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(54) Title: PROTEASE INHIBITORS

(57) Abstract

The present invention provides 4–amino–azepan–3–one protease inhibitors and pharmaceutically acceptable salts, hydrates and solvates thereof which inhibit proteases, including cathepsin K, pharmaceutical compositions of such compounds, novel intermediates of such compounds, and methods for treating diseases of excessive bone loss or cartilage or matrix degradation, including osteoporosis; gingival disease including gingivitis and periodontitis; arthritis, more specifically, osteoarthritis and rheumatoid arthritis; Paget's disease; hypercalcemia of malignancy; and metabolic bone disease, comprising inhibiting said bone loss or excessive cartilage or matrix degradation by administering to a patient in need thereof a compound of the present invention.

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PROTEASE INHIBITORS

FIELD OF THE INVENTION

This invention relates in general to 4-amino-azepan-3-one protease inhibitors, particularly such inhibitors of cysteine and serine proteases, more particularly compounds which inhibit cysteine proteases, even more particularly compounds which inhibit cysteine proteases of the papain superfamily, yet more particularly compounds which inhibit cysteine proteases of the cathepsin family, most particularly compounds which inhibit cathepsin K. Such compounds are particularly useful for treating diseases in which cysteine proteases are implicated, especially diseases of excessive bone or cartilage loss, e.g., osteoporosis, periodontitis, and arthritis.

BACKGROUND OF THE INVENTION

Cathepsins are a family of enzymes which are part of the papain superfamily of cysteine proteases. Cathepsins B, H, L, N and S have been described in the literature. Recently, cathepsin K polypeptide and the cDNA encoding such polypeptide were disclosed in U.S. Patent No. 5,501,969 (called cathepsin O therein). Cathepsin K has been recently expressed, purified, and characterized. Bossard, M. J., et al., (1996) *J. Biol. Chem.* **271**, 12517-12524; Drake, F.H., et al., (1996) *J. Biol. Chem.* **271**, 12511-12516; Bromme, D., et al., (1996) *J. Biol. Chem.* **271**, 2126-2132.

Cathepsin K has been variously denoted as cathepsin O or cathepsin O2 in the literature. The designation cathepsin K is considered to be the more appropriate one.

Cathepsins function in the normal physiological process of protein degradation in animals, including humans, e.g., in the degradation of connective tissue. However, elevated levels of these enzymes in the body can result in pathological conditions leading to disease. Thus, cathepsins have been implicated as causative agents in various disease states, including but not limited to, infections by pneumocystis carinii, trypsanoma cruzi, trypsanoma brucei brucei, and Crithidia fusiculata; as well as in schistosomiasis, malaria, tumor metastasis, metachromatic leukodystrophy, muscular dystrophy, amytrophy, and the like. *See* International Publication Number WO 94/04172, published on March 3, 1994, and references cited therein. *See also* European Patent Application EP 0 603 873 A1, and references cited therein. Two bacterial cysteine proteases from P. gingivallis, called

gingipains, have been implicated in the pathogenesis of gingivitis. Potempa, J., et al. (1994) *Perspectives in Drug Discovery and Design*, **2**, 445-458.

Cathepsin K is believed to play a causative role in diseases of excessive bone or cartilage loss. Bone is composed of a protein matrix in which spindle- or plate-shaped crystals of hydroxyapatite are incorporated. Type I collagen represents the major structural protein of bone comprising approximately 90% of the protein matrix. The remaining 10% of matrix is composed of a number of non-collagenous proteins, including osteocalcin, proteoglycans, osteopontin, osteonectin, thrombospondin, fibronectin, and bone sialoprotein. Skeletal bone undergoes remodelling at discrete foci throughout life. These foci, or remodelling units, undergo a cycle consisting of a bone resorption phase followed by a phase of bone replacement.

Bone resorption is carried out by osteoclasts, which are multinuclear cells of hematopoietic lineage. The osteoclasts adhere to the bone surface and form a tight sealing zone, followed by extensive membrane ruffling on their apical (i.e., resorbing) surface. This creates an enclosed extracellular compartment on the bone surface that is acidified by proton pumps in the ruffled membrane, and into which the osteoclast secretes proteolytic enzymes. The low pH of the compartment dissolves hydroxyapatite crystals at the bone surface, while the proteolytic enzymes digest the protein matrix. In this way, a resorption lacuna, or pit, is formed. At the end of this phase of the cycle, osteoblasts lay down a new protein matrix that is subsequently mineralized. In several disease states, such as osteoporosis and Paget's disease, the normal balance between bone resorption and formation is disrupted, and there is a net loss of bone at each cycle. Ultimately, this leads to weakening of the bone and may result in increased fracture risk with minimal trauma.

Several published studies have demonstrated that inhibitors of cysteine proteases are effective at inhibiting osteoclast-mediated bone resorption, and indicate an essential role for a cysteine proteases in bone resorption. For example, Delaisse, *et al.*, *Biochem. J.*, **1980**, *192*, 365, disclose a series of protease inhibitors in a mouse bone organ culture system and suggest that inhibitors of cysteine proteases (e.g., leupeptin, Z-Phe-Ala-CHN_2) prevent bone resorption, while serine protease inhibitors were ineffective. Delaisse, *et al.*, *Biochem. Biophys. Res. Commun.*, **1984**, *125*, 441, disclose that E-64 and leupeptin are also effective at preventing bone resorption *in vivo*, as measured by acute changes in serum calcium in rats on calcium deficient diets. Lerner, *et al.*, *J. Bone Min. Res.*, **1992**, *7*, 433, disclose that cystatin, an endogenous cysteine protease inhibitor, inhibits PTH stimulated

bone resorption in mouse calvariae. Other studies, such as by Delaisse, *et al.*, *Bone*, **1987**, *8*, 305, Hill, *et al.*, *J. Cell. Biochem.*, **1994**, *56*, 118, and Everts, *et al.*, *J. Cell. Physiol.*, **1992**, *150*, 221, also report a correlation between inhibition of cysteine protease activity and bone resorption. Tezuka, *et al.*, *J. Biol. Chem.*, **1994**, *269*, 1106, Inaoka, *et al.*, *Biochem. Biophys. Res. Commun.*, **1995**, *206*, 89 and Shi, *et al.*, *FEBS Lett.*, **1995**, *357*, 129 disclose that under normal conditions cathepsin K, a cysteine protease, is abundantly expressed in osteoclasts and may be the major cysteine protease present in these cells.

The abundant selective expression of cathepsin K in osteoclasts strongly suggests that this enzyme is essential for bone resorption. Thus, selective inhibition of cathepsin K may provide an effective treatment for diseases of excessive bone loss, including, but not limited to, osteoporosis, gingival diseases such as gingivitis and periodontitis, Paget's disease, hypercalcemia of malignancy, and metabolic bone disease. Cathepsin K levels have also been demonstrated to be elevated in chondroclasts of osteoarthritic synovium. Thus, selective inhibition of cathepsin K may also be useful for treating diseases of excessive cartilage or matrix degradation, including, but not limited to, osteoarthritis and rheumatoid arthritis. Metastatic neoplastic cells also typically express high levels of proteolytic enzymes that degrade the surrounding matrix. Thus, selective inhibition of cathepsin K may also be useful for treating certain neoplastic diseases.

Several cysteine protease inhibitors are known. Palmer, (1995) *J. Med. Chem.*, *38*, 3193, disclose certain vinyl sulfones which irreversibly inhibit cysteine proteases, such as the cathepsins B, L, S, O2 and cruzain. Other classes of compounds, such as aldehydes, nitriles, α-ketocarbonyl compounds, halomethyl ketones, diazomethyl ketones, (acyloxy)methyl ketones, ketomethylsulfonium salts and epoxy succinyl compounds have also been reported to inhibit cysteine proteases. *See* Palmer, *id*, and references cited therein.

U.S. Patent No. 4,518,528 discloses peptidyl fluoromethyl ketones as irreversible inhibitors of cysteine protease. Published International Patent Application No. WO 94/04172, and European Patent Application Nos. EP 0 525 420 A1, EP 0 603 873 A1, and EP 0 611 756 A2 describe alkoxymethyl and mercaptomethyl ketones which inhibit the cysteine proteases cathepsins B, H and L. International Patent Application No. PCT/US94/08868 and and European Patent Application No. EP 0 623 592 A1 describe alkoxymethyl and mercaptomethyl ketones which inhibit the cysteine protease IL-1βconvertase. Alkoxymethyl and mercaptomethyl ketones have also been described as

inhibitors of the serine protease kininogenase (International Patent Application No. PCT/GB91/01479).

Azapeptides which are designed to deliver the azaamino acid to the active site of serine proteases, and which possess a good leaving group, are disclosed by Elmore *et al.*, *Biochem. J.*, **1968**, *107*, 103, Garker *et al.*, *Biochem. J.*, **1974**, *139*, 555, Gray *et al.*, *Tetrahedron*, **1977**, *33*, 837, Gupton *et al.*, *J. Biol. Chem.*, **1984**, *259*, 4279, Powers *et al.*, *J. Biol. Chem.*, **1984**, *259*, 4288, and are known to inhibit serine proteases. In addition, *J. Med. Chem.*, **1992**, *35*, 4279, discloses certain azapeptide esters as cysteine protease inhibitors.

Antipain and leupeptin are described as reversible inhibitors of cysteine protease in McConnell et al., *J. Med. Chem.*, *33*, 86; and also have been disclosed as inhibitors of serine protease in Umezawa et al., 45 *Meth. Enzymol.* 678. E64 and its synthetic analogs are also well-known cysteine protease inhibitors (Barrett, *Biochem. J.*, *201*, 189, and Grinde, *Biochem. Biophys. Acta*, , *701*, 328).

1,3-diamido-propanones have been described as analgesic agents in U.S. Patent Nos.4,749,792 and 4,638,010.

Thus, a structurally diverse variety of protease inhibitors have been identified. However, these known inhibitors are not considered suitable for use as therapeutic agents in animals, especially humans, because they suffer from various shortcomings. These shortcomings include lack of selectivity, cytotoxicity, poor solubility, and overly rapid plasma clearance. A need therefore exists for methods of treating diseases caused by pathological levels of proteases, particularly cysteine proteases, more particularly cathepsins, most particularly cathepsin K, and for novel inhibitor compounds useful in such methods.

We have now discovered a novel class of 4-amino-azepan-3-one compounds which are protease inhibitors, most particularly of cathepsin K.

SUMMARY OF THE INVENTION

An object of the present invention is to provide 4-amino-azepan-3-one carbonyl protease inhibitors, particularly such inhibitors of cysteine and serine proteases, more particularly such compounds which inhibit cysteine proteases, even more particularly such compounds which inhibit cysteine proteases of the papain superfamily, yet more particularly such compounds which inhibit cysteine proteases of the cathepsin family, most

particularly such compounds which inhibit cathepsin K, and which are useful for treating diseases which may be therapeutically modified by altering the activity of such proteases.

Accordingly, in the first aspect, this invention provides a compound according to Formula I.

In another aspect, this invention provides a pharmaceutical composition comprising a compound according to Formula I and a pharmaceutically acceptable carrier, diluent or excipient.

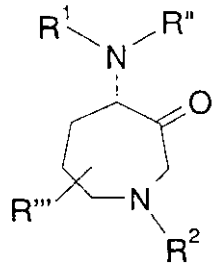
In yet another aspect, this invention provides intermediates useful in the preparation of the compounds of Formula I.

In still another aspect, this invention provides a method of treating diseases in which the disease pathology may be therapeutically modified by inhibiting proteases, particularly cysteine and serine proteases, more particularly cysteine proteases, even more particularly cysteine proteases of the papain superfamily, yet more particularly cysteine proteases of the cathepsin family, most particularly cathepsin K.

In a particular aspect, the compounds of this invention are especially useful for treating diseases characterized by bone loss, such as osteoporosis and gingival diseases, such as gingivitis and periodontitis, or by excessive cartilage or matrix degradation, such as osteoarthritis and rheumatoid arthritis.

DETAILED DESCRIPTION OF THE INVENTION

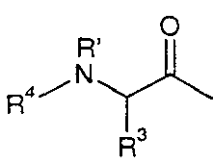
The present invention provides compounds of Formula I:



I

wherein:

R^1 is selected from the group consisting of: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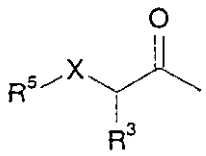
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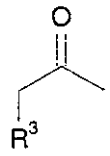
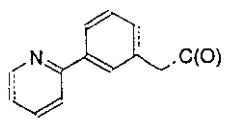

;

R^2 is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $R^9C(O)$-, $R^9C(S)$-, R^9SO_2-, $R^9OC(O)$-, $R^9R^{11}NC(O)$-, $R^9R^{11}NC(S)$-, $R^9(R^{11})NSO_2$-

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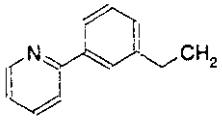
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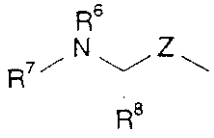

;

R^3 is selected from the group consisting of: H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, HetC_{0-6}alkyl and ArC_{0-6}alkyl;

R^3 and R' may be connected to form a pyrrolidine (204), piperidine or morpholine ring;

R^4 is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $R^5C(O)$-, $R^5C(S)$-, R^5SO_2-, $R^5OC(O)$-, $R^5R^{13}NC(O)$-, and $R^5R^{13}NC(S)$-;

R^5 is selected from the group consisting of: H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl;

R^6 is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R^7 is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $R^{10}C(O)$-, $R^{10}C(S)$-, $R^{10}SO_2$-, $R^{10}OC(O)$-, $R^{10}R^{14}NC(O)$-, and $R^{10}R^{14}NC(S)$-;

R^8 is selected from the group consisting of: H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, HetC_{0-6}alkyl and ArC_{0-6}alkyl;

R^9 is selected from the group consisting of: C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl;

R^{10} is selected from the group consisting of: C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl:

R^{11} is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R^{12} is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R^{13} is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R^{14} is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R' is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

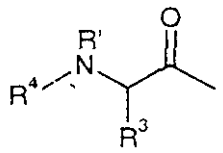
R" is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, or Het-C_{0-6}alkyl;

R'" is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

X is selected from the group consisting of: CH_2, S, and O;

Z is selected from the group consisting of: C(O) and CH_2;

and pharmaceutically acceptable salts, hydrates and solvates thereof.

In compounds of Formula I, when R^1 is  :

R^3 is selected from the group consisting of: H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, Het-C_{0-6}alkyl and Ar-C_{0-6}alkyl;

R^3 is preferably selected from the group consisting of: H, Ar-C_{0-6}alkyl, and C_{1-6}alkyl;

R^3 is more preferably selected from the group consisting of:

H, methyl, ethyl, n-propyl, prop-2-yl, n-butyl, isobutyl, but-2-yl, cyclopropylmethyl, cyclohexylmethyl, 2-methanesulfinyl-ethyl, 1-hydroxyethyl, toluyl, naphthalen-2-ylmethyl, benzyloxymethyl, and hydroxymethyl.

R^3 is even more preferably selected from the group consisting of: toluyl, isobutyl and cyclohexylmethyl.

R^3 is most preferably isobutyl.

R^4 is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $R^5C(O)$-, $R^5C(S)$-, R^5SO_2-, $R^5OC(O)$-, $R^5R^{13}NC(O)$-, and $R^5R^{13}NC(S)$-.

R^4 is preferably selected from the group consisting of: $R^5OC(O)$-, $R^5C(O)$- and R^5SO_2-.

R^4 is most preferably $R^5C(O)$-.

In some embodiments, R^4 is preferably methanesulfonyl.

R^5 is selected from the group consisting of: C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl or Het-C_{0-6}alkyl.

Preferably R^5 is selected from the group consisting of: C_{1-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl.

More preferably, and especially when R^4 is $R^5C(O)$-, R^5 is selected from the group consisting of:

methyl, especially halogenated methyl, more especially trifluoromethyl , especially alkoxy substituted methyl, more especially phenoxy-methyl , 4-fluoro-phenoxy-methyl , especially heterocycle substituted methyl, more especially 2-thiophenyl-methyl ;

butyl, especially aryl substituted butyl, more especially 4-(4-methoxy)phenyl-butyl;

isopentyl;

cyclohexyl;

pentanonyl, especially 4-pentanonyl;

butenyl, especially aryl substituted butenyl, more especially 4,4-bis(4-methoxyphenyl)-but-3-enyl;

acetyl;

phenyl, especially phenyl substituted with one or more halogens, more especially 3,4-dichlorophenyl and 4-fluorophenyl, especially phenyl substituted with one or more alkoxy groups, more especially 3,4-dimethoxy-phenyl, 3-benzyloxy-4-methoxy-phenyl, especially phenyl substituted with one or more sulfonyl groups, more especially 4-methanesulfonyl-phenyl;

benzyl;

naphthalenyl, especially naphthylen-2-yl;

benzo[1,3]dioxolyl. especially benzo[1,3]dioxol-5-yl,

furanyl, especially furan-2-yl, especially substituted furanyl, such as 5-nitro-furan-2-yl, 5-(4-nitrophenyl)-furan-2-yl, 5-(3-trifluoromethyl-phenyl)-furan-2-yl, more especially halogen substituted furanyl, even more especially 5-bromo-furan-2-yl, more especially aryl substituted furanyl, even more especially 5-(4-chloro-phenyl)-furan-2-yl;

tetrahydrofuran-2-yl;

benzofuranyl, especially benzofuran-2-yl, and substituted benzofuranyl, more especially 5-(2-piperazin-4-carboxylic acid *tert*-butyl ester- ethoxy) benzofuran-2-yl, 5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-yl, 5-(2-piperazin-1-yl-ethoxy)benzofuran-2-yl, 5-(2-cyclohexyl-ethoxy)-benzofuran-2-yl; especially alkoxy substituted benzofuranyl, more especially 7-methoxy-benzofuran-2-yl, 5-methoxy-benzofura-2-yl, 5,6-dimethoxy-benzofuran-2-yl, especially halogen substituted benzofuranyl, more especially 5-fluoro-benzofuran-2-yl(255), 5,6-difluoro-benzofuran-2-yl, especially alkyl substituted benzofuranyl, most especially 3-methyl-benzofuran-2-yl;

benzo[*b*]thiophenyl, especially benzo[*b*]thiophen-2-yl; especially alkoxy substituted benzo[*b*]thiophenyl, more especially 5,6-dimethoxy- benzo[*b*]thiophen-2-yl ;

quinolinyl, especially quinolin-2-yl, quinolin-3-yl, quinolin-4-yl, quinolin-6-yl, and quinolin-8-yl;

quinoxalinyl, especially quinoxalin-2-yl;

1,8 naphthyridinyl, especially 1,8 naphthyridin-2-yl;

indolyl, especially indol-2-yl, especially indol-6-yl, indol-5-yl, especially alkyl substituted indolyl, more especially N-methyl-indol-2-yl;

pyridinyl, especially pyridin-2-yl , pyridin-5-yl, especially 1-oxy-pyridin-2-yl, especially alkyl substituted pyridinyl, more especially 2-methyl-pyridin-5-yl;

thiophenyl, especially thiophen-3-yl, especially alkyl substituted thiophenyl, more especially 5-methyl-thiophen-2-yl, especially halogen substituted thiophenyl, more especially 4,5-dibromo-thiophen-2-yl;

thieno[3,2-*b*]thiophene, especially thieno[3,2-*b*]thiophene-2-yl, more especially alkyl substituted thieno[3,2-*b*]thiophene-2-yl, more especially 5-*tert*-butyl-3-methyl-thieno[3,2-*b*]thiophene-2-yl;

isoxazolyl, especially isoxazol-4-yl, especially alkyl substituted isoxazolyl, more especially 3,5-dimethyl- isoxazol-4-yl;

oxazolyl, especially oxazol-4-yl, more especially 5-methyl-2-phenyl oxazol-4-yl, 2-phenyl-5-trifluoromethyl-oxazol-4-yl;

When R^4 is R^5SO_2, R^5 is preferably pyridin-2-yl or 1-oxo-pyridin-2-yl.

R' is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl.

Preferably R' selected from the group consisting of: H and naphthalen-2-yl-methyl.

Most preferably R' is H.

R" selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl.

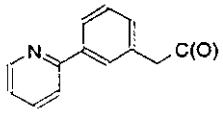
Most preferably R" is H.

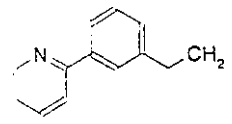
R'" is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, and Het-C_{0-6}alkyl.

R'" is preferably selected from the group consisting of: H and 6,6-dimethyl.

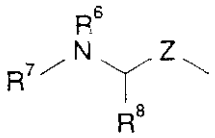
Most preferably R'" is H.

In compounds of Formula I, R^2 is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $R^9C(O)$-, $R^9C(S)$-, R^9SO_2-, $R^9OC(O)$-, $R^9R^{11}NC(O)$-, $R^9R^{11}NC(S)$-, $R^9R^{11}NSO_2$-,

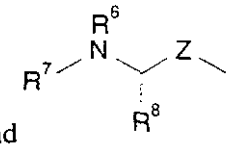




and



Preferably R^2 is selected from the group consisting of: Ar-C_{0-6}alkyl, $R^9C(O)$-,



R^9SO_2, $R^9R^{11}NC(O)$-, and .

More preferably, R^2 is selected from the group consisting of: Ar-C_{0-6}alkyl, $R^9C(O)$-, and R^9SO_2.

Most preferably R^2 is R^9SO_2.

In such embodiments:

R^6 is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, or Het-C_{0-6}alkyl, preferably H.

R^7 is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $R^{10}C(O)$-, $R^{10}C(S)$-, $R^{10}SO_2$-, $R^{10}OC(O)$-, $R^{10}R^{14}NC(O)$-, $R^{10}R^{14}NC(S)$-, R^7 is preferably $R^{10}OC(O)$.

R^8 is selected from the group consisting of: H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, HetC_{0-6}alkyl and ArC_{0-6}alkyl; preferably C_{1-6}alkyl, more preferably isobutyl.

R^9 is selected from the group consisting of: C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl.

R^9 is preferably selected from the group consisting of: C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl.

More preferably, R^9 is selected from the group consisting of:

methyl;

ethyl, especially C_{1-6}alkyl-substituted ethyl, more especially 2-cyclohexyl-ethyl;

butyl, especially C_{1-6}butyl, more especially 3-methylbutyl;

tert-butyl, particularly when R^2 is $R^9OC(O)$;

isopentyl;

phenyl, especially halogen substituted phenyl, more especially 3,4-dichlorophenyl , 4-bromophenyl, 2-fluorophenyl, 4-fluorophenyl, 3-chlorophenyl, 4-chlorophenyl, especially C_{1-6}alkoxy phenyl, more especially 3-methoxyphenyl, 4-methoxyphenyl, 3,4-dimethoxyphenyl, especially cyanophenyl, more especially 2-cyanophenyl;

toluyl, especially Het-substituted toluyl, more especially 3-(pyridin-2-yl)toluyl;

naphthylene, especially naphthyl-2-ene;

benzoic acid, especially 2-benzoic acid;

benzo[1,3]dioxolyl, especially benzo[1,3]dioxol-5-yl;

benzo[1,2,5]oxadiazolyl, especially benzo[1,2,5]oxadiazol-4-yl;

pyridinyl, especially pyridin-2-yl, pyridin-3-yl, especially 1-oxy-pyridinyl, more especially 1-oxy-pyridin-2-yl, 1-oxy-pyridin-3-yl; especially C_{1-6}alkylpyridinyl, more especially 3-methyl-pyridin-2-yl, 6-methyl-pyridin-2-yl,

thiophene, especially thiophene-2-yl;

thiazolyl, especially thiazol-2-yl;

1H-imidazolyl, especially 1H-imidazol-2-yl, 1H-imidazol-4-yl, more especially C_{1-6}alkyl substituted imidazolyl, even more especially 1-methyl-1H-imidazol-2-yl, 1-methyl-1H-imidazol-4-yl;

1H-[1,2,4]triazolyl, especially 1H-[1,2,4]triazol-3-yl, more especially C_{1-6}alkyl substituted 1H-[1,2,4]triazolyl, even more especially 5-methyl-1H-[1,2,4]triazol-3-yl.

When R^2 is R^9SO_2, R^9 is most preferably selected from the group consisting of: pyridin-2-yl and 1-oxy-pyridin-2-yl.

R^{10} is selected from the group consisting of: C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl or Het-C_{0-6}alkyl; preferably C_{1-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl.

Z is selected from the group consisting of: C(O) and CH_2.

R^2 is also preferably:

H;

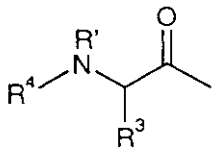
toluyl;

aryl substituted ethyl, especially 2-phenyl ethyl, 2-[3-(pyridin-2-yl) phenyl] ethyl.

Compounds of Formula I where R" and R"' are both H are preferred.

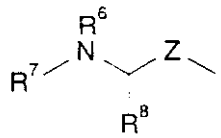
More preferred are compounds of Formula I wherein:

R^1 is



;

R^2 is selected from the group consisting of: Ar-C_{0-6}alkyl, $R^9C(O)$-, R^9SO_2,



$R^9R^{11}NC(O)$-, and ;

R^3 is selected from the group consisting of: H, C_{1-6}alkyl, and Ar-C_{0-6}alkyl;

R^4 is selected from the group consisting of: $R^5OC(O)$-, $R^5C(O)$- and R^5SO_2-;

$R^5$is selected from the group consisting of: C_{1-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl;

R^6 is H;

R^7 is $R^{10}OC(O)$;

R^8 is C_{1-6}alkyl:

R^9 is selected from the group consisting of: C_{1-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl;

R^{10} is selected from the group consisting of: C_{1-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl;

R' is H;

R" is H;

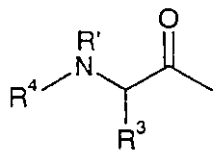
R'" is H; and

Z is selected from the group consisting of: C(O) and CH_2.

Even more preferred are such compounds of Formula I wherein R^2 is selected from the group consisting of: Ar-C_{0-6}alkyl, $R^9C(O)$-, R^9SO_2.

Yet more preferred are compounds of Formula I wherein:

R^1 is



;

R^2 is selected from the group consisting of: Ar-C_{0-6}alkyl, $R^9C(O)$- and R^9SO_2;

R^3 is selected from the group consisting of: H, methyl, ethyl, n-propyl, prop-2-yl, n-butyl, isobutyl, but-2-yl, cyclopropylmethyl, cyclohexylmethyl, 2-methanesulfinyl-ethyl, 1-hydroxyethyl, toluyl, naphthalen-2-ylmethyl, benzyloxymethyl, and hydroxymethyl;

R^4 is $R^5C(O)$-;

R^5 is selected from the group consisting of: methyl, especially halogenated methyl, more especially trifluoromethyl, especially alkoxy substituted methyl, more especially phenoxy-methyl, 4-fluoro-phenoxy-methyl, especially heterocycle substituted methyl, more especially 2-thiophenyl-methyl;

butyl, especially aryl substituted butyl, more especially 4-(4-methoxy)phenyl-butyl;

isopentyl;

cyclohexyl;

pentanonyl, especially 4-pentanonyl;

butenyl, especially aryl substituted butenyl, more especially 4,4-bis(4-methoxyphenyl)-but-3-enyl;

acetyl;

phenyl, especially phenyl substituted with one or more halogens, more especially 3,4-dichlorophenyl and 4-fluorophenyl, especially phenyl substituted with one or more alkoxy groups, more especially 3,4-dimethoxy-phenyl, 3-benzyloxy-4-methoxy-phenyl, especially phenyl substituted with one or more sulfonyl groups, more especially 4-methanesulfonyl-phenyl;

benzyl;

naphthylen-2-yl;

benzo[1,3]dioxolyl, especially benzo[1,3]dioxol-5-yl,

furanyl, especially furan-2-yl, especially substituted furanyl, such as 5-nitro-furan-2-yl, 5-(4-nitrophenyl)-furan-2-yl, 5-(3-trifluoromethyl-phenyl)-furan-2-yl, more especially halogen substituted furanyl, even more especially 5-bromo-furan-2-yl, more especially aryl substituted furanyl, even more especially 5-(4-chloro-phenyl)-furan-2-yl;

tetrahydrofuran-2-yl;

benzofuranyl, especially benzofuran-2-yl, and substituted benzofuranyl, more especially 5-(2-piperazin-4-carboxylic acid *tert*-butyl ester- ethoxy) benzofuran-2-yl, 5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-yl, 5-(2-piperazin-1-yl-ethoxy)benzofuran-2-yl, 5-(2-cyclohexyl-ethoxy)-benzofuran-2-yl; especially alkoxy substituted benzofuranyl, more especially 7-methoxy-benzofuran-2-yl, 5-methoxy-benzofura-2-yl, 5,6-dimethoxy-benzofuran-2-yl, especially halogen substituted benzofuranyl, more especially 5-fluoro-benzofuran-2-yl, 5,6-difluoro-benzofuran-2-yl, especially alkyl substituted benzofuranyl, most especially 3-methyl-benzofuran-2-yl;

benzo[*b*]thiophenyl, especially benzo[*b*]thiophen-2-yl; especially alkoxy substituted benzo[*b*]thiophenyl, more especially 5,6-dimethoxy- benzo[*b*]thiophen-2-yl;

quinolinyl, especially quinolin-2-yl, quinolin-3-yl, quinolin-4-yl, quinolin-6-yl, and quinolin-8-yl;

quinoxalinyl, especially quinoxalin-2-yl;

1,8 naphthyridinyl, especially 1,8 naphthyridin-2-yl;

indolyl, especially indol-2-yl, especially indol-6-yl, indol-5-yl, especially alkyl substituted indolyl, more especially N-methyl-indol-2-yl ;

pyridinyl, especially pyridin-2-yl , pyridin-5-yl, especially 1-oxy-pyridin-2-yl, especially alkyl substituted pyridinyl, more especially 2-methyl-pyridin-5-yl;

thiophenyl, especially thiophen-3-yl, especially alkyl substituted thiophenyl, more especially 5-methyl-thiophen-2-yl, especially halogen substituted thiophenyl, more especially 4,5-dibromo-thiophen-2-yl;

thieno[3,2-*b*]thiophene, especially thieno[3,2-*b*]thiophene-2-yl, more especially alkyl substituted thieno[3,2-*b*]thiophene-2-yl, more especially 5-*tert*-butyl-3-methyl-thieno[3,2-*b*]thiophene-2-yl;

isoxazolyl, especially isoxazol-4-yl, especially alkyl substituted isoxazolyl, more especially 3,5-dimethyl- isoxazol-4-yl;

oxazolyl, especially oxazol-4-yl, more especially 5-methyl-2-phenyl oxazol-4-yl , 2-phenyl-5-trifluoromethyl-oxazol-4-yl;

R^9 is selected from the group consisting of:

methyl;

ethyl, especially C_{1-6}alkyl-substituted ethyl, more especially 2-cyclohexyl-ethyl;

butyl, especially C_{1-6}butyl, more especially 3-methylbutyl;

tert-butyl, particularly when R^2 is $R^9OC(O)$;

isopentyl;

phenyl, especially halogen substituted phenyl, more especially 3,4-dichlorophenyl , 4-bromophenyl, 2-fluorophenyl, 4-fluorophenyl , 3-chlorophenyl, 4-chlorophenyl, especially C_{1-6}alkoxy phenyl, more especially 3-methoxyphenyl, 4-methoxyphenyl, 3,4-dimethoxyphenyl, especially cyanophenyl, more especially 2-cyanophenyl ;

toluyl, especially Het-substituted toluyl, more especially 3-(pyridin-2-yl)toluyl;

naphthylene, especially naphthyl-2-ene;

benzoic acid, especially 2-benzoic acid;

benzo[1,3]dioxolyl, especially benzo[1,3]dioxol-5-yl;

benzo[1,2,5]oxadiazolyl, especially benzo[1,2,5]oxadiazol-4-yl;

pyridinyl, especially pyridin-2-yl, pyridin-3-yl, especially 1-oxy-pyridinyl, more especially 1-oxy-pyridin-2-yl, 1-oxy-pyridin-3-yl; especially C_{1-6}alkylpyridinyl, more especially 3-methyl-pyridin-2-yl, 6-methyl-pyridin-2-yl,

thiophene, especially thiophene-2-yl;

thiazolyl, especially thiazol-2-yl;

1H-imidazolyl, especially 1H-imidazol-2-yl(74), 1H-imidazol-4-yl, more especially C_{1-6}alkyl substituted imidazolyl, even more especially 1-methyl-1H-imidazol-2-yl, 1-methyl-1H-imidazol-4-yl;

1H-[1,2,4]triazolyl, especially 1H-[1,2,4]triazol-3-yl, more especially C_{1-6}alkyl substituted 1H-[1,2,4]triazolyl, even more especially 5-methyl-1H-[1,2,4]triazol-3-yl;

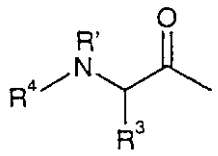
R' is H;

R" is H; and

R'" is H.

Most preferred are compounds of Formula I wherein:

R^1 is



;

R^2 is R^9SO_2;

R^3 is isobutyl;

R^4 is $R^5C(O)$;

R^5 is selected from the group consisting of: 3-methyl-benzofuran-2-yl, thieno[3,2-b]thiophen-2-yl, 5-methoxybenzofuran-2-yl, quinoxalin-2-yl, and quinolin-2-yl, preferably 3-methyl-benzofuran-2-yl;

R^9 is selected from the group consisting of: pyridin-2-yl and 1-oxy-pyridin-2-yl, preferably 1-oxy-pyridin-2-yl.

R' is H; and

R'" is H;

Compounds of Formula I selected from the following group are particularly preferred embodiments of the present invention:

Example No.	**Chemical Name**
1	{(S)-1-[1-((S)-2-Benzyloxycarbonylamino-4-methyl-pentanoyl)-3-oxo-azepan-4-ylcarbamoyl}carbamic acid benzyl ester
2	Naphthylene-2-carboxylic acid[(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

3	Benzo[1,3]dioxole-5-carboxylic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide
4	Benzofuran-2-carboxylic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide
5	Benzo[b]thiophene-2-carboxylic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide
6	Naphthylene-2-sulphonyl [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide
7	Quinoline-2-carboxylic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide
8	3,4-dichlorobenzoic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide
9	4-{(S)-Methyl-2-[(quinoline-2-carbonyl)-amino]pentanoylamino}-3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]azepanium
10	1-((S)-2-Benzyloxycarbonylamino-4-methyl-pentyl)-4-{(S)-4-methyl-2-[(2-quinoiline-2-carbonyl)-amino]-pentanoylamino)-3-oxo-azepanium
11	1-Benzoyl-4-((S)-2-(benzo[1,3]dioxole-carbonylamino)-4-methyl-pentanoylamino)-3-oxo-azepanium
12	1-Benzoyl-4-((S)-2-(4-fluoro-benzoylamino)-4-methyl-pentanoylamino)-3-oxo-azepanium
13	3-Oxo-4-((S)-4-methyl-2-{[5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]amino}-pentanoylamino)-1-(4-methyl-pentanoyl)-azepanium
14	5-(2-Morpholin-4-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide
15	4-((S)-4-Methyl-2-{[5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]amino}-pentanoylamino)-3-oxo-azepane-1-carboxylic acid phenylamide
16	5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)acetyl]-azepan-4-ylcarbamoyl}-butyl)amide

17	5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-1-(benzoyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide
18	5-(2-Pyrrolidin-1-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide
19	5-(2-Piperidin-1-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide
20	5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide
21	Naphthlene-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide
22	1H_Indole-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide
23	1H-Indole-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide
24	Benzofuran-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide
25	Benzofuran-2-carboxylic acid [(S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide
26	5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-3-methyl-1-(3-oxo-1-phenethyl-azepan-4-ylcarbamoyl]-butyl}amide
27	Naphthylene-2-carboxylic acid [(S)-3-methyl-1-(3-oxo-1-phenethyl-azepan-4-ylcarbamoyl]-butyl}amide
28	Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide
29	Naphthylene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide
30	5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

31	4-((S)-4-Methyl-2-{[(5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]-amino}-pentanoylamino)-3-oxo-azepane-1-carboxylic acid tert-butyl ester
32	4-((S)-4-Methyl-2-{[(5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-3-methyl-1-(3-oxo-azepan-4-ylcarbamoyl]-butyl}amide
33	4-Methyl-pentanoic acid {3-oxo-1-[2-(3-pyridin-2-yl-phenyl-acetyl]-azepan-4-yl}-amide
34	((S)-3-Methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-ylcarbamoyl}-butyl)-naphthylene-2-methyl-carbamic acid tert-butyl ester
35	(S)-4-Methyl-2-[(naphthylen-2-ylmethyl)-amino]-pentenoic acid [3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-yl}-amide
36	4-[2-(2-{(S)-3-Methyl-1-[3-oxo-1-(pyidine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butylcarbamoyl}-benzofuran-5-yloxy)-ethyl]-piperazine-1-carboxylic acid tert-butyl ester
37	5-(2-Piperizin-1-yl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-3-butyl}-amide
38	5-(2-Cyclohexyl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
39	5-(2-Cyclohexyl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide
40	4-[2-(2-{(S)-3-Methyl-1-[3-oxo-1-(3-pyridin-2-yl-phenyl)-ethyl [azepan-4-ylcarbamoyl]-butylcarbamoyl}-benzofuran-5-yloxy)-ethyl]-piperazine-1-carboxylic acid *tert*-butyl ester
41	5-(2-piperizin-1-yl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide
42	(S)-4-Methyl-2-(methyl-naphthalen-2-ylmethyl-amino)pentanoic acid [3-oxo-1-(pyridine-2-sulphonyl)-azepan-4-yl]-amide

43	(S)-4-Methyl-2-(methyl-naphthalen-2-ylmethyl-amino)pentanoic acid {3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-yl}-amide
44	5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid methyl ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)acetyl]-azepan-4-ylcarbamoyl}-butyl)amide
45	Benzofuran-2-carboxylic acid methyl {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide
46	2,2,2-Trifluoro-N-((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-ylcarbamoyl}-butyl)-N-naphthylen-2-ylmethyl-acetamide
47	4-[(S)-(Methanesulphonyl-naphthylen-2-ylmethyl-amino)-4-methyl-pentanoylamino]-3-oxo-azepane-1-carboxylic acid benzyl ester
48	Quinoline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
49	Quinoline-8-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
50	Quinoline-6-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
51	Quinoline-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
52	Quinoline-3-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
53	Isoquinoline-3-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
54	Isoquinoline-1-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
55	Quinoxaline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
56	Benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

57 1,8-Naphthyridine-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

58 1H-Indole-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

59 5-Methoxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

60 5-Bromo-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

61 Furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

62 5-Nitro-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

63 5-(4-Nitro-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

64 5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

65 Tetrahydro-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

66 (S)-4-Methyl-2-(2-phenoxy-acetylamino)-pentanoic acid [3-oxo-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

67 (S)-2-[2-(4-Fluoro-phenoxy)-acetylamino]-4-methyl-pentanoic acid [3-oxo-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

68 Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-carbonyl)-azepan-4-ylcarbamoyl)-3- butyl]-amide

69 Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-carbonyl)-azepan-4-ylcarbamoyl]-butyl}amide

70 4-((S)-2-tert-Butylcarbonylamino-4-methyl-pentanoylamino)-3-oxo-azepane-1-carboxylic acid benzyl ester

71 5,6-Dimethoxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-methyl-1H-imidazole-4-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

72 Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(5-methyl-1H-[1,2,4]triazole-3-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

73 Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1-methyl-1H-imidazole-3-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

74 Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1H-imidazole-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

75 Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

76 Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1-methyl-1H-imidazole-4-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

77 5-(4-Oxy-morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

78 Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-3-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

79 Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-3-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

80 Quinoline-3-carboxylic acid {(S)-1-(3,4-dichloro-benzene-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl)]-3-methyl-butyl}-amide

81 5-Hydroxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1-methyl-1H-imidazole-4-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

82 Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)]-3-methyl-butyl}-amide

83 2-(4-{(S)-2-{(Benzofuran-2-carbonyl)-amino}-4-methyl-pentanoylamino}-3-oxo-azepane-1-sulfonyl)-benzoic acid

84 3-(4-{(S)-2-{(Benzofuran-2-carbonyl)-amino]-4-methyl-pentanoylamino}-3-oxo-azepane-1-sulfonyl)-benzoic acid

85 Benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

86	5-Bromo-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
87	5,6-Dimethoxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
88	1-Oxy-pyridine-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
89	(S)-4-Methyl-2-(pyridine-2-sulfonylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide
90	(S)-2-(3-Benzyl-ureido)-4-methyl-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide
91	(S)-4-Methyl-2-(3-phenyl-uriedo)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide
92	Benzofuran-2-carboxylic acid {(S)-1-[6,6-dimethyl-3-oxo-1(pyridine-sulphonyl)-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide
93	5-Methoxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
94	Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
95	Quinoxaline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
96	Quinoline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
97	Thiophene-3-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
98	1H-Indole-5-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
99	Benzo[1,3]dioxole-5-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
100	Furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

101	(S)-4-Methyl-2-(2-thiophen-2-yl-acetylamino)-pentanoic acid [3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-yl]-amide
102	1H-Indole-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
103	4-Fluoro-{(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulphonyl)-azepan-4-carbamoyl]-butyl}-benzamide
104	5-(2-Morpholin-4-yl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-(1-oxy-pyridine2-sulphonyl)-azepan-4-ylcarbamoyl]- -buty}-amide
105	Thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
106	3-Methyl-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
107	6-Methyl-N-{(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-nicotinamide
108	(S)-4-Methyl-2-(2-thiophen-yl-acetylamino)-pentanoic acid-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-butyl}amide
109	1H-Indole-6-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
110	Benzo[1,3]dioxole-5-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
111	3,4-Dihydro-2H-benzo[b][1,4]dioxepine-7-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl] butyl}amide
112	5-Methyl-thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
113	4,5-Dibromo-thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
114	3,5-Dimethyl-isoxazole-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
115	(S)-2-(2-Benzyloxy-acetylamino)-4-methyl-pentanoic acid[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-yl]-amide

116	5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
117	5-Methyl-2 –phenyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
118	Benzofuran-2-carboxylic acid {(S)-1-[1-(3,4-dimethoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}-amide
119	Benzofuran-2-carboxylic acid {(S)-1-[1-(4-bromo-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide
120	Benzofuran-2-carboxylic acid {(S)-1-[1-(benzo[1,2,5]oxadiazole-4-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide
121	Benzofuran-2-carboxylic acid {(S)-1-[1-(3,5-dimethyl-oxazole-4 -sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide
122	3-Methyl-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
123	Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
124	5-*tert*-Butyl-3-methyl-thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
125	5-Methyl-2-phenyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
126	2-Phenyl-5-trifluoromethyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
127	Quinoline-2-carboxylic acid [(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide
128	1-Methyl-1H-indole-2-carboxylic acid [(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide
129	Furan-2-carboxylic acid {[(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butylcarbamoyl]-methyl}-amide

130 5-Methoxy-benzofuran-2-carboxylic acid [(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

131 Quinoxaline-2-carboxylic acid [(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

132 5-(4-Chloro-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

133 (S)-2-[2-(4-Methoxy-phenyl)-acetylamino)-4-methyl-pentanoic acid (1-methanesulfonyl-3-oxo-azepan-4-yl)-amide

134 Quinoline-2-carboxylic acid {[(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

135 1-Methyl-1H-indole -2-carboxylic acid {[(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

136 Furan-2-carboxylic acid ({(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butylcarbamoyl}-methyl)-amide

137 5-Methoxy-benzofuran-2-carboxylic acid {(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

138 Quinoxaline-2-carboxylic acid {(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

139 (S)-2-[2-(4-Methoxy-phenyl)-acetylamino)-4-methyl-pentanoic acid [1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-yl]-amide

140 Quinoline-2-carboxylic acid {[(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

141 1-Methyl-1H-indole-2-carboxylic acid {[(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

142	Furan-2-carboxylic acid ({(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butylcarbamoyl}-methyl)-amide
143	5-Methoxy-benzofuran-2-carboxylic acid {[(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide
144	Quinoxaline-2-carboxylic acid {[(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide
145	(S)-2-[2-(4-Methoxy-phenyl)-acetylamino)-4-methyl-pentanoic acid [1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-yl]-amide
146	1-Methyl-1H-indole-2-carboxylic acid {[(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide
147	Furan-2-carboxylic acid ({(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butylcarbamoyl}-methyl)-amide
148	5-Methoxy-benzofuran-2-carboxylic acid {[(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide
149	Quinoxaline-2-carboxylic acid {[(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide
150	(S)-2-[2-(4-Methoxy-phenyl)-acetylamino)-4-methyl-pentanoic acid [1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-yl]-amide
151	Benzofuran-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide
152	5-Methoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

153 7-Methoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

154 5,6-Dimethoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

155 3-Methyl-benzofuran-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

156 Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

157 1-Methyl-1H-indole-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

158 Quinoxaline-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

159 Benzofuran-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

160 5-Methoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

161 7-Methoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

162 5,6-Dimethoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

163 5-Methyl-benzofuran-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

164	Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide
165	1-Methyl-1H-indole-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide
166	(S)-4-Methyl-2-(1-oxy-pyridine-2-sulfonylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide
167	Quinoxaline-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide
168	5-Methoxy-benzofuran-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide
169	7-Methoxy-benzofuran-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide
170	5,6-Dimethoxy-benzofuran-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide
171	3-Methyl-benzofuran-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide
172	Benzo[b]thiophene-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide
173	1-Methyl-1-H-indole-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide
174	Quinoxaline-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide
175	Benzofuran-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide
176	5-Methoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

177 7-Methoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

178 5,6-Dimethoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

179 3-Methyl-benzofuran-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

180 Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

181 1-Methyl-1H-indole-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

182 Quinoxaline-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

183 Benzofuran-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

184 5-Methoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

185 7-Methoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

186 5,6-Dimethoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

187 3-Methyl-benzofuran-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

188	Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide
189	1-Methyl-1H-indole-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide
190	Quinoxaline-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide
191	Benzofuran-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide
192	Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[(2,2',4-tridueterio)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
193	Benzofuran-2-carboxylic acid {(S)-2-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide
194	Benzofuran-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-propyl}-amide
195	Benzofuran-2-carboxylic acid {(S)-2-cyclohexyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide
196	Benzofuran-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide
197	Benzofuran-2-carboxylic acid {(S)-3-methanesulfinyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-propyl}-amide
198	Benzofuran-2-carboxylic acid {[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-methyl}-amide
199	Benzofuran-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-pentyl}-amide
200	Benzofuran-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide
201	Benzofuran-2-carboxylic acid {(S)-2-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-propyl}-amide

202	Benzofuran-2-carboxylic acid {(S)-2-hydroxy-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-propyl}-amide
203	Benzofuran-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-2-phenyl-ethyl}-amide
204	1-(Benzofuran-2-carbonyl)-pyrrolidine-2-carboxylic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide
205	3,4-Dimethoxy-N-{(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-benzamide
206	Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(4-imethoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide
207	Benzo[1,3]dioxole-5-carboxylic acid {(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3methyl-butyl}-amide
208	(S)-2-(2-Benzyloxy-acetylamino)-4-methyl-pentanoic acid[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-yl]-amide
209	Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-yl carbamoyl]-3-methyl-butyl}-amide
210	Benzofuran-2-carboxylic acid {(S)-1-[1-benzoyl-3-oxo-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide
211	(S)-4-Methyl-2-(quinoline-8-sulfonylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide
212	(S)-4-Methyl-2-(naphthylene-2-sulfonylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide
213	Benzofuran-2-carboxylic acid-{(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-yl carbamoyl]-3-methyl-butyl}-amide
214	N-{(S)-1-[1-(4-Fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl}-3-methyl-butyl}-3,4-dimethoxy-benzamide
215	Cyclohexanecarboxylic acid {(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl}-3-methyl-butyl}-amide

216	(S)-2-(2-Benzyloxy-acetylamino)-4-methyl-pentanoic acid[1-(methanesulfonyl)-3-oxo-azepan-4-yl]-amide
217	Benzo[b]thiophene-2-carboxylic acid-{(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-yl carbamoyl)-3-methyl-butyl]-amide
218	Benzo[1,3]dioxole-5-carboxylic acid-{(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-yl carbamoyl)-3-methyl-butyl]-amide
219	Benzofuran-2-carboxylic acid-{(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-yl carbamoyl)-3-methyl-butyl]-amide
220	N-[(S)-1-(1-Methanesulfonyl)-3-oxo-azepan-4-ylcarbamoyl}-3-methyl-butyl}-3,4-dimethoxy-benzamide
221	(S)-2-(2-Benzyloxy-acetylamino)-4-methyl-pentanoic acid[1-(2-cyano-benzensulfonyl)-3-oxo-azepan-4-yl]-amide
222	N-{(S)-1-[1-(2-Cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl}-3-methyl-butyl}-4-methanesulfonyl-1-benzamide
223	Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-yl carbamoyl)-3-methyl-butyl]-amide
224	Benzo[1,3]dioxole-5-carboxylic acid-{(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide
225	(S)-4-Methyl-2-[4-oxo-4-((4-phenoxy-phenyl)-butyrylamino}-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide
226	N-{(S)-1-[(1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl}-3-methyl-butyl}-3,4-dimethoxy-benzamide
227	Cyclohexanecarboxylic acid {(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl}-3-methyl-butyl}-amide
228	4-Methansulfonyl-N-{(S)-1-[4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-carbamoyl]-3-methyl-butyl-benzamide
229	4-Methansulfonyl-N-{(S)-1-[4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-carbamoyl]-3-methyl-butyl-benzamide
230	({(S)-3-Methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butylcarbamoyl}-carbamic acid benzyl ester

231	(S)-2-[5-(4-Methoxy-phenyl)-pentanoylamnio]-4-methyl-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide
232	(S)-2-[2-(3-Benzyloxy-4-methoxy-phenyl)-acetylamnio]-4-methylpentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide
233	5,6-Difluoro-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide
234	(S)-4-Methyl-2-(5-oxo-hexanoylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide
235	Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide
236	5-Methoxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide
237	3-Methyl-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide
238	7-Methoxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide
239	5,6-Dimethoxy-benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide
240	(R)-1-Benzyl-5-oxo-pyrrolidine-2-carboxylic acid {(S)-3-methyl-1-{3-oxo-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
241	(S)-1-Benzyl-5-oxo-pyrrolidine-2-carboxylic acid {(S)-3-methyl-1-{3-oxo-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
242	Benzofuran-2-carboxylic acid {(S)-2-cyclopropyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-ethyl]-amide
243	Benzofuran-2-carboxylic acid {(S)-3-methylsulfanyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-propyl]-amide

244	Benzofuran-2-carboxylic acid {(S)-2-naphthylen-2-yl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-ethyl]-amide
245	Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide
246	Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide
247	3-Methyl-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide
248	5-Methoxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide
249	5,6-Difluoro-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
250	5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid{(S)-2-cyclohexyl-1-{3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide
251	5-(4-Chloro-phenyl)-furan-2-carboxylic acid{(S)-2-cyclohexyl-1-{3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide
252	Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[6-methyl-3-oxo-1-(pyridine-sulphonyl)-azepan-4-ylcarbamoyl]-butyl}-amide
253	5-(4-Chloro-phenyl)-furan-2-carboxylic acid{(S)-2-cyclohexyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide
254	5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid{(S)-2-cyclohexyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide
255	5-Fluoro-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

256	5,6-Dimethoxy-benzofuran-2-carboxylic acid{(S)-2-cyclohexyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide
257	5,5-Bis-(4-methoxy-phenyl)-pent-4-enoic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]}-butyl}-amide
258	Quinoline-8-carboxylic acid {(S)-2-naphthylen-2-yl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-ethyl]-amide
259	Naphthylene-1-carboxylic acid {(S)-2-naphthylen-2-yl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-ethyl]-amide
260	Quinoline-8-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2 -sulfonyl)-azepan-4-ylcarbamoyl]-2-phenyl-ethyl}-amide
261	Naphthyridine-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide
262	Naphthylene-1-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2 -sulfonyl)-azepan-4-ylcarbamoyl]-2-phenyl-ethyl}-amide
263	3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(cyclohexyl-proprionyl)-azepan-4-ylcarbamoyl]-butyl}-amide
264	3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(4-methyl-pentanoyl)-azepan-4-ylcarbamoyl]-butyl}-amide
265	3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-carbonyl)-azepan-4-ylcarbamoyl]-butyl}-amide
266	(S)-Acetylamino-4-methyl-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide
267	Quinoline-2-carboxylic acid {1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-pentyl}-amide
268	Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo -1-(cyclohexyl-proprionyl)-azepan-4-ylcarbamoyl]-butyl}-amide

269	Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(4-methyl-pentanoyl)-azepan-4-ylcarbamoyl]-butyl}-amide
270	Quinoline-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-2-phenyl-ethyl}-amide
271	Benzofuran-2-carboxylic acid{(S)-2-benzyloxy-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepane-4-ylcarbamoyl]-ethyl}-amide
272	Benzofuran-2-carboxylic acid{(S)-2-hydroxy-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepane-4-ylcarbamoyl]-ethyl}-amide
273	5-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
274	7-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
275	3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
276	Benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
277	1-Methyl-1H-indole-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
278	Quinoxaline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide
279	Quinoline-2-carboxylic acid {[(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Specific representative compounds of the present invention are set forth in Examples 1-279.

