-phenyl-1-cyclopropyl, 1-(4-methylphenyl)-1-cyclopropyl, 1-(4-fluorophenyl)-1-cyclopropyl, 1-(4-methoxyphenyl)-1-cyclopropyl, 1-(2,4-dichlorophenyl)-1-cyclopropyl, 1-phenyl-1-cyclopentyl, 1-phenyl-1-cyclohexyl, 1-(4-fluorophenyl)-1-cyclohexyl, 3-hydroxy-2-methyl-3-phenyl-2-propyl, 2-(4-cyanophenoxy)-2-propyl or 2-(4-chlorophenoxy)-2-propyl;

or R^8 is NR^9R^{10};

R^9 is hydrogen, butyl, isobutyl, t-butyl, pentyl, hexyl, 2,2-dimethyl-1-pentyl, 2-methyl-2-hexyl, 2,4,4-trimethyl-2-pentyl, allyl, 2-(cyclopropyl)ethyl, cyclohexylmethyl, 2-(cyclohexyl)methyl, cyclohexyl, 2-methoxyethyl, benzyl, 2-phenylethyl, 3-phenylpropyl, 3-(4-fluorophenyl)-2-methyl-2-propyl, 3-fluorophenyl, 3-(trifluoromethyl)phenyl, or 2-(aminocarbonyl)-2-methyl-1-propyl,

R^{10} is hydrogen, methyl, or isobutyl;

or R^9-R^{10} is $-(CH_2)_5-$ or $-(CH_2)_2O(CH_2)_2-$;

X^1 is tert-butoxycarbonyl;

X^2 together with X^3 is isopropylidene;

and the salts thereof;

26. A composition comprising an effective amount of a compound of claim 1 or enantiomer, diastereomer, or salt thereof, and a pharmaceutically acceptable carrier therefor.

27. A composition of claim 26 further comprising α-blockers, β-blockers, calcium channel blockers, diuretics, angiotensin converting enzyme (ACE) inhibitors, dual ACE and neutral endopeptidase (NEP) inhibitors, angiotensin-receptor blockers (ARBs), aldosterone synthase inhibitors, aldosterone-receptor antagonists, or endothelin receptor antagonists.

28. A composition of claim 26 comprising compounds having a mean inhibition constant (IC_{50}) against renin of between about 50,000 nM to about 0.001 nM; preferably between about 100 nM to about 0.001 nM; and more preferably between about 10 nM to about 0.001 nM.

29. A method of inhibiting renin which comprises administering to a subject in need thereof a therapeutically effective amount of a compound of claim 1 or enantiomer, diastereomer, or salt thereof.

30. A method of claim 28 which comprisies administering compounds having an IC_{50} for renin of between about 50,000 nM to about 0.001 nM; preferably between about 100 nM to about 0.001 nM; and more preferably between about 10 nM to about 0.001 nM.

31. A method for treating or ameliorating an renin mediated disorder in a subject in need thereof comprising administering to said subject a therapeutically effective amount of a compound of claim 1, or enantiomer, diastereomer, or salt thereof or composition thereof.

32. A method of claim 31, wherein said disorder is hypertension, congestive heart failure, cardiac hypertrophy, cardiac fibrosis, cardiomyopathy post-infarction, nephropathy, vasculopathy and neuropathy, diseases of the coronary vessels, post-

surgical hypertension, restenosis following angioplasty, raised intra-ocular pressure, glaucoma, abnormal vascular growth, hyperaldosteronism, anxiety states, or cognitive disorders.

33. A method of claim 31 further comprising administering said compound of claim 1 or enantiomer, diastereomer, or salt thereof or composition thereof in combination with one or more additional agents selected from the group consisting of α-blockers, β-blockers, calcium channel blockers, diuretics, angiotensin converting enzyme (ACE) inhibitors, dual ACE and neutral endopeptidase (NEP) inhibitors, angiotensin-receptor blockers (ARBs), aldosterone synthase inhibitors, aldosterone-receptor antagonists, and endothelin receptor antagonist.