Compared to the corresponding 5 and 6 membered ring compounds, the 7 membered ring compounds of the present invention are configurationally more stable at the carbon center alpha to the ketone.

The present invention includes deuterated analogs of the inventive compounds. A representative example of such a deuterated compound is set forth in Example 192. A

representative synthetic route for the deuterated compounds of the present invention is set forth in Scheme 4, below. The deuterated compounds of the present invention exhibit superior chiral stability compared to the protonated isomer.

Definitions

The present invention includes all hydrates, solvates, complexes and prodrugs of the compounds of this invention. Prodrugs are any covalently bonded compounds which release the active parent drug according to Formula I *in vivo*. If a chiral center or another form of an isomeric center is present in a compound of the present invention, all forms of such isomer or isomers, including enantiomers and diastereomers, are intended to be covered herein. Inventive compounds containing a chiral center may be used as a racemic mixture, an enantiomerically enriched mixture, or the racemic mixture may be separated using well-known techniques and an individual enantiomer may be used alone. In cases in which compounds have unsaturated carbon-carbon double bonds, both the cis (Z) and trans (E) isomers are within the scope of this invention. In cases wherein compounds may exist in tautomeric forms, such as keto-enol tautomers, each tautomeric form is contemplated as being included within this invention whether existing in equilibrium or predominantly in one form.

The meaning of any substituent at any one occurrence in Formula I or any subformula thereof is independent of its meaning, or any other substituent's meaning, at any other occurrence, unless specified otherwise.

Abbreviations and symbols commonly used in the peptide and chemical arts are used herein to describe the compounds of the present invention. In general, the amino acid abbreviations follow the IUPAC-IUB Joint Commission on Biochemical Nomenclature as described in *Eur. J. Biochem.*, 158, 9 (1984).

"Proteases" are enzymes that catalyze the cleavage of amide bonds of peptides and proteins by nucleophilic substitution at the amide bond, ultimately resulting in hydrolysis. Such proteases include: cysteine proteases, serine proteases, aspartic proteases, and metalloproteases. The compounds of the present invention are capable of binding more strongly to the enzyme than the substrate and in general are not subject to cleavage after enzyme catalyzed attack by the nucleophile. They therefore competitively prevent proteases from recognizing and hydrolyzing natural substrates and thereby act as inhibitors.

The term "amino acid" as used herein refers to the D- or L- isomers of alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine and valine.

"C_{1-6}alkyl" as applied herein is meant to include substituted and unsubstituted methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and t-butyl, pentyl, n-pentyl, isopentyl, neopentyl and hexyl and the simple aliphatic isomers thereof. C_{1-6}alkyl may be optionally substituted by a moiety selected from the group consisting of: OR^{12}, $C(O)R^{12}$, SR^{12}, $S(O)R^{12}$, $NR^{12}{}_2$, $R^{12}NC(O)OR^5$, CO_2R^{12}, $CO_2NR^{12}{}_2$, $N(C{=}NH)NH_2$, Het, C_{3-6}cycloalkyl, and Ar; where R^5 is selected from the group consisting of: H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl; and R^{12} is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

"C_{3-6}cycloalkyl" as applied herein is meant to include substituted and unsubstituted cyclopropane, cyclobutane, cyclopentane and cyclohexane.

"C_{2-6} alkenyl" as applied herein means an alkyl group of 2 to 6 carbons wherein a carbon-carbon single bond is replaced by a carbon-carbon double bond. C_{2-6}alkenyl includes ethylene, 1-propene, 2-propene, 1-butene, 2-butene, isobutene and the several isomeric pentenes and hexenes. Both cis and trans isomers are included.

"C_{2-6}alkynyl" means an alkyl group of 2 to 6 carbons wherein one carbon-carbon single bond is replaced by a carbon-carbon triple bond. C_{2-6} alkynyl includes acetylene, 1-propyne, 2-propyne, 1-butyne, 2-butyne, 3-butyne and the simple isomers of pentyne and hexyne.

"Halogen" means F, Cl, Br, and I.

"Ar" or "aryl" means phenyl or naphthyl, optionally substituted by one or more of Ph-C_{0-6}alkyl; Het-C_{0-6}alkyl; C_{1-6}alkoxy; Ph-C_{0-6}alkoxy; Het-C_{0-6}alkoxy; OH, $(CH_2)_{1-6}NR^{15}R^{16}$; $O(CH_2)_{1-6}NR^{15}R^{16}$; C_{1-6}alkyl, OR^{17}, $N(R^{17})_2$, SR^{17}, CF_3, NO_2, CN, CO_2R^{17}, $CON(R^{17})$, F, Cl, Br or I; where R^{15} and R^{16} are H, C_{1-6}alkyl, Ph-C_{0-6}alkyl, naphthyl-C_{0-6}alkyl or Het-C_{0-6}alkyl; and R^{17} is phenyl, naphthyl, or C_{1-6}alkyl.

As used herein "Het" or "heterocyclic" represents a stable 5- to 7-membered monocyclic, a stable 7- to 10-membered bicyclic, or a stable 11- to 18-membered tricyclic heterocyclic ring which is either saturated or unsaturated, and which consists of carbon atoms and from one to three heteroatoms selected from the group consisting of N, O and S,

and wherein the nitrogen and sulfur heteroatoms may optionally be oxidized, and the nitrogen heteroatom may optionally be quaternized, and including any bicyclic group in which any of the above-defined heterocyclic rings is fused to a benzene ring. The heterocyclic ring may be attached at any heteroatom or carbon atom which results in the creation of a stable structure, and may optionally be substituted with one or two moieties selected from $C_{0-6}Ar$, $C_{1-6}alkyl$, OR^{17}, $N(R^{17})_2$, SR^{17}, CF_3, NO_2, CN, CO_2R^{17}, $CON(R^{17})$, F, Cl, Br and I, where R^{17} is phenyl, naphthyl, or $C_{1-6}alkyl$. Examples of such heterocycles include piperidinyl, piperazinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolodinyl, 2-oxoazepinyl, azepinyl, pyrrolyl, 4-piperidonyl, pyrrolidinyl, pyrazolyl, pyrazolidinyl, imidazolyl, pyridinyl, 1-oxo-pyridinyl, pyrazinyl, oxazolidinyl, oxazolinyl, oxazolyl, isoxazolyl, morpholinyl, thiazolidinyl, thiazolinyl, thiazolyl, quinuclidinyl, indolyl, quinolinyl, quinoxalinyl, isoquinolinyl, benzimidazolyl, benzopyranyl, benzoxazolyl, furanyl, benzofuranyl, thiophenyl, benzo[b]thiophenyl, thieno[3,2-b]thiophenyl, benzo[1,3]dioxolyl, 1,8 naphthyridinyl, pyranyl, tetrahydrofuranyl, tetrahydropyranyl, thienyl, benzoxazolyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone, and oxadiazolyl, as well as triazolyl, thiadiazolyl, oxadiazolyl, isothiazolyl, imidazolyl, pyridazinyl, pyrimidinyl, triazinyl and tetrazinyl which are available by routine chemical synthesis and are stable. The term heteroatom as applied herein refers to oxygen, nitrogen and sulfur.

Here and throughout this application the term C_0 denotes the absence of the substituent group immediately following; for instance, in the moiety $ArC_{0-6}alkyl$, when C is 0, the substituent is Ar, e.g., phenyl. Conversely, when the moiety $ArC_{0-6}alkyl$ is identified as a specific aromatic group, e.g., phenyl, it is understood that the value of C is 0.

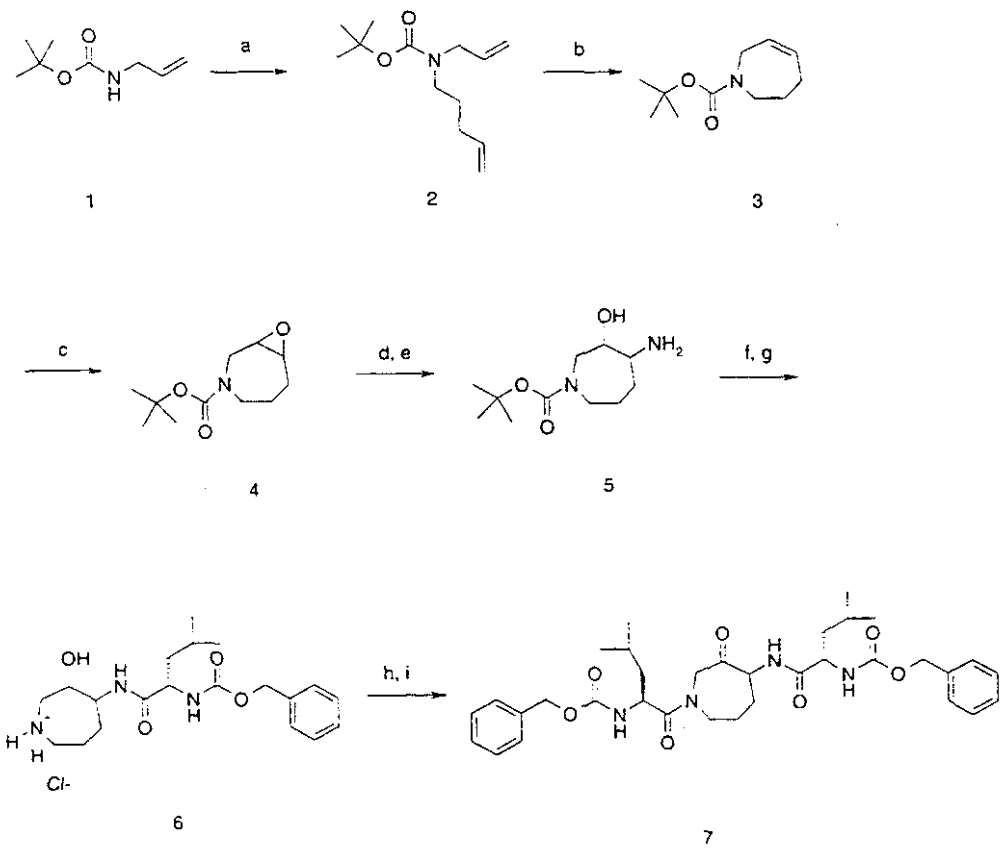
Certain radical groups are abbreviated herein. t-Bu refers to the tertiary butyl radical, Boc refers to the t-butyloxycarbonyl radical, Fmoc refers to the fluorenylmethoxycarbonyl radical, Ph refers to the phenyl radical, Cbz refers to the benzyloxycarbonyl radical.

Certain reagents are abbreviated herein. m-CPBA refers to 3-chloroperoxybenzoic acid, EDC refers to N-ethyl-N'(dimethylaminopropyl)-carbodiimide, DMF refers to dimethyl formamide, DMSO refers to dimethyl sulfoxide, TEA refers to triethylamine, TFA refers to trifluoroacetic acid, and THF refers to tetrahydrofuran.

Methods of Preparation

Compounds of the general formula I may be prepared in a fashion analogous to that outlined in Schemes 1, 2 and 3. Alkylation of *tert*-butyl N-allylcarbamate (**1**) with a base such as sodium hydride and 5-bromo-1-pentene provides the diene **2**. Treatment of **2** with either 2,6-diisopropylphenylimido neophylidene molybenum bis(tert-butoxide) or bis(tricyclohexylphosphine)benzylidine ruthenium (IV) dichloride olefin metathesis catalysts developed by Grubbs provides the azepine **3**. Epoxidation of **3** with standard oxidizing agents common to the art such as *m*-CPBA provide the epoxide **4**. Nucleophilic epoxide ring opening may be effected with a reagent such as sodium azide to provide the azido alcohol (not shown) which may be reduced to the amino alcohol **5** under conditions common to the art such as 1,3-propanedithiol and triethylamine in methanol or with hydrogen gas in the presence of a catalyst such as palladium on carbon. Acylation of **5** with an acid such as Cbz-leucine in the presence of a coupling agent such as EDC followed by removal of the BOC protecting group under acidic conditions provides the amine salt **6**. Coupling of **6** with Cbz-leucine may be effected with a coupling agent such as EDC to provide the intermediate alcohol (not shown) which was oxidized with an oxidant such as pyridine sulfur trioxide complex in DMSO and triethylamine to provide the ketone **7**.

Scheme 1



1 2 3 4 5 6 7

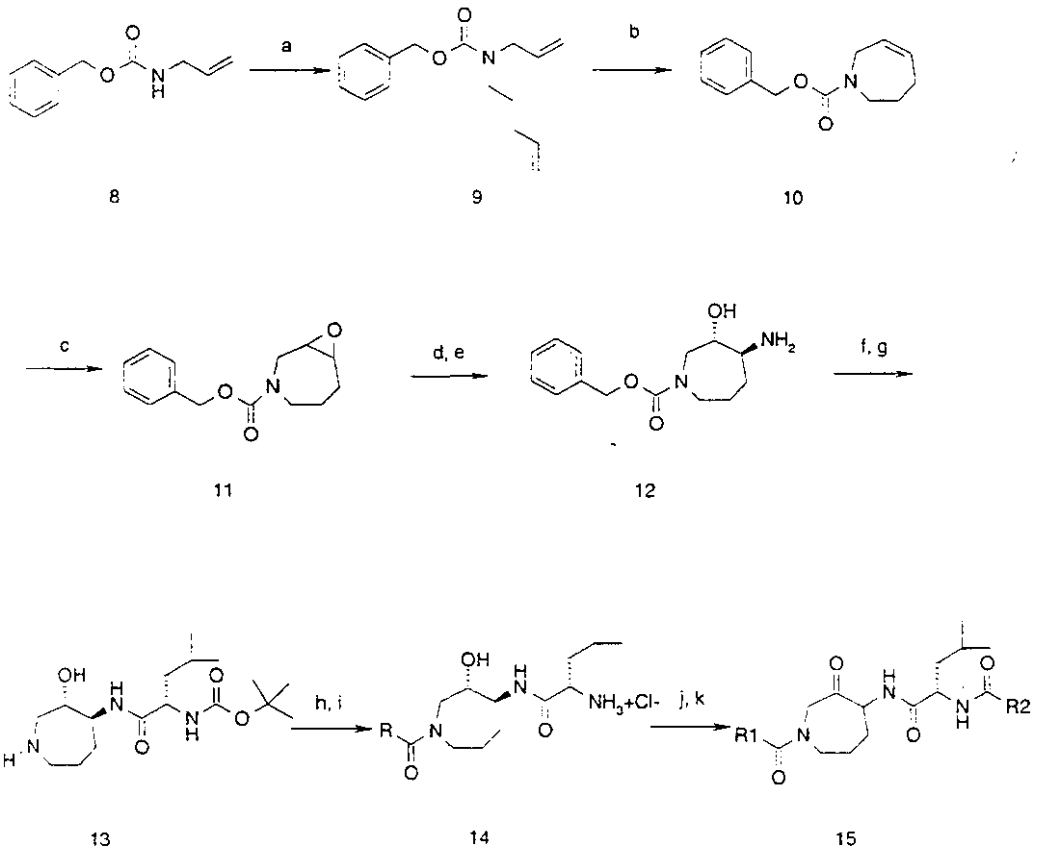
Reagents and conditions: a.) NaH, 5-bromo-1-pentene, DMF; b.) 2,6-diisopropylphenylimido neophylidene molybenum bis(tert-butoxide) or bis(tricyclohexylphosphine)benzylidine ruthenium (IV) dichloride catalyst, toluene c.) *m*-CPBA, CH_2Cl_2; d.) NaN_3, CH_3OH, H_2O, NH_4Cl; e.) 10% *Pd/C*, H_2, *f.) Cbz-leucine, EDC, CH_2Cl_2; g.) HCl, EtOAc; h.) Cbz-leucine, EDC, CH_2Cl_2; i.)* pyridine sulfur trioxide complex, DMSO, TEA.

Compounds of the general formula I wherein R^1 and R^2 are amides may be prepared in the general fashion outlined in Scheme 2. Alkylation of N-Cbz allyl amine (**8**) with a base such as sodium hydride and 5-bromo-1-pentene provides the diene **9**. Treatment of **9** with bis(tricyclohexylphosphine)benzylidine ruthenium(IV)dichloride olefin metathesis catalyst developed by Grubbs provides the azepine **10**. Epoxidation of **10** with standard oxidizing agents common to the art such as *m*-CPBA provide the epoxide **11**. Nucleophilic epoxide ring opening may be effected with a reagent such as sodium azide to provide the azido alcohol (not shown) which may be reduced to the amino alcohol **12** with a reducing agent such as propanedithiol in the presence of triethylamine. Acylation of **12** with N-Boc-

leucine and a coupling agent such as EDC followed by removal of the Cbz protecting group under hydrogenolysis conditions provides the amine **13**. Coupling of **13** with a carboxylic acid was effected with a coupling agent such as EDC followed by removal of the acid labile N-Boc protecting group with an acid such as HCl or TFA provides intermediate **14**.

Acylation of **14** may be effected with a carboxylic acid in the presence of a coupling agent common to the art such as EDC to give the intermediate alcohol (not shown) which is oxidized with an oxidant such as pyridine sulfur trioxide complex in DMSO and triethylamine to provide the ketone **15**.

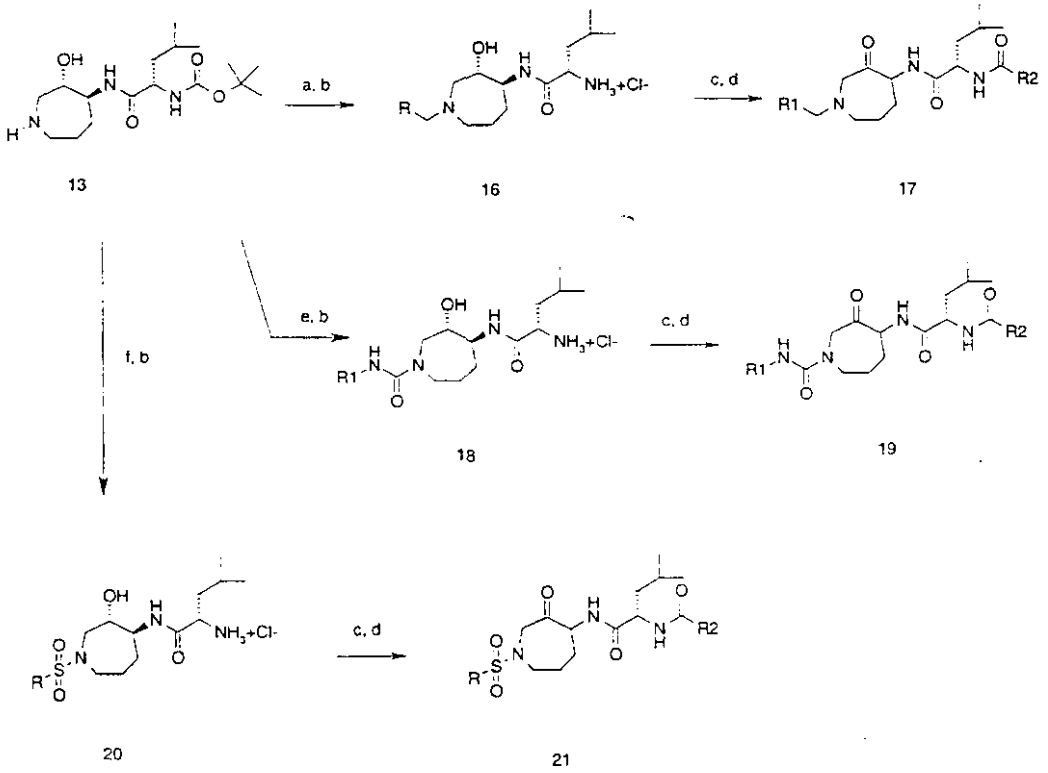
Scheme 2



Reagents and conditions: a.) NaH, 5-bromo-1-pentene, DMF; b.) bis(tricyclohexylphosphine)benzylidine ruthenium (IV) dichloride catalyst, CH_2Cl_2; c.) *m*-CPBA, CH_2Cl_2; d.) NaN_3, CH_3OH, H_2O, NH_4Cl; e.) propanedithiol, CH_3OH, TEA; f.) Boc-leucine, EDC, CH_2Cl_2; g.) 10% Pd/C, H_2; h.) R_1CO_2H, EDC, CH_2Cl_2 or R_1COCl, CH_2Cl_2; i.) HCl/ EtOAc; j.) R_2CO_2H, EDC, CH_2Cl_2; k.) pyridine sulfur trioxide complex, DMSO, TEA.

Compounds of the general formula I wherein R^2 is an alkyl, urea or sulphonamide group and R^1 is an amide may be prepared in the general fashion outlined in Scheme 3. Reductive amination of **13** may be effected by treatment with an aldehyde followed by a reducing agent such as sodium triacetoxyborohydride. Subsequent deprotection of the N-Boc group under acidic conditions provides the amine salt **16**. Coupling of **16** with an acid chloride or with a carboxylic acid in the presence of a coupling agent common to the art such as EDC followed by oxidation of the intermediate alcohol (not shown) with an oxidant such as pyridine sulfur trioxide complex provides the ketone **17**. Alternatively, treatment of amine **13** with an isocyanate followed by deprotection of the N-Boc group provides the amine salt **18**. Acylation and oxidation provides the ketone **19**. Further derivatization of amine **13** may be effected by treatment with a sulphonyl chloride followed by deprotection of the N-Boc group to provide the amine salt **20**. Acylation and oxidation provides the ketone **21**.

Scheme 3

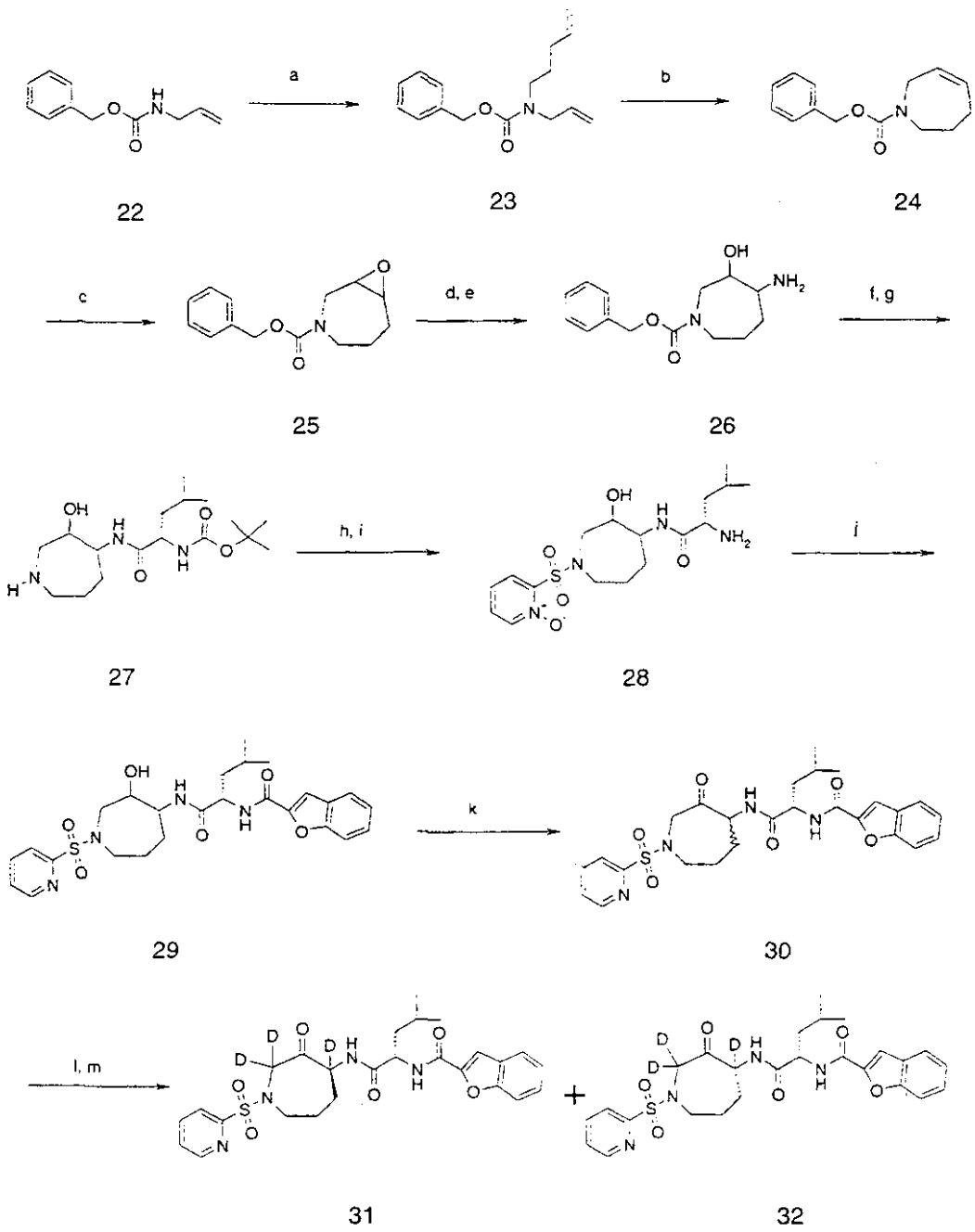


Reagents and conditions: a.) R_1CHO, $NaBH(OAc)_3$; b.) HCl; c.) R_2CO_2H, EDC, CH_2Cl_2; d.) pyridine sulfur trioxide complex, DMSO, TEA; e.) R_1NCO, base; f.) R_1SO_2Cl, TEA, CH_2Cl_2.

The deuterated compound of the Example 192 may be conveniently prepared according to Scheme 4. The skilled artisan will understand from Example 192 and Scheme 4 how to make any of the the deuterated compounds of the present invention.

The individual diastereomers of benzofuran-2-carboxylic acid {(S)-3-methyl-1-[(2,2',4-trideuterio)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide **31** and **32** may be prepared as outlined in Scheme 4. Alkylation of allyl-carbamic acid benzyl ester **22** with 5-bromo-1-pentene in the presence of a base such as sodium hydride provides the diene **23**. Treatment of diene **23** with bis(tricyclohexylphosphine)benzylidine ruthenium (IV) dichloride developed by Grubbs provides the 2,3,4,7-tetrahydro-azepine-1-carboxylic acid benzyl ester **24**. Epoxidation of azepine **24** may be effected with standard oxidizing agents common to the art such as *m*-CPBA to provide epoxide **25**. Nucleophilic epoxide ring opening of **25** may be effected with a reagent such as sodium azide to provide the azido alcohol (not shown).

Scheme 4

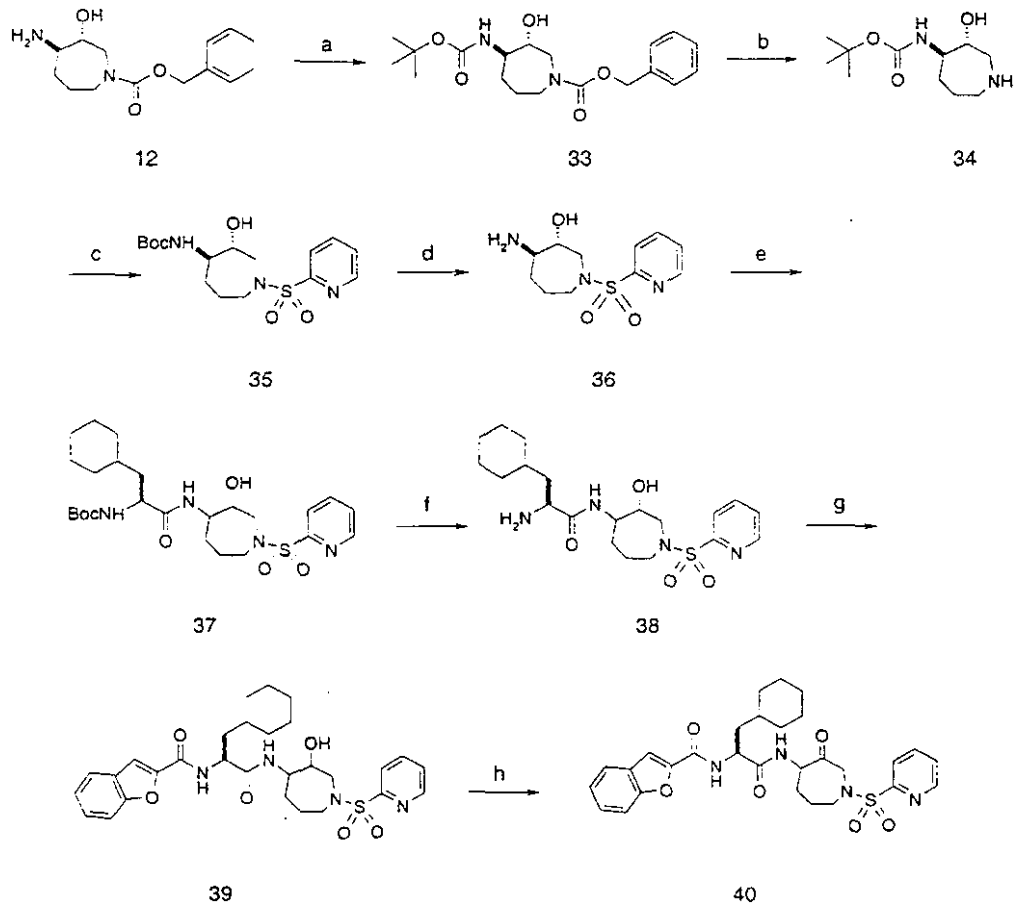


Reagents and Conditions: a.) NaH, 5-bromo-1-pentene, DMF; b.) bis(tricyclohexylphosphine)benzylidine ruthenium (IV) dichloride, CH_2Cl_2; c.) *m*-CPBA, CH_2Cl_2; d.) NaN_3, CH_3OH, H_2O, NH_4Cl; e.) 1,3-propanedithiol, TEA, methanol; f.) N-Boc-leucine, EDC, CH_2Cl_2; g.) 10% Pd/C, H_2; h.) 2-pyridinesulphonyl chloride, TEA, CH_2Cl_2; i.) 4 N HCl/dioxane, methanol; j.) benzofuran-2-carboxylic acid, EDC, CH_2Cl_2; k.) pyridine sulfur trioxide complex, DMSO, TEA; l.) CD_3OD;D_2O (10:1), TEA; m.) HPLC separation.

The intermediate azido alcohol may be reduced to the amino alcohol **26** under conditions common to the art such as 1,3-propanedithiol and triethylamine in methanol or with triphenylphosphine in tetrahydrofuran and water. Acylation of **26** may be effected with an acid such as N-Boc-leucine in the presence of a coupling agent such as EDC. Removal of the benzyloxycarbonyl protecting group with hydrogen gas in the presence of 10% Pd/C provides the amine **27**. Treatment of the amine **27** with 2-pyridinesulphonyl chloride in the presence of triethylamine or saturated sodium bicarbonate and CH_2Cl_2 followed by removal of the *tert*-butoxycarbonyl protecting group under acidic conditions provides **28**. Coupling of **28** with benzofuran-2-carboxylic acid may be effected with a coupling agent such as EDC to provide intermediate alcohol **29**. Alcohol **29** may be oxidized with an oxidant such as sulfur trioxide pyridine complex in DMSO and triethylamine to provide the ketone **30** as a mixture of diastereomers. Treatment of ketone **30** with triethylamine in CD_3OD:D_2O at reflux provides the deuterated analog as a mixture of diastereomers which are separated by HPLC to provide the deuterated compounds **31** and **32**.

Compounds of the general formula I may also be prepared as outlined in Scheme 5. The amine of compound **12** may be protected with with di-*tert*-butyldicarbonate to provide the N-Boc derivative **33** (Scheme 2). Removal of the benzyloxycarbonyl protecting group may be effected by treatment of **33** with hydrogen gas in the presence of a catalyst such as 10% Pd/C to provide the amine **34**. Treatment of amine **34** with a sulfonyl chloride such as 2-pyridinesulfonyl chloride in the presence of a base such as N-methylmorpholine or triethylamine provides the sulfonamide derivative **35**. Removal of the *tert*-butoxycarbonyl protecting group may be effected with an acid such as hydrochloric acid to provide intermediate **36**. Coupling of **36** with an acid such as N-Boc-cyclohexylalanine in the presence of a coupling agent common to the art such as HBTU or polymer supported EDC provides the alcohol intermediate **37**. Removal of the *tert*-butoxycarbonyl protecting group under acidic conditions provides amine **38**. Coupling of **38** with an acid such as benzofuran-2-carboxylic acid in the presence of a coupling agent such as HBTU or polymer supported EDC provides alcohol **39**. Alcohol **39** may be oxidized with an oxidant common to the art such as pyridine sulfur trioxide complex in DMSO and triethylamine or the Dess-Martin periodinane to provide the ketone **40**.

Scheme 5



Reagents and Conditions: (a) Di-*tert*-butyldicarbonate, THF; (b) H_2, 10% Pd/C, EtOAc; (c) 2-pyridylsulfonyl chloride, TEA ; (d) HCl, EtOAc; (e) N-Boc-cylohexylalanine, P-EDC, CH_2Cl_2; (f) HCl. CH_2Cl_2; (g) benzofuran-2-carboxylic acid, P-EDC, CH_2Cl_2; (h) Dess-Martin periodinane, methylene chloride.

The starting materials used herein are commercially available amino acids or are prepared by routine methods well known to those of ordinary skill in the art and can be found in standard reference books, such as the COMPENDIUM OF ORGANIC SYNTHETIC METHODS, Vol. I-VI (published by Wiley-Interscience).

Coupling methods to form amide bonds herein are generally well known to the art. The methods of peptide synthesis generally set forth by Bodansky *et al.*, THE PRACTICE OF PEPTIDE SYNTHESIS, Springer-Verlag, Berlin, 1984; E. Gross and J. Meienhofer, THE PEPTIDES, Vol. 1, 1-284 (1979); and J.M. Stewart and J.D. Young, SOLID PHASE

PEPTIDE SYNTHESIS, 2d Ed., Pierce Chemical Co., Rockford, Ill., 1984. are generally illustrative of the technique and are incorporated herein by reference.

Synthetic methods to prepare the compounds of this invention frequently employ protective groups to mask a reactive functionality or minimize unwanted side reactions. Such protective groups are described generally in Green, T.W, PROTECTIVE GROUPS IN ORGANIC SYNTHESIS, John Wiley & Sons, New York (1981). The term "amino protecting groups" generally refers to the Boc, acetyl, benzoyl, Fmoc and Cbz groups and derivatives thereof as known to the art. Methods for protection and deprotection, and replacement of an amino protecting group with another moiety are well known.

Acid addition salts of the compounds of Formula I are prepared in a standard manner in a suitable solvent from the parent compound and an excess of an acid, such as hydrochloric, hydrobromic, hydrofluoric, sulfuric, phosphoric, acetic, trifluoroacetic, maleic, succinic or methanesulfonic. Certain of the compounds form inner salts or zwitterions which may be acceptable. Cationic salts are prepared by treating the parent compound with an excess of an alkaline reagent, such as a hydroxide, carbonate or alkoxide, containing the appropriate cation; or with an appropriate organic amine. Cations such as Li^+, Na^+, K^+, Ca^{++}, Mg^{++} and NH_4^+ are specific examples of cations present in pharmaceutically acceptable salts. Halides, sulfate, phosphate, alkanoates (such as acetate and trifluoroacetate), benzoates, and sulfonates (such as mesylate) are examples of anions present in pharmaceutically acceptable salts.

This invention also provides a pharmaceutical composition which comprises a compound according to Formula I and a pharmaceutically acceptable carrier, diluent or excipient. Accordingly, the compounds of Formula I may be used in the manufacture of a medicament. Pharmaceutical compositions of the compounds of Formula I prepared as hereinbefore described may be formulated as solutions or lyophilized powders for parenteral administration. Powders may be reconstituted by addition of a suitable diluent or other pharmaceutically acceptable carrier prior to use. The liquid formulation may be a buffered, isotonic, aqueous solution. Examples of suitable diluents are normal isotonic saline solution, standard 5% dextrose in water or buffered sodium or ammonium acetate solution. Such formulation is especially suitable for parenteral administration, but may also be used for oral administration or contained in a metered dose inhaler or nebulizer for insufflation. It may be desirable to add excipients such as polyvinylpyrrolidone, gelatin,

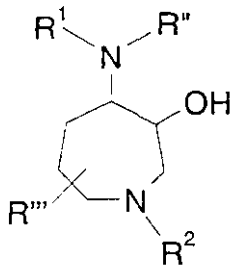
hydroxy cellulose, acacia, polyethylene glycol, mannitol, sodium chloride or sodium citrate.

Alternately, these compounds may be encapsulated, tableted or prepared in an emulsion or syrup for oral administration. Pharmaceutically acceptable solid or liquid carriers may be added to enhance or stabilize the composition, or to facilitate preparation of the composition. Solid carriers include starch, lactose, calcium sulfate dihydrate, terra alba, magnesium stearate or stearic acid, talc, pectin, acacia, agar or gelatin. Liquid carriers include syrup, peanut oil, olive oil, saline and water. The carrier may also include a sustained release material such as glyceryl monostearate or glyceryl distearate, alone or with a wax. The amount of solid carrier varies but, preferably, will be between about 20 mg to about 1 g per dosage unit. The pharmaceutical preparations are made following the conventional techniques of pharmacy involving milling, mixing, granulating, and compressing, when necessary, for tablet forms; or milling, mixing and filling for hard gelatin capsule forms. When a liquid carrier is used, the preparation will be in the form of a syrup, elixir, emulsion or an aqueous or non-aqueous suspension. Such a liquid formulation may be administered directly p.o. or filled into a soft gelatin capsule.

For rectal administration, the compounds of this invention may also be combined with excipients such as cocoa butter, glycerin, gelatin or polyethylene glycols and molded into a suppository.

Novel Intermediates

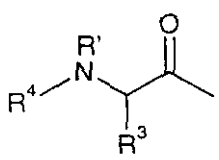
Referring to the methods of preparing the compounds of Formula I set forth in Schemes 1-4 above, the skilled artisan will appreciate that the present invention includes all novel intermediates required to make the compounds of Formula I. In particular, the present invention provides the compounds of Formula II:



II

wherein:

R^1 is selected from the group consisting of: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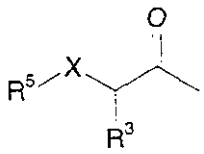
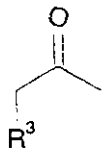
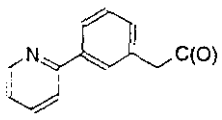

and

;

R^2 is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $R^9C(O)$-, $R^9C(S)$-, R^9SO_2-, $R^9OC(O)$-, $R^9R^{11}NC(O)$-, $R^9R^{11}NC(S)$-, $R^9(R^{11})NSO_2$-

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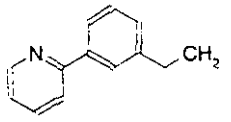
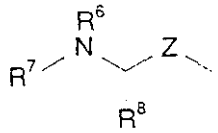


and ;

R^3 is selected from the group consisting of: H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, HetC_{0-6}alkyl and ArC_{0-6}alkyl;

R^3 and R' may be connected to form a pyrrolidine, piperidine or morpholine ring;

R^4 is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $R^5C(O)$-, $R^5C(S)$-, R^5SO_2-, $R^5OC(O)$-, $R^5R^{13}NC(O)$-, and $R^5R^{13}NC(S)$-;

R^5 is selected from the group consisting of: H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl;

R^6 is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, or Het-C_{0-6}alkyl;

R^7 is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $R^{10}C(O)$-, $R^{10}C(S)$-, $R^{10}SO_2$-, $R^{10}OC(O)$-, $R^{10}R^{14}NC(O)$-, and $R^{10}R^{14}NC(S)$-;

R^8 is selected from the group consisting of: H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, HetC_{0-6}alkyl and ArC_{0-6}alkyl;

R^9 is selected from the group consisting of: C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl:

R^{10} is independently selected from the group consisting of: C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl;

R^{11} is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R^{12} is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R^{13} is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R^{14} is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R' is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R" is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, or Het-C_{0-6}alkyl;

R'" is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

X is selected from the group consisting of: CH_2, S, and O;

Z is selected from the group consisting of: C(O) and CH_2;

and pharmaceutically acceptable salts, hydrates and solvates thereof.