34. A method of claim 33 wherein:

α-blockers include doxazosin, prazosin, tamsulosin, and terazosin;

β-blockers include atenolol, bisoprol, metoprolol, acetutolol, esmolol, celiprolol, taliprolol, acebutolol, oxprenolol, pindolol, propanolol, bupranolol, penbutolol, mepindolol, carteolol, nadolol, carvedilol, and their pharmaceutically acceptable salts;

calcium channel blockers include dihydropyridines (DHPs) and non-DHPs, wherein the DHPs are selected from the group consisting of amlodipine, felodipine, ryosidine, isradipine, lacidipine, nicardipine, nifedipine, nigulpidine, niludipine, nimodiphine, nisoldipine, nitrendipine, and nivaldipine and their pharmaceutically acceptable salts and the non-DHPs are selected from the group consisting of flunarizine, prenylamine, diltiazem, fendiline, gallopamil, mibefradil, anipamil, tiapamil, and verampimil, and their pharmaceutically acceptable salts;

the diuretics include a thiazide derivative selected from amiloride, chlorothiazide, hydrochlorothiazide, methylchlorothiazide, and chlorothalidon;

ACE inhibitors include alacepril, benazepril, benazaprilat, captopril, ceronapril, cilazapril, delapril, enalapril, enalaprilat, fosinopril, lisinopril, moexipiril, moveltopril, perindopril, quinapril, quinaprilat, ramipril, ramiprilat, spirapril, temocapril, trandolapril, and zofenopril;

dual ACE/NEP inhibitors include omapatrilat, fasidotril, and fasidotrilat;

ARBs include candesartan, eprosartan, irbesartan, losartan, olmesartan, tasosartan, telmisartan, and valsartan;

aldosterone synthase inhibitors include anastrozole, fadrozole, and exemestane;

aldosterone-receptor antagonists include spironolactone and eplerenone; and

endothelin antagonists include bosentan, enrasentan, atrasentan, darusentan, sitaxentan, and tezosentan, and their pharmaceutically acceptable salts.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/003489

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07C233/36 C07C233/62 C07C275/24 C07C311/13 C07C335/12
C07D295/20 A61K31/165 A61K31/17 A61K31/18 A61K31/4453
A61P9/12 C07D263/04

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)
C07C C07D A61K A61P

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 627 182 A (GOESCHKE ET AL) 6 May 1997 (1997-05-06) column 12, line 59 - column 14, line 30; claims; examples	1,14,21, 26-34
A	WOOD J M ET AL: "Structure-based design of aliskiren, a novel orally effective renin inhibitor" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, ACADEMIC PRESS INC. ORLANDO, FL, US, vol. 308, no. 4, 5 September 2003 (2003-09-05), pages 698-705, XP004447169 ISSN: 0006-291X page 700, column 1, line 1 - page 704, column 1, line 17	1,14,21, 26-34

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 June 2006	20/06/2006

Name and mailing address of the ISA/	Authorized officer
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Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/003489

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 03/050073 A (ELAN PHARMACEUTICALS, INC; PHARMACIA & UPJOHN COMPANY; TENBRINK, RUTH;) 19 June 2003 (2003-06-19) claims; example 8	1,14,21, 26-34
P,X	WO 2005/070877 A (SPEEDEL EXPERIMENTA AG; HEROLD, PETER; STUTZ, STEFAN; STOJANOVIC, ALEK) 4 August 2005 (2005-08-04) claims; examples	1-9, 14-20, 26-34

1

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2006/003489

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

Although claims 29 - 34 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/US2006/003489

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5627182 A	06-05-1997	US 5654445 A	05-08-1997
		US 5646143 A	08-07-1997
WO 03050073 A	19-06-2003	AU 2002360508 A1	23-06-2003
		BR 0214736 A	23-11-2004
		CA 2469622 A1	19-06-2003
		EP 1453788 A1	08-09-2004
		JP 2005511735 T	28-04-2005
		MX PA04005428 A	06-12-2004
WO 2005070877 A	04-08-2005	NONE	