The following compounds are preferred novel intermediates:

[(S)-1(3-Hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-carbamic acid benzyl ester;

(S)-2-Amino-4-methyl-pentanoic acid (1-benzyl-3-hydroxy-azepan-4-yl)-amide;

(S)-2-Amino-4-methyl-pentanoic acid{3-hydroxy-1-{2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-yl}-amide;

{(S)-1-[4-((S)-2-Amino-4-methyl-pentanoylamino)-3-hydroxy-azepan-1-ylmethyl]-3-methyl-butyl}-carbamic acid benzyl ester;

(S)-2-Amino-4-methyl-pentanoic acid-(1-benzoyl-3-hydroxy-azepan-4-yl)-amide;

(S)-2-Amino-4-methyl-pentanoic acid [3-hydroxy-1-(4-methyl-pentanoyl)-azepan-4-yl]-amide;

(S)-2-Amino-4-methyl-pentanoic acid (1-benzenesulfonyl-3-hydroxy-azepan-4-yl)-amide;

thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

5-methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

3-methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

quinoline-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide; and

quinoxaline-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide.

Process for Synthesis of Inventive Compounds

Referring to Schemes 1-5 herein above, the present invention provides a process for the synthesis of compounds of Formula (I) comprising the step of oxidizing the appropriate compound of Formula (II) with an oxidant to provide the compound of Formula (I) as a mixture of diastereomers. Preferably the oxidant is sulfur trioxide pyridine complex in DMSO and triethylamine.

Referring to Scheme 4, the present invention also provides a process for the synthesis of deuterated compounds of Formula (I). Specifically, when a deuterated isomer is desired, an additional step, following the oxidation step, of deuterating the protonated isomer with a deuterating agent to provide the deuterated compound of Formula (I) as a mixture of diastereomers is added to the synthesis. Preferably, the deuterating agent is CD_3OD:D_2O (10:1) in triethylamine.

The process further comprises the step of separating the diasteromers of Formula (I) by separating means, preferably by high presssure liquid chromatography (HPLC).

Utility of the Present Invention

The compounds of Formula I are useful as protease inhibitors, particularly as inhibitors of cysteine and serine proteases, more particularly as inhibitors of cysteine proteases, even more particularly as inhibitors of cysteine proteases of the papain superfamily, yet more particularly as inhibitors of cysteine proteases of the cathepsin family, most particularly as inhibitors of cathepsin K. The present invention also provides useful compositions and formulations of said compounds, including pharmaceutical compositions and formulations of said compounds.

The present compounds are useful for treating diseases in which cysteine proteases are implicated, including infections by pneumocystis carinii, trypsanoma cruzi, trypsanoma brucei, and Crithidia fusiculata; as well as in schistosomiasis, malaria, tumor metastasis, metachromatic leukodystrophy, muscular dystrophy, amytrophy; and especially diseases in which cathepsin K is implicated, most particularly diseases of excessive bone or cartilage loss, including osteoporosis, gingival disease including gingivitis and periodontitis, arthritis, more specifically, osteoarthritis and rheumatoid arthritis, Paget's disease; hypercalcemia of malignancy, and metabolic bone disease.

Metastatic neoplastic cells also typically express high levels of proteolytic enzymes that degrade the surrounding matrix, and certain tumors and metastatic neoplasias may be effectively treated with the compounds of this invention.

The present invention also provides methods of treatment of diseases caused by pathological levels of proteases, particularly cysteine and serine proteases, more particularly cysteine proteases, even more particularly cysteine proteases of the papain superfamily, yet more particularly cysteine proteases of the cathepsin family, which methods comprise administering to an animal, particularly a mammal, most particularly a human in need thereof a compound of the present invention. The present invention especially provides methods of treatment of diseases caused by pathological levels of cathepsin K, which methods comprise administering to an animal, particularly a mammal, most particularly a human in need thereof an inhibitor of cathepsin K, including a compound of the present invention. The present invention particularly provides methods for treating diseases in which cysteine proteases are implicated, including infections by pneumocystis carinii, trypsanoma cruzi, trypsanoma brucei, and Crithidia fusiculata; as well as in schistosomiasis, malaria, tumor metastasis, metachromatic leukodystrophy, muscular dystrophy, amytrophy, and especially diseases in which cathepsin K is implicated,

most particularly diseases of excessive bone or cartilage loss, including osteoporosis, gingival disease including gingivitis and periodontitis, arthritis, more specifically, osteoarthritis and rheumatoid arthritis, Paget's disease, hypercalcemia of malignancy, and metabolic bone disease.

This invention further provides a method for treating osteoporosis or inhibiting bone loss which comprises internal administration to a patient of an effective amount of a compound of Formula I, alone or in combination with other inhibitors of bone resorption, such as bisphosphonates (i.e., allendronate), hormone replacement therapy, anti-estrogens, or calcitonin. In addition, treatment with a compound of this invention and an anabolic agent, such as bone morphogenic protein, iproflavone, may be used to prevent bone loss or to increase bone mass.

For acute therapy, parenteral administration of a compound of Formula I is preferred. An intravenous infusion of the compound in 5% dextrose in water or normal saline, or a similar formulation with suitable excipients, is most effective, although an intramuscular bolus injection is also useful. Typically, the parenteral dose will be about 0.01 to about 100 mg/kg; preferably between 0.1 and 20 mg/kg, in a manner to maintain the concentration of drug in the plasma at a concentration effective to inhibit cathepsin K. The compounds are administered one to four times daily at a level to achieve a total daily dose of about 0.4 to about 400 mg/kg/day. The precise amount of an inventive compound which is therapeutically effective, and the route by which such compound is best administered, is readily determined by one of ordinary skill in the art by comparing the blood level of the agent to the concentration required to have a therapeutic effect.

The compounds of this invention may also be administered orally to the patient, in a manner such that the concentration of drug is sufficient to inhibit bone resorption or to achieve any other therapeutic indication as disclosed herein. Typically, a pharmaceutical composition containing the compound is administered at an oral dose of between about 0.1 to about 50 mg/kg in a manner consistent with the condition of the patient. Preferably the oral dose would be about 0.5 to about 20 mg/kg.

No unacceptable toxicological effects are expected when compounds of the present invention are administered in accordance with the present invention.

Biological Assays

The compounds of this invention may be tested in one of several biological assays to determine the concentration of compound which is required to have a given pharmacological effect.

Determination of cathepsin K proteolytic catalytic activity

All assays for cathepsin K were carried out with human recombinant enzyme. Standard assay conditions for the determination of kinetic constants used a fluorogenic peptide substrate, typically Cbz-Phe-Arg-AMC, and were determined in 100 mM Na acetate at pH 5.5 containing 20 mM cysteine and 5 mM EDTA. Stock substrate solutions were prepared at concentrations of 10 or 20 mM in DMSO with 20 uM final substrate concentration in the assays. All assays contained 10% DMSO. Independent experiments found that this level of DMSO had no effect on enzyme activity or kinetic constants. All assays were conducted at ambient temperature. Product fluorescence (excitation at 360 nM; emission at 460 nM) was monitored with a Perceptive Biosystems Cytofluor II fluorescent plate reader. Product progress curves were generated over 20 to 30 minutes following formation of AMC product.

Inhibition studies

Potential inhibitors were evaluated using the progress curve method. Assays were carried out in the presence of variable concentrations of test compound. Reactions were initiated by addition of enzyme to buffered solutions of inhibitor and substrate. Data analysis was conducted according to one of two procedures depending on the appearance of the progress curves in the presence of inhibitors. For those compounds whose progress curves were linear, apparent inhibition constants ($K_{i,app}$) were calculated according to equation 1 (Brandt *et al.*, *Biochemitsry*, **1989**, 28, 140):

$$v = V_m A / [K_a(1 + I/K_{i,\,app}) + A] \qquad (1)$$

where v is the velocity of the reaction with maximal velocity V_m , A is the concentration of substrate with Michaelis constant of K_a, and I is the concentration of inhibitor.

For those compounds whose progress curves showed downward curvature characteristic of time-dependent inhibition, the data from individual sets was analyzed to give k_{obs} according to equation 2:

$$[AMC] = v_{ss}\, t + (v_0 - v_{ss})\,[1 - exp\,(-k_{obs}t)] / k_{obs} \quad (2)$$

where [AMC] is the concentration of product formed over time t, v_0 is the initial reaction velocity and v_{ss} is the final steady state rate. Values for k_{obs} were then analyzed as a linear function of inhibitor concentration to generate an apparent second order rate constant (k_{obs} / inhibitor concentration or k_{obs} / [I]) describing the time-dependent inhibition. A complete discussion of this kinetic treatment has been fully described (Morrison *et al.*, *Adv. Enzymol. Relat. Areas Mol. Biol.*, **1988**, *61*, 201).

Human Osteoclast Resorption Assay

Aliquots of osteoclastoma-derived cell suspensions were removed from liquid nitrogen storage, warmed rapidly at 37°C and washed x1 in RPMI-1640 medium by centrifugation (1000 rpm, 5 min at 4°C). The medium was aspirated and replaced with murine anti-HLA-DR antibody, diluted 1:3 in RPMI-1640 medium, and incubated for 30 min on ice The cell suspension was mixed frequently.

The cells were washed x2 with cold RPMI-1640 by centrifugation (1000 rpm, 5 min at 4°C) and then transferred to a sterile 15 mL centrifuge tube. The number of mononuclear cells were enumerated in an improved Neubauer counting chamber.

Sufficient magnetic beads (5 / mononuclear cell), coated with goat anti-mouse IgG, were removed from their stock bottle and placed into 5 mL of fresh medium (this washes away the toxic azide preservative). The medium was removed by immobilizing the beads on a magnet and is replaced with fresh medium.

The beads were mixed with the cells and the suspension was incubated for 30 min on ice. The suspension was mixed frequently. The bead-coated cells were immobilized on a magnet and the remaining cells (osteoclast-rich fraction) were decanted into a sterile 50 mL centrifuge tube. Fresh medium was added to the bead-coated cells to dislodge any trapped osteoclasts. This wash process was repeated x10. The bead-coated cells were discarded.

The osteoclasts were enumerated in a counting chamber, using a large-bore disposable plastic pasteur pipette to charge the chamber with the sample. The cells were pelleted by centrifugation and the density of osteoclasts adjusted to $1.5x10^4$/mL in EMEM medium, supplemented with 10% fetal calf serum and 1.7g/litre of sodium bicarbonate. 3 mL aliquots of the cell suspension (per treatment) were decanted into 15 mL centrifuge tubes. These cells were pelleted by centrifugation. To each tube 3 mL of the appropriate treatment was added (diluted to 50 uM in the EMEM medium). Also included were appropriate vehicle controls, a positive control (87MEM1 diluted to 100 ug/mL) and an isotype control (IgG2a diluted to 100 ug/mL). The tubes were incubate at 37°C for 30 min.

0.5 mL aliquots of the cells were seeded onto sterile dentine slices in a 48-well plate and incubated at 37°C for 2 h. Each treatment was screened in quadruplicate. The slices were washed in six changes of warm PBS (10 mL / well in a 6-well plate) and then placed into fresh treatment or control and incubated at 37°C for 48 h. The slices were then washed in phosphate buffered saline and fixed in 2% glutaraldehyde (in 0.2M sodium cacodylate) for 5 min., following which they were washed in water and incubated in buffer for 5 min at 37°C. The slices were then washed in cold water and incubated in cold acetate buffer / fast red garnet for 5 min at 4°C. Excess buffer was aspirated, and the slices were air dried following a wash in water.

The TRAP positive osteoclasts were enumerated by bright-field microscopy and were then removed from the surface of the dentine by sonication. Pit volumes were determined using the Nikon/Lasertec ILM21W confocal microscope.

General

Nuclear magnetic resonance spectra were recorded at either 250 or 400 MHz using, respectively, a Bruker AM 250 or Bruker AC 400 spectrometer. $CDCl_3$ is deuteriochloroform, DMSO-d_6 is hexadeuteriodimethylsulfoxide, and CD_3OD is tetradeuteriomethanol. Chemical shifts are reported in parts per million (d) downfield from the internal standard tetramethylsilane. Abbreviations for NMR data are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, app = apparent, br = broad. J indicates the NMR coupling constant measured in Hertz. Continuous wave infrared (IR) spectra were recorded on a Perkin-Elmer 683 infrared spectrometer, and Fourier transform infrared (FTIR) spectra were recorded on a Nicolet Impact 400 D infrared spectrometer. IR and FTIR spectra were

recorded in transmission mode, and band positions are reported in inverse wavenumbers (cm^{-1}). Mass spectra were taken on either VG 70 FE, PE Syx API III, or VG ZAB HF instruments, using fast atom bombardment (FAB) or electrospray (ES) ionization techniques. Elemental analyses were obtained using a Perkin-Elmer 240C elemental analyzer. Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. All temperatures are reported in degrees Celsius.

Analtech Silica Gel GF and E. Merck Silica Gel 60 F-254 thin layer plates were used for thin layer chromatography. Both flash and gravity chromatography were carried out on E. Merck Kieselgel 60 (230-400 mesh) silica gel.

Where indicated, certain of the materials were purchased from the Aldrich Chemical Co., Milwaukee, Wisconsin, Chemical Dynamics Corp., South Plainfield, New Jersey, and Advanced Chemtech, Louisville, Kentucky.

Examples

In the following synthetic examples, temperature is in degrees Centigrade (°C). Unless otherwise indicated, all of the starting materials were obtained from commercial sources. Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. These Examples are given to illustrate the invention, not to limit its scope. Reference is made to the claims for what is reserved to the inventors hereunder.

Example 1

Preparation of {(S)-1-[1-((S)-2-Benzyloxycarbonylamino-4-methyl-pentanoyl)-3-oxo-azepan-4-ylcarbamoyl}carbamic acid benzyl ester

a.) Allyl-pent-4-enyl-carbamic acid *tert*-butyl ester

To a suspension of NaH (3.05 g, 76.33 mmol of 60% NaH in oil; washed with hexanes) in DMF (30 mL) was added *tert*-butyl N-allylcarbamate (6.0 g, 38.2 mmol) in a dropwise fashion. The mixture was stirred at room temperature for approximately 10 minutes whereupon 5-bromo-1-pentene (6.78 mL, 57.24 mmol) was added in a dropwise fashion. The reaction was heated to 40°C for approximately 2 hours whereupon the reaction was partitioned between ethyl acetate and water. The organic layer was washed with water (2 x's), brine, dried ($MgSO_4$), filtered and concentrated to give 10 grams of the title compound as an oil: MS(EI) 226 ($M+H^+$).

b.) 2,3,4,7-Tetrahydro-azepine-1-carboxylic acid *tert*-butyl ester

To a solution of compound of Example 1a (4.5 g) in benzene was added the 2,6-diisopropylphenylimidoneophylidene molybdenum bis(*t*-butoxide) (600 mg). The reaction was heated to reflux for 1.5 hours whereupon the reaction was concentrated *in vacuo*. Chromatography (50% CH_2Cl_2:hexanes) of the residue gave 3.92 g of the product:

c.) 8-Oxa-3-aza-bicyclo[5.1.0]octane-3-carboxylic acid *tert*-butyl ester

To a solution of the compound of Example 1b (3.0 g, 15.2 mmol) in CH_2Cl_2 was added m-CPBA (7.8 g, 45.6 mmol). The mixture was stirred overnight at room temperature whereupon it was partitioned between CH_2Cl_2 and staurated K_2CO_3. The organic layer was washed with sat. $NaHCO_3$, water, brine, dried ($MgSO_4$), filtered and concentrated to give 3.11 g of the title compound as an oil: MS(EI) 214 ($M+H^+$).

d.) 4-Azido-3-hydroxy-azepane-1-carboxylic acid *tert*-butyl ester

To a solution of the epoxide from Example 1c (3.92 g, 20 mmol) in methanol:water (180 mL of an 8:1 solution) was added NH_4Cl (3.18 g, 60 mmol) and sodium azide (3.9 g, 60 mmol). The reaction was heated to 40°C until complete consumption of the starting epoxide was observed by TLC analysis. The majority of the

solvent was removed *in vacuo* and the remaining solution was diluted with ethyl acetate and washed with water, brine dried (Na_2SO_4), filtered and concentrated. Column chromatography (40% ethyl acetate:hexanes) of the residue provided 3.43 g of the title compound.

e.) 4-Amino-3-hydroxy-azepane-1-carboxylic acid *tert*-butyl ester

To a solution of the azido alcohol of Example 1d (3.4 g) and 10% Pd/C (catalytic) in ethyl acetate:methanol (2:1 solution) was affixed a balloon of hydrogen. The reaction was stirred until complete consumption of the starting material was observed by TLC analysis. The reaction was filtered to remove the catalyst and the filtrate was concentrated *in vacuo*. Column chromatography of the residue (25% methanol:dichloromethane) provided 2.57 g of the title compound: MS(EI) 231 ($M+H^+$).

f.) 4-((S)-2-benzyloxycarbonylamino-4-methyl-pentanoylamino)-3-hydroxy-azepane-1-carboxylic acid *tert* butyl ester

To a solution of the amino alcohol of Example 1e (160 mg, 0.70 mmol) in CH_2Cl_2 was added EDC (134 mg), HOBt (94 mg) and Cbz-leucine (185 mg). The reaction was maintained at room temperature until complete consumption of the starting material was observed by TLC analysis. The reaction was diluted with ethyl acetate and washed with 1N HCl, sat. K_2CO_3, water, brine, dried ($MgSO_4$), filtered and concentrated. Column chromatography of the residue (3% methanol:dichloromethane) gave 200 mg of the title compound: MS(EI) 478 ($M+H^+$), 500 ($M+Na^+$).

g.) [(S)-1-(3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-carbamic acid benzyl ester

A solution of the compound of Example 1f (200 mg, 0.42 mmol) in methanol (5 mL) was added 4M HCl in dioxane (5 mL). The reaction was stirred at room temperature for approximately 2 hours whereupon the solvent was removed *in vacuo* to provide 168 mg of the title compound: MS(EI) 378 ($M+H^+$).

h.) {(S)-1-[4-((S)-2-Benzyloxycarbonylamino-4-methyl-pentanoylamino)-3-hydroxy-azepane-1-carbonyl]-3-methyl-butyl}carbamic acid benzyl ester

To a solution of the amine salt of Example 1g (168 mg, 0.42 mmol) in CH_2Cl_2 was added EDC (81 mg), HOBt (57 mg), triethylamine (0.09 mL) and Cbz-leucine (111 mg). The reaction was stirred until complete by TLC analaysis. Workup followed by column chromatography (5% CH_3OH:CH_2Cl_2) provided 159 mg of the title compound: MS(EI) 625 ($M+H^+$).

i.) {(S)-1-[4-((S)-2-Benzyloxycarbonylamino-4-methyl-pentanoylamino)-3-oxo-azepane-1-carbonyl]-3-methyl-butyl}carbamic acid benzyl ester

To a solution of the alcohol of Example 1h (130 mg, 0.21 mmol) in DMSO was added TEA (0.17 mL) and pyridine sulfur trioxide complex (97 mg, 0.62 mmol). The reaction was stirred at room temperature for approximately 2 hours whereupon it was partitioned between ethyl acetate and water. The organic layer was washed with brine, dried ($MgSO_4$), filtered and concentrated. Column chromatography of the residue (5% CH_3OH:CH_2Cl_2) provided 100 mg of the title compound as a mixture of diastereomers: ^1H NMR ($CDCl_3$): δ 1.0 (m, 12H), 1.5-2.1 (m, 8H), 2.2 (m, 4H), 3.0 (m, 1H), 3.5 (d, 1H). 3.6 (d, 1H), 4.01 (m, 1H), 4.5 (m, 2H), 4.7 (m, 1H), 5.0 (m, 5H), 7.3 (m, 10H): MS (EI) 623($M+H^+$), 645 ($M+Na^+$). Separation of the diastereomers by HPLC provided diastereomer 1:MS (EI) 623 ($M+H^+$), 645 ($M+Na^+$) and diastereomer 2: MS (ES) 623 ($M+H^+$), 645 ($M+Na^+$).

Example 2

Preparation of Naphthylene-2-carboxylic acid[(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

a.) Allyl-pent-4-enyl-carbamic acid benzyl ester

To a suspension of NaH (1.83 g, 76.33 mmol of 90% NaH) in DMF was added benzyl allyl-carbamic acid benzyl ester (7.3 g, 38.2 mmol) in a dropwise fashion. The mixture was stirred at room temperature for approximately 10 minutes whereupon 5-bromo-1-pentene (6.78 mL, 57.24 mmol) was added in a dropwise fashion. The reaction was heated to 40°C for approximately 4 hours whereupon the reaction was partitioned between dichloromethane and water. The organic layer was washed with water (2x's), brine, dried ($MgSO_4$), filtered and concentrated. Column chromatography of the residue (10% ethyl acetate:hexanes) provided 10.3 grams of the title compound as an oil: MS(EI) 260 ($M+H^+$).

b.) 2,3,4,7-Tetrahydro-azepine-1-carboxylic acid benzyl ester

To a solution of compound of Example 2a (50 g) in dichloromethane was added bis(tricyclohexylphosphine)benzylidine ruthenium (IV) dichloride (5.0 g). The reaction was heated to reflux until complete as determined by TLC analysis. The reaction was concentrated *in vacuo*. Column chromatography of the residue (50% dichloromethane:hexanes) gave 35 g of the title compound: MS(EI) 232 ($M+H^+$).

c.) 8-Oxa-3-aza-bicyclo[5.1.0]octane-3-carboxylic acid benzyl ester

Following the general procedure of Example 1c except substituting the compound of Example 2b the title compound was prepared: MS(EI) 248 ($M+H^+$), 270 ($M+Na^+$).

d.) 4-azido-3-hydroxy-azepane-1-carboxylic acid benzyl ester

To a solution of the epoxide from Example 2c (2.0 g, 8.1 mmol) in methanol:water (8:1 solution) was added NH_4Cl (1.29 g, 24.3 mmol) and sodium azide (1.58 g, 24.30 mmol). The reaction was heated to 40°C until complete consumption of the starting epoxide was observed by TLC analysis. The majority of the solvent was removed *in vacuo* and the remaining solution was partitioned between ethyl acetate and pH 4 buffer. The

organic layer was washed with sat. $NaHCO_3$, water, brine dried ($MgSO_4$), filtered and concentrated. Column chromatography (20% ethyl acetate:hexanes) of the residue provided 1.3 g of the title compound: MS(EI) 291 ($M+H^+$) plus 0.14 g of trans-4-hydroxy-3-azido-hexahydro-1H-azepine

e.) 4-amino-3-hydroxy-azepane-1-carboxylic acid benzyl ester

To a solution of the azido alcohol of Example 2d (1.1 g, 3.79 mmol) in methanol was added triethylamine (1.5 mL, 11.37 mmol) and 1,3-propanedithiol (1.1 mL, 11.37 mL). The reaction was stirred until complete consumption of the starting material was observed by TLC analysis whereupon the reaction was concentrated *in vacuo*. Column chromatography of the residue (20% methanol:dichloromethane) provided 0.72 g of the title compound: MS(EI) 265 ($M+H^+$).

f.) 4-((S)-2-*tert*-Butoxycarbonylamino-4-methyl-pentanoylamino)-3-hydroxy-azepan-1-carboxylic acid benzyl ester

To a solution of the amino alcohol of Example 2e (720 mg, 2.72 mmol) in CH_2Cl_2 was added EDC (521 mg), HOBt (368 mg) and N-Boc-leucine (630 mg). The reaction was maintained at room temperature until complete consumption of the starting material was observed by TLC analysis. The reaction was diluted with ethyl acetate and washed with 1N HCl, sat. K_2CO_3, water, brine, dried ($MgSO_4$), filtered and concentrated. Column chromatography of the residue (3% methanol:dichloromethane) gave 1.0 g of the title compound: MS(EI) 478 ($M+H^+$).

g.) [(S)-1-(3-Hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-carbamic acid *tert* butyl ester

To a solution of the compound of Example 2f (1.0 g) and 10% Pd/C (catalytic) in ethyl acetate:methanol (2:1 solution) was affixed a balloon of hydrogen. The reaction was stirred until complete consumption of the starting material was observed by TLC analysis. The reaction was filtered to remove the catalyst and the filtrate was concentrated *in vacuo* to provide 0.82 g of the title compound: MS(EI) 344 ($M+H^+$).

h.) [(S)-1-(1-Benzyl-3-Hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-carbamic acid *tert* butyl ester

To a solution of the compound of Example 2g (0.69 g, 2.01 mmol) in CH_2Cl_2 was added benzaldehyde (0.32 mL, 3.01 mmol) followed by sodium triacetoxyborohydride (0.85 g, 4.02 mmol). The reaction was stirred until complete as determined by TLC analysis whereupon several drops of water were added to the reaction to destroy the excess sodium triacetoxyborohydride. The mixture was diluted with ethyl acetate washed with sat. $NaHCO_3$, water, brine, dried (Na_2SO_4), filtered and concentrated. Column chromatography of the residue (5% methanol:dichloromethane) gave 800 mg of the title compound: MS(ES) 434 ($M+H^+$).

i.) (S)-2-Amino-4-methyl-pentanoic acid (1-benzyl-3-hydroxy-azepan-4-yl)-amide

To a solution of the compound of Example 2h (800 mg) in methanol (15 mL) was added 4M HCl in dioxane (15 mL). The reaction was stirred at room temperature overnight whereupon it was concentrated *in vacuo* to give 800 mg of the title compound: MS(ES) 334 (M+H+).

j.) Naphthylene-2-carboxylic acid [(S)-1-(1-benzyl-3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

To a solution of the amine salt of Example 2i (200 mg, 0.49 mmol) in CH_2Cl_2 was added triethylamine (0.17 mL, 1.22 mmol), EDC (103.5 mg, 0.54 mmol), HOBt (73 mg, 0.54 mmol) and 2-naphthoic acid (93 mg, 0.54 mmol). The reaction was stirred until complete by TLC analysis. The reaction was diluted with ethyl acetate and washed with sat. $NaHCO_3$, water, brine, dried (Na_2SO_4), filtered and concentrated. Column chromatography of the residue (5% methanol:dichloromethane) gave 0.14 g of the title compound: MS(EI) 488 ($M+H^+$).

k.) Naphthylene-2-carboxylic acid[(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

Following the general procedure of Example 1i except substituting the compound of Example 2j for the compound of Example 1i the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.9 (m, 1H), 3.2 (dd, 1H). 3.4 (m, 1H), 3.7 (m, 2H), 4.7 (m, 1H), 5.2 (m, 1H), 7.2-8.4 (m, 12H): MS(EI): 486

(M+H$^+$,100%). Separation of the diastereomers by HPLC provided diastereomer 1: MS (EI) 486.3 (M+H$^+$), and diastereomer 2: MS (ES) 486.3 (M+H$^+$).

Example 3

Preparation of Benzo[1,3]dioxole-5-carboxylic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

a.) Benzo[1,3]dioxole-5-carboxylic acid [(S)-1-(1-benzyl-3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the general procedure of Example 2j except substituting piperonylic acid for 2-naphthoic acid the title compound was prepared: MS(ES) 482 (M+H$^+$).

b.) Benzo[1,3]dioxole-5-carboxylic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the general procedure of Example 1i except substituting the compound of Example 3a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.9 (m, 1H), 3.0 (m, 1H). 3.2 (d, 1H), 3.5 (q, 1H), 3.7 (m, 2H), 4.7 (m, 1H), 5.2 (m, 1H), 6.0 (s, 2H), 6.8 (m, 2H).7.2 (m, 6H); MS(EI): 480 (M+H$^+$,100%). The diastereomers were separated by preparative scale HPLC. Lyophilisation of the eluents provided diastereomer 1: MS (EI) 480.3 (M+H$^+$), 959.6 2M+H$^+$) and diastereomer 2: MS (EI) 480.3 (M+H$^+$), 959.6 2M+H$^+$).

Example 4

Preparation of Benzofuran-2-carboxylic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

a.) Benzofuran-2-carboxylic acid [(S)-1-(1-benzyl-3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the general procedure of Example 2j except substituting benzofuran-2-carboxylic acid for 2-naphthoic acid the title compound was prepared: MS(ES) 478 ($M+H^+$).

b.) Benzofuran-2-carboxylic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the general procedure of Example 1i except substituting the compound of Example 4a the title compound was prepared: 476 MS(EI): 492 ($M+H^+$,100%). The diastereomers were separated by preparative scale HPLC. Lyophilisation of the eluents provided diastereomer 1: MS (EI) 476.4 ($M+H^+$), 951.6 ($M+H^+$) and diastereomer 2: MS (EI) 476.4 ($M+H^+$), 951.6 $2M+H^+$).

Example 5

Preparation of Benzo[b]thiophene-2-carboxylic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

a.) Benzo[b]thiophene-2-carboxylic acid [(S)-1-(1-benzyl-3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the general procedure of Example 2j except substituting benzothiophene-2-carboxylic acid for 2-naphthoic acid the title compound was prepared: MS(ES) 494 ($M+H^+$).

b.) Benzo[b]thiophene-2-carboxylic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the general procedure of Example 1i except substituting the compound of Example 5a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.9 (m, 1H), 3.2 (dd, 1H). 3.4 (m, 1H), 3.7 (m, 2H), 4.7 (m, 1H), 5.2 (m, 1H), 7.2-8.4 (m, 10H): MS(EI): 492 ($M+H^+$,100%)

The diastereomers were separated by preparative scale HPLC. Lyophilisation of the eluents provided diastereomer 1: MS (EI) 492.4 ($M+H^+$), 983.7 $2M+H^+$) and diastereomer 2: MS (EI) 492.4 ($M+H^+$), 983.7 $2M+H^+$).

Example 6

Preparation of Naphthylene-2-sulphonyl [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

a.) Naphthylene-2-sulphonyl [(S)-1-(1-benzyl-3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

To a solution of the amine salt of Example 2i (200 mg, 0.49 mmol) in CH_2Cl_2 was added triethylamine (0.24 mL, 1.72 mmol) and 2-naphthalenesulphonyl chloride (122 mg, 0.54 mmol). The reaction was stirred at room temperature until complete as determined by TLC analysis. The reaction was worked-up, dried (Na_2SO_4), filtered and concentrated. Column chromatography of the residue (10% methanol:dichloromethane) provided 52 mg of the title compound: MS(EI) 524 ($M+H^+$).

b.) Naphthylene-2-sulphonyl [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

Following the general procedure of Example 1i except substituting the compound of Example 6a the title compound was prepared: : ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.0 (dd, 1H). 3.3 (m, 1H), 3.6 (m, 2H), 3.7 (m, 1H), 4.7 (m, 1H), 5.3 (m, 1H), 7.2-8.4 (m, 12H): MS(EI): 522 ($M+H^+$,100%)

Example 7

Preparation of Quinoline-2-carboxylic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

a.) Quinoline-2-carboxylic acid [(S)-1-(1-benzyl-3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the general procedure of Example 2j except substituting 2-quinolinecarboxylic acid for 2-naphthoic acid the title compound was prepared: MS(ES) 489 ($M+H^+$).

b.) Quinoline-2-carboxylic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the general procedure of Example 1i except substituting the compound of Example 7a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.9 (m, 1H), 3.2 (dd, 1H). 3.4 (m, 1H), 3.7 (m, 2H), 4.7 (m, 1H), 5.2 (m, 1H), 7.2-8.4 (m, 11H); MS(EI): 487 ($M+H^+$,100%). The diastereomers were separated by preparative scale HPLC. Lyophilisation of the eluents provided diastereomer 1: MS (EI) 492.4 ($M+H^+$), 983.7 $2M+H^+$) and diastereomer 2: MS (EI) 492.4 ($M+H^+$), 983.7 $2M+H^+$).

Example 8

Preparation of 3,4-dichlorobenzoic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

a.) 3,4-dichlorobenzoic acid [(S)-1-(1-benzyl-3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the general procedure of Example 2j except substituting 3,4-dichlorbenzoic acid for 2-naphthoic acid the title compound was prepared: MS(ES) 506 ($M+H^+$).

b.) 3,4-dichlorobenzoic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the general procedure of Example 1i except substituting the compound of Example 8a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.9 (m, 1H), 3.2 (dd, 1H). 3.4 (m, 1H), 3.7 (m, 2H), 4.7 (m, 2H), 5.2 (m, 1H), 7.2-8.4 (m, 8H); MS(EI): 504 (M^+,100%) .

Example 9

Preparation of 4-{(S)-Methyl-2-[(quinoline-2-carbonyl)-amino]pentanoylamino}-3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]azepanium

a.) 4-((S)-2-*tert*-Butoxycarbonylamino-4-methyl-pentanoylamino)-3-hydroxy-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepanium

To a solution of the compound of Example 2g (0.5g, 1.46 mmol) in CH_2Cl_2 was added EDC (307 mg, 1.60 mmol), HOBt (216 mg, 1.60 mmol) and 3-(2-pyridyl)phenyl acetic acid (341 mg, 1.60 mmol). The reaction was stirred at room temperature until complete as determined by TLC analysis. Workup and column chromatography (2% methanol:dichloromethane) provided the title compound: MS(ES) 539 ($M+H^+$).

b.) 4-((S)-Amino-4-methyl-pentanoylamino)-3-hydroxy-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepanium

To a solution of the compound of Example 9a (1.3 g) dissolved in methanol (20 mL was added 4M HCl in dixoane (20 mL). The reaction was stirred until complete by TLC analysis whereupon it was concentrated *in vacuo* to give 1.1 g of the title compound: MS(EI) 439 ($M+H^+$).

c.) 4-{(S)-Methyl-2-[(quinoline-2-carbonyl)-amino]pentanoylamino}-3-hydroxy-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]azepanium

Following the procedure of Example 7a except substituting the compound of Example 9b the title compound was prepared: MS(EI) 594 ($M+H^+$).

d.) 4-{(S)-Methyl-2-[(quinoline-2-carbonyl)-amino]pentanoylamino}-3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]azepanium

Following the procedure of Example 1i except substituting the compound of Example 9c the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.9 (m, 1H), 3.4 (dd, 1H). 3.8 (m, 3H), 4.1 (m, 2H), 4.7 (m, 3H), 5.4 (m, 1H), 7.2-8.4 (m, 14H); MS(EI): 592 ($M+H^+$,100%) .

Example 10

Preparation of 1-((S)-2-Benzyloxycarbonylamino-4-methyl-pentyl)-4-{(S)-4-methyl-2-[(2-quinoiline-2-carbonyl)-amino]-pentanoylamino)-3-oxo-azepanium

a.) 1-((S)-2-Benzyloxycarbonylamino-4-methyl-pentyl)-4-((S)-2-*tert*-butoxycarbonylamino-4-methyl-pentanoylamino)-3-hydroxy-azepanium

Following the procedure of Example 2h except substituting Cbz-leucinal for benzaldehyde the title compound was prepared: MS(EI) 577 ($M+H^+$).

b.) 4-((S)-2-Amino-4-methy-pentanoylamino)-1-((S)-2-*tert*-benzylxycarbonylamino-4-methyl-pentyl)-3-hydroxy-azepanium

Following the procedure of Example 2i except substituting the compound of Example 10a the title compound was prepared: MS(EI) 477 ($M+H^+$).

c.) 1-((S)-2-Benzyloxycarbonylamino-4-methyl-pentyl)-4-{(S)-4-methyl-2-[(2-quinoiline-2-carbonyl)-amino]-pentanoylamino)-3-hydroxy-azepanium

Following the procedure of Example 7a except substituting the compound of Example 10b the title compound was prepared: MS(EI) 632 (M+H+).

d.) 1-((S)-2-Benzyloxycarbonylamino-4-methyl-pentyl)-4-{(S)-4-methyl-2-[(2-quinoiline-2-carbonyl)-amino]-pentanoylamino)-3-oxo-azepanium

Following the procedure of Example 1i except substituting the compound of Example 10c the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m. 12H), 1.5-2.1 (m, 10H),

2.2 (m, 4H), 2.9 (m, 1H), 3.4 (M, 2H). 3.7 (m, 1H), 4.7 (m, 2H), 5.2 (m, 3H), 7.2 (m, 4H), 7.5 (m, 1H), 7.6 (m, 1H), 7.7 (m, 1H), 8.1 (m, 1H), 8.2 (m, 2H), 8.5 (m, 1H); MS(EI): 630 ($M+H^+$,100%) .

Example 11

Preparation of 1-Benzoyl-4-((S)-2-(benzo[1,3]dioxole-carbonylamino)-4-methyl-pentanoylamino)-3-oxo-azepanium

a.) 1-Benzoyl-4-((S)-2-*tert*-butoxycarbonylamino-4-methyl-pentanoylamino)-3-hydroxy-azepanium

Following the procedure of Example 9a except substituting benzoic acid for 3-(2-pyridyl)phenyl acetic acid the title compound was prepared: MS(EI) 448($M+H^+$).

b.) 4-((S)-2-Amino-4-methyl-pentanoylamino)-1-benzoyl-3-hydroxy-azepanium

Following the procedure of Example 2i except substituting the compound of Example 11a the title compound was prepared: MS(EI) 348 ($M+H^+$).

c.) 1-Benzoyl-4-((S)-2-(benzo[1,3]dioxole-carbonylamino)-4-methyl-pentanoylamino)-3-hydroxy-azepanium

Following the procedure of Example 2j except substituting the compound of Example 11b for the compound of Example 2j and piperonylic acid for 2-naphthoic acid the title compound was prepared: MS(EI) 496 (M+H+).

d.) 1-Benzoyl-4-((S)-2-(benzo[1,3]dioxole-carbonylamino)-4-methyl-pentanoylamino)-3-oxo-azepanium

Following the procedure of Example 1i except substituting the compound of Example 11c the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.9 (m, 1H), 3.2 (dd, 1H). 3.4 (m, 1H), 3.7 (m, 2H), 4.7 (m, 1H), 5.2 (m, 1H), 6.0 (s, 2H), 7.2-8.4 (m, 8H); MS(EI): 494 ($M+H^+$, 70%).

Example 12

Preparation of 1-Benzoyl-4-((S)-2-(4-fluoro-benzoylamino)-4-methyl-pentanoylamino)-3-oxo-azepanium

a.) 1-Benzoyl-4-((S)-2-(4-fluoro-benzoylamino)-4-methyl-pentanoylamino)-3-hydroxy-azepanium

Following the procedure of Example 11c except substituting 4-fluorobenzoic acid for piperonylic acid the title compound was prepared: MS(EI) 470 (M+H+).

b.) 1-Benzoyl-4-((S)-2-(4-fluoro-benzoylamino)-4-methyl-pentanoylamino)-3-oxo-azepanium

Following the procedure of Example 1i except substituting the compound of Example 12a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.0 (dd, 1H). 3.6 (m, 1H), 4.0 (m, 2H), 4.7 (m, 1H), 5.2 (m, 1H), 7.2-8.4 (m, 9H); MS(EI): 468 ($M+H^+$, 10%).

Example 13

Preparation of 3-Oxo-4-((S)-4-methyl-2-{[5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]amino}-pentanoylamino)-1-(4-methyl-pentanoyl)-azepanium

a.) 4-((S)-2-*tert*-butoxycarbonylamino-4-methyl-pentanoylamino)-3-hydroxy-1-(4-methyl-pentanoyl)-azepanium

Following the procedure of Example 9a except substituting iso-caproic acid for 3-(2-pyridyl)phenyl acetic acid the title compound was prepared: MS(EI) 442 ($M+H^+$).

b.) 4-((S)-2-Amino-4-methyl-pentanoylamino)-3-hydroxy-1-(4-methyl-pentanoyl)-azepanium

Following the procedure of Example 2i except substituting the compound of Example 13a the title compound was prepared: MS(EI) 342 ($M+H^+$).

c.) 3-Hydroxy-4-((S)-4-methyl-2-{[5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]amino}-pentanoylamino)-1-(4-methyl-pentanoyl)-azepanium

To a solution of the compound of Example 13b (200 mg, 0.53 mmol) in dichloromethane was added EDC (111 mg, 0.58 mmol), HOBt (78 mg, 0.58 mmol), TEA (0.11 mL, 0.79 mmol) and 5-(2-morpholin-4-yl-ethyloxy)benzofuran-2-carboxylic acid. The reaction was stirred at room temperature until complete as indicated by TLC analysis. Workup and column chromatography (5% methanol:dichloromethane) provided 160 mg of the title compound: MS(EI) 615 ($M+H^+$).

d.) 3-Oxo-4-((S)-4-methyl-2-{[5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]amino}-pentanoylamino)-1-(4-methyl-pentanoyl)-azepanium

Following the procedure of Example 1i except substituting the compound of Example 13d the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 12H), 1.5-2.1 (m, 8H), 2.2 (m, 2H), 2.3 (m, 1H), 2.4-2.5 (m, 2H), 2.6 (m 5H), 2.7 (m, 2H), 2.9 (m, 1H), 3.4 (m, 1H), 3.7 (m, 4H), 4.1 (m, 2H), 4.5-4.6 (m, 2H), 5.2 (m, 1H), 7.2-8.4 (m, 4H): MS(EI): 613 ($M+H^+$,100%). The diastereomers were separated by preparative scale HPLC. Lyophilisation of the eluents provided diastereomer 1 and diastereomer 2.

Example 14

Preparation of 3-Oxo-4-((S)-4-methyl-2-{[5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]amino}-pentanoylamino)-1-benzenesulphonyl-azepanium

a.) 1-Benzenesulphonyl-4-((S)-2-*tert*-butoxycarbonylamino-methyl-pentanoylamino)-3-hydroxy-azepanium

To a solution of the amine of Example 2g (0.5 g, 1.46 mmol) in dichloromethane was added triethylamine (0.4 mL, 2.92 mmol) followed by benzenesulphonyl chloride (0.28 mL, 2.18 mmol). The reaction was stirred at room temperature until complete as determined by TLC analysis. Workup and column chromatography (10% methanol:dichloromethane) provided 450 mg of the title compound: MS(EI) 484 ($M+H^+$).

b.) 4-((S)-2-Amino-methyl-pentanoylamino) 1-benzenesulphonyl-3-hydroxy-azepanium

Following the procedure of Example 2i except substituting the compound of Example 14a the title compound was prepared: MS(EI) 384 (M+H+).

c.) 3-Hydroxy-4-((S)-4-methyl-2-{[5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]amino}-pentanoylamino)-1-benzenesulphonyl-azepanium

Following the procedure of Example 13c except substituting the compound of Example 14b the title compound was prepared: MS(EI) 657 (M+H+).

d.) 3-Oxo-4-((S)-4-methyl-2-{[5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]amino}-pentanoylamino)-1-benzenesulphonyl-azepanium

Following the procedure of Example 1i except substituting the compound of Example 14c the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.4 (m, 1H), 2.7 (m, 4H), 2.8 (m, 2H), 3.5 (m, 1H), 3.8 (m, 4H), 4.0 (m, 1H), 4.1 (m, 2H), 4.4 (m, 1H), 4.5 (m, 1H), 4.7 (m, 1H), 5.1 (m, 1H), 7.0 (m, 3H), 7.3 (m, 2H), 7.5 (m, 3H), 7.7 (m, 2H): MS(EI): 655 ($M+H^+$,100%) .

Analysis of the diastereomeric mixture by analytical HPLC (40:60 to 45:55 CH_3CN:20 mm $KHPO_4$ (pH 7 buffer) 60 min. gradient 1 mL/min.; inertsil ODS-3 column 4.6 x 250 mm; UV detection at 215 nM) showed two peaks (R_t = 44.6 mins. and 45.9 mins). The diastereomers were separated by preparative scale HPLC (40:60 to 50:50 CH_3CN: mm $KHPO_4$ (pH 7 buffer)gradient, 12 mL/min.. 60 mins; inertsil ODS-3 column 250 x 20 mm; UV detection at 215 nM). Lyophilisation of the eluents provided diastereomer 1 (anal. R_t = 44.6 mins.) and diastereomer 2 (anal. Rt = 45.9 mins).

Example 15

Preparation of 4-((S)-4-Methyl-2-{[5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]amino}-pentanoylamino)-3-oxo-azepane-1-carboxylic acid phenylamide

a.) [(S)-1-(3-Hydroxy-1-phenylcarbamoyl-azepan-4-ylcarbamoyl)-3-methyl-butyl]-carbamic acid *tert*-butyl ester

To a solution of the amine of Example 2g (0.5 g, 1.46 mmol) in dichloromethane (20 mL) was added phenyl isocyanate (0.24 mL, 2.18 mmol). The reaction was stirred at room temperature until complete as determined by TLC analysis. Workup and column chromatography (5% methanol:dichloromethane) provided 578 mg of the title compound: MS(EI) 463 ($M+H^+$).

b.) 4-((S)-2-Amino-methyl-pentanoylamino)-3-hydroxy-azepane-1-carboxylic acid phenyl amide

Following the procedure of Example 2i except substituting the compound of Example 15a the title compound was prepared: MS(EI) 363 ($M+H^+$).

c.) 3-Hydroxy-4-((S)-4-Methyl-2-{[5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]amino}-pentanoylamino)-azepane-1-carboxylic acid phenylamide

Following the procedure of Example 13c except substituting the compound of Example 15b the title compound was prepared: MS(EI) 636 ($M+H^+$).

d.) 4-((S)-4-Methyl-2-{[5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]amino}-pentanoylamino)-3-oxo-azepane-1-carboxylic acid phenylamide

Following the procedure of Example 1i except substituting the compound of Example 15c the title compound was prepared: ^1H NMR ($CDCl_3$):): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 4H), 3.0 (m, 2H), 3.1 (m, 1H), 3.8 (m, 1H), 3.9 (m, 4H), 4.2 (m, 1H), 4.3 (m, 2H), 4.9 (m, 2H), 5.2 (m, 1H), 7.2-8.4 (m, 9H): MS(EI): 634 ($M+H^+$,100%)

Analysis of the diastereomeric mixture by analytical HPLC (40:60 CH_3CN:20 mM $KHPO_4$ (pH 7 buffer) isocratic, 1 mL/min.; inertsil ODS-3 column 4.6 x 250 mm: UV

detection at 215 nM) showed two peaks (R_t = 27.3 mins. and 30.1 mins). The diastereomers were separated by preparative scale HPLC (40:60 to 50:50 CH_3CN: 20 mM $KHPO_4$ (pH 7 buffer) gradient, 12 mL/min., 60 mins; inertsil ODS-3 column 250 x 20 mm; UV detection at 215 nM). Lyophilisation and desalting of the eluents by $NaHCO_3$:ethyl acetate extraction provided diastereomer 1 (anal. R_t = 27.3 mins.) and diastereomer 2 (anal. Rt = 30.1 mins).

Example 16

Preparation of 5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)acetyl]-azepan-4-ylcarbamoyl}-butyl)amide

a.) 5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-hydroxy-1-[2-(3-pyridin-2-yl-phenyl)acetyl]-azepan-4-ylcarbamoyl}-butyl)amide

Following the procedure of Example 13c except substituting the compound of Example 9b the title compound was prepared: MS(EI) 712 ($M+H^+$).

b.) 5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)acetyl]-azepan-4-ylcarbamoyl}-butyl)amide

Following the procedure of Example 1i except substituting the compound of Example 16c the title compound was prepared: ^1H NMR ($CDCl_3$):): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 4H), 2.8 (m, 2H), 2.9 (m, 1H), 3.5 (m, 1H), 3.7 (m, 4H), 3.9 (m, 3H), 4.3 (m, 2H), 4.7 (m, 2H), 5.4 (m, 1H), 7.2-8.0 (m, 13H), 8.5 (m, 1H); MS(EI): 710 ($M+H^+$,100%) MS(EI).

Analysis of the diastereomeric mixture by analytical HPLC (40:60 CH_3CN:20 mM $KHPO_4$ (pH 7 buffer) isocratic, 1 mL/min.; inertsil ODS-3 column 4.6 x 250 mm; UV detection at 215 nM) showed two peaks (R_t = 33.9 mins. and 37.9 mins). The diastereomers were separated by preparative scale HPLC (40:60 to 45:55 CH_3CN: 20 mM $KHPO_4$ (pH 7 buffer) gradient, 12 mL/min., 60 mins; inertsil ODS-3 column 250 x 20 mm; UV detection at 215 nM). Lyophilisation and desalting of the eluents by $NaHCO_3$:ethyl acetate extraction provided diastereomer 1: MS(EI) 710.3 ($M+H^+$) (anal. R_t = 33.9 mins.) and diastereomer 2: MS(EI) 710.3 ($M+H^+$) (anal. Rt = 37.9 mins).

Example 17

Preparation of 5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-1-(benzoyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

a.) 5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-1-(benzoyl-3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the procedure of Example 13c except substituting the compound of Example 11b the title compound was prepared: MS(EI) 621 ($M+H^+$).

b.) 5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-1-(benzoyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the procedure of Example 1i except substituting the compound of Example 17a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 4H), 2.9 (m, 2H), 3.0 (m, 1H), 3.7 (m, 5H), 4.0 (m, 1H), 4.1 (m, 2H), 4.7 (m, 2H), 5.4 (m, 1H), 7.2-8.4 (m, 11H): MS(EI): 619 ($M+H^+$,100%)

Analysis of the diastereomeric mixture by analytical HPLC (40:60 to 55:45 CH_3CN:20 mM $KHPO_4$ (pH 7 buffer) 30 min. gradient, 1 mL/min.; inertsil ODS-3 column 4.6 x 250 mm; UV detection at 215 nM) showed two peaks (R_t = mins. 13.5 and 17.6 mins). The diastereomers were separated by preparative scale HPLC (40:60 to 45:55 CH_3CN: mM $KHPO_4$ (pH 7 buffer) 60 min. gradient, 15 mL/min., 60 mins; inertsil ODS-3 column 250 x 20 mm; UV detection at 215 nM). Lyophilisation and desalting of the eluents by $NaHCO_3$:ethyl acetate extraction provided diastereomer 1 (anal. R_t = 13.5 mins.) and diastereomer 2 (anal. Rt = 17.6 mins).

Example 18

Preparation of 5-(2-Pyrrolidin-1-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

a.) 5-(2-Pyrrolidin-1-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the procedure of Example 14c except substituting 5-(2-pyrrolidin-1-yl-ethyloxy)-benzofuran-2-carboxylic acid for 5-(2-morpholin-4-yl-ethyloxy)benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 641 ($M+H^+$).

b.) 5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-1-(benzoyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the procedure of Example 1i except substituting the compound of Example 18a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 9H), 2.2 (m, 2H), 2.5 (m, 1H), 2.7 (m, 4H), 3.0 (m, 2H), 3.4 (m, 1H), 4.0 (m, 1H), 4.1 (m, 2H), 4.5 (m, 1H), 4.6 (m, 1H), 5.0 (m, 1H), 7.2-8.4 (m, 11H): MS(EI): 639 ($M+H^+$,100%) .

Example 19

Preparation of 5-(2-Piperidin-1-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

a.) 5-(2-Piperidin-1-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the procedure of Example 14c except substituting 5-(2-piperidin-1-yl-ethyloxy)-benzofuran-2-carboxylic acid for 5-(2-morpholin-4-yl-ethyloxy)benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 655 ($M+H^+$).

b.) 5-(2-Piperidin-1-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the procedure of Example 1i except substituting the compound of Example 18a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 11H), 2.2 (m, 2H), 2.5 (m, 5H), 2.7 (m, 2H), 3.5 (m, 1H), 4.0 (m, 1H), 4.1 (m, 2H), 4.5 (m, 1H), 4.6 (m, 1H), 5.0 (m, 1H), 7.2-8.4 (m, 11H): MS(EI): 653 ($M+H^+$,100%) .

Example 20

Preparation of 5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide

a.) 5-(2-morpholin-4-yl-ethyloxy)benzofuran-2-carboxylic acid methoxy methyl amide

To a solution of 3-(2-pyridyl)phenyl acetic acid (1g) in dichloromethane was added N, O-dimethylhydroxylamine hydrochloride (0.92 g), triethylamine (1.3 mL), HOBt (0.96 g) and EDC (1.1 g). The reaction was stirred until complete. Workup and column chromatography (40% ethyl acetate:hexanes provided 1.1 g of the title compound: MS(EI) 257 ($M+H^+$).

b.) 5-(2-morpholin-4-yl-ethyloxy)benzofuran-2-carbaldehyde

To a solution of 5-(2-morpholin-4-yl-ethyloxy)benzofuran-2-carboxylic acid methoxy methyl amide (0.2 g) of Example 20a in THF was added LAH (2.0 mL of a 1 M solution in THF). The reaction was stirred until complete consumption of the starting material. Workup gave 160 mg of the title compound.

c.) ((S)-{3-hydroxy-1-[2-(3-pyridin-2-yl-phenyl)-ethyl]-azepan-4-ylcarbamoyl}-3-methyl-butyl)-carbamic acid *tert* butyl ester

Following the general procedure of Example 2g except substituting 5-(2-morpholin-4-yl-ethyloxy)benzofuran-2-carbaldehyde for benzaldehyde the title compound was prepared: MS(EI) 525 ($M+H^+$).

d.) (S)-2-Amino-4-methyl-pentanoic acid-{3-hydroxy-1-[2-(3-pyridin-2-yl-phenyl)-ethyl]-azepan-4-yl}-amide.

Following the procedure of Example 2i except substituting the compound of Example 20c the title compound was prepared.

e.) 5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3hydroxy--1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide

Following the procedure of Example 13c except substituting the compound of Example 20d the title compound was prepared.

f.) 5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-oxy-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide

Following the procedure of Example 1i except substituting the compound of Example 20e the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 4H), 2.8 (m, 6H), 3.1 (m, 1H), 3.3 (m, 1H), 3.5 (m, 1H), 3.7 (m, 4H), 4.2 (m, 3H), 4.6 (m, 1H), 5.2 (m, 1H), 7.2-8.4 (m, 13H), 8.6 (m, 1H); MS(EI): 696 ($M+H^+$, 80%).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 696 ($M+H^+$, 100%), and the slower eluting diastereomer; MS(EI): 696 ($M+H^+$, 100%).

Example 21

Preparation of Naphthlene-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide

a.) Naphthlene-2-carboxylic acid ((S)-3-methyl-1-{3-hydroxy-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide

Following the procedure of Example 20f except substituting 2-naphthoic acid for 5-(2-morpholin-4-yl-ethyloxy)benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 579 ($M+H^+$).

b.) Naphthlene-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide

Following the procedure of Example 1i except substituting the compound of Example 21b the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 6H), 2.2 (m, 2H), 2.9 (m, 4H), 3.0 (m, 1H), 3.4 (d, 1H). 3.5 (m, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 6.8-7.2 (m, 6H), 7.3 (m, 1H), 7.5 (m, 2H), 7.9 (m, 6H), 8.2 (M, 1H), 8.7 (m, 1H): MS(EI):577 ($M+H^+$,100%) .

Example 22

Preparation of 1H-Indole-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide

a.) ((S)-3-methyl-1-{3-hydroxy-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide

Following the procedure of Example 20f except substituting 1H-indole-2-carboxylic acid for 5-(2-morpholin-4-yl-ethyloxy)benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 568 ($M+H^+$).

b.) ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide

Following the procedure of Example 1i except substituting the compound of Example 22b the title compound was prepared: : ^{1}H NMR ($CDCl_3$):): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.9 (m, 4H), 3.0 (m, 1H), 3.4 (d, 1H). 3.5 (m, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 6.8-7.2 (m, 6H), 7.0-7.9 (m, 12H), 8.7 (m, 1H), 9.5 (m, 1H): MS(EI): 566 ($M+H^+$,100%)

Example 23

Preparation of 1H-Indole-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

a.) 1H-Indole-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the procedure of Example 2j except substituting the compound of Example 14b and substituting 1H-indole-2-carboxylic acid for naphthoic acid the title compound was prepared: MS(EI) 527 ($M+H^+$).

b.) 1H-Indole-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the procedure of Example 1i except substituting the compound of Example 23b the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.5 (m, 1H), 3.5 (dd, 1H). 3.9 (m, 1H), 4.5 (dd, 2H), 4.7 (m, 1H), 5.0 (m, 1H), 7.2 –7.6 (m, 10H). 9.5 (b, 1H); MS(EI): 525 ($M+H^+$, 10%).

Example 24

Preparation of Benzofuran-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

a.) Benzofuran-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the procedure of Example 23a except substituting benzofuran-2-carboxylic acid for 1H-indole 2-carboxylic acid the title compound was prepared: MS(EI) 528 ($M+H^+$).

b.) Benzofuran-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide

Following the procedure of Example 1i except substituting the compound of Example 24b the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (

m, 5H), 2.2 (m, 2H), 2.6 (m, 1H), 3.5 (d, 1H). 4.1 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7.2-7.2 (m, 10H).

Example 25

Preparation of Benzofuran-2-carboxylic acid [(S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide

a.) Benzofuran-2-carboxylic acid [(S)-3-methyl-1-{3-hydroxy-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide

Following the procedure of Example 20e except substituting benzofuran-2-carboxylic acid for 5-(2-morpholin-4-yl-ethyloxy)benzofuran-2-carboxylic the title compound was prepared: MS(EI) 569 ($M+H^+$).

b.) Benzofuran-2-carboxylic acid [(S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide

Following the procedure of Example 1i except substituting the compound of Example 25b the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 5H), 3.0 (m, 1H). 3.3 (m, 1H), 3.5 (m, 1H), 4.7 (m, 1H). 5.2 (m. 1H), 7.2-7.7 (m, 14H), 8.7 (m, 1H); MS(EI): 567 ($M+H^+$,100%)

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 656 ($M+H^+$,100%), and the slower eluting diastereomer; MS(EI): 656 ($M+H^+$,100%).

Example 26

Preparation of 5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-3-methyl-1-(3-oxo-1-phenethyl-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedures of Examples 20c-f except substituting phenylacetaldehyde for 5-(2-morpholin-4-yl-ethyloxy)benzofuran-2-carbaldehyde of Example 20c the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.4 (m, 1H), 2.6 (m,4H), 2.7 (m, 6H), 3.0 (m, 1H), 3.3 (dd, 1H), 3.5

(q, 1H), 3.7 (m, 4H). 4.2 (m, 2H), 4.7 (m,1H), 5.0 (m, 1H), 7.2-7.2 (m, 11H); MS(EI): 619 ($M+H^+$, 80%)

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 619 ($M+H^+$,100%), and the slower eluting diastereomer; MS(EI): 619 ($M+H^+$,100%).

Example 27

Preparation of Naphthylene-2-carboxylic acid [(S)-3-methyl-1-(3-oxo-1-phenethyl-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedures of Examples 2h-k except substituting phenylacetaldehyde for benzaldehyde of Example 2h the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.4 (m, 1H), 2.7 (m, 4H), 3.0 (m, 1H), 3.7 (d, 1H), 3.5 (q, 1H), 4.7 (m, 1H), 5.1 (m, 1H), 6.9 -7.2 (m, 7H), 7.5 (m, 2H), 7.9 (m, 4H) 8.4 (m, 1H); MS(EI): 500 ($M+H^+$,100%) .

Example 28

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) (S)-2-Amino-4-methyl-pentanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Examples 14a-b except substituting 2-pyridinesulfonyl chloride for benzenesulfonyl chloride of Example 14a the title compound was prepared: MS(EI) 385 ($M+H^+$).

b.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

To a solution of (S)-2-amino-4-methyl-pentanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide of Example 28a (0.15 g) in dichloromethane was added TEA (0.11 mL), HOBt (49 mg), EDC (69 mg) and benzofuran-2-carboxylic acid (58 mg). The

reaction was stirred until complete. Workup and column chromatography (5% methanol:ethyl acetate) provided the title compound: MS(EI) 529 ($M+H^+$).

c.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 28b the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (dd, 1H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7.2-7.3 (m, 3H), 7.4 (m, 4H), 7.6 (m, 1H), 8.0 (m, 2H), 8.7 (m, 1H); MS(EI): 527 ($M+H^+$, 40%).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; ^{1}HNMR: δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (t, 1H), 3.7 (d, 1H); 4.0 (d, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7.2-7.3 (m, 3H), 7.4 (m, 4H), 7.6 (m, 1H), 8.0 (m, 2H), 8.7 (m, 1H); MS(EI): 527 ($M+H^+$, 100%), and the slower eluting diastereomer; ^{1}HNMR: δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (t, 1H), 3.7 (d, 1H); 4.0 (d, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7.2-7.3 (m, 3H), 7.4 (m, 4H), 7.6 (m, 1H), 8.0 (m, 2H), 8.7 (m, 1H); MS(EI): 527 ($M+H^+$, 100%).

Example 29

Preparation of Naphthylene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Naphthylene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 2-naphthoic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 539 ($M+H^+$).

b.) Naphthylene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 29a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H). 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (dd, 1H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H),

7.2-7.3 (m, 2H), 7.5 (m, 3H), 7.9 (m, 6H), 8.3 (m, 1H), 8.4 (m, 1H); MS(EI): 537 ($M+H^+$, 50%).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 537 ($M+H^+$, 100%), and the slower eluting diastereomer; MS(EI): 537 ($M+H^+$, 100%).

Example 30

Preparation of 5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 13c except substituting the compound of Example 28a the title compound was prepared: MS(EI) 658 ($M+H^+$).

b.) 5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 29a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.5 (m, 4H). 3.7 (m, 6H), 4.1 (m, 1H), 4.5 (m, 2H), 4.7 (m, 2H), 5.0 (m, 1H), 7.2-7.3 (m, 4H), 7.4 (m, 2H), 8.0 (m, 2H), 8.7 (m, 1H), 8.7 (m, 1H); MS(EI): 656 ($M+H^+$,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 656 ($M+H^+$, 100%), and the slower eluting diastereomer; MS(EI): 656 ($M+H^+$, 100%).

Example 31

Preparation of 4-((S)-4-Methyl-2-{[(5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]-amino}-pentanoylamino)-3-oxo-azepane-1-carboxylic acid *tert*-butyl ester

a.) 4-((S)-2-Amino-4-methyl-pentanoylamino)-3-hydroxy-azepane-1-carboxylic acid *tert*-butyl ester

To a solution of the compound of Example 1f (0.89 g) in ethyl acetate:methanol (30 mL of a 2:1 mixture) was added 10 % Pd/C and a balloon of hydrogen gas was attached. The reaction was stirred until complete by TLC analysis whereupon it was filtered and concentrated to provide the title compound (0.57 g).

b.) 4-((S)-4-Methyl-2-{[(5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]-amino}-pentanoylamino)-3-hydroxy-azepane-1-carboxylic acid *tert*-butyl ester

Following the procedure of Example 13c except substituting the compound of Example 31a the title compound was prepared.

c.) 4-((S)-4-Methyl-2-{[(5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]-amino}-pentanoylamino)-3-oxo-azepane-1-carboxylic acid *tert*-butyl ester

Following the procedure of Example 1i except substituting the compound of Example 31b the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5 (m, 9H), 1.7 (m, 5H), 2.2 (m, 2H), 2.5 (m, 5H), 2.7 (m, 2H), 3.5 (m , 1H). 3.8 (m, 4H), 4.1 (m, 3H), 4.2 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7.2-7.3 (m, 5H); MS(EI): 615 ($M+H^+$,100%) .

Example 32

Preparation of 4-((S)-4-Methyl-2-{[(5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-3-methyl-1-(3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

To a solution of the compound of Example 31c in THF (5 mL) was added 1M HCl in ether (5 mL). Th reaction was stirred overnight whereupon it was concentrated to provide the title compound: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H),

2.7 (m, 4H), 3.2 (dd, 3H). 3.7 (m, 6H), 4.0 (m, 3H), 4.5 (m, 2H), 5.0 (m, 1H), 7.2-7.3 (m, 6H); MS(EI): 515 ($M+H^+$,100%) .

Example 33

Preparation of 4-Methyl-pentanoic acid {3-oxo-1-[2-(3-pyridin-2-yl-phenyl-acetyl]-azepan-4-yl}-amide

a.) 3-Hydroxy-4-(4-methyl-pentanoylamino)-azepane-1-carboxylic acid *tert*-butyl ester

Following the procedure of Example 1f except substituting 4-methylpentanoic acid for Cbz-leucine the title compound was prepared: MS(EI) 329 ($M+H^+$).

b.) 4-Methyl pentanoic acid (3-hydroxy-azepan-4-yl)-amide

To a solution of the compound of Example 33a (200 mg) in methanol (5 mL) was added 4M HCl dioxane (5 mL). The reaction was stirred until complete whereupon it was concentrated to provide the title compound (132 mg): MS(EI) 229 ($M+H^+$).

c.) 4-Methyl-pentanoic acid {3-hydroxy-1-[2-(3-pyridin-2-yl-phenyl-acetyl]-azepan-4-yl} amide

Following the procedure of Example 9a except substituting the compound of Example 33b the title compound was prepared: MS(EI) 424 ($M+H^+$).

d.) 4-Methyl-pentanoic acid {3-oxo-1-[2-(3-pyridin-2-yl-phenyl-acetyl]-azepan-4-yl}-amide

Following the procedure of Example 1i except substituting the compound of Example 33c the title compound was prepared: ^{1}H NMR ($CDCl_3$) δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 2.9 (m, 1H), 3.5 (m, 1H), 3.7 (m, 2H), 4.1 (m, 3H), 4.6 (m, 1H), 5.3 (m, 1H), 7.2-8.0 (m, 7H), 8.7 (m, 1H); MS(EI): 422 ($M+H^+$,100%) .

Example 34

Preparation of ((S)-3-Methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-ylcarbamoyl}-butyl)-naphthylene-2-methyl-carbamic acid *tert*-butyl ester

a.) (S)-4-Methyl-2-[naphthalene-2-ylmethyl)-amino]-pentanoic acid methyl ester

To a solution of leucine methyl ester hydrochloride (0.5 g) in dichlormethane was added triethylamine (0.9 mL), 2-naphthaldehyde (0.43 g) and sodium triacetoxyborohydride (0.87 g). The mixture was stirred until complete. Workup and column chromatography (5% ethyl acetate:dichloromethane) provided 0.4 g of the title compound: MS(EI) 286 ($M+H^+$).

b.) (S)-2-(*tert*-Butoxycarbonyl-naphthlen-2-ylmethyl-amino)-4-metyhyl pentanoic acid methyl ester

To a solution of the compound of Example 34a (0.35 g) in dichloromethane was added di-*tert*-butyldicarbonate (0.29 g). After 2 hours at room temperature triethylamine was added and the reaction heated to reflux. Upon completion, the reaction was concentrated and the residue was purified by column chromatography (50% hexane:dichloromethane) to provide 0.17 g of the title compound: MS(EI) 386 ($M+H^+$).

c.) (S)-2-(*tert*-Butoxycarbonyl-naphthlen-2-ylmethyl-amino)-4-methyl pentanoic acid

To a solution of the compound of Example 34b (0.17 g) in THF:methanol (15 mL of a 2:1 solution) was added LiOH (0.019 g). The reaction was stirred overnight whereupon it was concentrated to provide the title compound .

d.) 4-[(S)-*tert*-butoxycarbonyl-naphthylen-2-ylmethyl-amino)-4-methyl-pentanoylamino]-3-hydroxy-azepane-1-carboxylic acid benzyl ester

To a sloution of the compound of Example 2e (0.11 g) in dichloromethane was added EDC (0.08 g). HOBt (0.06 g) and the acid of Example 34c. Upon completion the reaction was worked up and chromatographed (5% methanol:dichloromethane) to provide the title compound (0.18 g): MS(EI) 618 ($M+H^+$).

e.) [(S)-1-(3-Hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-naphthylen-2-ylmethyl carbamic acid *tert*-butyl ester

To a solution of the compound of Example 34d (0.17 g) in ethyl acetate:methanol (20:10 mL) was added 10% Pd/C. A balloon of hydrogen was attached and the reaction was stirred until complete consumption of the starting material. The reaction was filtered and concentrated to provide the title compound (0.10g): MS(EI) 484 ($M+H^+$).

f.) ((S)-3-Methyl-1-{3-hydroxy-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-ylcarbamoyl}-butyl)-naphthylene-2-methyl-carbamic acid *tert*-butyl ester

Following the procedure of Example 9a except substituting the compound of Example 34e the title compound was prepared: MS(EI) 679 ($M+H^+$).

g.) ((S)-3-Methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-ylcarbamoyl}-butyl)-naphthylene-2-methyl-carbamic acid *tert*-butyl ester

Following the procedure of Example 1i except substituting the compound of Example 34f the title compound was prepared: : ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 16H), 2.7 (m, 1H), 3.2 (m, 1H). 3.7 (m, 3H), 4.0 (m, 1H), 4.7 (m, 2H), 5.2 (m, 1H), 7.2-7.3 (m, 16H), 8.6 (m, 1H); MS(EI): 677 ($M+H^+$,100%) .

Example 35

Preparation of (S)-4-Methyl-2-[(naphthylen-2-ylmethyl)-amino]-pentenoic acid [3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-yl}-amide

To a solution of the compound of Example 34g (20 mg) in THF was added 1M HCl in ether. The reaction was stirred until complete consumption of the starting material whereupon it was concentrated to provide the title compound: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.5 (m, 1H), 3.5 (m, 5H), 4.0 (m, 1H), 4.7 (m, 2H), 4.4 (m, 1H), 7.2-8.0 (m, 16H), 8.7 (m, 1H); MS(EI): 577 ($M+H^+$,100%) .

Example 36

Preparation of 4-[2-(2-{(S)-3-Methyl-1-[3-oxo-1-(pyidine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butylcarbamoyl}-benzofuran-5-yloxy)-ethyl]-piperazine-1-carboxylic acid *tert*-butyl ester

a.) 4-[2-(2-{(S)-3-Methyl-1-[3-hydroxy-1-(pyidine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butylcarbamoyl}-benzofuran-5-yloxy)-ethyl]-piperazine-1-carboxylic acid *tert*-butyl ester

To a solution of the compound of Example 28a (0.15 g) in dichloromethane was added EDC (0.07 g), HOBt (0.05 g), triethylamine (0.11 mL) and 4-[2-(2-carboxy-benzofuran-5-yloxy)-ethyl]-piperazine-1-carboxylic acid *tert*-butyl ester. The reaction was stirred until complete. Work up and column chromatography (10 % methanol: ethyl acetate) provided the title compound (0.10 g): MS(EI) 757 ($M+H^+$).

b.) 4-[2-(2-{(S)-3-Methyl-1-[3-oxo-1-(pyidine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butylcarbamoyl}-benzofuran-5-yloxy)-ethyl]-piperazine-1-carboxylic acid *tert*-butyl ester

Following the procedure of Example 1i except substituting the compound of Example 36a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 14H), 2.2 (m, 2H), 2.7 (m, 1H), 3.0 (m, 2H), 3.5 (m, 4H). 3.7 (m, 6H), 4.1 (m, 1H), 4.5 (m, 2H), 4.7 (m, 2H), 5.0 (m, 1H), 7.0-7.6 (m, 6H), 8.0 (m, 2H), 8.7 (m, 1H); MS(EI): 755 ($M+H^+$,100%) .

Example 37

Preparation of 5-(2-Piperizin-1-yl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-3-butyl]-amide

The compound of Example 36b (0.02 g) was dissolved in 4M HCl in dioxane. The reaction was stirred until complete whereupon it was concentrated to provide the title compound: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5- 1.7 (m, 7H), 2.7 (m, 2H), 3.3 (M, 2H), 3.5 (m , 1H). 3.8 (m, 5H), 4.1 (m, 3H), 4.7 (m, 4H), 5.0 (m, 1H), 7.0-7.3 (m, 2H), 7.4 (m, 6H), 8.0 (m, 2H), 8.7 (m, 1H): MS(EI): 655 ($M+H^+$,100%) .

Example 38

Preparation of 5-(2-Cyclohexyl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5-(2-Cyclohexyl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

To a solution of the compound of Example 28a (0.15 g) in dichloromethane was added EDC (0.07 g), HOBt (0.05 g), triethylamine (0.11 mL) and 5-(2-cyclohexyl-ethoxy)-benzofuran carboxylic acid (0.01 g). The reaction was stirred until complete by TLC analysis. Workup and column chromatography (100% ethyl acetate) provided the title compound (0.15 g): MS(EI) 655 ($M+H^+$).

b.) 5-(2-Cyclohexyl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 38a the title compound was prepared: MS(EI) 653 ($M+H^+$).

Example 39

Preparation of 5-(2-Cyclohexyl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide

a.) 5-(2-Cyclohexyl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-hydroxy-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide

To a solution of the compound of Example 20d (0.15 g) in dichloromethane was added EDC (0.06 g), HOBt (0.04 g), triethylamine (0.14 mL) and 5-(2-cyclohexyl-ethoxy)-benzofuran carboxylic acid (0.09 g). The reaction was stirred until complete by TLC analysis. Workup and column chromatography (100% ethyl acetate) provided the title compound (0.10 g): MS(EI) 695 ($M+H^+$).

b.) 5-(2-Cyclohexyl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide

Following the procedure of Example 1i except substituting the compound of Example 39a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 18H), 2.2 (m, 2H), 2.7 (m, 3H), 3.2 (m, 1H), 3.5 (m, 1H). 3.9 (m, 4H), 4.7 (m, 2H), 5.0 (m, 1H), 7.2-7.3 (m, 13H), 8.7 (m, 1H): MS(EI): 693 ($M+H^+$,100%)

Example 40

Preparation of 4-[2-(2-{(S)-3-Methyl-1-[3-oxo-1-(3-pyridin-2-yl-phenyl)-ethyl [azepan-4-ylcarbamoyl]-butylcarbamoyl}-benzofuran-5-yloxy)-ethyl]-piperazine-1-carboxylic acid *tert*-butyl ester

a.) 4-[2-(2-{(S)-3-Methyl-1-[3-hydroxy-1-(3-pyridin-2-yl-phenyl)-ethyl [azepan-4-ylcarbamoyl]-butylcarbamoyl}-benzofuran-5-yloxy)-ethyl]-piperazine-1-carboxylic acid *tert*-butyl ester

To a solution of the compound of Example 20d (0.15 g) in dichloromethane was added EDC (0.06 g), HOBt (0.04 g), triethylamine (0.14 mL) and 4-[2-(2-carboxy-benzofuran-5-yloxy)-ethyl]-piperazine-1-carboxylic acid *tert*-butyl ester (0.12 g). The reaction was stirred until complete by TLC analysis. Workup and column chromatography (10% methanol:ethyl acetate) provided the title compound (0.09 g): MS(EI) 797 ($M+H^+$).

b.) 4-[2-(2-{(S)-3-Methyl-1-[3-oxo-1-(3-pyridin-2-yl-phenyl)-ethyl [azepan-4-ylcarbamoyl]-butylcarbamoyl}-benzofuran-5-yloxy)-ethyl]-piperazine-1-carboxylic acid *tert*-butyl ester

Following the procedure of Example 1i except substituting the compound of Example 40a the title compound was prepared: MS(EI) 795.9 ($M+H^+$).

Example 41

Preparation of 5-(2-piperizin-1-yl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide

Following the procedure of Example 37 except substituting the compound of Example 40b the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 3.4-3.6 (m, 19H), 4.5 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7.2 (m, 1H), 7.4 (m, 1H), 7.5 (m, 2H), 7.7 (m, 2H), 7.8 (m, 1H), 8.1 (m, 2H), 8.4 (m, 1H), 8.7 (m, 1H); MS(EI): 695 ($M+H^+$, 70%).

Example 42

Preparation of (S)-4-Methyl-2-(methyl-naphthalen-2-ylmethyl-amino)pentanoic acid [3-oxo-1-(pyridine-2-sulphonyl)-azepan-4-yl]-amide

a.) 4-[(S)-2-(*tert*-Butoxycarbonyl-methyl-amino)-4-methyl-pentanoylamino]-3-hydroxy-azepane-1-carboxylic acid benzyl ester

To a solution of the compound of Example 2e (0.35 g)in dichloromethane was added N-methyl-N-Boc-leucine (0.36 g), HOBt (0.2 g) and EDC (0.28 g). The reaction was stirred until complete. Workup and column chromatography (5% methanol:dichloromethane) provided 0.6 g of the title compound: MS(EI) 492 ($M+H^+$).

b.) [(S)-1-(3-Hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-methyl-carbamic acid *tert*-butyl ester

To a solution of the compound of Example 42a (0.6 g) in methanol:ethyl acetate (10:20 mL) was added 10% Pd/C and a balloon of hydrogen was attached. The reaction was stirred overnight whereupon it was filtered and concentrated to provide 0.50 g of the title: MS(EI) 358 ($M+H^+$).

c.) {(S)-1-[3-Hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-3-methyl-butyl}-methyl-carbamic acid *tert*-butyl ester

To a solution of the compound of Example 42b (0.2 g) in dichloromethane was added triethylamine (0.16 mL) and 2-pyridinesulfonyl chloride (0.15 g). The reaction was

stirred until complete. Workup and column chromatography (5% methanol:ethyl acetate) provided the title compound (0.23 g): MS(EI) 499 ($M+H^+$).

d.) (S)-4-Methyl-2-methylamino-pentanoic acid [3-hydroxy-1-(2-pyridine-2-sulfonyl)-azepan-4-yl]-amide

To a solution of the compound of Example 42c (0.23 g) in methanol (3.0 mL) was added 4M HCl in dioxane (3.0 mL). The reaction was stirred until complete. Concentration provided the title compound: MS(EI) 399 ($M+H^+$).

e.) (S)-4-Methyl-2-(methyl-naphthalen-2-ylmethyl-amino)pentanoic acid [3-hydroxy-1-(pyridine-2-sulphonyl)-azepan-4-yl]-amide

To a solution of the compound of Example 42d (0.05 g) in dichloromethane was added triethylamine (0.07 mL), 2-naphthaldehyde (0.05 g) and sodium triacetoxyborohydride (0.11 g). The reaction was stirred until complete. Workup and column chromatography (5% methanol ethyl acetate) provided the title compound (0.03 g): MS(EI) 539 ($M+H^+$).

f.) (S)-4-Methyl-2-(methyl-naphthalen-2-ylmethyl-amino)pentanoic acid [3-oxo-1-(pyridine-2-sulphonyl)-azepan-4-yl]-amide

Following the procedure of Example 1i except substituting the compound of Example 42e the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 5H), 2.6 (m, 1H), 3.3 (m, 1H), 3.7 (m, 2H), 4.1 (m, 1H), 4.7 (m, 1H), 5.2 (m, 1H), 7.2-8.0 (m, 10H), 8.7 (m, 1H); MS(EI): 537 ($M+H^+$,100%).

Example 43

Preparation of (S)-4-Methyl-2-(methyl-naphthalen-2-ylmethyl-amino)pentanoic acid {3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-yl}-amide

a.) ((S)-1-{3-Hydroxy-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-ylcarbamoyl}-3-methyl-butyl)-methyl-carbamic acid *tert*-butyl ester

To a solution of the compound of Example 42b (0.25 g) was added 3-(2-pyridyl)phenyl acetic acid (0.16 g), HOBt (0.12 g) and EDC (0.15 g). The reaction was

stirred until complete. Workup and column chromatography (5% methanol:ethyl acetate) provided the title compound (0.24 g): MS(EI) 553 ($M+H^+$).

b.) (S)-4-Methyl-2-methylamino-pentanoic acid {3-hydroxy-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-yl}-amide

Following the procedure of Example 42d except substituting the compound of Example 43a the title compound was produced: MS(EI) 453 ($M+H^+$).

c.) (S)-4-Methyl-2-(methyl-naphthalen-2-ylmethyl-amino)pentanoic acid {3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-yl}-amide

Following the procedures of Examples 42e-f except substituting the compound of Example 43b the title compound was produced: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 5H), 3.0 (m, 1H), 3.5 (m, 1H), 3.7 (m, 4H), 4.1 (m, 1H), 4.7 (m, 2H), 5.2 (m, 1H), 7.2-8.0 (m, 15H), 8.7 (m, 1H); MS(EI): 591 ($M+H^+$,100%) .

Example 44

Preparation of 5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid methyl ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)acetyl]-azepan-4-ylcarbamoyl}-butyl)amide

a.) 5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid methyl ((S)-3-methyl-1-{3-hydroxy-1-[2-(3-pyridin-2-yl-phenyl)acetyl]-azepan-4-ylcarbamoyl}-butyl)amide

To a solution of the compound of Example 43b (0.1 g) in dichloromethane was added 5-(2-morpholin-4-yl-ethyloxy)benzofuran-2-carboxylic acid (0.06 g), HOBt (0.026 g), TEA (0.07 mL) and EDC (0.04 g). The reaction was stirred until complete. Workup and chromatography (20% methanol:ethyl acetate) provided the title compound (0.07 g): MS(EI) 726 ($M+H^+$).

b.) 5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid methyl ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)acetyl]-azepan-4-ylcarbamoyl}-butyl)amide

Following the procedure of Example 1i except substituting the compound of Example 44a the title compound was prepared: ^{1}H NMR ($CDCl_3$):): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 5H), 2.7 (m, 4H), 2.8 (m, 2H), 2.9 (m, 1H), 3.5 (m, 1H), 3.7 (m, 4H),

3.9 (m, 3H), 4.3 (m, 2H), 4.7 (m, 2H), 5.4 (m, 1H), 7.2-8.0 (m, 12H), 8.5 (m, 1H); MS(EI): 724 ($M+H^+$,100%) .

Example 45

Preparation of Benzofuran-2-carboxylic acid methyl {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

a.) Benzofuran-2-carboxylic acid methyl {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

To a solution of the compound of Example 42d (0.1 g) in dichloromethane was added benzofuran-2-carboxylic acid (0.04 g), TEA (excess), HOBt (0.03 g), and EDC (0.04 g). The reaction was stirred until complete. Workup and column chromatography (5% methanol:dichloromethane) provided the title compound (0.04 g): MS(EI) 542.9 ($M+H^+$).

b.) Benzofuran-2-carboxylic acid methyl {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

Following the procedure of Example 1i except substituting the compound of Example 45a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 8H), 2.2 (m, 2H), 2.7 (m, 1H), 3.0 (m, 1H), 3.7 (m, 2H), 4.1 (m, 1H), 4.7 (m, 1H), 5.2 (m, 1H), 7.2-8.0 (m, 8H), 8.7 (m, 1H); MS(EI): 541 ($M+H^+$, 10%).

Example 46

Preparation of 2,2,2-Trifluoro-N-((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-ylcarbamoyl}-butyl)-N-naphthylen-2-ylmethyl-acetamide

a.) (S)-4-Methyl-2-[naphthylen-2-ylmethyl-(2,2,2-trifluoro-acetyl)-amino]-pentanoic acid methyl ester

To a solution of the compound of Example 34a (0.5 g) in dichloromethane was added potassium carbonate (catalytic amount), and trifluoroacetic acid (0.44 g). The reaction was stirred at room temperature for 1 hour whereupon it was concentrated and chromatographed (20% ethyl acetate:hexane) to provide the title compound.

b.) (S)-4-Methyl-2-[naphthylen-2-ylmethyl-(2,2,2-trifluoro-acetyl)-amino]-pentanoic acid lithium salt

To a solution of the compound of Example 46a (0.49 g) in THF:water (3 mL of a 2:1 solution) was added lithium hydroxide monohydrate (0.06 g). The reaction was stirred overnight whereupon it was concentrated to provide the title compound (0.46 g): MS(EI) 366 ($M+H^+$).

c.) 3-Hydroxy-4-{(S)-4-methyl-2-[naphthylen-2-ylmethyl-(2,2,2-trifluoro-acetyl)-amino]-pentanoylamino}-azepane-1-carboxylic acid benzyl ester

To a solution of the compound of Example 2e (0.29 g) in dichloromethane was added EDC (0.24 g), HOBt (0.16 g) and the compound of Example 46b (0.46 g). The reaction was stirred until complete. Workup and column chromatography (5% methanol:ethyl acetate) provided the title compound (0.25 g): MS(EI) 614 ($M+H^+$).

d.) 2,2,2-Trifluoro-N-[(S)-1-(3-hydroxy-azepan-ylcarbamoyl)-3-methyl-butyl]-N-naphthlen-2-ylmethyl-acetamide

Following the procedure of Example 42b except substituting the compound of Example 46c the title compound was produced: MS(EI) 480 ($M+H^+$).

e.) 2,2,2-Trifluoro-N-((S)-3-methyl-1-{3-hydroxy-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-ylcarbamoyl}-butyl)-N-naphthylen-2-ylmethyl-acetamide

Following the procedure of Example 43a except substituting the compound of Example 46d the title compound was produced: MS(EI) 675 ($M+H^+$).

f.) 2,2,2-Trifluoro-N-((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-ylcarbamoyl}-butyl)-N-naphthylen-2-ylmethyl-acetamide

Following the procedure of Example 1i except substituting the compound of Example 46e the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.2 (m, 1H), 3.7 (m, 3H), 4.1 (m, 1H), 4.5 (m, 2H), 4.7 (m, 2H), 5.2 (m, 1H), 7.2-8.0 (m, 14H), 8.7 (m, 1H): MS(EI): 673 ($M+H^+$,100%) .

Example 47

Preparation of 4-[(S)-(Methanesulphonyl-naphthylen-2-ylmethyl-amino)-4-methyl-pentanoylamino]-3-oxo-azepane-1-carboxylic acid benzyl ester

a.) (S)-2-(Methanesulfonyl-naphthylen-2-ylmethyl-amino)-4-methyl-pentanoic acid methyl ester

To a solution of the compound of Example 34a (0.5 g) in dichloromethane was added triethylamine (0.36 mL) and methansulfonyl chloride (0.16 mL). The reaction was stirred at room temperature until complete. Workup and chromatography (20% ethyl acetate:hexanes) provided the title compound (0.24 g).

b.) (S)-2-(Methanesulfonyl-naphthylen-2-ylmethyl-amino)-4-methyl-pentanoic acid lithium salt

Following the procedure of Example 46b except substituting the compound of Example 47a the title compound was prepared: MS(EI) 348 ($M+H^+$).

c.) 4-[(S)-(Methanesulphonyl-naphthylen-2-ylmethyl-amino)-4-methyl-pentanoylamino]-3-hydroxy-azepane-1-carboxylic acid benzyl ester

Following the procedure of Example 46c except substituting the compound of Example 47b the title compound was prepared: MS(EI) 596 ($M+H^+$).

d.) 4-[(S)-(Methanesulphonyl-naphthylen-2-ylmethyl-amino)-4-methyl-pentanoylamino]-3-oxo-azepane-1-carboxylic acid benzyl ester

Following the procedure of Example 1i except substituting the compound of Example 47c the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 5H), 3.0 (m, 1H), 3.5 (m, 1H), 4.1 (m, 1H), 4.5 (m, 3H), 4.7 (m, 1H), 5.2 (m, 3H), 7.2-8.0 (m, 13H); MS(EI): 596 ($M+3H^+$,100%) .

Example 48

Preparation of Quinoline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Quinoline-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting quinoline-2-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 540 ($M+H^+$).

b.) Quinoline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 48a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H). 4.1 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7.0-7.2 (m, 1H), 7.3 (m, 1H), 7.5 (m, 1H), 7.7 (m, 1H), 7.8 (m, 3H), 8.1 (m, 1H), 8.3 (m, 2H), 8.7 (m, 2H); MS(EI): 538 ($M+H^+$,100%).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 538 ($M+H^+$,100%). and the slower eluting diastereomer: MS(EI): 538 ($M+H^+$,100%).

Example 49

Preparation of Quinoline-8-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Quinoline-8-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting quinoline-8-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 540 ($M+H^+$).

b.) Quinoline-8-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 49a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7.5 (m, 4H), 7.6 (m, 1H), 7.7 (m, 3H), 8.2 (m, 1H), 8.6 (m, 1H), 8.7 (m, 1H), 8.9 (m, 1H); MS(EI): 538 ($M+H^+$,100%) .

Example 50

Preparation of Quinoline-6-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Quinoline-6-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting quinoline-6-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 540 ($M+H^+$).

b.) Quinoline-6-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 50a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7.0 (m, 2H), 7.5 (m, 2H), 7.9 (m, 2H), 8.0 (m, 3H), 8.2 (m, 1H), 8.7 (m, 1H), 8.9 (m, 1H); MS(EI): 538 ($M+H^+$,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 538 ($M+H^+$,100%), and the slower eluting diastereomer; MS(EI): 538 ($M+H^+$,100%).

Example 51

Preparation of Quinoline-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Quinoline-4-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting quinoline-4-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 540 ($M+H^+$).

b.) Quinoline-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 51a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 6.5-7.2 (m, 2H), 7.4 (m, 2H), 7.5 (m, 1H), 7.7 (m, 1H), 7.9 (m, 2H), 8.0 (m, 1H), 8.2 (m, 1H), 8.7 (m, 1H), 8.9 (m, 1H); MS(EI): 538 ($M+H^+$,100%)

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 538 ($M+H^+$,100%), and the slower eluting diastereomer; MS(EI): 538 ($M+H^+$,100%).

Example 52

Preparation of Quinoline-3-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Quinoline-3-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting quinoline-3-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 540 ($M+H^+$).

b.) Quinoline-3-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 52a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7.2 (m 2H), 7.5 (m, 1H), 7.6 (m, 1H), 7.7-7.9 (m, 4H), 8.1 (m, 1H), 8.5 (m, 1H), 8.6 (m, 1H), 9.3 (m, 1H); MS(EI): 538 ($M+H^+$,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 538 ($M+H^+$,100%), and the slower eluting diastereomer; MS(EI): 538 ($M+H^+$,100%).

Example 53

Preparation of Isoquinoline-3-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Isoquinoline-3-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting isoquinoline-3-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 540 ($M+H^+$).

b.) Isoquinoline-3-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 53a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7.0 (m, 1H). 7.5 (m, 1H), 7.7 (m, 2H), 7.9 (m, 4H), 8.7 (m, 3H), 9.2 (m, 1H); MS(EI): 538 ($M+H^+$,100%) .

Example 54

Preparation of Isoquinoline-1-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Isoquinoline-1-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting isoquinoline-1-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 540 ($M+H^+$).

b.) Isoquinoline-1-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 54a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7.3 (m, 1H), 7.5 (m, 1H), 7.7-8.0 (m, 6H), 8.7 (m, 3H), 9.5 (m, 1H); MS(EI): 538 ($M+H^+$,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 537 (M^+,100%), and the slower eluting diastereomer; MS(EI): 537 (M^+,100%).

Example 55

Preparation of Quinoxaline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Quinoxaline-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting quinoxaline-2-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 541 ($M+H^+$).

b.) Quinoxaline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 55a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7..0-7.2 (m, 2H), 7.5 (m, 1H), 7.7 (m, 3H), 8.2 (m, 2H), 8.3 (m, 1H), 8.7 (m, 1H), 9.5 (m, 1H); MS(EI): 539 ($M+H^+$, 30%).

Example 56

Preparation of Benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting benzo[b]thiophene-2-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 545 ($M+H^+$).

b.) Benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 56a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 6.8-7.2 (m, 1H), 7.5 (m, 3H), 8.0 (m, 6H), 8.7 (m, 1H); MS(EI): 543 ($M+H^+$, 60%).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; ^{1}HNMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.7 (m, 1H), 3.8 (m,1H), 4.1 (m, 1H), 4.7 (m, 2H), 5.1 (m, 1H), 7.4-8.0 (m, 8H), 8.7 (m, 1H); MS(EI): 543 ($M+H^+$,100%), and the slower eluting diastereomer; 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.7 (m, 1H), 3.8 (m,1H), 4.1 (m, 1H), 4.7 (m, 2H), 5.1 (m, 1H), 7.4-8.0 (m, 8H), 8.7 (m, 1H); MS(EI): 543 ($M+H^+$,100%).

Example 57

Preparation of 1,8-Naphthyridine-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 1,8-Naphthyridine-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 1,8-naphthyridine-2-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 541 ($M+H^+$).

b.) 1,8-Naphthyridine-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 57a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7.2 (m, 1H), 7.6 (m, 2H), 7.9 (m, 2H), 8.3 (m, 1H), 8.4 (m, 2H), 8.5 (m, 2H), 9.2 (m, 1H); MS(EI): 539 ($M+H^+$,100%)

Example 58

Preparation of 1H-Indole-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 1H-Indole-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 1H-indole-2-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 528 ($M+H^+$).

b.) 1H-Indole-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 58a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1

(m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 6.8 (m, 1H), 7.1 (m, 1H), 7.3 (m, 3H), 7.4 (m, 1H), 7.5 (m, 1H), 7.6 (m, 1H), 8.0 (m, 2H), 8.7 (m, 1H), 9.4 (b, 1H); MS(EI): 526 ($M+H^+$, 80%).

Example 59

Preparation of 5-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 5-methoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 559 ($M+H^+$).

b.) 5-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 59a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 4H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7.0 (m, 4H), 7.6 (m, 3H), 8.0 (m, 2H), 8.7 (m, 1H); MS(EI): 557 ($M+H^+$, 70%).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; ^{1}HNMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (t, 1H), 3.7 (m, 4H). 4.0 (d, 1H), 4.7 (m, 2H), 5.0 (d, 1H), 7.0 (m, 4H), 7.6 (m, 3H), 8.0 (m, 2H), 8.7 (d, 1H); MS(EI): 557 ($M+H^+$,100%), and the slower eluting diastereomer; MS(EI): 557 ($M+H^+$,100%).

Example 60

Preparation of 5-Bromo-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5-Bromo-furan-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 5-bromo-2-furoic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 558 ($M+H^+$).

b.) 5-Bromo-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 60a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 6.5 (m, 1H), 6.7 (m, 1H), 7.1 (m, 2H), 7.5 (m, 1H), 8.0 (m, 2H), 8.7 (m, 1H); MS(EI): 555 ($M+H^+$, 60%).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 555 ($M+H^+$,100%), and the slower eluting diastereomer; MS(EI): 555 ($M+H^+$,100%).

Example 61

Preparation of Furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Furan-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 2-furoic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 479 ($M+H^+$).

b.) Furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 61a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 6.5 (m, 1H), 7.2 (m, 3H), 7.5 (m, 2H), 8.0 (m, 2H), 8.7 (m, 1H); MS(EI): 477 ($M+H^+$, 50%).

Example 62

Preparation of 5-Nitro-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5-Nitro-furan-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 5-nitro-2-furoic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 524 ($M+H^+$).

b.) 5-Nitro-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 62a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7.2 (m, 1H), 7.3 (m, 1H), 7.5 (m, 1H), 7.9 (m, 2H), 8.7 (m, 1H); MS(EI): 522 ($M+H^+$, 80%).

Example 63

Preparation of 5-(4-Nitro-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5-(4-Nitro-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 5-(4-nitrophenyl)-2-furoic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 600 ($M+H^+$).

b.) 5-(4-Nitro-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 63a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 6.9 (m, 1H), 7.2 (m, 1H), 7.5 (m, 2H), 7.9-8.0 (m, 4H), 8.5 (m, 1H), 8.6 (m, 1H); MS(EI): 598 ($M+H^+$, 80%).

Example 64

Preparation of 5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 5-[3-(trifluoromethyl)phenyl]-2-furoic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 623 ($M+H^+$).

b.) 5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 64a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1

(m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H). 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7.1 (m, 1H), 7.5 (m, 3H), 8.0 (m, 4H) 8.7 (m, 1H); MS(EI): 621 ($M+H^+$, 80%).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 621 ($M+H^+$,100%), and the slower eluting diastereomer; MS(EI): 621 ($M+H^+$,100%).

Example 65

Preparation of Tetrahydro-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Tetrahydro-furan-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting tetrahydrofuran-2-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 483 ($M+H^+$).

b.) Tetrahydro-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 65a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 12H), 2.7 (m, 1H), 3.8 (m, 3H). 4.0 (m, 1H), 4.5 (m, 2H), 4.8 (m, 1H), 5.0 (m, 1H), 7.0 (m, 1H), 7.5 (m, 1H), 7.9 (m, 2H), 8.7 (m, 1H). MS(EI): 481 ($M+H^+$, 80%).

Example 66

Preparation of (S)-4-Methyl-2-(2-phenoxy-acetylamino)-pentanoic acid [3-oxo-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

a.) (S)-4-Methyl-2-(2-phenoxy-acetylamino)-pentanoic acid [3-hydroxy-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 28b except substituting phenoxyacetic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 519 ($M+H^+$).

b.) (S)-4-Methyl-2-(2-phenoxy-acetylamino)-pentanoic acid [3-oxo-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 1i except substituting the compound of Example 66a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H). 4.0 (m, 1H), 4.5 (m, 3H), 4.7 (m, 1H), 5.1 (m, 1H), 7.0 (m, 3H), 7.3 (m, 2H), 7.5 (m, 1H), 7.9 (m, 2H), 8.6 (m, 1H); MS(EI): 517 ($M+H^+$, 60%).

Example 67

Preparation of (S)-2-[2-(4-Fluoro-phenoxy)-acetylamino]-4-methyl-pentanoic acid [3-oxo-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

a.) (S)-2-[2-(4-Fluoro-phenoxy)-acetylamino]-4-methyl-pentanoic acid [3-hydroxy-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 28b except substituting 4-fluorophenoxyacetic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 537 ($M+H^+$).

b.) (S)-2-[2-(4-Fluoro-phenoxy)-acetylamino]-4-methyl-pentanoic acid [3-oxo-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 1i except substituting the compound of Example 67a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.6 (d, 1H). 4.0 (m, 1H), 4.5 (, 3H), 4.8 (m, 1H), 5.1 (m, 1H), 7.0 (m, 4H), 7.5 (m, 1H), 7.9 (m, 2H), 8.6 (m, 1H); MS(EI): 535 ($M+H^+$, 50%).

Example 68

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-carbonyl)-azepan-4-ylcarbamoyl)-3- butyl]-amide

a.) {(S)-1-[3-Hydroxy-1-(pyridine-2-carbonyl)-azepan-4-ylcarbamoyl]-3-methyl-butyl}-carbamic acid *tert*-butyl ester

To a solution of the compound of Example 2g (0.25 g) in dichloromethane was added picolinic acid (0.09g), EDC (0.14 g) and HOBt (0.10 g). The reaction was stirred until complete. Workup and column chromatography (5% methanol:ethyl acetate) provided the title compound (0.35 g).

b.) (S)-2-Amino-4-methylpentanoic acid [3-hydroxy-1-(pyridine-2-carbonyl)-azepan-4-yl]-amide

To a solution of the compound of Example 68a (0.34 g) in methanol (6 mL) was added 4M HCl in dioxane (6 mL). The reaction was stirred until complete whereupon it was concentrated to provide the title compound (0.34 g): MS(EI) 349 ($M+H^+$).

c.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-carbonyl)-azepan-4-ylcarbamoyl)-3- butyl]-amide

Following the procedure of Example 28b except substituting the compound of Example 68b the title compound was prepared: MS(EI) 493 ($M+H^+$).

d.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-carbonyl)-azepan-4-ylcarbamoyl)-3- butyl]-amide

Following the procedure of Example 1i except substituting the compound of Example 68c the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.5 (m, 1H), 3.7 (m, 1H), 4.7 (m, 4H). 5.0 (m, 1H), 7.0-7.5 (m, 8H), 8.2 (m, 1H); MS(EI): 491 (M^+,100%).

Example 69

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-carbonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedures of Examples 68a-d except substituting picolinic acid N-oxide for picolinic acid of Example 68c the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.5 (m, 1H), 3.5 (d, 1H). 4.0 (m, 1H), 4.7 (m, 3H), 5.5 (m, 1H), 7.0 (m, 2H), 7.2-7.5 (m, 7H), 8.1 (m, 2H); MS(EI): 507 (M^+, 20%).

Example 70

Preparation of 4-((S)-2-*tert*-Butylcarbonylamino-4-methyl-pentanoylamino)-3-oxo-azepane-1-carboxylic acid benzyl ester

Following the procedure of Example 92j, except substituting 4-((S)-2-*tert*-Butoxycarbonylamino-4-methyl-pentanoylamino)-3-hydroxy-azepane-1-carboxylic acid benzyl ester for benzofuran-2-carboxylic acid {(S)-1-[3-hydroxy-6,6-dimethyl-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 476.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 7.40-6.95(m, 7H), 5.25-4.60(m, 4H), 4.40-4.06(m, 2H), 3.70-3.58(t, 1H), 2.70-2.50(m, 1H), 2.25-1.30(m, 1 6H); and the second eluting diastereomer:, 1.00-0.85(d, 6H); and the second eluting diastereomer: MS ($M+H^+$) 476.2.

Example 71

Preparation of 5,6-Dimethoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-methyl-1H-imidazole-4-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) {(S)-1-[3-Hydroxy-1-(1-methyl-1H-imidazole-2-sulfonyl)-azepan-4-ylcarbamoyl}-3-methyl-butyl}-carbamic acid *tert*-butyl ester

To a solution of the amine of Example 2g in methylene chloride (5ml) was added pyridine (92μL, 1.14mmol) followed by 1-methylimidazole-4-sulfonylchloride (0.112g,

0.623mmol). The reaction was allowed to stir for 16h at room temperature. The solution was then washed with saturated aqueous $NaHCO_3$, water and brine. The product was purified by column chromatography (silica gel: methanol/ methylenechloride) to yield the title compound as a white solid (0.172g, 68%): ^{1}HNMR (400MHz, $CDCl_3$) δ 7.6 (d, 1H), 7.5 (d, 1H), 6.6 (d, 1H), 3.8 (s, 3H), 1.5 (s, 9H), 1 (d, 6H); MS(ESI): 488.2 $(M+H)^+$

b.) (S)-2-Amino-4-methyl-pentanoic acid [3-hydroxy-1-(1-methyl-1H-imidazole-2-sulfonyl)-azepan-4-yl]-amide

To a solution of the compound of Example 71a (0.172g, 0.353mmol) in minimal MeOH was added 4M HCl in dioxane (10mL) and stirred for 4h at room temperature. The reaction mixture was concentrated and azeotroped with toulene (2x's) to yield the title compound as an off white solid: MS(ESI): 388.2 $(M+H)^+$

c.) 5,6-Dimethoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-methyl-1H-imidazole-4-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

To a stirring solution of the compound of Example 71b (0.137g, 0.353 mmol), 5,6-dimethoxybenzofuran-2-carboxylic acid (0.86g, 0.388mmol), triethylamine (246 mL, 1.77 mmol) and 1-hydroxybenzotriazole (0.01g, 0.070mmol) in DMF (5mL) was added 1-(3-dimethylaminopropyl)3-ethylcarbodimide hydrochloride (0.074g, 0.388mmol). After stirring at room temperature for 16h, the solution was diluted with EtOAc and washed successively with saturated aqueous sodium bicarbonate, water (2x's), and saturated brine. The organic layer was dried over Na_2SO_4, filtered and concentrated. The product was purified by column chromatography (silica gel; methanol/dichloromethane) to yield the title compound as a white solid (0.088g, 42%): MS(ESI): 592.1 $(M+H)^+$

d.) 5,6-Dimethoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-methyl-1H-imidazole-4-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Oxalyl chloride (52μL, 0.596mmol) chloride was cooled to –78°. To this was added dimethyl sulfoxide (106μL, 1.49mmol) in methylene chloride dropwise. After stirring for 15min at –78°, the alcohol in methylene chloride was added slowly and allowed to stir for 1h when Et_3N (416μL,2.98mmol) was added. The solution was then brought to room temperature and quenched with water and extracted into methylene chloride. The organic layer was separated and washed with brine, dried over $MgSO_4$, filtered and concentrated. The product was purified by column chromatography (silica gel: methanol/methylene

chloride) to yield the title compound as white solid (0.068g, 78%): ^{1}H NMR (400MHz, $CDCl_3$) δ 6.8-7.6 (m, 14H), 4 (d, 12H), 1 (d, 12H); MS(ESI): 590.1 $(M+H)^+$

Example 72

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(5-methyl-1H-[1,2,4]triazole-3-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

a.) 4-((S)-2-Amino-4-methyl-pentanoylamino)-3-hydroxy-azepane-1-carboxylic acid benzyl ester

To a stirring solution of the compound of Example 2f (3.5 g, 7.33 mmol) in EtOAc (0.5 mL) was added 4M HCl in dioxane (12.8 mL). The mixture was stirred for 1h at room temperature. The reaction mixture was then concentrated and azeotroped with toluene (2x20 mL) to yield the title compound as a pale yellow oil (3.13g, 100%): MS(ESI) 378.4 $(M+H)^+$

b.) 4-{(S)-2-[(Benzofuran-2-carbonyl)-amino]-4-methyl-pentanoylamino}-3-hydroxy-azepane-1-carboxylic acid benzyl ester

To a stirring solution of the compound of Example 72a (3.13g, 7.57mmol), benzofuran-2-carboxylic acid (1.35g, 8.32mmol), triethylamine (1.17ml, 8.25mmol) and 1-hydroxybenzotriazole (0.2g, 1.48mmol) in DMF (30mL) was added 1-(3-dimethylaminopropyl)3-ethylcarbodimide hydrochloride (1.6g, 8.33mmol). After stirring at room temperature for 16h, the solution was diluted with EtOAc and washed successively with saturated aqueous sodium bicarbonate, water (2X), and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated. The product was purified by column chromatography (silica gel; ethylacetate/dichloromethane) to yield the title compound (3.7g, 93%). ^{1}HNMR (400MHz, $CDCl_3$) δ 6.8-7.7 (m, 12H), 5.35 (s, 2H), 1.0 (d, 6H): MS(ESI): 522 $(M+H)^+$

c.) Benzofuran-2-carboxylic acid [(S)-1-(3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

To a solution the compound of Example 72b (2.6 g, 4.9 mmol) in EtOAc (150 mL) was added 10% palladium on carbon (1.3 g) and stirred at room temperature for 64 h under

a hydrogen atmosphere. The mixture was then filtered through celite and the filtrate concentrated to yield the title compound as a white solid (1.92 g, 100%): ^{1}H NMR (400MHz, $CDCl_3$) δ 6.8-7.7(m, 7H), 1.02 (d, 6H); MS(ESI) 388 $(M+H)^+$

d.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(5-methyl-1H-[1,2,4]triazole-3-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide

To a stirring solution of the compound of Example 72c (0.100g, 0.25mmol) and triethylamine (35μL, 0.25mmol) in methylene chloride (2mL) was added 5-methyl-1H-1,2,4-triazolesulfonylchloride (0.043g, 0.25mmol). The reaction was allowed to stir for 10 min and washed with saturated aqueous $NaHCO_3$, water and saturated brine. The organic layer was dried over Na_2SO_4, filtered and concentrated. The compound was purified by column chromatography (silica gel; ethylacetate/ hexane) to yield the title compound as a pale yellow oil (0.111, 84%): MS(ESI) 532.73 $(M+H)^+$

e.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(5-methyl-1H-[1,2,4]triazole-3-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

To a stirring solution of the compound of Example 72d (0.108g, , 0.206mmol) in dimethylsulfoxide (2mL) was added triethylamine (172μL, 1.23mmol) followed by sulfur trioxide pyridine (0.116g, 0.718mmol) and stirred for 16h at room temperature. The reaction mixture was diluted with EtOAc and washed with water (X2). The organic layer was dried over Na_2SO_4, filtered and conentrated. The crude product was purified by column chromatography (silica gel; methanol/methylenechloride) to yield the title compound as a white solid (0.08g, 81%): ^{1}HNMR (400MHz, $CDCl_3$) δ 7.1-7.7 (m, 7H), 2.65 (s, 3H), 1.0 (d, 6H); MS(ESI): 552.71 $(M+Na)^+$

Example 73

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1-methyl-1H-imidazole-3-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

a.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1-methyl-1H-imidazole-3-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide

To a stirring solution of the compound of Example 72c (0.100g, 0.25mmol) and triethylamine (35µL, 0.25mmol) was added l-methylimidazole sulfonyl chloride (0.046g, 0.255mmol). The reaction was allowed to stir for 10min and washed with saturated aqueous $NaHCO_3$, water and saturated brine. The organic layer was dried over Na_2SO_4, filtered and concentrated. The compound was purified by column chromatography (silica gel; ethylacetate /hexane) to yield the title compound as a pale yellow oil (0.113g, 82%): ^{1}HNMR (400 MHz, $CDCl_3$) δ 6.9-7.7 (m, 9H), 3.9 (2s, 3H), 1.0 (d, 6H); MS(ESI): 531.8 $(M+H)^+$

b.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1-methyl-1H-imidazole-3-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

To a stirring solution of the compound of Example 73a (0.085g, 0.159mmol) in dimethylsulfoxide was added triethylamine (133µL, 0.95mmol) followed by sulfurtrioxide pyridine (0.08g, 0.5mmol) and stirred for 16h at room temperature. The reaction mixture was diluted with EtOAc and washed with water (X2). The organic layer was dried over Na_2SO_4, filtered and conentrated. The crude product was purified by column chromatography (silica gel; methanol/methylenechloride) to yield the title compound as a white solid (0.072g, 83%). MS(ESI): 529.76 $(M+H)^+$

Example 74

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1H-imidazole-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

a.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1H-imidazole-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

To a stirring solution of the compound of Example 72c (0.100g, 0.25mmol) and triethylamine (35µL, 0.25mmol) was added 2-imidazolesulfonyl chloride (0.046g, 0.255mmol). The reaction was allowed to stir for 10min and washed with saturated aqueous $NaHCO_3$, water and saturated brine. The organic layer was dried over Na_2SO_4, filtered and concentrated. The compound was purified by column chromatography (silica gel; ethylacetate/hexane) to yield the title compound as a pale yellow oil (0.113g, 82%): ^{1}HNMR (400MHz, $CDCl_3$) δ 7.1-7.7 (m, 9H), 4.8 (s, 1H), d, 6H); MS(ESI): 517.76 $(M+H)^+$

b.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1H-imidazole-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

To a stirring solution of the compound of Example 74a (0.107g, 0.206mmol) in dimethylsulfoxide (2mL) was added triethylamine (172µL, 1.23mmol) followed by sulfurtrioxide pyridine (0.115g, 0.718mmol) and stirred for 16h at room temperature. The reaction mixture was diluted with EtOAc and washed with water (X2). The organic layer was dried over Na_2SO_4, filtered and conentrated. The crude product was purified by column chromatography (silica gel; methanol/methylenechloride) to yield the title compound as a white solid (0.09g, 85%); MS(ESI): 515.84 $(M+H)^+$

Example 75

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) {(S)-1-[3-Hydroxy-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl}-3-methyl-butyl}-carbamic acid *tert*-butyl ester

To a solution of the compound of Example 2g (2.50g, 7.29mmol) in DCE (100 mL) was added P-NMM (4.0 g) and thioazole-2-sulphonyl chloride (1.6 g, 8.75 mmol). After shaking at room temperature overnight, the solution was filtered. The filtrate was concentrated to yield the title compound as white solid (2.50 g, 5.10 mmol, 70%); MS: 490.91 $(M+H)^+$.

b.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hyroxy-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

To a solution of the compound of Example 75b (0.15 g, 0.45 mmol) in CH_2Cl_2 (20 mL) was added benzofuran-2-carboxylic acid (0.109 g, 0.172 mmol), 1-hydroxybenzotriazole (0.106 g, 0.762mmol), and P-EDC (0.85g, 1mmol/g) in CH_2Cl_2 (10 mL) . After shaking at room temperature overnight, the solution was treated with tisamine (0.589g, 3.75mmol/g). After shaking for another 2hr, the solution was filtered and concentrated to yield the title compound as a white solid (166.7 mg, 70%); MS (ESI): 535.3 $(M+H)^+$.

c.) Benzofuran-2-carboxylic acid{S}-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

To a stirring solution of the compound of Example 75c (166.7 mg, 0.313 mmol) in dichloromethane (4 mL) was added Dess-Martin reagent (265.5 mg, 0.626 mmol). After stirring at room temperature for 2 h, solutions of sodium thiosulfate (2 mL of 10% in water) and saturated aqueous sodium bicarbonate (2 mL) were added simultaneously to the solution. The aqueous was extracted with dichloromethane (2x). The organic phases were combined, washed with saturated brine, dried ($MgSO_4$), filtered and concentrated. The residue was purified by HPLC (50:50 ethanol: hexane, 20mL/min, 25min, WhelkO-1(R,R) 21x250mm column, UV detection at 280 nm and 305 nm) to yield the first elution as a

white solid (84.8mg, 50.8 %). MS (ESI): 533.2 $(M+H)^+$ and the second elution as a white solid (50.1mg, 30.0%) MS: 533.2 $(M+H^+)$.

Example 76

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1-methyl-1H-imidazole-4-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

a.) {(S)-1-[3-Hydroxy-1-(1-methyl-1H-imidazole-2-sulfonyl)-azepan-4-ylcarbamoyl}-3-methyl-butyl}-carbamic acid *tert*-butyl ester

To a solution of the amine of Example 2g in methylenechloride (5ml) was added pyridine (92µL, 1.14mmol) followed by 1-methylimidazole-4-sulfonylchloride (0.112g, 0.623mmol). The reaction was allowed to stir for 16h at room temperature. The solution was then washed with saturated aqueous $NaHCO_3$, water and brine. The product was purified by column chromatography (silica gel: methanol/ methylenechloride) to yield the title compound as a white solid (0.172g, 68%): ^{1}HNMR (400MHz, $CDCl_3$) δ 7.6 (d, 1H), 7.5 (d, 1H), 6.6 (d, 1H), 3.8 (s, 3H), 1.5 (s, 9H), 1 (d, 6H); MS(ESI): 488.2 $(M+H)^+$

b.) (S)-2-Amino-4-methyl-pentanoic acid [3-hydroxy-1-(1-methyl-1H-imidazole-2-sulfonyl)-azepan-4-yl]-amide

To a solution of the compound of Example 76a (0.172g, 0.353mmol) in minimal MeOH was added 4M HCl in dioxane (10mL) and stirred for 4h at room temperature. The reaction mixture was concentrated and azeotroped with toulene (2x's) to yield the title compound as an off white solid. MS(ESI): 388.2 $(M+H)^+$

c.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1-methyl-1H-imidazole-4-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide

To a stirring solution of the compound of Example 72c (0.2g, 0.471mmol), benzofuran-2-carboxylic acid (0.084 g, 0.388 mmol), triethylamine (72µL, 0.517mmol) and 1-hydroxybenzotriazole (0.012 g, 0.088 mmol) in DMF (5 mL) was added 1-(3-dimethylaminopropyl)3-ethylcarbodimide hydrochloride (0.099g, 0.515mmol). After stirring at room temperature for 16h, the solution was diluted with EtOAc and washed successively with saturated aqueous sodium bicarbonate, water (2x's), and saturated brine. The organic layer was dried over Na_2SO_4, filtered and concentrated. The product was

purified by column chromatography (silica gel; methanol/dichloromethane) to yield the title compound as a white solid (0.226g, 90%): ^{1}HNMR (400MHz, $CDCl_3$) δ 6.9-8.1 (m, 18H), 3.75 (2s, 6H), 1 (d, 12H); MS(ESI): 531.80$(M+H)^+$

d.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1-methyl-1H-imidazole-4-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

To a stirring solution of the compound of Example 76a (0.226 g, 0.426mmol) in dimethylsulfoxide (2mL) was added triethylamine (355µL, 2.55mmol) followed by sulfur trioxide pyridine (0.238g, 1.48mmol) and stirred for 16h at room temperature. The reaction mixture was diluted with EtOAc and washed with water (X2). The organic layer was dried over Na_2SO_4, filtered and conentrated. The crude product was purified by column chromatography (silica gel; methanol/methylenechloride) to yield the title compound as a white solid (0.168g, 76%): ^{1}HNMR (400MHz, $CDCl_3$) δ 7.1-7.7 9m, 18H), 3.7 (2s, 6H), 0.9 (d, 12H); MS(ESI): 529.80 $(M+H)^+$

Example 77

Preparation of 5-(4-Oxy-morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

To a solution of the compound of Example 30b (0.01 g) in dichloromethane (2 mL) was added m-CPBA (0.008 g). The reaction was stirred overnight. Workup and column chromatography (30% methanol:dichloromethane) provided the title compound: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.5 (m, 4H), 2.7 (m, 1H), 2.8 (m 2H), 3.7 (m, 4H), 3.8 (q, 1H). 4.0 (m, 3H), 4.7 (m, 1H), 4.8 (m, 1H), 5.0 (m, 1H), 7.0 (m, 3H), 7.4 (m, 2H), 7.5 (m, 1H), 7.9 (m, 2H), 8.6 (m, 1H); MS(EI): 671 (M^+,100%) .

Example 78

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-3-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 4-((S)-2-Amino-4-methyl-pentanoylamino)-3-hydroxy-azepane-1-carboxylic acid benzyl ester

To a solution of 4-((S)-2-*tert*-butoxycarbonylamino-4-methyl-pentanoylamino)-3-hydroxy-azepan-1-carboxylic acid benzyl ester of Example 2f (4.0 g) in methanol (20 mL) was added 4M HCl in dioxane (20 mL). The reaction was stirred at room temperature for 2 hours whereupon it was concentrated to provide the title compound (3.8 g): MS(EI) 378 ($M+H^+$).

b.) 4-{(S)-2-[(Benzofuran-2-carbonyl)-amino]-4-methyl-pentanoylamino}-3-hydroxy-azepane-1-carboxylic acid benzyl ester

To a solution of 4-((S)-2-amino-4-methyl-pentanoylamino)-3-hydroxy-azepane-1-carboxylic acid benzyl ester of Example 78a (3.2 g) in dichloromethane (200 mL) was added EDC (1.48 g), HOBt (1.05 g), TEA (1.29 mL) and benzofuran-2-carboxylic acid. The reaction was stirred until complete. Workup and column chromatography (2% methanol:dichloromethane) provided the title compound (3.78 g): MS(EI) 521 ($M+H^+$).

c.) Benzofuran-2-carboxylic acid [(S)-1-(3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

To a solution of 4-{(S)-2-[(benzofuran-2-carbonyl)-amino]-4-methyl-pentanoylamino}-3-hydroxy-azepane-1-carboxylic acid benzyl ester of Example 78b (1.6 g) in methanol:ethyl acetate (50 mL:100 mL) was added 10% Pd/C. The reaction was stirred under a balloon of hydrogen for 2 hours whereupon it was filtered and concentrated to provide the title compound (1.16 g): MS(EI) 387 ($M+H^+$).

d.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-3-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

To a solution of benzofuran-2-carboxylic acid [(S)-1-(3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide of Example 78c (0.3 g) in dichloromethane was added triethylamine (0.17 mL) followed by 3-pyridinesulfonyl chloride (0.25 g). The reaction was

stirred at room temperature until complete as determined by TLC analysis. Workup and column chromatography (5% methanol:ethyl acetate) provided 0.32 g of the title compound: MS(EI) 528 ($M+H^+$).

e.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-3-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-3-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 78d the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.5 (m, 1H), 3.5 (d, 1H). 4.0 (m, 1H), 4.7 (m, 1H), 4.8 (m, 1H), 5.0 (m, 1H), 7.0 (m, 2H), 7.2-7.5 (m, 6H), 8.1 (m, 1H), 8.9-9.0 (m, 2H); MS(EI): 526 (M^+,100%).

Example 79

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-3-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-3-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

To a solution of benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-3-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 78d (0.05g) in dichloromethane was added m-CPBA (0.05 g). The reacrton was stirred overnight. Workup and column chromatography (10% methanol:dichloromethane) provided the title compound (0.03 g): MS(EI) 544 ($M+H^+$).

b.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-3-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-3-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 79a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.5 (m, 1H), 3.5 (d, 1H). 4.0 (m, 1H), 4.5 (m, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.2-7.5 (m, 7H), 8.1-8.2 (m, 2H). MS(EI): 542 (M^+, 50%).

Example 80

Preparation of Quinoline-3-carboxylic acid {(S)-1-(3,4-dichloro-benzene-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl)]-3-methyl-butyl}-amide

Following the procedures of Example 75a-d except substituting 3,4-dichlorosulfonyl chloride for thioazole-2-sulphonyl chloride of Example 75a and quinoline-3-carboxylic acid for benzofura-2-carboxylic acid the title compound was prepared: ^{1}H NMR($CDCl_3$, 400 MHz) δ 9.34 (s, 1H), 8.61 (s, 1H), 8.14 (m, 1H), 7.81 (m, 3H), 7.60 (m, 3H), 7.19 m, 2H), 5.09 (m, 1H), 4.88 (m, 1H), 4.50 (m, 1H), 3.92 (m, 1H), 3.51 (m, 1H), 2.57 (m, 1H), 2.23 (m, 2H), 1.60 (m, 5H), 1.01 (m, 6H).

Example 81

Prepeparation of 5-Hydroxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1-methyl-1H-imidazole-4-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5-Hydroxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1-methyl-1H-imidazole-4-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide

To a stirring solution of the compound of Example 76b (0.1 g, 0.235 mmol), 5-hydroxybenzofuran-2-carboxylic acid(0.046g, 0.256mmol), triethylamine (36 µL, 0.258 mmol) and 1-hydroxybenzotriazole (0.006g, 0.044mmol) in DMF (5mL) was added 1-(3-dimethylaminopropyl)3-ethylcarbodimide hydrochloride (0.05g, 0.26mmol). After stirring at room temperature for 16h, the solution was diluted with EtOAc and washed successively with saturated aqueous sodium bicarbonate, water (2X), and saturated brine. The organic layer was dried over Na_2SO_4, filtered and concentrated. The product was purified by column chromatography (silica gel; methanol/dichloromethane) to yield the title compound as a white solid (0.129g, 100%). ^{1}HNMR (400MHz, $CDCl_3$) δ 6.8-8 (m, 16H), 3.6 (2s, 6H), 0.85 (d, 12H).

MS(ESI): 547.88$(M+H)^+$

b.) 5-Hydroxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1-methyl-1H-imidazole-4-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

Oxalyl chloride (13 µL, 0.149 mmol) chloride was taken to –78°. To this was added dimethyl sulfoxide (28 µL, 0.394mmol) in methylene chloride dropwise. After stirring for 15min at –78 °, the alcohol of Example 81a in methylene chloride was added slowly and allowed to stir for 1h when Et_3N (7 µL, 0.05 mmol) was added. The solution was then brought to room temperature and quenched with water and extracted into methylene chloride. The organic layer was separated and washed with brine, dried over $MgSO_4$, filtered and concentrated. The product was purified by column chromatography (silica gel: methanol/methylene chloride) to yield the title compound as white solid (0.021g, 78%): MS(ESI) 545.9$(M+H)^+$

Example 82

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)]-3-methyl-butyl}-amide

a.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)]-3-methyl-butyl}-amide

To a solution of benzofuran-2-carboxylic acid [(S)-1-(3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide of Example 78c (0.10 g) in dichloromethane was added triethylamine (0.07 mL) followed by 2-pyidinesulphonylchloride N-oxide. The reaction was stirred at room temperature overnight. Workup and chromatography (10% methanol:dichloromethane) provided the title compound (0.01 g): MS(EI) 544 $(M+H^+)$.

b.) {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)]-3-methyl-butyl}-amide

Following the procedure of Example 1i except substituting benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)]-3-methyl-butyl}-amide of Example 82a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (q, 1H). 4.0 (m, 1H), 4.7 (m, 1H), 4.8 (m, 1H), 5.0 (m, 1H), 7.0 –7.5 (m, 9H), 8.1-8.2 (m, 2H). MS(EI): 542 (M^+, 20%).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; ^{1}HNMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m. 5H), 2.2 (m, 2H), 2.7 (t, 1H), 3.8 (d, 1H). 4.0 (d, 1H), 4.7 (m, 1H), 4.8 (d, 1H), 5.0 (m, 1H), 7.0 –7.5 (m, 9H), 8.1-8.2 (m, 2H); MS(EI): 542 (M^+,100%), and the slower eluting diastereomer; MS(EI): 542 ($M+H^+$,100%).

Example 83

Preparation of 2-(4-{(S)-2-{(Benzofuran-2-carbonyl)-amino}-4-methyl-pentanoylamino}-3-oxo-azepane-1-sulfonyl)-benzoic acid

a.) 2-(4-{(S)-2-[(Benzofuran-2-carbonyl)-amino]-4-methyl-pentanoylamino}-3-hydroxy-azepane-1-sulfonyl)-benzoic acid methyl ester

Following the procedure of Example 75a-c, except substituting 2-carboxymethylsulphonyl chloride for 2-thiazolesulfonyl chloride, the title compound was prepared: MS ($M+H^+$) = 585.56, $M+Na^+$ = 607.76, $2M+H^+$ = 1170.48.

b.) 2-(4-{(S)-2-[(Benzofuran-2-carbonyl)-amino]-4-methyl-pentanoylamino}-3-hydroxy-azepane-1-sulfonyl)-benzoic acid

2-(4-{(S)-2-[(benzofuran-2-carbonyl)-amino]-4-methyl-pentanoylamino}-3-hydroxy-azepane-1-sulfonyl)-benzoic acid methyl ester (compound 83a, 180 mg, 0.309 mmol) was dissolved in 5:1 MeOH/water (6 ml) LiOH (14 mg, 0.34 mmol) was added and the reaction mixture was stirred and refluxed for 6 h. The reaction mixture was then quenched with water and 6 N HCl (adjusted to pH=2), extracted with EtOAc (3 x 10 ml), dried with $MgSO_4$, filtered, concentrated, and chromatographed (silica gel, 1% acetic acid/

4% MeOH/ CH_2Cl_2) to yield the title compound as a white solid (48 mg, 27%): $M+H^+$ = 572.2

c.) 2-(4-{(S)-2-[(Benzofuran-2-carbonyl)-amino]-4-methyl-pentanoylamino}-3-oxo-azepane-1-sulfonyl)-benzoic acid

Following the procedure of Example 75d, except substituting 2-(4-{(S)-2-[(benzofuran-2-carbonyl)-amino]-4-methyl-pentanoylamino}-3-hydroxy-azepane-1-sulfonyl)-benzoic acid for benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide, the title compound was prepared: MS ($M+H^+$): 570.2 ($M+H^+$). ^1H NMR(400Hz,$CDCl_3$-CD_3OD): δ 8.05-7.95 (m, 1H), 7.70-7.15 (m, 8H), 5.15-5.00 (m,1H), 4.95-4.75 (m, 2H), 4.15-4.00 (m, 1H), 3.65 (d, 1H), 2.85-2.70 (m, 1H), 2.25-2.05 (m, 2H), 1.90-1.70 (m, 4H), 1.60-1.45 (m, 1H), 0.95 (d, 6H).

Example 84

Preparation of 3-(4-{(S)-2-[(Benzofuran-2-carbonyl)-amino]-4-methyl-pentanoylamino}-3-oxo-azepane-1-sulfonyl)-benzoic acid

Following the procedure of Example 83, except substituting 3-carboxymethylbenzenesulphonyl chloride for 2-carboxymethylbenzenesulfonyl chloride, the title compound was prepared: MS 570.2 ($M+H^+$); ^1H NMR (400Hz,$CDCl_3$-CD_3OD): δ 8.46 (d,1H), 8.31-8.25 (m,1H), 8.00-7.97 (m,1H), 7.70-7.62 (m, 2H), 7.55-7.46 (m, 1H), 7.45-7.35 (m,1H), 7.30-7.25 (m, 1H), 5.10-5.05 (m,1H), 4.95-4.78 (m,1H), 4.75-4.55 (q,1H), 4.00 (d,1H), 3.5 (d, 1H), 2.60-2.40 (m, 2H), 2.25-2.15 (m,1H), 1.95-1.70 (m, 4H), 1.55-1.40 (m,1H), 0.98 (t, 6H).

Example 85

Preparation of Benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) {(S)-1-[3-Hydroxy-1-(1-oxy-pyridine-sulfonyl)-azepan-4-ylcarbamoyl]-3-methyl-butyl-carbamic acid *tert*-butyl ester

To a solution of [(S)-1-(3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-carbamic acid *tert* butyl ester of Example 2g (2.5 g) in dichloromethane (100 mL) and saturated sodium bicarbonate was added freshly prepared 2-pyidinesulphonyl chloride N-oxide (prepared by bubbling chlorine gas through a solution of 2-mercaptopyridine-N-oxidein 9M HCl for approximately 90 minutes. Removal of excess chlorine under vacuum provided the 2-pyridinesulfonyl chloride-N-oxide). The reaction was stirred at room temperature for 1 hour. Workup and column chromatography (10% methanol:dichloromethane) provided the title compound (2.0 g): MS(EI) 500 ($M+H^+$).

b.) (S)-2-Amino-4-methyl-pentanoic acid [3-hydroxy-1-(1-oxy-pyyridine-sulfonyl)-azepan-4-yl]-amide

To a solution of {(S)-1-[3-hydroxy-1-(1-oxy-pyridine-sulfonyl)-azepan-4-ylcarbamoyl]-3-methyl-butyl-carbamic acid *tert*-butyl ester of Example 85a (2.0 g) in methanol (20 mL) was added 4M HCl in dioxane (20 mL). The reaction was stirred at room temperature for 1.5 hours whereupon it was concentrated to provide the title compound (1.8 g): MS(EI) 400 ($M+H^+$).

c.) Benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

To a solution of (S)-2-amino-4-methyl-pentanoic acid [3-hydroxy-1-(1-oxy-pyyridine-sulfonyl)-azepan-4-yl]-amide of Example 85b (0.25 g) in dichloromethane (12 mL) was added triethylamine (0.12 mL), EDC (0.11 g), HOBt (0.077 g) and benzo[b]thiophene-2-carboxylic acid. The reaction was stirred until complete. Workup and column chromatography (10% methanol: dichloromethane) provided the title compound (0.26 g): MS(EI) 560 ($M+H^+$).

d.) Benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 85c the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (q, 1H). 4.0 (m, 1H), 4.7 (m, 1H), 4.8 (m, 1H), 5.0 (m, 1H), 7.5 (m, 4H), 7.8 (m, 3H), 8.1-8.2 (m, 2H). MS(EI): 558 (M^+,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 558 (M^+,100%), and the slower eluting diastereomer; MS(EI): 558 (M^+,100%).

Example 86

Preparation of 5-Bromo-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a. 5-Bromo-furan-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting 5-bromo-2-furoic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 574 ($M+H^+$).

b.) 5-Bromo-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting 5-bromo-furan-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 86a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (q, 1H). 4.0 (m, 1H), 4.7 (m, 1H), 4.8 (m, 1H), 5.0 (m, 1H), 7.0 (m, 2H), 7.4 (m, 2H), 8.1-8.2 (m, 2H); MS(EI): 570 (M^+,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 572 ($M+H^+$,100%), and the slower eluting diastereomer; MS(EI): 572 ($M+H^+$,100%).

Example 87

Preparation of 5,6-Dimethoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5,6-Dimethoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting 5,6-dimethoxybenzofuran-2-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 604 ($M+H^+$).

b.) 5,6-Dimethoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting 5,6-dimethoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 87a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (m, 7H). 4.0 (m, 1H), 4.7 (m, 1H), 4.8 (m, 1H), 5.0 (m, 1H), 7.0-7.5 (m, 5H), 8.1-8.2 (m, 2H); MS(EI): 602 (M^+,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 602 (M^+,100%), and the slower eluting diastereomer; MS(EI): 602 (M^+,100%).

Example 88

Preparation of 1-Oxy-pyridine-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 1-Oxy-pyridine-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting picolinic acid N-oxide for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 505 ($M+H^+$).

b.) 1-Oxy-pyridine-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting 1-oxy-pyridine-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 88a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (q, 1H). 4.1 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 7.5 (m, 3H), 7.9 (m 2H), 8.3-8.4 (m, 2H), 8.6 (m, 1H); MS(EI): 503 (M^+,100%) .

Example 89

Preparation of (S)-4-Methyl-2-(pyridine-2-sulfonylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

a.) (S)-4-Methyl-2-(pyridine-2-sulfonylamino)-pentanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

To a solution of (S)-2-amino-4-methyl-pentanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide of Example 28a (0.25 g) in dichloromethane was added triethylamine (0.27 mL) and 2-pyridinesulfonyl chloride (0.15 g). The reaction was stirred until complete. Workup and column chromatography (5% methanol:dichloromethane) provided the title compound (0.09 g): MS(EI) 525 ($M+H^+$).

b.) (S)-4-Methyl-2-(pyridine-2-sulfonylamino)-pentanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 1i except substituting (S)-4-methyl-2-(pyridine-2-sulfonylamino)-pentanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide of Example 89a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (q, 1H). 4.0 (m, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 5.5 (m, 1H), 7.0 (m 1H), 7.5 (m, 2H), 7.9 (m 3H), 8.6 (m, 2H). MS(EI): 523 (M^+,100%) .

Example 90

Preparation of (S)-2-(3-Benzyl-ureido)-4-methyl-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

a.) (S)-2-(3-Benzyl-ureido)-4-methyl-pentanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

To a solution of (S)-2-amino-4-methyl-pentanoic acid [3-hydroxy-1-(pyyridine-sulfonyl)-azepan-4-yl]-amide of Example 28a (0.25 g) in dichloromethane was added triethylamine (0.17 mL) and benzyl isocyanate (0.088g). The reaction was stirred until complete. Workup and column chromatography (5% methanol:dichloromethane) provided the title compound (0.12 g).

b.) (S)-2-(3-Benzyl-ureido)-4-methyl-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 1i except substituting (S)-2-(3-benzyl-ureido)-4-methyl-pentanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide of Example 89a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (q, 1H). 4.0 (m, 3H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.2 (, 5H), 7.5 (m, 1H), 7.9 (m, 2H), 8.6 (m, 1H); MS(EI): 515 (M^+, 60%).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 516 ($M+H^+$,100%), and the slower eluting diastereomer; MS(EI): 516 ($M+H^+$,100%).

Example 91

Preparation of (S)-2-(3-Phenyl-uriedo)-4-methyl pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

a.) (S)-2-(3-Phenyl-ureido)-4-methyl-pentanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 90a except substituting phenyl isocyante for benzyl isocyanate the title compound was prepared: : MS(EI) 503 ($M+H^+$).

b.) (S)-2-(3-Phenyl-ureido)-4-methyl-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 1i except substituting (S)-2-(3-phenyl-ureido)-4-methyl-pentanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide of Example 91a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (q, 1H). 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.0-7.9 (m, 8H), 8.6 (m, 1H). MS(EI): 501 (M^+, 60%).

Example 92

Preparation of Benzofuran-2-carboxylic acid {(S)-1-[6,6-dimethyl-3-oxo-1(pyridine-sulphonyl)-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide

a.) Allyl-(2,2-dimethyl-pent-4-enylidene)-amine

2,2-Dimethyl-4-pentenal (2.8 g, 25 mmol) was dissolved in 15 mL benzene. To this solution allylamine (2.85 g, 50 mmol) was added. A few molecular sieves were used to absorb water generated during the reaction. The mixture was stirred at room temperature overnight. Removal of the solvent and excess amount of allylamine on rotavapor provided 3.76 g of the title compound as clear liquid (yield 100%). ^{1}H-NMR (400 MHz, $CDCl_3$): • 7.52(s, 1H), 5.99-5.90(m, 1H), 5.80-5.70(m, 1H), 5.15-4.99(m, 4H), 4.01-3.99(m, 2H), 2.17(d, 2H), 1.06(s, 6H).

b.) Allyl-(2,2-dimethyl-pent-4-enyl)-amine

Allyl-(2,2-dimethyl-pent-4-enylidene)-amine of Example 92a (3.76g, 25mmol) was diluted in 5ml MeOH. To the solution $NaBH_4$ (0.95g, 25mmol) was added at 0°C. After addition the mixture was stirred at r.t. for 5h. Methanol was removed on rotavapor and the residue was partitioned between EtOAc/ 20% NaOH. The organic layer was dried over Na_2SO_4, fitered and evaperated to give 2.26 g of the title compound: MS ($M+H^+$): 154.0; ^{1}H-NMR (400 MHz, $CDCl_3$): 5.93-5.76(m, 2H), 5.29-4.99(m, 4H), 3.22(d, 2H), 2.34(s, 2H), 2.01(d, 2H), 0.94(s, 6H).

c.) Pyridine-2-sulfonic acid allyl-(2,2-dimethyl-pent-4-enyl)-amide

Allyl-(2,2-dimethyl-pent-4-enyl)-amine (0.43 g, 2.8 mmol) and NMM (0.57g, 5.6mmol) were mixed in 30 mL CH_2Cl_2. 2-pryridinesulphonyl chloride was added slowly to the solution while it was cooled in an ice-water bath. After addition, the reaction mixture was stirred at r.t. overnight. Washed by 10% $NaHCO_3$ and the brine. Purified by column chromatography gave 0.6 g colorless oil in 73% yield. MS ($M+H^+$): 295.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.71-8.70(d, 1H), 7.98-7.86(m, 2H), 7.48-7.46(m, 1H), 5.88-5.77(m, 1H), 5.55-5.45(m, 1H), 5.13-5.00(m, 4H), 4.05-4.04(d, 2H), 3.24(s, 2H), 2.07-2.05(d, 2H), 0.96(s, 6H)

d.) .3,3-Dimethyl-1-(pyridine-2-sulfonyl)-2,3,4,7-tetrahydro-1H-azepine

Pyridine-2-sulfonic acid allyl-(2.2-dimethyl-pent-4-enyl)-amide (0.6g, 2mmol) was diluted in CH_2Cl_2 (50ml). After carefully degass by Ar, Grubbs catalyst (0.17g, 0.2mmol) was added under Ar protection. The mixture was then refluxed for 2h before the solvent was removed on rotavapor. The crude product was purified by column chromatography (5%-20% E/H) to give 0.47g of the title compound in 87% yield. MS ($M+H^+$): 267.0; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.70-8.69(d, 1H), 7.96-7.88(m, 2H), 7.49-7.46(m, 1H), 5.81-5.70(m, 2H), 3.93-3.92(d, 2H), 3.26(s, 2H), 2.13-2.12(d, 2H), 1.00(s, 6H)

e.) 5,5-Dimethyl-3-(pyridine-2-sulfonyl)-8-oxa-3-aza-bicyclo[5.1.0]octane

To the solution of the compound of Example 92d (1.2 g, 4.5 mmol) in 50 mL CH_2Cl_2 was added $NaHCO_3$ (2.4 g, 13.5 mmol) and then MCPBA (1.2 g, 13.5 mmol) in portions. The reaction was stirred at r.t. for 4h before it was worked up by washing with 15% NaOH, saturated K_2CO_3, brine and dried (Na_2SO_4) to give 1.0g crude product in 79

% yield (good enough for next reaction without further purification.) MS ($M+H^+$): 283.0; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.68-8.67(d, 1H), 8.03-7.87(m, 2H), 7.49-7.40(m, 1H), 4.44-3.89(q, 1H), 3.62-3.59(d, 1H), 3.50(m, 1H), 3.00(m, 1H), 2.78-2.62(m, 2H), 2.12-2.06(m, 1H), 1.52-1.46(q, 1H), 1.20(s, 3H), 0.89(s, 3H).

f.) 4-Azido-6,6-dimethyl-1-(pyridine-2-sulfonyl)-azepan-3-ol

5,5-Dimethyl-3-(pyridine-2-sulfonyl)-8-oxa-3-aza-bicyclo[5.1.0]octane from Example 92e (1.2 g, 4.3 mmol) was dissolved in the mixture of 7 ml MeOH and 1 ml H_2O. NaN_3 (0.83 g, 13 mmol) and NH_4Cl (0.7 g, 13 mmol) were added to the solution. The resulting mixture was refluxed overnight. After the removal of MeOH, the residue was diluted in EtOAc and washed with 10% $NaHCO_3$ and brine. Purified on column chromatography gave 0.4g 4-azido-6,6-dimethyl-1-(pyridine-2-sulfonyl)-azepan-3-ol (yield 29%); MS ($M+H^+$): 326.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.68-8.67(m, 1H), 8.05-7.90(m, 2H), 7.53-7.50(m, 1H), 3.75-3.60(m, 3H), 3.49-3.30(m, 3H), 1.73-1.66(m, 1H), 1.56-1.52(d, 1H), 1.07(s, 3H), 0.99(s, 3H)

g.) 4-Amino-6,6-dimethyl-1-(pyridine-2-sulfonyl)-azepan-3-ol

4-Azido-6,6-dimethyl-1-(pyridine-2-sulfonyl)-azepan-3-ol from Example 92f (0.4 g, 1.23 mmol) was dissolved in THF (50 ml) and H_2O (0.2 ml). PPh_3 (0.48 g, 1.85 mmol) was added to this solution. The reaction mixture was stirred at 45°C over night. TLC showed no starting material left. THF was evaporated, azeotroped with toluene (2x's). The resulting thick oil was dissolved in MeOH, treated with HCl in ether to adjust pH to acidic. More ether was added and the solution turned cloudy. 0.22 g white precipitate of the title compound was collected. (45% yield); ^{1}H-NMR (400 MHz, CD_3OD): • 8.68(m, 1H), 8.10-7.93(m, 2H), 7.62(m, 1H), 3.90(m, 1H), 3.68(m,1H), 3.40-2.90(m, 4H), 1.82(m, 1H), 1.53(d, 1H), 1.05(s, 6H)

h.) {(S)-1-[3-Hydroxy-6,6-dimethyl-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-3-methyl-butyl}-carbamic acid *tert*-butyl ester

4-Amino-6,6-dimethyl-1-(pyridine-2-sulfonyl)-azepan-3-ol HCl salt from Example 92g (0.22 g, 0.6 mmol) was dissolved in 5ml DMF. To this solution, was added Boc-Leu-OH (0.22 g, 0.9 mmol)and HBTU (0.34 g, 0.9 mmol) and then NMM (0.24 g, 2.4 mmol). The mixture was stirred at r.t. overnight. DMF was removed under high vacuum. The

residue was diluted with EtOAc and washed with H_2O, 10% $NaHCO_3$ and brine. Purification by column chromatography gave 0.22 g of the title compound (72% yield); MS ($M+H^+$): 512.9; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.68-8.67(d, 1H), 7.97-7.88(m, 2H), 7.69-7.64(m, 1H), 6.62-6.53(m, 1H), 5.06-5.00(m, 1H), 4.03-3.18(m, 7H), 1.80-1.42(m, 15H), 1.04-0.92(m, 12H).

i.) Benzofuran-2-carboxylic acid {(S)-1-[3-hydroxy-6,6-dimethyl-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

To {(S)-1-[3-Hydroxy-6,6-dimethyl-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-3-methyl-butyl}-carbamic acid *tert*-butyl ester of Example 92h (0.22g, 0.43mmol) was added HCl/dioxane (4M, 20 ml, 80 mmol). The mixture was stirred at r.t. for 2h before solvents and excess amount of HCl was removed on rotavapor. The resulting white solid was dissolved in 5 ml DMF. To the solution was added 2-benzofurancarboxylic acid (84 mg, 0.52 mmol), HBTU (0.2 g, 0.52 mmol) and NMM (0.2 g, 2 mmol). The mixture was stirred at r.t. overnight. DMF was then removed and the residue was re-dissolved in EtOAc (50 ml), washed with 10% $NaHCO_3$ (50 ml x 2) and brine (50 ml). Evaporation of the solvent gave crude product 0.26 g. Purification by column chromatograghy gave the title compound 0.15 g in 63% total yield; MS ($M+H^+$): 556.8; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.66-8.63(m, 1H), 7.94-7.11(m, 10H), 4.72(m, 1H), 4.01-2.98(m, 7H), 1.78-1.39(m, 5H), 1.02-0.85(m, 12H).

j.) Benzofuran-2-carboxylic acid {(S)-1-[3-oxo-6,6-dimethyl-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

To a solution of benzofuran-2-carboxylic acid {(S)-1-[3-hydroxy-6,6-dimethyl-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide from Example 92i (100 mg, 0.18mmol) in 2 ml CH_2Cl_2, was added Dess-Martin reagent (76 mg, 0.18 mmol) at r.t.. The solution was stirred for 2h when 20 ml CH_2Cl_2 was added and then washed with $NaHCO_3$ and brine. Purification by column chromatograghy (50% ethyl acetate in hexane) gave 70 mg of the title compound in 70% yield. MS (M+H+): 555.4; 1H-NMR (400 MHz, $CDCl_3$): • 8.68-8.67(d, 1H), 7.97-7.93(m, 2H), 7.69-7.28(m, 6H), 7.32-6.92(m, 2H), 5.24(m, 1H), 4.79-4.69(m, 2H), 3.80-3.71(m, 2H), 2.54-2.50(d, 1H), 1.92-1.76(m, 4H), 1.45-1.40(m, 4H), 1.01-0.91(m, 9H).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS ($M+H^+$): 555.2, and the slower eluting diastereomer; MS ($M+H^+$): 555.2.

Example 93

Preparation of 5-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting 5-methoxybenzofuran-2-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 574 ($M+H^+$).

b.) 5-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting 5-methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 93a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (m, 4H). 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-8.6 (m, 8H) 8.0-8.2 (m, 2H); MS(EI): 572 (M^+, 30%).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; ^{1}HNMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (t, 1H), 3.7 (s, 3H), 3.8 (d, 1H). 4.0 (d, 1H), 4,7 (m, 1H), 4.8 (d, 1H), 5.0 (m, 1H), 7.4-8.6 (m, 8H) 8.0-8.2 (m, 2H); MS(EI): 573 ($M+H^+$,100%) and the slower eluting diastereomer; MS(EI): 573 ($M+H^+$,100%).

Example 94

Preparation of Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting thieno[3,2-b]thiophene-2-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 566 ($M+H^+$).

b.) Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 94a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m,6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (q, 1H). 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-7.5 (m, 6H), 7.7 (d, 1H), 8.0-8.2 (m, 2H). MS(EI): 564 (M^+,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; ^{1}HNMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (t, 1H), 3.8 (d, 1H). 4.0 (d, 1H), 4,5 (m, 1H), 4.7 (d, 1H). 5.0 (m, 1H), 7.4-7.5 (m, 6H), 7.7 (d, 1H), 8.0-8.2 (m, 2H); MS(EI): 565 ($M+H^+$,100%) and the slower eluting diastereomer; MS(EI): 565 ($M+H^+$,100%).

Example 95

Preparation of Quinoxaline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Quinoxaline-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting quinoxaline-2-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 556 ($M+H^+$).

b.) Quinoxaline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting quinoxaline-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

of Example 95a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (q, 1H). 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-7.5 (m, 2H), 7.9 (m, 1H), 8.0-8.4 (m, 4H, 9.6 (d, 1H); MS(EI): 554 (M^+,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 555 ($M+H^+$,100%) and the slower eluting diastereomer; MS(EI): 555 ($M+H^+$,100%).

Example 96

Preparation of Quinoline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Quinoline-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting quinoline-2-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 555 ($M+H^+$).

b.) Quinoline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting quinoline-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 96a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (q, 1H). 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-8.6 (m, 10H); MS(EI): 553 (M^+,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 554 ($M+H^+$,100%) and the slower eluting diastereomer; MS(EI): 554 ($M+H^+$,100%).

Example 97

Preparation of Thiophene-3-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Thiophene-3-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting thiophene-3-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 510 ($M+H^+$).

b.) Thiophene-3-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting thiophene-3-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 97a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (q, 1H). 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-8.0 (m, 4H), 7.8 (m, 1H), 8.1-8.2 (m, 2H); MS(EI): 508 (M^+, 80%).

Example 98

Preparation of 1H-Indole-5-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 1H-Indole-5-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting 1H-indole-5-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 543 (M^+).

b.) 1H-Indole-5-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting of 1H-indole-5-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 98a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H) , 2.7 (m, 1H), 3.8 (q, 1H); 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-8.0 (m, 7H), 8.1-8.2 (m, 2H), 8.6 (b, 1H); MS(EI): 541 (M^+,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 542 ($M+H^+$,80%) and the slower eluting diastereomer; MS(EI): 542 ($M+H^+$,80%).

Example 99

Preparation of Benzo[1,3]dioxole-5-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Benzo[1,3]dioxole-5-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting Benzo[1,3]dioxole-5-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 548 (M^+).

b.) Benzo[1,3]dioxole-5-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting benzo[1,3]dioxole-5-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 99a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (q, 1H); 4.0 (m, 1H), 4.5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 6.0 (s, 2H), 7.4-8.0 (m, 5H), 8.1-8.2 (m, 2H); MS(EI): 546 (M^+,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer; MS(EI): 547 ($M+H^+$,100%) and the slower eluting diastereomer; MS(EI): 547 ($M+H^+$,100%).

Example 100

Preparation of Furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Furan-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting furoic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 494 (M^+).

b.) Furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting furan-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 100a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (q, 1H); 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-8.0 (m, 5H), 8.1-8.2 (m, 2H); MS(EI): 492 (M^+,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer MS(EI): 493 ($M+H^+$,100%) and the slower eluting diastereomer; MS(EI): 493 ($M+H^+$,100%).

Example 101

Preparation of (S)-4-Methyl-2-(2-thiophen-2-yl-acetylamino)-pentanoic acid [3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-yl]-amide

a.) (S)-4-Methyl-2-(2-thiophen-2-yl-acetylamino)-pentanoic acid [3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 85c except substituting thiophene-2-acetic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared.

b.) (S)-4-Methyl-2-(2-thiophen-2-yl-acetylamino)-pentanoic acid [3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 1i except substuting (S)-4-methyl-2-(2-thiophen-2-yl-acetylamino)-pentanoic acid [3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-yl]-amide of

Example 101a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (m, 3H); 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-8.0 (m, 5H), 8.1-8.2 (m, 2H); MS(EI): 522 (M^+, 20%).

Example 102

Preparation of 1H-Indole-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 1H-Indole-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting 1H-indole-2-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 543 (M^+).

b.) 1H-Indole-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting 1H-indole-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-

butyl}amide of Example 102a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (q, 1H); 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H),7.4-8.0 (m, 7H), 8.1-8.2 (m, 2H), 9.4 (b, 1H); MS(EI): 541 (M^+,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereomer: MS(EI): 542 ($M+H^+$,100%) and the slower eluting diastereomer; MS(EI): 542 ($M+H^+$,100%).

Example 103

Preparation of 4-Fluoro-{(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulphonyl)-azepan-4-carbamoyl]-butyl}-benzamide

a.) 4-Fluoro-{(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulphonyl)-azepan-4-carbamoyl]-butyl}-benzamide

Following the procedure of Example 85c except substituting 4-fluorobenzoic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 522 (M^+).

b.) 4-Fluoro-{(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulphonyl)-azepan-4-carbamoyl]-butyl}-benzamide

Following the procedure of Example 1i except substuting 4-fluoro-{(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulphonyl)-azepan-4-carbamoyl]-butyl}-benzamide of Example 103a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (q, 1H); 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H),7.4-8.0 (m, 6H), 8.1-8.2 (m, 2H); MS(EI): 520 (M^+,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereomer: MS(EI): 521 ($M+H^+$,100%) and the slower eluting diastereomer MS(EI): 521 ($M+H^+$,100%).

Example 104

Preparation of 5-(2-Morpholin-4-yl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-(1-oxy-pyridine2-sulphonyl)-azepan-4-ylcarbamoyl]-buty}-amide

a.) 5-(2-Morpholin-4-yl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-(1-oxy-pyridine2-sulphonyl)-azepan-4-ylcarbamoyl]-buty}-amide

Following the procedure of Example 85c except substituting 5-(2-morpholin-4-yl-ethyloxy)benzofuran-2-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 673 (M^+).

b.) 5-(2-Morpholin-4-yl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-(1-oxy-pyridine2-sulphonyl)-azepan-4-ylcarbamoyl]-buty}-amide

Following the procedure of Example 1i except substuting 5-(2-morpholin-4-yl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-(1-oxy-pyridine2-sulphonyl)-azepan-4-ylcarbamoyl]-buty}-amide of Example 104a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.5 (m, 4H), 2.7 (m, 3H), 3.7 (m, 4H); 3.9 (m, 1H), 4,5 (m, 3H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-8.0 (m, 6H), 8.1-8.2 (m, 2H); MS(EI): 671 (M^+,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereomer: MS(EI): 672 ($M+H^+$,100%) and the slower eluting diastereomer MS(EI): 672 ($M+H^+$,100%).

Example 105

Preparation of Thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting thiophene-2-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 510 (M^+).

b.) Thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 105a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (q, 1H); 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-8.0 (m, 5H), 8.1-8.2 (m, 2H); MS(EI): 508 (M^+,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereomer: MS(EI): 509 ($M+H^+$,100%) and the slower eluting diastereomer MS(EI): 509 ($M+H^+$,100%).

Example 106

Preparation of 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting 3-methylbenzofuran-2-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 558 (M^+).

b.) 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting 3-methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 106a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.5 (d, 3H), 2.7 (m, 1H), 3.8 (q, 1H); 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-8.0 (m, 6H), 8.1-8.2 (m, 2H); MS(EI): 556 (M^+,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.6 (s, 3H), 2.7 (t, 1H), 3.8 (d, 1H); 4.1 (d, 1H), 4,7 (m, 1H), 4.7 (d, 1H), 5.0 (m, 1H), 7.0 (m, 2H), 7.3

(m, 2H), 7.4 (m, 4H), 8.1 (d, 1H), 8.2 (d, 1H); MS(EI): 557 ($M+H^+$,100%) and the slower eluting diastereomer MS(EI): 557 ($M+H^+$,100%).

Example 107

Preparation of 6-Methyl-N-{(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-nicotinamide

a.) 6-Methyl-N-{(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-nicotinamide

Following the procedure of Example 85c except substituting 6-methylnicotinic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 519 (M^+).

b.) 6-Methyl-N-{(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-nicotinamide

Following the procedure of Example 1i except substuting of 6-methyl-N-{(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-nicotinamide Example 107a the title compound was prepared: : ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.6 (s, 3H), 2.7 (m, 1H), 3.8 (q, 1H); 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-8.0 (m, 3H), 8.1-8.2 (m, 3H), 9.0 (m, 1H); MS(EI): 517 (M^+,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer: MS(EI): 518 ($M+H^+$,100%) and the slower eluting diastereomer MS(EI): 518 ($M+H^+$,100%).

Example 108

Preparation of (S)-4-Methyl-2-(2-thiophen-yl-acetylamino)-pentanoic acid-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-butyl}amide

a.) (S)-4-Methyl-2-(2-thiophen-yl-acetylamino)-pentanoic acid-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-butyl}amide

Following the procedure of Example 28b except substituting thiophene-2-acetic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(ESI) 508.8 ($M+H^+$).

b.) (S)-4-Methyl-2-(2-thiophen-yl-acetylamino)-pentanoic acid-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-butyl}amide

Following the procedure of Example 1i except substuting (S)-4-methyl-2-(2-thiophen-yl-acetylamino)-pentanoic acid-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-butyl}amide of Example 108a the title compound was prepared: MS(ESI) 506.8 ($M+H^+$).

Example 109

Preparation of 1H-Indole-6-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 1H-Indole-6-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 1H-indole-6-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 527 ($M+H^+$).

b.) 1H-Indole-6-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting 1H-indole-6-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 109a the title compound was prepared: MS(EI) 525 ($M+H^+$).

Example 110

Preparation of Benzo[1,3]dioxole-5-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Benzo[1.3]dioxole-5-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting piperonylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 532.7 ($M+H^+$).

b.) Benzo[1,3]dioxole-5-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting benzo[1,3]dioxole-5-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 110a the title compound was prepared: MS(EI) 530.8 ($M+H^+$).

Example 111

Preparation of 3,4-Dihydro-2H-benzo[b][1,4]dioxepine-7-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 3,4-Dihydro-2H-benzo[b][1,4]dioxepine-7-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting 3,4-dihydro-2H-1,5-benzodioxepine-7-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 576 (M^+).

b.) 3,4-Dihydro-2H-benzo[b][1,4]dioxepine-7-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting 3,4-dihydro-2H-benzo[b][1,4]dioxepine-7-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 111a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 4H), 2.5 (d, 3H), 2.7

(m, 1H), 3.8 (q, 1H); 4.0 (m, 1H), 4.2 (m, 4H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-8.0 (m, 5H), 8.1-8.2 (m, 2H); MS(EI): 575 ($M+H^+$,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer: MS(EI): 575 ($M+H^+$,100%) and the slower eluting diastereomer MS(EI): 575 ($M+H^+$,100%).

Example 112

Preparation of 5-Methyl-thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5-Methyl-thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting 5-methyl thiophene-2-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 524 (M^+).

b.) 5-Methyl-thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting 5-methyl-thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 112a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.5 (d, 3H), 2.7 (m, 1H), 3.8 (q, 1H); 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-8.0 (m, 4H), 8.1-8.2 (m, 2H); MS(EI): 523 ($M+H^+$,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer: MS(EI): 523 ($M+H^+$,100%) and the slower eluting diastereomer MS(EI): 523 ($M+H^+$,100%).

Example 113

Preparation of 4,5-Dibromo-thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 4,5-Dibromo-thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting 4,5-dibromo-thiophene-2-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 668 (M^+).

b.) 4,5-Dibromo-thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

**Following the procedure of Example 1i except substuting 4,5-dibromo-thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 113a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (q, 1H); 4.0 (m, 1H), 4.5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-8.0 (m, 3H), 8.1-8.2 (m, 2H); MS(EI): 665 ($M+H^+$,100%) .

Example 114

Preparation of 3,5-Dimethyl-isoxazole-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 3,5-Dimethyl-isoxazole-4-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting 3,5-dimethyl-isoxazole-4-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 524 ($M+H^+$).

b.) 3,5-Dimethyl-isoxazole-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting 3,5-dimethyl-isoxazole-4-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 114a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.4 (m, 3H), 2.6 (m, 3H), 2.7 (m, 1H), 3.8 (q, 1H); 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-8.0 (m, 5H), 8.1-8.2 (m, 2H); MS(EI): 521 (M^+,100%) .

Example 115

Preparation of (S)-2-(2-Benzyloxy-acetylamino)-4-methyl-pentanoic acid[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-yl]-amide

a.) {(S)-1-[3-Hydroxy-1-(4-methoxy-benzenesulfonyl)-azepan-4-ylcarbamoyl]-3-methyl-butyl}-carbamic acid-*tert*-butyl ester

[(S)-1-(3-Hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-carbamic acid-*tert*-butyl ester (compound 2g, 0.8 g, 2.33 mmol) was dissolved in 1,2-dichloroethane (DCE, 20 ml). Then, morpholinemethyl polystyrene resin beads (1.26 g, 3.7 mmol/g, Nova) were added and the solution was shaken for 5 minutes. Then, p-methoxybenzenesulfonyl chloride (0.48 g, 2.33 mmol) was dissolved in DCE (10 ml), and this solution was added to the reaction mixture. The reaction was shaken overnight, filtered, washed with DCE (2 x 10 ml), then CH_2Cl_2 (10 ml). The combined organics were concentrated *in vacuo*, and used in the next reaction without further purification: $M+H^+$ = 514.2.

b.) (S)-2-Amino-4-methyl-pentanoic acid [3-hydroxy-1-(4-methoxy-benzenesulfonyl)-azepan-4-yl]-amide-HCl salt

{(S)-1-[3-Hydroxy-1-(4-methoxy-benzenesulfonyl)-azepan-4-ylcarbamoyl]-3-methyl-butyl}-carbamic acid-*tert*-butyl ester (compound 207a, 0.59 g, 1.15 mmol) was dissolved in CH_2Cl_2 (8 ml), then a solution of 4 M HCl in dioxane (8 ml) was added and the reaction was stirred at RT for 4h. The reaction mixture was concentrated *in vacuo*, azeotroped from toluene twice (10 ml) *in vacuo*, and was used in the next reaction without further purification: $M+H^+$ = 413.8.

c.) (S)-2-(2-Benzyloxy-acetylamino)-4-methyl-pentanoic acid [3-hydroxy-1-(4-methoxy-benzenesulfonyl)-azepan-4-yl]-amide

(S)-2-Amino-4-methyl-pentanoic acid [3-hydroxy-1-(4-methoxy-benzenesulfonyl)-azepan-4-yl]-amide-HCl salt (crude product from reaction mixture of 115b) was dissolved in MeOH (10 ml) and was treated with carbonate-polystyrene resin beads (1.75 g, 2.63 mmol/g, 4.6 mmol) and was shaken for 2h, filtered, washed with MeOH (10 ml) and the combined organics were concentrated *in vacuo*. The product was then dissolved in DCE (2 ml) and morpholinemethyl polystyrene resin beads (0.25 g, 3.77 mmol/g, 0.91 mmol, Nova) were added and the reaction was shaken for 5 minutes. Then, benzylacetyl chloride (0.081 g, 0.44 mmol) was added and the reaction mixture was shaken overnight. Then, trisamine polystyrene beads (0.1g, 3.66 mmol/g, 0.366 mmol) was added and the reaction mixture was shaken for 1.5 h. The reaction mixture was then filtered, washed with DCE (2x10 ml) and CH_2Cl_2 (10 ml), and the combined organics were concentrated *in vacuo*. The crude product was used in the next reaction without further purification: $M+H^+ = 562.2$.

d.) (S)-2-(2-Benzyloxy-acetylamino)-4-methyl-pentanoic acid [1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan- 4-yl]-amide

(S)-2-(2-Benzyloxy-acetylamino)-4-methyl-pentanoic acid [3-hydroxy-1-(4-methoxy-benzenesulfonyl)-azepan-4-yl]-amide (compound 207c, 0.24 g, 0.44 mmol) was dissolved in CH_2Cl_2 (5 ml), then Dess-Martin periodinane (0.3 g, 0.7 mmol) was added and the reaction was stirred for 30 min. The reaction was diluted with CH_2Cl_2 (20 ml), then was extracted with aqueous 10% $Na_2S_2O_5$ (10 ml), then aqueous 10% $NaHCO_3$ (10 ml), water (10 ml), brine (10 ml). The combined organics were concentrated *in vacuo*. The residue was purified by HPLC (50:50 Ethanol: hexanes, 20mL/min, 25min, WhelkO-1(R,R) 21x250mm column, UV detection at 280nm and 305nm) to yield the first elution as a white solid (47 mg, 43 %): MS 560.4 ($M+H^+$). ^1H NMR (400Hz,$CDCl_3$): δ 7.73 (d, 2H), 7.40-7.30 (m, 5H), 7.05 (d, 2H), 3.99 (s, 2H), 3.88 (s, 3H), 2.28-2.10 (m, 2H), 0.95 (t, 6H) and second eluting diastereomer: MS 560.2 ($M+H^+$).

Example 116

Preparation of 5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting 5-(3-trifluoromethyl-phenyl)-furan-2-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 638 (M^+).

b.) 5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting 5-(3-trifluoromethyl-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 116a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.6 (d, 3H), 2.7 (m, 1H), 3.8 (q, 1H); 4.1 (m, 1H), 4,7 (t, 1H), 4.8 (m, 1H), 5.0 (m, 1H), 7.4-8.0 (m, 9H), 8.1-8.2 (m, 2H); MS(EI): 637 ($M+H^+$,100%) .

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer: MS(EI): 637 ($M+H^+$, 100%) and the slower eluting diastereomer MS(EI): 637 ($M+H^+$, 100%) .

Example 117

Preparation of 5-Methyl-2 –phenyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5-Methyl-2 –phenyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c except substituting 5-methyl-2-phenyl-oxazole-4-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(EI) 585 (M^+).

b.) 5-Methyl-2 –phenyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substuting 5-methyl-2 –phenyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 117a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.6 (d, 3H), 2.7 (m, 1H), 3.8 (q, 1H); 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-8.0 (m, 7H), 8.1-8.2 (m, 2H); MS(EI): 584 ($M+H^+$, 100%).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer: MS(EI): 584 ($M+H^+$, 100%) and the slower eluting diastereomer MS(EI): 584 ($M+H^+$, 100%) .

Example 118

Preparation of Benzofuran-2-carboxylic acid {(S)-1-[1-(3,4-dimethoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}-amide

a.) Benzofuran-2-carboxylic acid {(S)-1-[1-(3,4-dimethoxy-benzenesulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}-amide

To a solution of benzofuran-2-carboxylic acid {(S)-1-[1-(3,4-dimethoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}-amide of Example 78c (0.175 g) in dichloromethane was added triethylamine (0.1 mL) and 3,4-dimethoxybenzenesulfonyl chloride (0.12 g). The reaction was stirred until complete. Workup and column chromatography (5% methanol:dicloromethane) provided the title compound (0.21 g): MS(EI) 587 (M^+).

b.) Benzofuran-2-carboxylic acid {(S)-1-[1-(3,4-dimethoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedure of Example 1i except substuting benzofuran-2-carboxylic acid {(S)-1-[1-(3,4-dimethoxy-benzenesulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}-amide of Example 118a the title compound was prepared: : ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 6H), 2.6 (m, 1H), 3.5 (d. 1H); 3.7 (t, 6H), 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-8.0 (m, 8H); MS(EI): 586 ($M+H^+$, 100%).

Example 119

Preparation of Benzofuran-2-carboxylic acid {(S)-1-[1-(4-bromo-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide

a.) Benzofuran-2-carboxylic acid {(S)-1-[1-(4-bromo-benzenesulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide

Following the procedure of Example 118a except substituting 4-bromobenzenesulfonyl chloride for 3,4-dimethoxybenzenesulfonyl chloride the title compound was prepared: MS(EI) 606 (M^+).

b.) Benzofuran-2-carboxylic acid {(S)-1-[1-(4-bromo-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide

Following the procedure of Example 1i except substituting benzofuran-2-carboxylic acid {(S)-1-[1-(4-bromo-benzenesulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide of Example 119a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 6H), 2.6 (m, 1H), 3.5 (d, 1H); 4.0 (m, 1H), 4,5 (t, 1H), 4.7 (m, 1H), 5.0 (m, 1H), 7.4-8.0 (m, 9H); MS(EI): 604 (M^+, 100%).

Example 120

Preparation of Benzofuran-2-carboxylic acid {(S)-1-[1-(benzo[1,2,5]oxadiazole-4-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide

a.) Benzofuran-2-carboxylic acid {(S)-1-[1-(benzo[1,2,5]oxadiazole-4-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide

Following the procedure of Example 118a except substituting benzofurazan-4-sulfonyl chloride for 3,4-dimethoxybenzenesulfonyl chloride the title compound was prepared: MS(EI) 569 (M^+).

b.) Benzofuran-2-carboxylic acid {(S)-1-[1-(benzo[1,2,5]oxadiazole-4-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide

Following the procedure of Example 1i except substituting Benzofuran-2-carboxylic acid {(S)-1-[1-(benzo[1,2,5]oxadiazole-4-sulfonyl)-3-hydroxy-azepan-4-

ylcarbamoyl]-3-methyl–butyl}-amide of Example 120a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 6H), 2.6 (m, 1H), 3.7 (m, 1H); 4.1 (m, 1H), 4.7 (m, 2H), 5.2 (m, 1H), 7.4-8.0 (m, 8H); MS(EI): 568 ($M+H^+$, 100%).

Example 121

Preparation of Benzofuran-2-carboxylic acid {(S)-1-[1-(3,5-dimethyl-oxazole-4 -sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide

a.) Benzofuran-2-carboxylic acid {(S)-1-[1-(3,5-dimethyl-oxazole-4 -sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide

Following the procedure of Example 118a except substituting 3,5-dimethyloxazole-4-sulphonyl chloride for 3,4-dimethoxybenzenesulfonyl chloride the title compound was prepared: MS(EI) 546 (M^+).

b.) Benzofuran-2-carboxylic acid {(S)-1-[1-(3,5-dimethyl-oxazole-4 -sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide

Following the procedure of Example 1i except substituting benzofuran-2-carboxylic acid {(S)-1-[1-(3,5-dimethyl-oxazole-4-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide of Example 121a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.2 (m, 2H), 2.4 (d, 3H), 2.7 (t, 3H), 3.6 (d, 1H), 4.1 (m, 1H), 4.4 (t, 1H), 4.7 (m, 1H), 5.2 (m, 1H), 7.4-8.0 (m, 5H); MS(EI): 544 (M^+, 100%).

Example 122

Preparation of 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 3-methylbenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 542 (M^+).

b.) 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting 3-methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 122a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.2 (m, 2H), 2.6 (d, 3H), 2.7 (m, 1H), 3.8 (m, 1H), 4.1 (m, 1H), 4.7 (m, 2H), 5.2 (m, 1H), 7.4-8.0 (m, 7H): 8.7 (m, 1H); MS(EI): 540 (M^+, 100%).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.2 (m, 2H), 2.6 (s, 3H), 2.7 (m, 1H), 3.8 (d, 1H); 4.1 (d, 1H), 4.7 (m, 2H), 5.2 (m, 1H), 7.4-8.0 (m, 7H); 8.7 (m, 1H); MS(EI): 541 ($M+H^+$,100%) and the slower eluting diastereomer MS(EI): 541 ($M+H^+$, 100%).

Example 123

Preparation of Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting thieno[3,2-b]thiophene-2-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 550 (M^+).

b.) Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 123a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (m, 1H); 4.1 (m, 1H), 4.7 (m, 2H), 5.2 (m, 1H), 7.4-8.0 (m, 8H); 8.7 (m, 1H): MS(EI): 548 (M^+, 100%).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer: ^{1}HNMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.2 (m, 2H) 2.7 (t, 1H), 3.8 (d, 1H); 4.1 (d, 1H), 4.7 (m, 2H), 5.2 (m, 1H), 7.4-8.0 (m, 8H); 8.7 (d, 1H); MS(EI): 549 ($M+H^+$,100%) and the slower eluting diastereomer MS(EI): 549 ($M+H^+$, 100%) .

Example 124

Preparation of 5-*tert*-Butyl-3-methyl-thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5-*tert*-Butyl-3-methyl-thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 5-*tert*-butyl-3-methyl-thieno[3,2-b]thiophene-2-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 620 (M^+).

b.) 5-*tert*-Butyl-3-methyl-thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting 5-*tert*-butyl-3-methyl-thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 124a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.45 (s, 9H), 1.5-2.2 (m, 6H), 2.2 (m, 2H) 2.4 (d, 3H), 2.7 (m, 1H), 3.8 (m, 1H); 4.1 (m, 1H), 4.7 (m, 2H), 5.2 (m, 1H), 7.4-8.0 (m, 4H); 8.7 (m, 1H); MS(EI): 618 (M^+, 100%).

Example 125

Preparation of 5-Methyl-2-phenyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5-Methyl-2-phenyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 5-methyl-2-phenyl-oxazole-4-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 569 (M^+).

b.) 5-Methyl-2-phenyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting 5-methyl-2-phenyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 125a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.2 (m, 2H), 2.7 (m, 1H), 2.6 (m, 3H), 3.8 (m, 1H); 4.1 (m, 1H), 4.7 (m, 2H), 5.2 (m, 1H), 7.4-8.0 (m, 8H); 8.7 (m, 1H); MS(EI): 567 (M^+, 100%).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer: MS(EI): 568 ($M+H^+$,100%) and the slower eluting diastereomer MS(EI): 568 ($M+H^+$,100%)

Example 126

Preparation of 2-Phenyl-5-trifluoromethyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 2-Phenyl-5-trifluoromethyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-hydrox-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 2-phenyl-5-trifluoromethyl-oxazole-4-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 623 (M^+).

b.) 2-Phenyl-5-trifluoromethyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting 2-phenyl-5-trifluoromethyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-hydrox-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 126a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.2 (m, 2H), 2.7 (m, 1H), 3.8 (m, 1H); 4.1 (m, 1H), 4.7 (m, 2H), 5.2 (m, 1H), 7.4-8.0 (m, 8H); 8.7 (m, 1H); MS(EI): 621 (M^+, 100%).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer: MS(EI): 622 ($M+H^+$,100%) and the slower eluting diastereomer: MS(EI): 622 ($M+H^+$,100%).

Example 127

Preparation of Quinoline-2-carboxylic acid [(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

Following the procedure of Example 75, except substituting methanesulfonyl chloride for thiazole-2-sulfonyl chloride and 2-quinoline carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 475.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.65(d, 1H), 8.35-8.28(q, 2H), 8.20-8.18(d, 1H), 7.91-7.89(d, 1H), 7.80-7.78(t, 1H), 7.67-7.65(t, 1H), 7.10(d, 1H), 5.08(m, 1H), 4.73 (m, 1H), 4.56-4.51(d, 1H), 4.00(m, 1H), 3.67-3.62(d, 1H), 2.91(s, 3H), 2.70(m, 1H), 2.32-2.10(m, 2H), 1.95-1.40(m, 5H), 1.02-1.00(m, 6H); and the second eluting diastereomer: MS ($M+H^+$): 475.2

Example 128

Preparation of 1-Methyl-1H-indole-2-carboxylic acid [(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

Following the procedure of Example 75, except substituting methanesulfonyl chloride for thiazole-2-sulfonyl chloride and N-methylindole-2-carboxylic acid for

benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 477.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 7.65-7.63(d, 1H), 7.39-7.33(m, 2H), 7.17-7.14(t, 1H), 6.98-6.95(m, 2H), 6.65(d, 1H), 5.08(m, 1H), 4.68 (m, 1H) 4.56-4.52(d, 1H), 4.03(m, 4H), 3.67-3.63(d, 1H), 2.92(s, 3H), 2.71(m, 1H), 2.32-2.10(m, 2H), 1.95-1.40(m, 5H), 1.02-1.00(d, 6H); and the second eluting diastereomer: MS ($M+H^+$): 477.2

Example 129

Preparation of Furan-2-carboxylic acid {[(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butylcarbamoyl]-methyl}-amide

Following the procedure of Example 75, except substituting methanesulfonyl chloride for thiazole-2-sulfonyl chloride and N-(2-furan-carbonyl)-glycine for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 471.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 7.50(m, 1H), 7.15(m, 1H), 7.05(m, 1H), 6.90(d, 1H), 6.55(m, 2H), 5.08(m, 1H), 4.55 (m, 2H), 4.12(m, 2H), 4.05(m, 1H), 3.70(d, 1H), 2.92(s, 3H), 2.75(m, 1H), 2.20-1.40(m, 7H), 0.95 (m, 6H); and the second eluting diastereomer: MS ($M+H^+$): 471.4.

Example 130

Preparation of 5-Methoxybenzofuran-2-carboxylic acid [(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

Following the procedure of Example 75, except substituting methanesulfonyl chloride for thiazole-2-sulfonyl chloride and 5-methoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 494.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 7.42-7.40(d, 2H), 7.08-6.94(m, 4H), 5.10(m, 1H), 4.71(m, 1H), 4.56-4.52(d, 1H), 4.02(m, 1H), 3.86(s, 3H), 3.68-3.63(d, 1H), 2.92(s, 3H), 2.72(m, 1H), 2.30-1.15(m, 2H), 1.95-1.40(m, 5H), 0.99 (d, 6H); and the second eluting diastereomer: MS ($M+H^+$): 494.2.

Example 131

Preparation of Quinoxaline-2-carboxylic acid [(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

Following the procedure of Example 75, except substituting methanesulfonyl chloride for thiazole-2-sulfonyl chloride and quinoxaline-2-carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 476.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 9.66(s, 1H), 8.38(d, 1H), 8.20-8.18(m, 2H), 7.88(m, 2H), 7.01(d, 1H), 5.10(m, 1H), 4.77(m, 1H), 4.57-4.52(d, 1H), 4.08-4.00(m, 1H), 3.69-3.64(d, 1H), 2.92(s, 3H), 2.71(m, 1H), 2.42-2.15(m, 2H), 1.95-1.42(m, 5H), 1.02-1.01(d, 6H); and the second eluting diastereomer: MS ($M+H^+$): 476.2.

Example 132

Preparation of 5-(4-Chloro-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5-(4-Chloro-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 5-(4-chlorophenyl)-2-furoic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 590 ($M+H^+$).

b.) 5-(4-Chloro-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting 5-(4-chloro-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 132a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.1 (m, 5H), 2.2 (m, 2H), 2.7 (m, 1H), 3.7 (d, 1H), 4.0 (m, 1H), 4.7 (m, 2H), 5.0 (m, 1H), 6.7 (m, 1H), 7.2 (m, 1H), 7.3 (m, 2H), 7.5 (m, 1H), 7.7 (m, 2H), 8.0 (m, 2H), 8.7 (m, 1H): MS(EI): 587 (M^+, 80%)

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer: MS(EI): 587 ($M+H^+$,100%) and the slower eluting diastereomer: MS(EI): 587 ($M+H^+$,100%).

Example 133

Preparation of (S)-2-[2-(4-Methoxy-phenyl)-acetylamino)-4-methyl-pentanoic acid (1-methanesulfonyl-3-oxo-azepan-4-yl)-amide

Following the procedure of Example 75, except substituting 4- methanesulfonyl chloride for thiazole-2-sulfonyl chloride and 2-(4-methoxyphenyl)-acetic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 468.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 7.19-7.17(d, 2H), 6.90-6.88(d, 3H), 5.83-5.81(d, 1H), 5.00(m, 1H), 4.53-4.40(m, 2H), 4.03-3.99(m, 1H), 3.81(s, 3H), 3.66-3.61(d, 1H), 3.53(s, 2H), 2.91(s, 3H), 2.73(t, 1H), 2.22-2.10(m, 2H), 1.99(m, 1H), 1.62-1.35(m, 4H), 0.90-0.88(d, 6H); and the second eluting diastereomer: MS ($M+H^+$): 468.2.

Example 134

Preparation of Quinoline-2-carboxylic acid {[(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 75, except substituting 2-cyanobenzenesulfonyl chloride for thiazole-2-sulfonyl chloride and quinoline-2-carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 562.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.65(d, 1H), 8.48-8.40(q, 2H), 8.25-8.10(q, 2H), 7.91-7.65(m, 6H); and the second eluting diastereomer:, 7.12(d, 1H), 5.10(m, 1H), 4.73 (m, 1H) 4,61-4.56(d, 1H),4.20(m, 1H),3.73-3.68(d, 1H), 2.80(m, 1H), 2.27(m, 2H), 1.91-1.40(m, 5H), 1.03-1.01(m, 6H); and the second eluting diastereomer: MS ($M+H^+$): 562.2.

Example 135

Preparation of 1-Methyl-1H-indole -2-carboxylic acid {[(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 75, except substituting 2-cyanophenylsulfonyl chloride for thiazole-2-sulfonyl chloride and N-methylindole-2-carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 564.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.13(d, 1H), 7.89(d, 1H), 7.77-7.67(m, 3H), 7.38-7.16(m, 4H), 6.97(s, 1H), 6.70(d, 1H), 5.05(m, 1H), 4.70-4.60 (m, 1H), 4.55-4.50(d, 1H), 4.07(m, 1H), 4.05(s, 3H), 3.76-3.71(d, 1H), 2.75(m, 1H), 2.30(m, 2H), 2.00-1.45(m, 5H), 1.00(d, 6H); and the second eluting diastereomer: MS ($M+H^+$) 564.2.

Example 136

Preparation of Furan-2-carboxylic acid ({(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butylcarbamoyl}-methyl)-amide

Following the procedure of Example 75, except substituting 2-cyanophenylsulfonyl chloride for thiazole-2-sulfonyl chloride and N-(2-furan-carbonyl)-glycine for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 558.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.14-8.12(d, 1H), 7.91-7.90(d, 1H), 7.80-7.72(m, 2H), 7.48(s, 1H), 7.14(d, 2H), 6.98(d, 1H), 6.80(d, 1H), 6.52-6.51(t, 1H), 5.03(m, 1H), 4.60-4.53 (m, 2H), 4.17-4.14(m, 3H), 3.74-3.69(d, 1H), 2.80(m, 1H), 2.25(m, 2H), 2.00-1.40(m, 5H), 1.03-1.01(m, 6H); and the second eluting diastereomer: MS ($M+H^+$) 558.2.

Example 137

Preparation of 5-Methoxybenzofuran-2-carboxylic acid {(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 75, except substituting 2-cyanophenylsulfonyl chloride for thiazole-2-sulfonyl chloride and 5-methoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 581.4; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.15-8.13(d, 1H), 7.92-7.90(d, 1H), 7.81-7.74(m, 2H), 7.42-7.40(m, 2H), 7.08-7.03(m, 3H), 6.96(d, 1H), 5.10(m, 1H), 4.72-4.60 (m, 2H), 4.17 (d, 1H), 3.85(s, 3H), 3.75-3.70(d, 1H), 2.83-2.76(t, 1H), 2.27(m, 2H), 1.92-1.51(m, 5H), 1.02-1.01(m, 6H); and the second eluting diastereomer: MS ($M+H^+$) 581.2.

Example 138

Preparation of Quinoxaline-2-carboxylic acid {(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 75, except substituting 2-cyanophenylsulfonyl chloride for thiazole-2-sulfonyl chloride and quinoxaline-2-carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 563.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 9.65(s, 1H), 8.40(m, 1H), 8.22-8.10(m, 3H), 7.90-7.22(m, 5H), 7.00(d, 1H), 5.10(m, 1H), 4.75(m, 1H), 4.65-4.60(d, 1H), 4.20-4.10(m, 1H), 3.72-3.70(d, 1H), 2.70(m, 1H), 2.38(m, 2H), 1.95-1.40(m, 5H), 1.02(d, 6H); and the second eluting diastereomer: MS ($M+H^+$) 563.2.

Example 139

Preparation of (S)-2-[2-(4-Methoxy-phenyl)-acetylamino)-4-methyl-pentanoic acid [1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-yl]-amide

Following the procedure of Example 75, except substituting 2-cyanophenylsulfonyl chloride for thiazole-2-sulfonyl chloride and 2-(4-methoxyphenyl)-acetic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 555.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.14-8.12(d, 1H), 7.91-7.89(d, 1H), 7.79-7.73(m, 2H), 7.19-7.17(d, 2H), 6.90-6.88(d, 3H), 5.80(d, 1H), 5.02(m, 1H), 4.59-4.55(d, 1H), 4.45-4.42(m, 1H), 4.18-4.15(m, 1H), 3.82(s, 3H), 3.72-3.67(d, 1H), 3.53(s, 2H), 2.82-2.79(t, 1H), 2.22(m, 2H), 1.92(m, 1H), 1.60-1.30(m, 4H), 0.91-0.89(d, 6H); and the second eluting diastereomer: MS ($M+H^+$) 555.2.

Example 140

Preparation of Quinoline-2-carboxylic acid {[(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 75, except substituting 4-methoxybenzenesulfonyl chloride for thiazole-2-sulfonyl chloride and 2-quinoline carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 567.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.72-8.61(d, 1H), 8.35-8.28(q, 2H) 8.21-8.18(d, 1H), 7.91-7.60(m, 5H), 7.10-6.99(m, 3H), 5.05(m, 1H), 4.73 (m, 1H) 4,59-4.52(d, 1H),4.00(m, 1H), 3.88(s, 3H), 3.45-3.38(d, 1H), 2.42(m, 1H), 2.30-1.35 (m, 7H), 1.03-1.01(m, 6H); and the second eluting diastereomer: MS ($M+H^+$) 567.2.

Example 141

Preparation of 1-Methyl-1H-indole-2-carboxylic acid {[(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 75, except substituting 4-methoxyphenylsulfonyl chloride for thiazole-2-sulfonyl chloride and N-methyl-indole-2-carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 569.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 7.78-7.72(d, 2H), 7.70-7.65(d, 1H), 7.42-7.30(m, 2H), 7.17-7.14(t, 1H), 7.05-6.95(m, 4H), 6.65(d, 1H), 5.05(m, 1H), 4.70-4.50 (m, 2H), 4.03(s, 3H), 3.88(s, 3H), 3.45-3.40(d, 1H), 2.45(m, 1H), 2.30-2.10(m, 2H), 1.90-1.35(m, 6H); and the second eluting diastereomer:, 1.00(d, 6H); and the second eluting diastereomer: MS ($M+H^+$) 569.2.

Example 142

Preparation of Furan-2-carboxylic acid ({(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butylcarbamoyl}-methyl)-amide

Following the procedure of Example 75, except substituting 4-methoxyphenylsulfonyl chloride for thiazole-2-sulfonyl chloride and N-(2-furan-carbonyl)-glycine for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 563.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 7.74-7.72(d, 2H), 7.47 (s, 1H), 7.15-6.99(m, 4H), 6.91(d, 1H), 6.70(d, 1H), 6.52-6.51(m, 1H), 5.01(m, 1H), 4.53-4.49 (m, 2H), 4.17-4.14(m, 2H), 4.00-3.90(m, 1H), 3.88(s, 3H), 3.45-3.41(d, 1H), 2.47(m, 1H), 2.17(m, 2H), 1.85-1.40(m, 5H), 0.95(m, 6H); and the second eluting diastereomer: MS ($M+H^+$) 563.2.

Example 143

Preparation of 5-Methoxybenzofuran-2-carboxylic acid {[(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 75, except substituting 4-methoxyphenylsulfonyl chloride for thiazole-2-sulfonyl chloride and 5-methoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 586.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 7.75-7.73(d, 2H), 7.42-7.40(m, 2H), 7.08-6.99(m, 5H), 6.91(d, 1H), 5.05(m, 1H), 4.70-4.55(m, 2H), 4.05-4.00(m, 1H), 3.89(s, 3H), 3.86(s, 3H), 3.45-3.40(d, 1H), 2.50-2.40(m, 1H), 2.30-2.10(m, 2H), 1.90-1.35(m, 5H), 1.01(m, 6H); and the second eluting diastereomer: MS ($M+H^+$) 586.2.

Example 144

Preparation of Quinoxaline-2-carboxylic acid {[(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 75, except substituting 4-methoxyphenylsulfonyl chloride for thiazole-2-sulfonyl chloride and quinoxaline-2-carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 568.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 9.66(s, 1H), 8.40-8.35(m, 1H), 8.19(m, 2H), 7.88(m, 2H), 7.75-7.73(d, 2H), 7.02-6.90(m, 3H), 5.10-5.05(m, 1H), 4.75(m, 1H), 4.60-4.55(d, 1H), 4.05-3.95(m, 1H), 3.89(s, 3H), 3.45-3.41(d, 1H), 2.45(m, 1H), 2.30-2.10(m, 2H), 1.95-1.40(m, 5H), 1.04-1.02(d, 6H); and the second eluting diastereomer: MS ($M+H^+$) 568.2.

Example 145

Preparation of (S)-2-[2-(4-Methoxy-phenyl)-acetylamino)-4-methyl-pentanoic acid [1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-yl]-amide

Following the procedure of Example 75, except substituting 4-methoxyphenylsulfonyl chloride for thiazole-2-sulfonyl chloride and 2-(4-methoxyphenyl)-acetic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 560.4; ^{1}H-NMR (400 MHz, $CDCl_3$): • 7.74-7.71(d, 2H), 7.19-7.17(d, 2H), 7.01-6.99(d, 2H), 6.90-6.88(d, 2H), 6.85(d, 1H), 5.81(d, 1H), 4.99(m, 1H), 4.55-4.44(m, 2H), 3.97(m, 1H), 3.88(s, 3H), 3.81(s, 3H), 3.53(s, 2H), 3.43-3.38(d, 1H), 2.43(t, 1H), 2.14(m, 2H), 1.85-1.35(m, 5H), 0.90-0.89(d, 6H); and the second eluting diastereomer: MS ($M+H^+$) 560.2.

Example 146

Preparation of 1-Methyl-1H-indole-2-carboxylic acid {[(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 75, except substituting 4-fluorophenylsulfonyl chloride for thiazole-2-sulfonyl chloride and N-methyl-indole-2-carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 557.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 7.84-7.80(m, 2H), 7.66-7.65(d, 1H), 7.40-7.14(m, 5H), 6.95(m, 2H), 6.65-6.63(d, 1H), 5.07(m, 1H), 4.68-4.55 (m, 2H), 4.04(s, 3H), 3.48-3.43(d, 1H), 2.49(m, 1H), 2.25(m, 2H), 1.89-1.38(m, 6H); and the second eluting diastereomer:, 1.01(d, 6H); and the second eluting diastereomer: MS ($M+H^+$) 557.4.

Example 147

Preparation of Furan-2-carboxylic acid {{(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butylcarbamoyl}-methyl)-amide

Following the procedure of Example 75, except substituting 4-fluorophenylsulfonyl chloride for thiazole-2-sulfonyl chloride and N-(2-furan-carbonyl)-glycine for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 551.4; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.81(m, 2H), 7.48(s, 1H), 7.27-7.16(m, 3H), 7.05(m, 1H), 6.90(d, 1H), 6.52(m, 2H), 5.00(m, 1H), 4.60-4.48 (m, 2H), 4.14(m, 2H), 4.00-3.90(d, 1H), 3.48-3.44(d, 1H), 2.50(m, 1H), 2.20(m, 2H), 1.90-1.40(m, 5H), 0.95(m, 6H); and the second eluting diastereomer: MS ($M+H^+$) 551.2.

Example 148

Preparation of 5-Methoxybenzofuran-2-carboxylic acid {[(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 75, except substituting 4-fluorophenylsulfonyl chloride for thiazole-2-sulfonyl chloride and 5-methoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 574.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 7.84-7.81(m, 2H), 7.42-7.40(m, 2H), 7.27-7.22(m, 2H), 7.08-7.04(m, 3H), 6.93(d, 1H), 5.10-5.02(m, 1H), 4.69-4.55(m, 2H), 4.05-4.00(m, 1H), 3.86(s, 3H), 3.47-3.43(d, 1H), 2.49(m, 1H), 2.24(m, 2H), 1.90-1.40(m, 5H), 1.01(m, 6H); and the second eluting diastereomer: MS ($M+H^+$): 574.2

Example 149

Preparation of Quinoxaline-2-carboxylic acid {[(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 75, except substituting 4-fluorophenylsulfonyl chloride for thiazole-2-sulfonyl chloride and quinoxaline-2-carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 556.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 9.66(s, 1H), 8.40-8.35(d, 1H), 8.21-8.18(m, 2H), 7.90-7.81(m, 4H), 7.27-7.22(m, 2H), 6.97(d, 1H), 5.10-5.02(m, 1H), 4.75(m, 1H), 4.59-4.55(d, 1H), 4.05-4.39(m, 1H), 3.48-3.44(d, 1H), 2.49(m, 1H), 2.32-2.10(m, 2H), 1.90-1.40(m, 5H), 1.03-1.02(d, 6H); and the second eluting diastereomer: MS ($M+H^+$) 556.2.

Example 150

Preparation of (S)-2-[2-(4-Methoxy-phenyl)-acetylamino)-4-methyl-pentanoic acid [1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-yl]-amide

Following the procedure of Example 75, except substituting 4-fluorophenylsulfonyl chloride for thiazole-2-sulfonyl chloride and 2-(4-methoxyphenyl)-acetic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 548.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 7.83-7.80(m, 2H), 7.27-7.17(m, 4H), 6.90-6.88(d, 3H), 5.85(d, 1H), 4.98(m, 1H), 4.55-4.43(m, 2H), 4.00-3.97(m, 1H), 3.81(s, 3H), 3.53(s, 2H), 3.45-3.41(d, 1H), 2.48(t, 1H), 2.17-2.14(m, 2H), 1.90-1.30(m, 5H), 0.90-0.88(d, 6H); and the second eluting diastereomer: MS ($M+H^+$): 548.4.

Example 151

Preparation of Benzofuran-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

a.) {(S)-1-[1-(3-Chloro-benzenesulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-3-methyl-butyl}-carbamic acid *tert*-butyl ester

To a solution of the compound of Example 2g (2.50g, 7.29mmol) in DCE (100ml) was added P-NMM (4.0g) and 3-chlorobenzenesulphonyl chloride (1.85g, 8.75mmol). After shaking at room temperature overnight, the solution was filtered. The filtrate was concentrated to yield the title compound as white solid (3.13g, 83.3%). MS: 539.78 $(M+Na)^+$.

b.) (S)-2-Amino-4-methyl-pentanoic acid [1-(3-chloro-benzenesulfonyl)-3-hydroxy-azepan-4-yl]-amide

To a stirring solution of the compound of Example 151a (1.0g, 1.93mmol) in methnol (10 ml) was added HCl (4M in Dioxane) (10 ml). After stirring at room temperature for 3 hr the solution was concentrated to provide a white solid. To a solution of the white solid (0.68 g, 1.50 mmol, 78%) in methnol (37 ml) was added P-CO_3 (2.85g, 2.63mmol/g). After shaking for 2hr, the solution was filtered and concentrated to yield the title compound as white solid (0.59 g, 1.42 mmol, 95%). MS: 417.86 $(M+H)^+$.

c.) Benzofuran-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

To a solution of the compound of Example 151b (0.14 g, 0.33 mmol) in CH_2Cl_2 (20 mL) was added benzofuran-2-carboxylic acid (0.81, 0.50 mmol), 1-hydroxybenzotriazole (0.77 g, 0.57 mmol), and P-EDC (0.67g, 1 mmol/g) in CH_2Cl_2 (10 mL) . After shaking at room temperature overnight, the solution was treated with tisamine (0.45 g, 3.75 mmol/g). After shaking for another 2 hr, the solution was filtered and concentrated to yield the title compound as a white solid (122 mg, 65%). MS (ESI): 562.2 $(M+H)^+$.

d.) Benzofuran-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

To a stirring solution of the compound of Example 151c (122 mg, 0.22 mmol) in dichloromethane (4 mL) was added Dess-Martin reagent (185 mg, 0.44 mmol). After stirring at room temperature for 2 h, solutions of sodium thiosulfate (2 mL of 10% in water) and saturated aqueous sodium bicarbonate (2 mL) were added simultaneously to the solution. The aqueous layer was extracted with dichloromethane (2x). The organic phases were combined, washed with saturated brine, dried ($MgSO_4$), filtered and concentrated. The residue was purified by HPLC to yield the first eluting diastereomer as a white solid (62.7 mg, 51.6 %), MS (ESI): 560.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (40.2 mg, 33.1 %). MS (ESI): 560.2 $(M+H)^+$

Example 152

Preparation of 5-Methoxybenzofuran-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 151c-d, except substituting 5-methoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid of Example 151c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (64.4 mg, 50.3%): MS (ESI): 590.2 $(M+H)^+$ and the second eluting distereomer as a white solid (44.4 mg, 34.7%): MS (ESI): 590.2 $(M+H)^+$

Example 153

Preparation of 7-Methoxybenzofuran-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 151c-d except substituting 7-methoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid of Example 151c provided the title compound which was separated by HPLC to give first eluting diastereomer as a white solid (51.1mg, 39.9%), MS (ESI): 590.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (36.7 mg, 28.7%): MS (ESI): 590.2 $(M+H)^+$

Example 154

Preparation of 5,6-Dimethoxybenzofuran-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 151c-d except substituting 5,6-dimethoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid of Example 151c provided the title compound which was separated by HPLC to give first eluting diastereomer as a white solid (51.1mg, 39.9%), MS (ESI): 622.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (36.7 mg, 28.7%): MS (ESI): 622.2 $(M+H)^+$

Example 155

Preparation of 3-Methylbenzofuran-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 151c-d except substituting 3-methylbenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid in step 151c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (78.6mg, 63.1%), MS (ESI): 574.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (40.7mg, 32.6%). MS (ESI): 574.2 $(M+H)^+$

Example 156

Preparation of Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 151c-d except substituting benzo[b]thiophene-2-carboxylic acid for benzofuran-2-carboxylic acid in step 151c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (41.0 mg, 32.8%), MS (ESI): 576.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (31.0 mg, 24.8%). MS (ESI): 576.4 $(M+H)^+$

Example 157

Preparation of 1-Methyl-1H-indole-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 151c-d except substituting 1-methylindole-2-carboxylic acid for benzofuran-2-carboxylic acid in step 151c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (28.5 mg, 22.9%), MS (ESI): 573.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (28.5mg, 22.9%). MS (ESI): 573.2 $(M+H)^+$

Example 158

Preparation of Quinoxaline-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 151c-d except substituting quinoxaline-2-carboxylic acid for benzofuran-2-carboxylic acid in step 151c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (63.1 mg, 50.8%), MS (ESI): 572.2 $(M+H)^+$ and the second eluting distereomer as a white solid (43.2 mg, 34.8%), MS (ESI): 572.2 $(M+H)^+$

Example 159

Preparation of Benzofuran-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

a.) {(S)-1-[1-(2-Fluoro-benzenesulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-3-methyl-butyl}-carbamic acid *tert*-butyl ester

To a solution of the compound of Example 2g (1.03 g, 3.00 mmol) in DCE (20 ml) was added P-NMM (1.65 g, 3.64 mmol/g) and 2-fluorobenzenesulphony lchloride (0.70 g, 3.60 mmol). After shaking at room temperature overnight, the solution was filtered. The

filtrate was concentrated to yield the title compound as white solid (1.13 g, 75.1%): MS: 523.88 $(M+Na)^+$.

b.) (S)-2-Amino-4-methyl-pentanoic acid [1-(2-fluoro-benzenesulfonyl)-3-hydroxy-azepan-4-yl]-amide

To a stirring solution of the compound of Example 159a (1.13 g, 2.25 mmol) in methnol (15 ml) was added HCl (4M in dioxane) (15 ml). After stirring at room temperature for 3 hr, the solution was concentrated to get white solid. To a solution of the white solid (1.11 g, 2.60 mmol, 75%) in methnol (50 ml) was added P-CO_3 (5.70 g, 2.63 mmol/g). After shaking for 2hr, the solution was filtered and concentrated to yield the title compound as white solid (0.868g, 2.16mmol, 96%): MS: 401.96 $(M+H)^+$.

c.) Benzofuran-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

To a solution of the compound of Example 159b (0.11 g, 0.26 mmol) in CH_2Cl_2 (10 mL) was added benzofuran-2-carboxylic acid (64.7 mg, 0.39 mmol), 1-hydroxybenzotriazole (61.1g, 0.45 mmol), and P-EDC (0.53 g, 1 mmol/g) in CH_2Cl_2 (10 mL). After shaking at room temperature overnight, the solution was treated with tisamine (0.35 g, 3.75 mmol/g). After shaking for another 2 hr, the solution was filtered and concentrated to yield the title compound as a white solid (103.5 mg, 70%): MS (ESI) 546.2 $(M+H)^+$.

d.) Benzofuran-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

To a stirring solution of the compound of Example 159c (103.5 mg, 0.19 mmol) in dichloromethane (4 mL) was added Dess-Martin reagent (164.7 mg, 0.39 mmol). After stirring at room temperature for 2 h, solutions of sodium thiosulfate (2 mL of 10% in water) and saturated aqueous sodium bicarbonate (2 mL) were added simultaneously to the solution. The aqueous was extracted with dichloromethane (2x). The organic phases were combined, washed with saturated brine, dried ($MgSO_4$), filtered and concentrated. The residue was purified by HPLC to yield the first eluting diastereomer as a white solid (76.2 mg, 73.6 %): MS (ESI) 544.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (20.7mg, 20.0%) MS (ESI) 544.4 $(M+H)^+$

Example 160

Preparation of 5-Methoxybenzofuran-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 159c-d, except substituting 5-methoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid in step 159c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (48.3 mg, 59.2%) MS (ESI): 574.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (24.2mg, 29.6%) MS (ESI): 574.2 $(M+H)^+$

Example 161

Preparation of 7-Methoxybenzofuran-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 159c-d except substituting 7-methoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid in step 159c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (47.7 mg, 58.5%): MS (ESI) 574.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (27.7 mg, 33.9%).

Example 162

Preparation of 5,6-Dimethoxybenzofuran-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 159c-d except substituting 5,6-dimethoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid in step 159c provided the title compound which was separated by HPLC to give the first eluting diastereomer: MS (ESI) 606.4 $(M+H)^+$ and the second eluting diastereomer as a white solid MS(ESI) 606.4 $(M+H^+)$.

Example 163

Preparation of 3-Methylbenzofuran-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 159c-d except substituting 3-methylbenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid in step 160c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (50.5 mg, 63.7%): MS (ESI) 558.2 and the second elutinfg diastereoemer as a white solid (20.6 mg); MS 558.2 $(M+H)^+$.

Example 164

Preparation of Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 159c-d except substituting benzo[b]thiophene-2-carboxylic acid for benzofuran-2-carboxylic acid in step 159c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (52.5 mg, 65.9%): MS (ESI) 560.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (20.7mg, 26.0%): MS(ESI) 560.2 $(M+H)^+$

Example 165

Preparation of 1-Methyl-1H-indole-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 159c-d except substituting 1-methylindole-2-carboxylic acid for benzofuran-2-carboxylic acid in step 159c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (51.4 mg, 64.9%): MS (ESI) 557.2 $(M+H)^+$ and the seond eluting diastereoemer as a white solid (21.0 mg, 26.5%): MS 557.2 $(M+H)^+$

Example 166

Preparation of (S)-4-Methyl-2-(1-oxy-pyridine-2-sulfonylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

a.) (S)-4-Methyl-2-(1-oxy-pyridine-2-sulfonylamino)-pentanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

To a solution of the compound of Example 28a (0.1 g) in dichlorormethane (10 mL) and saturated $NaHCO_3$ was added 2-pryridinesulfonyl chloride N-oxide (0.9 mL) in a dropwise fashion over 3 minutes. The reaction was stirred at room temperature for 30 minutes. Workup and columnn chromatography provided 9.2 mg of the title compound: MS (ESI) 541 ($M+H^+$).

b.) (S)-4-Methyl-2-(1-oxy-pyridine-2-sulfonylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 1i except substituting the compound of Example 166a the title compound was prepared: MS (ESI) 539 ($M+H^+$).

Example 167

Preparation of Quinoxaline-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 159c-d except substituting quinoxaline-2-carboxylic acid for benzofuran-2-carboxylic acid in step 159c provided the title compound which was purified by HPLC to give the first eluting diastereomer as a white solid (49.7 mg, 62.9%): MS (ESI) 556.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (19.9 mg, 25.1%): MS 556.4 $(M+H)^+$

Example 168

Preparation of 5-Methoxybenzofuran-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedure of Example 75a-d except substituting 2-thiophensulfonyl chloride for 2-thiazolesupfonyl chloride of Example 75a and 5-methoxybenzofuran-2-

carboxylic acid for benzofuran-2-carboxylic acid in step 75c provided the title compound which was purified by HPLC to give the first eluting diastereomer as a white solid (71 mg, 65%): MS (ESI) 562.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (21.6 mg, 20.0%) MS (ESI): 562.2 $(M+H)^+$

Example 169

Preparation of 7-Methoxybenzofuran-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedure of Example 168 except substituting 7-methoxybenzofuran-2-carboxylic acid for 5-methoxybenzofuran-2-carboxylic acid provided the title compound which ws purified by HPLC to give the first eluting diastereomer as a white solid (88 mg, 80%): MS (ESI) 562.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (18 mg, 16%) MS (ESI): 562.2 $(M+H)^+$

Example 170

Preparation of 5,6-Dimethoxybenzofuran-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedure of Example 168 except substituting 5,6-dimethoxybenzofuran-2-carboxylic acid for 5-methoxybenzofuran-2-carboxylic acid provided the title compound which was purified by HPLC to give the first eluting diastereomer MS (ESI) 594.2 $(M+H)^+$ and the second eluting diastereomer.

Example 171

Preparation of 3-Methylbenzofuran-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedure of Example 168 except substituting 3-methybenzofuran-2-carboxylic acid for 5-methoxybenzofuran-2-carboxylic acid provided the title compound which was purified by HPLC to give the first eluting diastereomer as a white solid (88 mg, 83%): MS (ESI) 546.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (16 mg, 15%): MS (ESI) 546.2 $(M+H)^+$

Example 172

Preparation of Benzo[b]thiophene-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedure of Example 168 except substituting benzo[b]thiophene-2-carboxylic acid 5-methoxybenzofuran-2-carboxylic acid provided the title compound which was purified by HPLC to give the first eluting diastereomer as a white solid (43.4 mg, 41%): MS (ESI) 548.4 $(M+H)^+$ and the second eluting diastereomer as a white solid (33.4 mg, 31.5%): MS (ESI) 548.2 $(M+H)^+$

Example 173

Preparation of 1-Methyl-1H-indole-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedure of Example 168 except substituting 1-methylindole-2-carboxylic acid for 5-methoxybenzofuran-2-carboxylic acid provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (35.8 mg, 34.0%): MS (ESI) 545.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (45.8 mg, 43%): MS (ESI) 545.2 $(M+H)^+$

Example 174

Preparation of Quinoxaline-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedure of Example 168 except substituting quinoxaline-2-carboxylic acid for 5-methoxybenzofuran-2-carboxylic acid provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (60 mg, 56%): MS (ESI) 544.4 $(M+H)^+$ and the second eluting diastereomer as a white solid (38.7 mg, 37%): MS (ESI) 544.4 $(M+H)^+$

Example 175

Preparation of Benzofuran-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

a.) {(S)-1-[1-(3-Chloro-benzenesulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-3-methyl-butyl}-carbamic acid *tert*-butyl ester

To a solution of the compound of Example 2g (2.50 g, 7.29mmol) in DCE (100 ml) was added P-NMM (4.0g) and 4-chlorobenzenesulphonyl chloride (1.85g, 8.75mmol). After shaking at room temperature for over night, the solution was filtered. The filtrate was concentrated to yield the title compound as white solid (3.13g, 83.3%). MS: 539.78 $(M+Na)^+$.

b.) (S)-2-Amino-4-methyl-pentanoic acid [1-(3-chloro-benzenesulfonyl)-3-hydroxy-azepan-4-yl]-amide

To a stirring solution of the compound of example 175a (1.0 g, 1.93mmol) in methnol (10 ml) was added HCl (4M in dioxane) (10 ml). After stirring at room temperature for 3 hr, the solution was concentrated to provide a white solid. To a solution of the white solid (0.68 g, 1.50 mmol, 78%) in methnol (37 ml) was added P-CO_3 (2.85 g, 2.63 mmol/g). After shaking for 2hr, the solution was filtered and concentrated to yield the title compound as white solid (0.59 g, 1.42 mmol, 95%): MS: 417.86 $(M+H)^+$.

c.) Benzofuran-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

To a solution of the compound of Example 175b (0.14 g, 0.335 mmol) in CH_2Cl_2 (20 mL) was added benzofuran-2-carboxylic acid (0.81, 0.50 mmol), 1-hydroxybenzotriazole (0.77g, 0.569mmol), and P-EDC (0.67g, 1mmol/g) in CH_2Cl_2 (10 mL) . After shaking at room temperature overnight, the solution was treated with tisamine (0.446 g, 3.75 mmol/g). After shaking for another 2 hr, the solution was filtered and concentrated to yield the title compound as a white solid (122.2 mg, 65%). MS (ESI): 562.2 $(M+H)^+$.

d.) Benzofuran-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

To a stirring solution of the compound of Example 175c (122.2mg, 0.217mmol) in dichloromethane (4 mL) was added Dess-Martin reagent (184.8mg, 0.436mmol). After stirring at room temperature for 2 h, solutions of sodium thiosulfate (2 mL of 10% in water) and saturated aqueous sodium bicarbonate (2 mL) were added simultaneously to the solution. The aqueous was extracted with dichloromethane (2x). The organic phases were combined, washed with saturated brine, dried ($MgSO_4$), filtered and concentrated. The residue was purified by HPLC to yield the first eluting diastereomer as a white solid (62.7mg, 51.6 %): MS (ESI) 560.2 $(M+H)^+$ and the second elution as a white solid (32.7mg, 26.9 %): MS (ESI) 560.2 $(M+H)^+$

Example 176

Preparation of 5-Methoxybenzofuran-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 175c-d except substituting 5-methoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid in step 175c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (64.4 mg, 50%): MS (ESI) 590.2 $(M+H)^+$ and the second eluting diastereoemer as a white solid (32.2 mg, 25.2%): MS (ESI) 590.0 $(M+H)^+$

Example 177

Preparation of 7-Methoxybenzofuran-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 175c-d except substituting 7-methoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid in step 175c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (51.1 mg, 40%): MS (ESI) 590.2 $(M+H)^+$ and the second eluting diastereoemer as a white solid (41 mg, 32%): MS (ESI) 590.2 $(M+H)^+$

Example 178

Preparation of 5,6-Dimethoxybenzofuran-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 175c-d except substituting 5,6-dimethoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid in step 175c provided the title compound which was separated by HPLC to give the first eluting diastereomer: MS (ESI) 622.2 $(M+H)^+$ and the second eluting diastereoemer: MS (ESI) 622.2 $(M+H)^+$

Example 179

Preparation of 3-Methylbenzofuran-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 175c-d except substituting 3-methylbenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid in step 175c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (78.6 mg, 63%): MS (ESI) 574.2 $(M+H)^+$ and the second eluting diastereoemer as a white solid (27.6 mg, 22%): MS (ESI) 574.2 $(M+H)^+$

Example 180

Preparation of Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 175c-d except substituting benzo[b]thiophene-2-carboxylic acid for benzofuran-2-carboxylic acid in step 175c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (41 mg, 33%): MS (ESI) 576.2 $(M+H)^+$ and the second eluting diastereoemer as a white solid (32.6 mg, 26%): MS (ESI) 576.2 $(M+H)^+$

Example 181

Preparation of 1-Methyl-1H-indole-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 175c-d except substituting 1-methylindole-2-carboxylic acid for benzofuran-2-carboxylic acid in step 175c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (28.5 mg, 23%): MS (ESI) 573.2 $(M+H)^+$ and the second eluting diastereoemer as a white solid (38.5 mg, 31%): MS (ESI) 573.2 $(M+H)^+$

Example 182

Preparation of Quinoxaline-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 175c-d except substituting quinoxaline-2-carboxylic acid for benzofuran-2-carboxylic acid in step 175c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (63 mg, 51%): MS (ESI) 572.2 $(M+H)^+$ and the second eluting diastereoemer as a white solid (44.5 mg, 36%): MS (ESI) 572.2 $(M+H)^+$

Example 183

Preparation of Benzofuran-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

a.) {(S)-1-[1-(3-Methoxy-benzenesulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-3-methyl-butyl}-carbamic acid *tert*-butyl ester

To a solution of the compound of Example 2g (1.60g, 4.66mmol) in DCE (50ml) was added P-NMM (2.56g, 3.64mmol/g) and 3-methoxy-benzenesulphonyl chloride (1.15g, 5.59mmol). After shaking at room temperature for over night, the solution was

filtered. The filtrate was concentrated to yield the title compound as white solid (1.70g, 71.1%): MS 535.8 $(M+Na)^+$.

b.) (S)-2-Amino-4-methyl-pentanoic acid [1-(3-methoxy-benzenesulfonyl)-3-hydroxy-azepan-4-yl]-amide

To a stirring solution of the compound of example 183a (1.70 g, 3.31mmol) in methnol (22 ml) was added HCl (4M in dioxane) (22 ml). After stirring at room temperature for 3 hr, the solution was concentrated to get white solid. To a solution of the white solid (1.19 g, 2.64 mmol, 80%) in methnol (50 ml) was added P-CO_3 (5.02 g, 2.63 mmol/g). After shaking for 2 hr the solution was filtered and concentrated to yield the title compound as white solid (1.03 g, 2.49 mmol, 96%): MS 413.90 $(M+H)^+$.

c.) Benzofuran-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

To a solution of the compound of Example 183b (0.11 g, 0.26 mmol) in CH_2Cl_2 (10 mL) was added benzofuran-2-carboxylic acid (64.69mg, 0.399 mmol), 1-hydroxybenzotriazole (61.1g, 0.452mmol), and P-EDC (0.532g, 1mmol/g) in CH_2Cl_2 (10 mL) . After shaking at room temperature for over night, the solution was treated with tisamine (0.355g, 3.75mmol/g). After shaking for another 2hr, the solution was filtered and concentrated to yield the title compound as a white solid (103.5 mg, 70%): MS (ESI) 558.2 $(M+H)^+$.

d.) Benzofuran-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

To a stirring solution of the compound of Example 183c (103 mg, 0.19 mmol) in dichloromethane (4 mL) was added Dess-Martin reagent (157 mg, 0.37 mmol). After stirring at room temperature for 2 h, solutions of sodium thiosulfate (2 mL of 10% in water) and saturated aqueous sodium bicarbonate (2 mL) were added simultaneously to the solution. The aqueous was extracted with dichloromethane (2x). The organic phases were combined, washed with saturated brine, dried ($MgSO_4$), filtered and concentrated. The residue was purified by HPLC to yield the first eluting diastereomer as a white solid (76.2 mg, 73.6 %): MS (ESI: 556.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (24.1 mg, 23.3 %): MS (ESI) 556.2 $(M+H)^+$

Example 184

Preparation of 5-Methoxybenzofuran-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 183c-d except substituting 5-methoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid in step 183c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (33 mg, 31%): MS (ESI) 586.2 $(M+H)^+$ and the second eluting diastereoemer as a white solid (35.2 mg, 32%): MS (ESI) 586.2 $(M+H)^+$

Example 185

Preparation of 7-Methoxybenzofuran-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 183c-d except substituting 7-methoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid in step 183c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (41 mg, 38%): MS (ESI) 586.4 $(M+H)^+$ and the second eluting diastereoemer as a white solid (39.5 mg, 36%): MS (ESI) 586.2 $(M+H)^+$

Example 186

Preparation of 4,5-Dimethoxybenzofuran-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 183c-d except substituting 5,6-dimethoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid in step 183c provided the title compound which was separated by HPLC to give the first eluting diastereomer: MS (ESI) 618.4 $(M+H)^+$ and the second eluting diastereoemer.

Example 187

Preparation of 3-Methylbenzofuran-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 183c-d except substituting 3-methylbenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid in step 183c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (76 mg, 72%): MS (ESI) 570.2 $(M+H)^+$ and the second eluting diastereoemer as a white solid (23.2 mg, 22%): MS (ESI) 570.2 $(M+H)^+$

Example 188

Preparation of Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 183c-d except substituting benzo[b]thiophene-2-carboxylic acid for benzofuran-2-carboxylic acid in step 183c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (37 mg, 35%): MS (ESI) 572.2 $(M+H)^+$ and the second eluting diastereoemer as a white solid (31 mg, 29%): MS (ESI) 572.2 $(M+H)^+$

Example 189

Preparation of 1-Methyl-1H-indole-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 183c-d except substituting 1-methylindole-2-carboxylic acid for benzofuran-2-carboxylic acid in step 183c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (34 mg, 32%): MS (ESI) 569.2 $(M+H)^+$ and the second eluting diastereoemer as a white solid (38 mg, 38%): MS (ESI) 569.4 $(M+H)^+$

Example 190

Preparation of Quinoxaline-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 183c-d except substituting quinoxaline-2-carboxylic acid for benzofuran-2-carboxylic acid in step 183c provided the title compound which was separated by HPLC to give the first eluting diastereomer as a white solid (71 mg, 67%): MS (ESI) 568.2 $(M+H)^+$ and the second eluting diastereoemer as a white solid (27 mg, 24%): MS (ESI) 568.2 $(M+H)^+$

Example 191

Preparation of Benzofuran-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedure of Example 168 except substituting benzofuran-2-carboxylic acid for 5-methoxybenzofuran-2-carboxylic acid provided the title compound which ws purified by HPLC to give the first eluting diastereomer as a white solid (76 mg, 73%): MS (ESI) 532.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (25 mg, 23%) MS (ESI): 532.2 $(M+H)^+$

Example 192

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[(2,2',4-trideuterio)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

To a solution of benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide of Example 28c (0.03 g) in D_2O:CD_3OD (0.4:4 mL) was added triethylamine (0.04 mL). The reaction was heated to reflux for 2 hours whereupon it was concentrated and dried under vacuum. The residue was the redissolved in the same mixture and heated to reflux overnight. The reaction was concentrated and the residue purified by column chromatography (5% methanol:dichloromethane) to provide the title compound (0.02 g): ^{1}HNMR: δ 1.0 (m, 6H),

1.5-2.2 (m, 6H), 2.7 (m, 1H), 4.1 (m, 1H), 4.7 (m, 2H), 7.4-8.0 (m, 8H), 8.7 (m, 1H); MS(EI): 529 (M^+, 45%).

The diastereomeric mixture was separated by HPLC to provide the faster eluting diastereoemer: MS(EI): 530 ($M+H^+$,100%) and the slower eluting diastereomer: MS(EI): 530 ($M+H^+$,100%).

Example 193

Preparation of Benzofuran-2-carboxylic acid {(S)-2-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

a.) 4-*tert*-Butoxycarbonylamino-3-hydroxy-azepane-1-carboxylicacid benzyl ester

To a stirring solution of compound of Example 2e (1.04 g, 3.92mmol) in THF was added di-*tert*-butyldicarbonate (0.864 g). After stirring at room temperature for 30 minutes, the reaction mixture was diluted with diethylether and extracted with saturated $NaHCO_3$. The organic layer was dried over anhydrous Na_2SO_4, filtered, concentrated, and purified by silica gel column to give the title compound as a yellow oil (0.963 g, 2.64 mmol, 67%). MS (ESI): 365.03 $(M+H)^+$.

b.) (3-Hydroxy-azepan-4-yl)-carbamic acid *tert*-butyl ester

To a solution of compound of Example 193a (0.963g, 2.64mmol) in ethyl acetate (16 ml) was added 10% palladium on carbon (500 mg). After stirring the solution at room temperature for 48 hours, the mixture was filtered through celite. The filterate was concentrated to yield the title compound (0.529 g, 2.29mmol, 87%): MS(ESI): 231.92 $(M+H)^+$.

c.) [3-Hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-carbamic acid *tert*-butyl ester

To a solution of the compound of Example 193b (0.53, 2.29 mmol) in dichloromethane (20 ml) was added triethylamine (232 mg) and pyridine-2-sulfonyl chloride (410 mg, 2.32 mmol). After stirring at room temperature for 30 minutes, the mixture was washed with saturated $NaHCO_3$. The organic layer was dried, filtered, concentrated and purified on a silica gel column to give the title compound as a solid (0.58 g, 1.57 mmol, 68%): MS(ESI): 372.95 $(M+H)^+$.

d.) 4-Amino-1-(pryidine-2-sulfonyl)-azepan-3-ol

To a stirring solution of the compound of Example 193c (0.583 g, 1.57mmol) in ethyl acetate (0.5 ml) was added HCl (4M in dioxane, 3.9 ml). After stirring the reaction mixture for 30 minutes at room temperature, the mixture was concentrated to yield a white solid. The solid was treated with NaOH and then extracted with ethylacetate. The organic layer was dried, filtered, and concentrated to yield a yellow solid (0.35 g, 1.28 mmol, 81%): MS (ESI) 272.93 $(M+H)^+$.

e.) {(S)-1-[3-Hydroxy-1-(pryidine-2-sulfonyl)-azepan-4-ylcarbamoyl]-2-meth-butyl}-carbamic acid *tert*-butyl ester

To a solution of the compound of example 193d (19 mg, 0.070 mmol) in CH_2Cl_2 was added N-Boc-isoleucine (24.5 mg, 0.10 mmol), 1-hydroxybenzotriazole (16.1 mg, 0.12 mmol), and P-EDC (140 mg, 0.14 mmol) in CH_2Cl_2 . After shaking at room temperature overnight, the mixture was treated with PS-Trisamine. After shaking for another 2 hours, the mixture was filtered and concentrated to yield the title compound as a solid. MS (ESI) 484.97 $(M+H)^+$.

f.) (S)-2-Amino-3-methyl-penatanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

To a stirring solution of the compound of example 193e (34 mg, 0.07 mmol) in CH_2Cl_2 (0.50 ml) was added HCl (4M in dioxane) (0.165 ml). After stirring at room temperature for 30 minutes, the mixture was concentrated, giving a white solid. The white solid was azeotroped with toluene then treated with MP-carbonate (0.35 mmol) in methanol. After four hours of shaking, the mixture was filtered and concentrated to give the title compound as a solid.: MS(ESI) 384.9 $(M+H)^+$.

g.) Benzofuran-2-carboxylic acid {(S)-2-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

To a solution of the compound of example 193f (27 mg, 0.070 mmol) in CH_2Cl_2 was added 2-benzofurancarboxylic acid (17.0 mg, 0.106mmol), 1-hydroxybenzotriazole (16.1 mg, 0.12 mmol), and P-EDC (140 mg, 0.14 mmol) in CH_2Cl_2 . After shaking at room temperature overnight, the mixture was treated with PS-Trisamine. After shaking for

another 2 hours, the mixture was filtered and concentrated to yield the title compound as a solid: MS (ESI) 528.9 $(M+H)^+$.

h.) Benzofuran-2-carboxylic acid {(S)-2-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

To a stirring solution of the compound of example 193g (37 mg, 0.07 mmol) in CH_2Cl_2 (0.5 ml) was added Dess-Martin reagent (45 mg, 0.105 mmol). After stirring for 30 minutes, solutions of sodium thiosulfate (10% in water, 0.50 ml) and saturated aqueous sodium bicarbonate (0.50 ml) were added simultaneously to the reaction. The mixture was then extracted with dichloromethane (2 times). The organic layer was dried, filtered, and concentrated. The residue was purified by HPLC to yield the two diastereomers of the title compound as solids (first eluting: 7mg, second eluting: 5.5 mg): MS (ESI) 526.91 $(M+H)^+$.

Example 194

Preparation of Benzofuran-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-propyl}-amide

Following the procedure of Example 193e-h, except substituting N-Boc-alpha-aminobutyric acid in step 193e the title compound was purified to yield two diastereomers as solids (first eluting: 5 mg, second eluting: 5 mg) MS(ESI) 543.8 $(M+H)^+$.

Example 195

Preparation of Benzofuran-2-carboxylic acid {(S)-2-cyclohexyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide

Following the procedure of Example 193e-h, except substituting N-Boc-cyclohexylalanine in step 193e, the title compound was purified to yield two diastereomers as solids (first eluting: 4.5 mg second eluting: 4.5 mg): MS(ESI): 566.87 $(M+H)^+$.

Example 196

Preparation of Benzofuran-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide

Following the procedure of Example 193e-h, except substituting N-Boc-alanine for step 193e, the title compound was purified to yield two diastereomers as solids (first eluting: 5.5 mg, second eluting: 5 mg).

Example 197

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methanesulfinyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-propyl}-amide

Following the procedure of Example 193e-h, except substituting N-Boc-L-methionine for step 1(f), the title compound was purified to yield two diastereomers as solids (first eluting: 3 mg, second eluting: 3 mg). MS(ESI): 560.7 $(M+H)^+$.

Example 198

Preparation of Benzofuran-2-carboxylic acid {[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-methyl}-amide

Following the procedure of Example 193e-h, except substituting N-Boc-glycine for step 193e, the title compound was purified to yield two diastereomers as solids (first eluting: 3mg ,second eluting: 3 mg). MS(ESI): 470.81 $(M+H)^+$.

Example 199

Preparation of Benzofuran-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-pentyl}-amide

Following the procedure of Example 193e-h, except substituting N-Boc-norleucine for step 193e, the title compound was purified to yield two diastereomers as solids (first eluting: 4 mg, second eluting: 5 mg). MS(ESI): 526.85 $(M+H)^+$.

Example 200

Preparation of Benzofuran-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedure of Example 193e-h, except substituting N-Boc-norvaline for step 193e, the title compound was purified to yield two diastereomers as solids (first eluting: 7.5 mg, second eluting: 3.5 mg). MS(ESI): 512.8 $(M+H)^+$.

Example 201

Preparation of Benzofuran-2-carboxylic acid {(S)-2-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-propyl}-amide

Following the procedure of Example 193e-h, except substituting N-Boc-valine for step 193e, the title compound was purified to yield two diastereomers as solids (first eluting: 6 mg, second eluting: 4.5 mg). MS(ESI): 512.8 $(M+H)^+$.

Example 202

Preparation of Benzofuran-2-carboxylic acid {(S)-2-hydroxy-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-propyl}-amide

Following the procedure of Example 193e-h, except substituting N-Boc-L-threonine for step 193e, the title compound was purified to yield two diastereomers as solids (first eluting: 3 mg, second eluting: 3 mg).

Example 203

Preparation of Benzofuran-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-2-phenyl-ethyl}-amide

Following the procedure of Example 193e-h, except substituting N-Boc-phenylalanine for step 193e, the title compound was purified to yield two diastereomers as solids (first eluting:5mg, second eluting: 5mg). MS(ESI): 560.8 $(M+H)^+$.

Example 204

Preparation of 1(Benzofuran-2-carbonyl)-pyrrolidine-2-carboxylic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 193e-h, except substituting N-Boc-L-proline for step 193e, the title compound was purified to yield two diastereomers as solids (first eluting: 4 mg, second eluting: 5mg). MS(ESI): $(M+H)^+$.

Example 205

Preparation of 3,4-Dimethoxy-N- {(S)-1-[1-(4-imethoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-benzamide

Following the procedure of Example 115, except substituting 3,4-dimethoxybenzoyl chloride for benzyloxyacetyl chloride, the title compound was prepared.

The residue was purified by HPLC. First eluting diastereomer: MS 576.4($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 7.68 (d, 2H),7.00 (d,1H), 6.89 (s, 2H),3.84 (s, 3H),3.77 (s, 6H), 2.38 (t,1H), 0.94 (d, 6H): MS 576.4 ($M+H^+$).

Example 206

Preparation of Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(4-imethoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 115, except substituting 2-thiophene-carbonyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 572.2 ($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 7.80-7.68 (m, 5H), 7.38-7.34 (m, 2H), 7.01-6.93 (m, 4H), 3.83 (s, 3H), 2.38 (t, 1H), 0.97 (d, 6H). Second eluting diastereomer: MS 572.2 ($M+H^+$).

Example 207

Preparation of Benzo[1,3]dioxole-5-carboxylic acid {(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3methyl-butyl}-amide

Following the procedure of Example 115, except substituting 4-fluorobenzenesulphonyl chloride for 4-methoxybenzenesulfonyl chloride and 3,4-methylenedioxybenzoyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS 548.2 ($M+H^+$); ^1H NMR (400Hz.$CDCl_3$): δ 7.85-7.78 (m, 2H), 7.38-7.20 (m, 4H), 7.05 (d, 1H), 2.52-2.40 (m,1H), 1.0 (d, 6H). Second eluting diastereomer: MS 548.2 ($M+H^+$).

Example 208

Preparation of (S)-2-(2-Benzyloxy-acetylamino)-4-methyl-pentanoic acid[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-yl]-amide

Following the procedure of Example 115, except substituting 4-fluorobenzenesulphonyl chloride for 4-methoxybenzenesulfonyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 548.2 ($M+H^+$). ^1H NMR (400Hz,$CDCl_3$-CD_3OD) δ 7.88-7.80 (m, 2H), 7.45-7.30 (m, 5H), 7.30-7.20 (m, 2H), 4.00 (s, 2H), 2.60-2.48 (m,1H), 0.96 (t, 6H): MS 548.2 ($M+H^+$).

Example 209

Preparation of Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-yl carbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 115, except substituting 4-fluorobenzenesulphonyl chloride for 4-methoxybenzenesulfonyl chloride and benzo[b]thiophenecarbonyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 560.2 ($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 7.80-7.72 (m, 5H).7.37-7.34 (m, 2H), 7.33-7.15 (m. 4H), 2.43 (t, 1H), 0.96 (d, 6H). Second eluting diastereomer: MS 560.2 ($M+H^+$).

Example 210

Preparation of Benzofuran-2-carboxylic acid {(S)-1-[1-benzoyl-3-oxo-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide

a.) Benzofuran-2-carboxylic acid {(S)-1-[1-benzoyl-3-hydroxy-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide

To a solution of benzofuran-2-carboxylic acid [(S)-1-(3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide of Example 78c (0.2 g) in dichloromethane was added benzoic acid (0.12 g), HOBt (0.07 g) and EDC (0.99 g). The reaction was stirred until

complete. Workup and column chromatography (5% methanol:dichloromethane) provided the title compound (0.2 g): ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.7 (m, 1H), 3.8 (m,1H), 4.1 (m, 1H), 4.7 (m, 2H), 5.1 (m, 1H), 7.0-7.7 (m, 10H), 8.7 (m, 1H); MS(EI): 492 ($M+H^+$, 100%).

b.) Benzofuran-2-carboxylic acid {(S)-1-[1-benzoyl-3-oxo-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide

Following the procedure of Example 1i except substituting benzofuran-2-carboxylic acid {(S)-1-[1-benzoyl-3-hydroxy-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide of Example 210a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.7 (m, 1H), 3.7 (m,1H), 4.0 (m, 1H), 4.7 (m, 2H), 5.1 (m, 1H), 7.4-8.0 (m, 8H); MS(EI): 490 ($M+H^+$, 100%).

Example 211

Preparation of (S)-4-Methyl-2-(quinoline-8-sulfonylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

a.) (S)-4-Methyl-2-(quinoline-8-sulfonylamino)-pentanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 89a except substituting 8-quinolinesulfonyl chloride for 2-pyridinesulfonyl chloride the title compound was prepared: MS(EI) 576 ($M+H^+$).

b.) (S)-4-Methyl-2-(quinoline-8-sulfonylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 1i except substituting (S)-4-methyl-2-(quinoline-8-sulfonylamino)-pentanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide of Example 211a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 0.5-0.8 (m, 6H), 1.4-1.8 (m, 7H), 2.5 (m, 1H), 3.5-3.9 (m, 3H), 4.4 (m, 1H), 4.6 (m, 1H), 5.5 (m, 1H), 6.7 –7.0 (m, 2H), 7.5 (m, 3H), 8.0 (m, 2H), 8.3 (m, 2H), 8.6 (m, 1H), 9.0 (m, 1H); MS(EI): 674 ($M+H^+$, 100%).

Example 212

Preparation of (S)-4-Methyl-2-(naphthylene-2-sulfonylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

a.) (S)-4-Methyl-2-(naphthylene-2-sulfonylamino)-pentanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 89a except substituting 2-naphthylenesulfonyl chloride for 2-pyridinesulfonyl chloride the title compound was prepared: MS(EI) 575 ($M+H^+$).

b.) (S)-4-Methyl-2-(naphthylene-2-sulfonylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 1i except substituting (S)-4-methyl-2-(naphthylene-2-sulfonylamino)-pentanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide of Example 212a the title compound was prepared: ^1H NMR ($CDCl_3$): δ 0.5-0.8 (m, 6H), 1.4-1.8 (m, 7H), 2.5 (m, 1H), 3.5-3.9 (m, 3H), 4.5 (m, 1H), 4.6 (m, 1H), 5.5 (m, 1H), 6.7 (m, 1H), 7.5-8.0 (m, 9H), 8.5-8.6 (m, 2H); MS(EI): 673 ($M+H^+$, 100%).

Example 213

Preparation of Benzofuran-2-carboxylic acid-{(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-yl carbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 115, except substituting 4-fluorobenzenesulphonyl chloride for 4-methoxybenzenesulfonyl chloride and 2-benzofurancarbonyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 544.2.($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 7.79-7.77 (m, 2H), 7.61 (d, 1H), 7.46-7.38 (m, 3H), 7.25-7.06 (m, 5H), 2.43 (t, 1H), 0.95 (d, 6H). Second eluting diastereomer: MS 544.4 ($M+H^+$).

Example 214

Preparation of N-{(S)-1-[1-(4-Fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-3,4-dimethoxy-benzamide

Following the procedure of Example 115, except substituting 4-fluorobenzenesulphonyl chloride for 4-methoxybenzenesulfonyl chloride and 3,4-dimethoxybenzoyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 564.2.($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 7.80-7.76 (m, 2H),7.19 (t, 2H),7.05 (d, 1H), 6.88 (s, 2H), 6.78 (d, 1H), 6.53 (s, 1H), 3.77 (s, 6H), 2.43 (t, 1H), 0.94 (d, 6H). Second eluting diastereomer: MS 546.2 ($M+H^+$).

Example 215

Preparation of Cyclohexanecarboxylic acid {(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 115, except substituting 4-fluorobenzenesulphonyl chloride for 4-methoxybenzenesulfonyl chloride and cyclohexylcarbonyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 510.4.($M+H^+$).^1H NMR (400Hz,$CDCl_3$): δ 7.83-7.80 (m, 2H), 7.27-7.20 (m, 2H), 6.92 (d, 1H), 6.95 (d, 1H), 2.50 (t, 1H), 1.90-1.20 (m, 15H), 0.94 (t, 6H). Second eluting diastereomer: MS 510.2 ($M+H^+$).

Example 216

Preparation of (S)-2-(2-Benzyloxy-acetylamino)-4-methyl-pentanoic acid[1-(methanesulfonyl)-3-oxo-azepan-4-yl]-amide

Following the procedure of Example 115, except substituting methanesulphonyl chloride for 4-methoxybenzenesulfonyl chloride, the title compound was prepared. The

residue was purified by HPLC. First eluting diastereomer: MS 468.2 ($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 7.37-7.24 (m, 4H), 6.93-6.91 (m, 2H), 5.02-5.00 (m, 1H), 2.88 (s, 3H), 2.70 (t, 1H), 0.92 (t, 6H). Second eluting diastereomer: MS 468.2 ($M+H^+$).

Example 217

Preparation of Benzo[b]thiophene-2-carboxylic acid-{(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-yl carbamoyl)-3-methyl-butyl]-amide

Following the procedure of Example 115, except substituting methanesulphonyl chloride for 4-methoxybenzenesulfonyl chloride and benzo[b]thiophenecarbonyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 480.2 ($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 7.83-7.78 (m, 3H),7.42-7.37 (m, 2H),6.94 (d, 1H), 6.75 (d, 1H), 2.89 (s, 3H), 2.68 (t, 1H), 0.97 (d, 6H). Second eluting diastereomer: MS 480.2 ($M+H^+$).

Example 218

Preparation of Benzo[1,3]dioxole-5-carboxylic acid-{(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-yl carbamoyl)-3-methyl-butyl]-amide

Following the procedure of Example 115, except substituting methanesulphonyl chloride for 4-methoxybenzenesulfonyl chloride and piperonylcarbonyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 468.2 ($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 7.31-7.24 (m, 2H), 6.91 (d, 1H), 6.00 (s, 2H), 2.89 (s, 3H), 2.67 (t, 1H), 0.95 (d, 6H). Second eluting diastereomer: MS 468.2 ($M+H^+$).

Example 219

Preparation of Benzofuran-2-carboxylic acid-[(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-yl carbamoyl)-3-methyl-butyl]-amide

Following the procedure of Example 115, except substituting methanesulphonyl chloride for 4-methoxybenzenesulfonyl chloride and 2-benzofurancarbonyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 464.2 ($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 7.64 (d, 1H), 7.51-7.37 (m, 3H), 7.29-7.28 (m, 1H), 2.89 (s, 3H), 2.67 (t, 1H), 0.97 (d, 6H). Second eluting diastereomer: MS 464.2 ($M+H^+$).

Example 220

Preparation of N-[(S)-1-(1-Methanesulfonyl)-3-oxo-azepan-4-ylcarbamoyl}-3-methyl-butyl}-3,4-dimethoxy-benzamide

Following the procedure of Example 115, except substituting methanesulphonyl chloride for 4-methoxybenzenesulfonyl chloride and 3,4-dimethoxybenzoyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 484.2 ($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 6.94-6.88 (m, 3H), 6.58-6.55 (m, 2H), 3.80 (s, 6H), 2.89 (s, 3H), 0.95 (d, 6H). Second eluting diastereomer: MS 484.2 ($M+H^+$).

Example 221

Preparation of (S)-2-(2-Benzyloxy-acetylamino)-4-methyl-pentanoic acid[1-(2-cyano-benzensulfonyl)-3-oxo-azepan-4-yl]-amide

Following the procedure of Example 115, except substituting 2-cyanophenylsulphonyl chloride for 4-methoxybenzenesulfonyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 555.2 ($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 8.10 (d, 1H), 7.86 (d, 1H), 7.76-7.70 (m, 2H),

7.35-7.31 (m, 5H), 6.93 (d, 2H), 4.61-4.47 (m, 4H), 2.77 (t, 1H), 0.92 (t, 6H). Second eluting diastereomer: MS 555.2 ($M+H^+$).

Example 222

Preparation of N-{(S)-1-[1-(2-Cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl}-3-methyl-butyl}-4-methanesulfonyl-1-benzamide

Following the procedure of Example 115, except substituting 2-cyanophenylsulphonyl chloride for 4-methoxybenzenesulfonyl chloride and 4-methanesulfonylbenzoyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 589.2 ($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 8.10 (d,1H), 7.96 (s, 4H), 7.88 (d, 1H), 7.78-7.71 (m, 2H), 3.05 (s, 3H), 2.79 (t, 1H), 0.97 (t, 6H). Second eluting diastereomer: MS 589.2 ($M+H^+$).

Example 223

Preparation of Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-yl carbamoyl)-3-methyl-butyl]-amide.

Following the procedure of Example 115, except substituting 2-cyanophenylsulphonyl chloride for 4-methoxybenzenesulfonyl chloride and benzo[b]thiophene-2-carbonyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 567.2 ($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 8.10 (d, 1H), 7.86-7.70 (m, 6H), 7.37-7.30 (m, 2H), 2.76 (t, 1H), 0.98 (d, 6H). Second eluting diastereomer: MS 567.2 ($M+H^+$).

Example 224

Preparation of Benzo[1,3]dioxole-5-carboxylic acid-{(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

Following the procedure of Example 115, except substituting 2-cyanophenylsulphonyl chloride for 4-methoxybenzenesulfonyl chloride and piperonyloyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 555.2 ($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 8.11 (d, 1H), 7.87 (d, 1H), 7.76-7.71 (m, 2H), 7.31-7.24 (m, 2H), 6.00 (s, 2H), 2.77 (t, 1H), 0.97 (d, 6H). Second eluting diastereomer: MS 555.4 ($M+H^+$).

Example 225

Preparation of (S)-4-Methyl-2-[4-oxo-4-((4-phenoxy-phenyl)-butyrylamino}-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 75, except substituting 2-pyridylsulfonyl chloride for thiaxole-2-sulfonyl chloride and 4-phenoxyphenyl-carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$) 635.4; ^1H-NMR (400 MHz, $CDCl_3$): • 8.69(d, 1H), 7.99-7.94(m, 4H), 7.53-7.39(m, 3H), 7.23-6.95(m, 7H), 6.20(d, 1H), 5.07(m, 1H), 4.77-4.72(d, 1H), 4.46(m, 1H), 4.13-4.09(m, 1H), 3.85-3.80(d, 1H), 3.33(m, 2H), 2.70-2.64(m, 3H), 2.20-1.40(m, 6H); and the second eluting diastereomer:, 0.96-0.92(m, 6H); and the second eluting diastereomer: MS ($M+H^+$) 635.4.

Example 226

Preparation of N-{(S)-1-[(1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl}-3-methyl-butyl}-3,4-dimethoxy-benzamide

Following the procedure of Example 115, except substituting 2-cyanophenylsulphonyl chloride for 4-methoxybenzenesulfonyl chloride and 3,4-

dimethoxybenzoyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 571.4 ($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 8.10 (d, 1H), 7.87 (d, 1H), 7.76-7.70 (m, 2H), 6.98 (s, 2H), 6.89 (s, 2H), 3.79 (s, 6H), 2.76 (t, 1H), 0.96 (d, 6H). Second eluting diastereomer: MS 571.4 ($M+H^+$).

Example 227

Preparation of Cyclohexanecarboxylic acid {(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl}-3-methyl-butyl}-amide

Following the procedure of Example 115, except substituting cyclohexylcarbonyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 522.4 ($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 7.70 (d, 2H), 6.97 (d, 2H), 2.40 (t, 1H), 1.90-1.20 (m, 16H), 0.92 (d, 6H). Second eluting diastereomer: MS 522.4 ($M+H^+$).

Example 228

Preparation of 4-Methansulfonyl-N-{(S)-1-[4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-carbamoyl]-3-methyl-butyl-benzamide

Following the procedure of Example 115, except substituting 4-methanesulfonylbenzoyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 594.2 ($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 7.96 (s, 4H), 7.69 (d, 2H), 7.25 (d,1H), 6.98 (d,3H), 3.85 (s, 3H), 3.04 (d, 3H), 2.42 (t, 1H), 0.95 (d, 6H). Second eluting diastereomer: MS 594.2 ($M+H^+$).

Example 229

Preparation of 4-Methansulfonyl-N-{(S)-1-[4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-carbamoyl]-3-methyl-butyl-benzamide

Following the procedure of Example 115, except substituting 4-fluorophenylsulphonyl chloride for 4-methoxybenzenesulfonyl chloride and substituting 4-methanesulfonylbenzoyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 582.2 ($M+H^+$). ^1H NMR (500 MHz,$CDCl_3$): δ 7.94 (s, 4H), 7.80-7.77 (m, 2H), 7.25-7.19 (m, 3H), 7.00 (d, 1H), 3.04 (s, 3H), 0.96 (d, 6H). Second eluting diastereomer: MS 582.2 ($M+H^+$).

Example 230

Preparation of ({(S)-3-Methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butylcarbamoyl}-carbamic acid benzyl ester

Following the procedure of Example 75, except substituting 2-pyridylsulfonyl chloride for benzenesulfonyl chloride and N-carbobenzyloxycarbonyl-glycine for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 574.2; ^1H-NMR (400 MHz, $CDCl_3$): • 8.60(d, 1H), 7.97-7.90(m, 2H), 7.50(m, 1H), 7.42-7.25(m, 5H), 6.90(m, 1H), 6.42(m, 1H), 5.38(m, 1H), 5.18-5.10(m, 4H), 4.78-4.72(d, 1H), 4.50(m, 1H), 4.12-4.05(m, 1H), 3.95-3.85(m, 2H), 2.72(m, 1H), 2.25-2.10(m, 2H), 1.90-1.40(m, 5H), 0.92(m, 6H); and the second eluting diastereomer: MS ($M+H^+$) 574.2.

Example 231

Preparation of (S)-2-[5-(4-Methoxy-phenyl)-pentanoylamnio]-4-methyl-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 75, except substituting 2-pyridylsulfonyl chloride for benzenesulfonyl chloride and 5-(4-methoxyphenyl)-pentanoic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 573.4; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.59(d, 1H), 7.97-7.94(m, 2H), 7.53(m, 1H), 7.09-7.07(d, 2H), 6.89-6.81(m, 3H), 5.90(m, 1H), 5.12(m, 1H), 4.79-4.74(d, 1H), 4.48(m, 1H), 4.12(m, 1H), 3.86-3.81(d, 1H), 3.79(s, 3H), 2.69(m, 1H), 2.59-2.57(m, 2H), 2.23-2.10(m, 3H), 1.75-1.45(m, 10H), 0.96-0.95(m, 6H); and the second eluting diastereomer: MS ($M+H^+$) 573.4.

Example 232

Preparation of (S)-2-[2-(3-Benzyloxy-4-methoxy-phenyl)-acetylamnio]-4-methylpentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 75, except substituting 2-pyridylsulfonyl chloride for benzenesulfonyl chloride and (3-benzyloxy-4-methoxy-phenyl)-acetic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 637.4; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.69(d, 1H), 7.98-7.91(m, 2H), 7.53-7.30(m, 6H); and the second eluting diastereomer:, 6.89-6.82(m, 4H), 5.82(m, 1H), 5.14-5.07(m, 3H), 4.78-4.73(d, 1H), 4.43(m, 1H), 4.09(m, 1H), 3.89(s, 3H), 3.82(d, 1H), 3.49(s, 2H), 2.69(m, 1H), 2.14(m, 2H), 1.82-1.40(m, 5H), 0.89(d, 6H); and the second eluting diastereomer: MS ($M+H^+$) 637.4.

Example 233

Preparation of 5,6-Difluoro-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5,6-Difluoro-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(pyridine-2-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 5,6-difluorobenzofuran-2-carboxylic acid for bernzofuran-2-carboxylic acid provided the title compound: MS ($M+H^+$): 564

b.) 5,6-Difluoro-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting the compound of Example 233a provided the title compound. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 562; and the second eluting diastereomer: MS ($M+H^+$) 562.

Example 234

Preparation of (S)-4-Methyl-2-(5-oxo-hexanoylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 115, except substituting 2-pyridinesulphonyl chloride for 4-methoxybenzenesulfonyl chloride and substituting 5-oxo-hexanoyl chloride for benzyloxyacetyl chloride, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer: MS 495.4 ($M+H^+$); Second eluting diastereomer: MS 495.4 ($M+H^+$).

Example 235

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

a.) 6-methyl-pyridine-2-sulphonyl chloride

The title compound was prepared in a similar fashion as that described in Example 85a for the preparation of 2-pyridinesulfonyl chloride-N-oxide.

b.) {(S)-1-[3-Hydroxy-1-(6-methyl-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-3-methyl-butyl}-carbamic acid *tert*-butylester

To a solution of [(S)-1-(3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-carbamic acid *tert*-butyl ester of Example 2g (1.0 g) in dichloromethane (20 mL) was added saturated sodium bicarbonate (50 mL). To this solution was added 6-methyl-pyridine-2-sulphonyl chloride (6.44 mL of a 0.13 g/mL solution in 9M HCl). The reaction was stirred until complete. Workup and column chromatography (5% methanol:dichloromethane) provided the title compound (1.2 g).

c.) (S)-2-Amino-4-methyl-pentanoic acid [3-hydroxy-1-(6-methyl-pyridine-2-sulfonyl)-azepan-4-yl]-amide

To a solution of (S)-2-amino-4-methyl-pentanoic acid [3-hydroxy-1-(6-methyl-pyridine-2-sulfonyl)-azepan-4-yl]-amide of Example 235a (1.2 g) in methanol (20 mL) was added 4M HCl in diopxane (20 mL). The reaction was stirred until complete whereupon it was concentrated to provide the title compound (1 g).

d.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting (S)-2-amino-4-methyl-pentanoic acid [3-hydroxy-1-(6-methyl-pyridine-2-sulfonyl)-azepan-4-yl]-amide of Example 235c the title compound was prepared: MS(EI) 542 (M^+).

e.) Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide of Example 235d the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.6 (m, 3H), 2.7 (m, 1H), 4.1 (m, 1H), 4.7 (m, 2H), 5.3 (m, 1H), 7.4-8.0 (m, 8H); MS(EI); 540 (M^+, 100%).

Example 236

Preparation of 5-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 5-methoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid and (S)-2-amino-4-methyl-pentanoic acid [3-hydroxy-1-(6-methyl-pyridine-2-sulfonyl)-azepan-4-yl]-amide of Example 235c for (S)-2-amino-4-methyl-pentanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide of Example 28b the title compound was prepared: MS(EI) 572 (M^+).

b.) 5-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting 5-methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide of Example 236a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.6 (m, 3H), 2.7 (m, 1H), 3.8 (s, 3H); 4.1 (m, 1H), 4.7 (m, 2H), 5.3 (m, 1H), 7.4-8.0, (m, 7H); MS(EI): 570 (M^+, 100%).

Example 237

Preparation of 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

a.) 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 236a except substituting 3-methylbenzofuran-2-carboxylic acid for 5-methoxybenzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 556 (M^+).

b.) 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting 3-methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide of Example 237a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.6 (m, 3H), 2.7 (m, 1H), 3.8 (s, 1H); 4.1 (m, 1H), 4.7 (m, 2H), 5.3 (m, 1H), 7.4-8.0 (m, 6H); MS(EI): 564 (M^+, 100%).

Example 238

Preparation of 7-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

a.) 7-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 7-methoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 559 ($M+H^+$).

b.) 7-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting 7-methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-

ylcarbamoyl]-butyl}amide of Example 238a the title compound was prepared: MS(EI) 557 ($M+H^+$).

Example 239

Preparation of 5,6-Dimethoxy-benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5,6-Dimethoxy-benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 28b except substituting 5,6-dimethoxy-benzo[b]thiophene-2-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 604 (M^+).

b.) 5,6-Dimethoxy-benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting 5,6-dimethoxy-benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide of Example 239a the title compound was prepared: MS(EI) 602.9 ($M+H^+$).

Example 240

Preparation of (R)-1-Benzyl-5-oxo-pyrrolidine-2-carboxylic acid {(S)-3-methyl-1-{3-oxo-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 75, except substituting 2-pyridylsulfonyl chloride for thiazole-2-sulfonyl chloride and (R)-1-benzyl-5-oxo-pyrrolidine-2-carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 584.4; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.69(d, 1H), 7.99-7.92(m, 2H), 7.52(m, 1H), 7.32-7.22(m, 5H), 6.92(d, 1H), 6.38(d, 1H), 5.15-5.08(m, 2H), 4.80-4.75(d, 1H), 4.47-4.44(m, 1H), 4.14-4.10(m, 1H), 3.89-3.80(m, 3H), 2.75-2.63(m, 2H), 2.46-1.44(m, 10H), 0.95(d, 6H); and the second eluting diastereomer: MS ($M+H^+$) 584.4.

Example 241

Preparation of (S)-1-Benzyl-5-oxo-pyrrolidine-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 75, except substituting 2-pyridylsulfonyl chloride for benzenesulfonyl chloride and (S)-1-benzyl-5-oxo-pyrrolidine-2-carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 584.4; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.69(d, 1H), 7.98-7.92(m, 2H), 7.52(m, 1H), 7.32-7.22(m, 5H), 6.92(d, 1H), 6.38(d, 1H), 5.22-5.18(d, 1H), 5.10(m, 1H), 4.80-4.75(d, 1H), 4.51(m, 1H), 4.12-4.08 (m, 1H), 3.91-3.79(m, 3H), 2.71-1.38(m, 12H), 0.97(d, 6H); and the second eluting diastereomer: MS ($M+H^+$): 584.4.

Example 242

Preparation of Benzofuran-2-carboxylic acid {(S)-2-cyclopropyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-ethyl]-amide

Following the procedure of Example 193e-h except substituting N-Boc-cyclopropylalanine for step 193e, the title compound was purified to yield two diastereomers as solids (first eluting: 8 mg, second eluting: 8 mg): MS(ESI): 525 $(M+H)^+$.

Example 243

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methylsulfanyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-propyl]-amide

Following the procedures of Examples 193e-g except substituted N-Boc-L-methionine in step 193e. The oxidation of Example 193g was performed by adding sulfur trioxide-pyridine complex (34mg, 0.211 mmol) and triethylamine (0.077 ml) to the alcohol intermediate in DMSO solvent (0.200 ml). After stirring at room temperature for two hours, the mixture was diluted with water and extracted with ethyl acetate. The organic

layer was dried, filtered, concentrated, and purified by HPLC to yield two diastereomers of the title compound as solids (first eluting: 8mg, second eluting: 5 mg). MS(ESI): 545 $(M+H)^+$.

Example 244

Preparation of Benzofuran-2-carboxylic acid {(S)-2-naphthylen-2-yl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-ethyl]-amide

Following the procedure of Example 193e-h except substituting except substituting N-(t-butoxycarbonyl)-3-(2-naphthyl)-L-alanine, the title compound was purified to yield two diastereomers as solids (first eluting: 5.3 mg, second eluting: 3.3 mg): MS(ESI): 610.8 $(M+H)^+$.

Example 245

Preparation of Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

a.) Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 236a except substituting thieno[3,2-b]thiophene-2-carboxylic acid for 5-methoxybenzofuran-2-carboxylic acid the title compound was prepared: MS(EI) 564 (M^+).

b.) Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide of Example 245a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.6 (m, 3H) 2.7 (m, 1H), 3.8 (s, 1H); 4.1 (m, 1H), 4.7 (m, 2H), 5.3 (m, 1H), 7.4-8.0 (m, 6H); MS(EI): 562 (M^+, 100%).

Example 246

Preparation of Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

a.) (S)-2-Amino-4-methyl-pentanoic acid [3-hydroxy-1-(3-methyl-pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Examples 235b-c except substituting 3-methyl-pyridine-2-sulfonyl chloride for 6-methyl-pyridine-2-sulfonyl chloride the title compound was prepared: MS(EI) 399 (M^+).

b.) Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide

To a solution of (S)-2-amino-4-methyl-pentanoic acid [3-hydroxy-1-(3-methyl-pyridine-2-sulfonyl)-azepan-4-yl]-amide of Example 246a (0.25 g) in dichloromethane was added thieno[3,2-b]thiophene (0.10 g), triethylamine (0.12 mL), HOBt (0.085 g) and EDC (0.12 g). The reaction was stirred until complete. Workup and column chromatography (5% methanol: dichloromethane) provided the title compound (0.18 g): MS(EI) 564 (M^+).

c.) Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide of Example 245a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.6 (m, 3H) 3.0 (m, 1H), 3.8 (s, 3H); 4.1 (m, 2H), 4.7 (m, 2H), 5.3 (m, 1H), 7.4-8.0 (m, 5H), 8.4 (m, 1H); MS(EI): 562 (M^+, 100%).

Example 247

Preparation of 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

a.) 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 246c except substituting 3-methylbenzofuran-2-carboxylic acid for thieno[3,2-b]thiophene the title compound was prepared: MS(EI) 556 (M^+).

b.) 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting 3-methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide of Example 247a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.6 (d, 3H), 2.6 (m, 3H), 3.0 (m, 1H), 4.1 (m, 2H), 4.7 (m, 2H), 5.3 (m, 1H), 7.4-8.0 (m, 6H), 8.4 (m, 1H); MS(EI): 554 (M^+, 100%).

Example 248

Preparation of 5-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 246c except substituting 5-methoxybenzofuran-2-carboxylic acid for thieno[3,2-b]thiophene the title compound was prepared: MS(EI) 572 (M^+).

b.) 5-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i except substituting 5-methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-hydroxy-azepan-4-

ylcarbamoyl]-butyl}amide of Example 247a the title compound was prepared: ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 6H), 1.5-2.2 (m, 6H), 2.6 (d, 3H), 3.0 (m, 1H), 3.8 (s, 3H); 4.1 (m, 2H), 4.7 (m, 2H), 5.3 (m, 1H), 7.4-8.0 (m, 6H), 8.4 (m, 1H); MS(EI): 570 (M^+, 100%).

Example 249

Preparation of 5,6-Difluoro-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

a.) 5,6-Difluoro-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 85c exept substituting 5,6-difluorobenzofuran-2-carboxylic acid for benzo[b]thiophene-2-carboxylic acid the title compound was prepared: MS(ESI) 580.9 ($M+H^+$).

b.) 5,6-Difluoro-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 1i exept substituting the compound of Example 249a the title compound was prepared: MS(ESI) 578.87 ($M+H^+$).

Example 250

Preparation of 5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid{(S)-2-cyclohexyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide

a.) 4-((S)-2-*tert*-Butoxycarbonylamino-3-cyclohexyl-proprionylamino)-3-hydroxy-azepane-1-carboxylic acid benzyl ester

To a solution of the compound of Example 2e (3.2 g, 12.2 mmol) in DMF (35 mL) was added N-Boc-cyclohexylalanine (3.3 g), HOBt (1.8 g) and EDC (2.56 g). The reaction was stirred until complete. Workup and column chromatography of the residue (65% hexanes:ethyl acetate) provided 5.5 g of the title compound.

b.) [(S)-Cyclohexyl-1-(3-hydroxy-azepan-4-ylcarbamoyl)-ethyl]-carbamic acid *tert*-butyl ester

To a solution of the compound of Example 250a (5.5 g) in etyhl acetate:methanol (185 mL:40 mL) was added 10% Pd/C. This mixture was stirred under an atmosphere of hydrogen until complete consumption of the starting material was observed. The reaction was filtered and concentrated to provide 3.75 g of the title compound.

c.) {(S)-2-Cyclohexyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-carbamic acid *tert*-butyl ester

To a solution of the compound of Example 250 b (1.0 g, 1.91 mmol) in dichloromethane (5 mL) was added water (10 mL) and sodium bicarbonate (1 g). To this mixture was added 2-pryidinesulfonyl chloride (0.55 g in 5 mL dichloromethane) dropwise. The mixture was stirred for 20 minutes whereupon the organic layer was separated and washed with water, brine, dried filtered and concentrated. Column chromatography (2% methanol:dichloromethane) of the residue provided 1.0 g of the title compound: MS (ESI) 525 ($M+H^+$).

d.) (S)-2-Amino-3-cyclohexyl-N-[3-hydroxy-(pyridine-2-sulfonyl)-azepan-4-yl]-proprionamide

To a solution of the compound of Example 250c (1.0 g) in methanol (10 mL) was added HCl (10 mL of 4M HCl in dioxane). The reaction was stirred until complete consumption of the starting material whereupon it was concentrated. The residue was azeotroped with toluene then washed with ether to provide 0.95 g of the title compound.

e.) 5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid{(S)-2-cyclohexyl-1-{3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide

To a solution of the compound of Example 250d (0.20 g, 0.4 mmol) in DMF (0.5 mL) was added diisopropylethylamine (0.16 mL), HOBt (0.06 g), EDC (0.084 g) and 5-[3-(trifluoromethyl)phenyl]-2-furoic acid (0.11 g).). The reaction was stirred until complete consumption of the starting material. Workup and column chromatography 4% methanol:dichloromethane) provided 0.23 g of the title compound.

f.) 5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid{(S)-2-cyclohexyl-1-{3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide

Following the procedure of Example 75d except substituting the compound of Example 250e the title compound was prepared. Separation of the diastereomers by HPLC provided the first eluting disatereomer (52 mg): MS (ESI) 661.4 and the second eluting diastereomer (45.8 mg): MS (ESI) 661.6.

Example 251

Preparation of 5-(4-Chloro-phenyl)-furan-2-carboxylic acid{(S)-2-cyclohexyl-1-{3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide

Following the procedures of Example 250e-f except substituting 5-(4-chlorophenyl)-2-furoic acid for 5-[3-(trifluoromethyl)phenyl]-2-furoic acid of Example 252e the title compound was prepared. Separation of the diastereomers by HPLC provided the first eluting diastereomer (57 mg): MS (ESI) 627.4 and the second eluting diastereomer (53 mg): MS (ESI) 627.4.

Example 252

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[6-methyl-3-oxo-1-(pyridine-sulphonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedure of Example 92, except substituting, 2-methyl-4-pentenal for 2,2-dimethyl-4-pentenal the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 541.2; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.71-8.66(m, 1H), 7.98-7.93(m, 2H), 7.91(d, 1H), 7.67-7.29(m, 5H), 7.15-6.92(m, 2H), 5.28-5.20(m, 1H), 4.82-4.47(m, 2H), 3.97-3.78(m, 1H), 3.65-2.98(m, 1H), 2.37-2.34(m, 1H), 2.20-1.55(m, 3H), 1.22-1.19(m, 3H), 1.00-0.86(m, 9H).

Example 253

Preparation of 5-(4-Chloro-phenyl)-furan-2-carboxylic acid{(S)-2-cyclohexyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide

Following the procedures of Example 250c-f except substituting 2-pyridinesulfonyl chloride N-oxide for 2-pyridinesulfonyl chloride of Example 250c and substituting 5-(4-chlorophenyl)-2-furoic acid for 5-[3-(trifluoromethyl)phenyl]-2-furoic acid of Example 252e the title compound was prepared. Separation of the diastereomers by HPLC provided the first eluting diastereomer: MS (ESI) 643.4 and the second eluting diastereomer: MS (ESI) 643.2.

Example 254

Preparation of 5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid{(S)-2-cyclohexyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide

Following the procedures of Example 250c-f except substituting 2-pyridinesulfonyl chloride N-oxide for 2-pyridinesulfonyl chloride of Example 250c the title compound was prepared. Separation of the diastereomers by HPLC provided the first eluting diastereomer: MS (ESI) 677.2 and the second eluting diastereomer: MS (ESI) 677.4.

Example 255

Preparation of 5-Fluoro-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

a.) 5-Fluoro-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedure of Example 28b except substituting 5-fluorobenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared: MS (ESI) 547 ($M+H^+$).

b.) 5-Fluoro-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedure of Example 1i except substituting the compound of Example 255a the title compound was prepared: MS(ESI) 544.9 ($M+H^+$).

Example 256

Preparation of 5,6-Dimethoxybenzofuran-2-carboxylic acid{(S)-2-cyclohexyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide

Following the procedures of Example 250c-f except substituting 2-pyridinesulfonyl chloride N-oxide for 2-pyridinesulfonyl chloride of Example 250c and substituting 5,6-dimethoxybenzofuran-2-carboxylic acid for 5-[3-(trifluoromethyl)phenyl]-2-furoic acid of Example 252e the title compound was prepared. Separation of the diastereomers by HPLC provided the first eluting diastereomer: MS (ESI) 643.4 and the second eluting diastereomer: MS (ESI) 643.2.

Example 257

Preparation of 5,5-Bis-(4-methoxy-phenyl)-pent-4-enoic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]}-butyl}-amide

Following the procedure of Example 75 except substituting 2-pyridylsulfonyl chloride for thiazole-2-sulfonyl chloride and 5,5-bis-(4-methoxy-phenyl)-pent-4-enoic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$) 677.4; ^{1}H-NMR (400 MHz, $CDCl_3$): • 8.69(d, 1H), 7.98-7.92(m, 2H), 7.53-7.50(m, 1H), 7.27-6.77(m, 10H), 6.00-5.87(m, 2H), 5.08(m, 1H), 4.76-4.72(d, 1H), 4.48(m, 1H), 4.08(m, 1H), 3.83(s, 3H), 3.78(s, 3H), 2.70-1.35(m, 12H), 0.91(d, 6H); and the second eluting diastereomer: MS ($M+H^+$) 677.4.

Example 258

Preparation of Quinoline-8-carboxylic acid {(S)-2-naphthylen-2-yl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-ethyl]-amide

a.) 4-Amino-1-(pyridine-2-sulfonyl)-azepan-3-ol

To a solution of the compound of Example 193c (1.5 g) in methanol (10 mL) was added HCl (10 mL of 4M HCl in dioxane). The reaction was stirred until complete by TLC analysis whereupon it was concentrated to provide 1.2 g of the title compound as a white solid.

b.) {(S)-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-2-napthylene-2-yl-ethyl}-carbamic acid *tert*-butyl ester

To a solution of the compound of Example 258a (225 mg) in dichloromethane was added TEA (0.15 mL), HOBt (99 mg), EDC (140 mg) and N-Boc-L-2-naphthylalanine (230 mg). The reaction was stirred until complete. Workup and column chromatography of the residue (3% methanol:dichloromethane) provided 0.35g of the title compound: MS(ESI) 569 ($M+H^+$).

c.) (S)-2-Amino-N-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-3-naphthylen-2-yl-proprionamide

To a solution of the compound of Example 258b (0.35 g) in methanol (5 mL) was added HCl (5 mL of 4M HCl in dioxane). The reaction was stirred until complete by TLC analysis whereupon it was concentrated to provide 0.31 g of the title compound as a white solid.

d.) Quinoline-8-carboxylic acid {(S)-2-naphthylen-2-yl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-ethyl]-amide

To a solution of the compound of Example 258c (131 mg) in dichloromethane was added TEA, HOBt (39 mg), EDC (55 mg) and quinoline-8-carboxylic acid (51 mg). The reaction was stirred until complete. Workup and column chromatography of the residue (5% methanol:dichloromethane) provided 0.35g of the title compound: MS(ESI) 574 ($M+H^+$).

e.) Quinoline-8-carboxylic acid {(S)-2-naphthylen-2-yl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-ethyl]-amide

Following the procedure of Example 1i except substituting the compound of Example 258d the title compound was prepared.

Example 259

Preparation of Naphthylene-1-carboxylic acid {(S)-2-naphthylen-2-yl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-ethyl]-amide

Following the procedures of Examples 258d-e except substituting 1-naphthoic acid for quinoline-8-carboxylic acid the title compound was prepared.

Example 260

Preparation of Quinoline-8-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-2-phenyl-ethyl}-amide

Following the procedures of Examples 258a-e except substituting N-Boc-phenylalanine for N-Boc-L-2-naphthylalanine the title compound was prepared.

Example 261

Preparation of Naphthyridine-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedure of Example 28b-c exept subsituting 1,6-naphthyridine-2-carboxylic acid for benzofuran-2-carboxylic acid the title compound was prepared.

Example 262

Preparation of Naphthylene-1-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-2-phenyl-ethyl}-amide

Following the procedure of Example 260 except substituting 1-naphthoic acid for quinoline-8-carboxylic acid the title compound was prepared.

Example 263

Preparation of 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(cyclohexyl-proprionyl)-azepan-4-ylcarbamoyl]-butyl}-amide

a.) 4-{(S)-2-[(3-Methylbenzofuran-2-carbonyl)-amino]-4-methyl-pentanoylamino}-3-hydroxy-azepane-1-carboxylic acid benzyl ester

To a solution of the compound of Example 72a (1.2 g, 2.67 mmol) was added EDC (0.56 g), HOBt (0.36 g), TEA (0.67 g) and 3-methylbenzofuran-2-carboxylic acid (0.47 g). The reaction was stirred until complete consumption of the starting material was observed. Workup and colum chromatography (4:1 hexanes:ethyl acetate) provided 1.05 g of the title compound: MS (ESI) 536 ($M+H^+$).

b.) 3-Methylbenzofuran-2-carboxylic acid [(S)-1-(3-hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide

Following the procedure of Example 2g except substituting the compound of Example 263a the title compound was prepared: MS (ESI) 402 ($M+H^+$).

c.) 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(cyclohexyl-proprionyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedure of Example 263a except substituting the compound of Example 263b and 3-cyclohexylpropionic acid for 3-methylbenzofuran-2-carboxylic acid the title compound was prepared: MS (ESI) 540 ($M+H^+$).

d.) 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(cyclohexyl-propriony1)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedure of Example 1i except substituting the compound of Example 263c the title compound was prepared: MS (ESI) 538 ($M+H^+$).

Example 264

Preparation of 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(4-methyl-pentanoyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedures of Example 263c-d except substituting 4-methylpentanoic acid for 3-cyclohexylpropionic acid the title compound was prepared: MS (ESI) 498 ($M+H^+$).

Example 265

Preparation of 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-carbonyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedures of Example 263c-d except substituting picolinic acid N-oxide for 3-cyclohexylpropionic acid the title compound was prepared: MS (ESI) 498 ($M+H^+$).

Example 266

Preparation of (S)-Acetylamino-4-methyl-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

Following the procedure of Example 75c-d except substituting acetic acid for benzofuran-2-carboxylic acid in step 75c provided the title compound which was separated by HPLC to give the first eluting diastereoemer: MS ($M+H^+$) 425.2; ^{1}H-NMR (400Hz, $CDCl_3$): • 8.69(d, 1H), 7.96-7.94(m, 2H), 7.53-7.52(m, 1H), 7.05(m, 1H), 5.92(m, 1H), 5.08(m, 1H), 4.69-4.53(m, 2H), 4.05-3.90(m, 2H), 2.80(m, 1H), 2.25-2.12(m, 2H), 1.64(s,

3H), 1.90-1.40(m, 5H), 0.95(m, 6H); and the second eluting distereomer: MS ($M+H^+$): 425.2

Example 267

Preparation of Quinoline-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-pentyl}-amide

a.) 4-((S)-2-*tert*-Butoxycarbonylamino-hexanoylamino)-3-hydroxy-azepane-1-carboxylic acid benzyl ester

To a stirring solution of compound of the amino alcohol of Example 2e (200 mg, 0.74mmol) in DMF (4 ml) was added N-Boc-norleucine (175 mg, 0.76mmol), EDC-HCl (145 mg, 0.76mmol), and 1-hydroxybenzotriazole (21 mg, 0.16mmol). Reaction allowed to proceed overnight at room temperature. The following morning the mixture was diluted with ethyl acetate, washed with sat. $NaHCO_3$, H_2O, and brine. Dried on $MgSO_4$, filtered and purified by column chromatography to give 300 mg of the title compound: MS(ESI) 478.11 $(M+H)^+$.

b.) [(S)-1-(3-Hydroxy-azepan-4-ylcarbamoyl)-pentyl]-carbamic acid *tert*-butyl ester

To a solution of compound of Example 267a (300 mg, 0.6 3mmol) in ethyl acetate (5 ml) was added 10% palladium on carbon (160 mg) and H_2 from a filled balloon. After stirring the solution at room temperature for 48 hours, the mixture was filtered through celite. The filterate was concentrated to yield the title compound (crude, 161mg, 0.47mmol): MS(ESI): 344.19 $(M+H)^+$.

c.) {(S)-1-[3-Hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-pentyl}-carbamic acid *tert*-butyl ester

To a solution of the compound of Example 267b (161 mg,0.47 mmol) in dichloromethane (6 ml) was added triethylamine (0.065 ml, 0.47mmol) and pyridine-2-sulfonyl chloride (83mg, 0.47 mmol). After stirring at room temperature for 1 hr the mixture was washed with saturated $NaHCO_3$. The organic layer was dried, filtered, concentrated and purified on a silica gel column to give the title compound (142mg, 0.29mmol): MS(ESI): 485.10 $(M+H)^+$.

d.) (S)-2-Amino-hexanoic acid {3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide

To a stirring solution of the compound of Example 267c (142mg, 0.29mmol) in ethyl acetate was added HCl (4M in dioxane) (0.760 ml, 3.0 mmol). After stirring the reaction mixture for 1 hr at room temperature, the mixture was concentrated to yield a white solid. The solid was azeotroped with toluene twice on rotavap and then treated with a resin bound carbonate (1.47 mmol) in methanol and placed on a shaker. After 4 hr the suspension was filtered and concentrated to yield 104 mg crude product: MS (ESI) 385.08 $(M+H)^+$.

e.) Quinoline-2-carboxylic acid {(S)-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-pentyl}-amide

To a solution of the compound of Example 267d (104 mg, 0.27mmol) in CH_2Cl_2 was added quinaldic acid (47mg, 0.27 mmol), 1-hydroxybenzotriazole (7.4, .055 mmol), EDC-HCL (52 mg, 0.27 mmol) in DMF (2 ml). After stirring at room temperature overnight, the mixture was diluted with ethylacetate, washed with sat. $NaHCO_3$, H_2O, dried on $MgSO_4$, and filtered to obtain 172mg crude product: MS(ESI) 539.90 $(M+H)^+$.

f.) Quinoline-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-pentyl}-amide

To a stirring solution of the compound of Example 267e (172mg crude. 0.32mmol) in 1 ml DMSO was added sulfur trioxide-pyridine complex (260mg, 1.6 mmol)) and triethylamine (0.88 ml, 3.2mmol). After stirring at room temperature for two hours, the mixture was diluted with water and extracted with ethyl acetate. The organic layer was dried, filtered, concentrated, and purified by HPLC to yield two diastereomers of the title compound as solids (first: 40 mg: second:43mg): MS(ESI) 537.86 $(M+H)^+$.

Example 268

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(cyclohexyl-proprionyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedures of Example 263a-d except substituting benzofuran-2-carboxylic acid for 3-methylbenzofuran-2-carboxylic acid of Example 263a the title compound was prepared: MS(ESI) 524 ($M+H^+$).

Example 269

Preparation of Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(4-methyl-pentanoyl)-azepan-4-ylcarbamoyl]-butyl}-amide

Following the procedures of Example 263a-d except substituting benzofuran-2-carboxylic acid for 3-methylbenzofuran-2-carboxylic acid of Example 263a and 5-methyl pentanoic aicd for cyclohexyl propionic acid the title compound was prepared: MS(ESI) 484 ($M+H^+$).

Example 270

Preparation of Quinoline-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-2-phenyl-ethyl}-amide

Following the procedure of Example 267a-f except substituting N-Boc-phenylalanine for N-Boc-norleucine in step 267a the title compound was prepared. Separation of the mixture by HPLC provided two diastereomers as solids (first eluting: 20.5 mg; second eluting: 27 mg): MS(ESI) 571.95 $(M+H)^+$.

Example 271

Preparation of Benzofuran-2-carboxylic acid{(S)-2-benzyloxy-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepane-4-ylcarbamoyl]-ethyl}-amide

Following the procedure of Example 193e-h, except substituting N-Boc-O-benzyl-L-serine in step 193e the title compound was prepared as a mixture of distereoemers. To a solution of benzofuran-2-carboxylic acid {(S)-2-benzyloxy-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepane-4-ylcarbamoyl]-ethyl}-amide (90 mg) in ethyl acetate (2 mL) was added 10% Pd/C (50 mg). Upon hydrogenolysis of approximately 50% of the starting benzyl ether the reaction was filtered and concentrated. Purification of this 4 component mixture by HPLC provided the first eluting diastereomer of the title compound (1 mg) and the second eluting diastereomer of the title compound (0.3 mg): MS(ESI): 590.94$(M+H)^+$. Additionally the two individual diastereoemers of benzofuran-2-carboxylic acid{(S)-2-hydroxy-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepane-4-ylcarbamoyl]-ethyl}-amide were also isolated as described below in Example 272.

Example 272

Preparation of Benzofuran-2-carboxylic acid {(S)-2-hydroxy-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepane-4-ylcarbamoyl]-ethyl}-amide

The title compound was obtained as discussed above in Example 271. Purification of the mixture by HPLC provided the two diastereomers in solid form (first eluting: 1.6 mg; second eluting 2.1 mg): MS(ESI): 500.9 $(M+H)^+$.

Example 273

Preparation of 5-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 75c-d except substituting 5-methoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid in step 75c provided the title compound which was separated by HPLC to give the first eluting

diastereoemer as a white solid (144.3 mg, 85.1%): MS (ESI) 563.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (16.9mg, 10.0%) MS (ESI): 563.0 $(M+H)^+$

Example 274

Preparation of 7-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 75c-d except substituting 7-methoxybenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid in step 75c provided the title compound which was separated by HPLC to give the first eluting diastereoemer as a white solid (75 mg, 47%): MS (ESI) 563.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (57 mg, 35%): MS (ESI) 563.0 $(M+H)^+$

Example 275

Preparation of 3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 75c-d except substituting 3-methylbenzofuran-2-carboxylic acid for benzofuran-2-carboxylic acid in step 75c provided the title compound which was separated by HPLC to give the first eluting diastereoemer as a white solid (69.5 mg, 42%): MS (ESI) 547.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (65 mg, 40%): MS (ESI) 547.2 $(M+H)^+$

Example 276

Preparation of Benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 75c-d except substituting benzo[b]thiophene-2-carboxylic acid for benzofuran-2-carboxylic acid in step 75c provided the title compound which was separated by HPLC to give the first eluting diastereoemer as a white solid (79.5

mg, 48%): MS (ESI) 549.3 $(M+H)^+$ and the second eluting diastereomer as a white solid (50.5 mg, 31%): MS (ESI) 549.2 $(M+H)^+$

Example 277

Preparation of 1-Methyl-1H-indole-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 75c-d except substituting 1-methylindole-2-carboxylic acid for benzofuran-2-carboxylic acid in step 75c provided the title compound which was separated by HPLC to give the first eluting diastereoemer as a white solid (75 mg, 47%): MS (ESI) 563.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (57 mg, 35%): MS (ESI) 563.0 $(M+H)^+$

Example 278

Preparation of Quinoxaline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide

Following the procedure of Example 75c-d except substituting quinoxaline-2-carboxylic acid for benzofuran-2-carboxylic acid in step 75c provided the title compound which was separated by HPLC to give the first eluting diastereoemer as a white solid (126 mg, 77%): MS (ESI) 545.2 $(M+H)^+$ and the second eluting diastereomer as a white solid (25 mg, 15%): MS (ESI) 545.2 $(M+H)^+$

Example 279

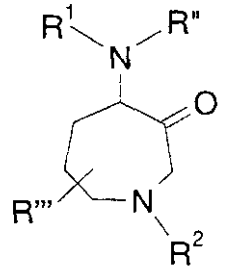
Preparation of Quinoline-2-carboxylic acid {[(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide

Following the procedure of Example 75, except substituting 4-fluorophenylsulfonyl chloride for benzenesulfonyl chloride and 2-quinoline carboxylic acid for benzofuran-2-carboxylic acid, the title compound was prepared. The residue was purified by HPLC. First eluting diastereomer; MS ($M+H^+$): 555.2; ^{1}H-NMR (400Hz, $CDCl_3$): • 8.62(d, 1H), 8.34-8.23(q, 2H) 8.19-8.17(d, 1H), 7.90-7.88(d, 1H), 7.88-7.80(m, 3H), 7.66-7.64(t, 1H), 7.25-7.07(m, 3H), 5.08(m, 1H), 4.72 (m, 1H), 4.58-4.53(d, 1H),4.00(m, 1H), 3.46-3.42(d, 1H), 2.47(m, 1H), 2.27-2.12(m, 2H), 1.90-1.40(m, 5H), 1.03-1.01(m, 6H); and the second eluting diastereomer: MS ($M+H^+$): 555.4.

The above specification and Examples fully disclose how to make and use the compounds of the present invention. However, the present invention is not limited to the particular embodiments described hereinabove, but includes all modifications thereof within the scope of the following claims. The various references to journals, patents and other publications which are cited herein comprise the state of the art and are incorporated herein by reference as though fully set forth.

We claim:

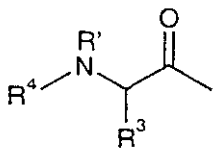
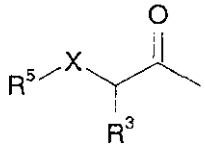
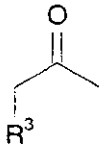
1. A compound of Formula I:

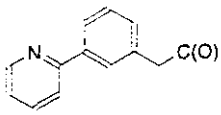
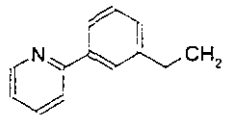
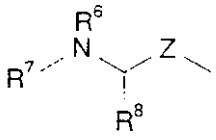


I

wherein:

R^1 is selected from the group consisting of:


; 
and 
;

R^2 is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $R^9C(O)$-, $R^9C(S)$-, R^9SO_2-, $R^9OC(O)$-, $R^9R^{11}NC(O)$-, $R^9R^{11}NC(S)$-, $R^9(R^{11})NSO_2$-  ,  and 
;

R^3 is selected from the group consisting of: H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, HetC_{0-6}alkyl and ArC_{0-6}alkyl;

R^3 and R' may be connected to form a pyrrolidine, piperidine or morpholine ring;

R^4 is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $R^5C(O)$-, $R^5C(S)$-, R^5SO_2-, $R^5OC(O)$-, $R^5R^{13}NC(O)$-, and $R^5R^{13}NC(S)$-;

R^5 is selected from the group consisting of: H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl;

R^6 is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, or Het-C_{0-6}alkyl;

R^7 is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $R^{10}C(O)$-, $R^{10}C(S)$-, $R^{10}SO_2$-, $R^{10}OC(O)$-, $R^{10}R^{14}NC(O)$-, and $R^{10}R^{14}NC(S)$-;

R^8 is selected from the group consisting of: H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, HetC_{0-6}alkyl and ArC_{0-6}alkyl;

R^9 is selected from the group consisting of: C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl;

R^{10} is selected from the group consisting of: C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl;

R^{11} is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R^{12} is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R^{13} is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R^{14} is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R' is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

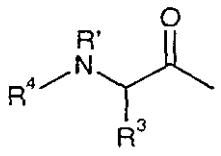
R" is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, or Het-C_{0-6}alkyl;

R'" is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

X is selected from the group consisting of: CH_2, S, and O; and

Z is selected from the group consisting of: C(O) and CH_2;

and pharmaceutically acceptable salts, hydrates and solvates thereof.

2. A compound according to Claim 1 wherein R^1 is  .

3. A compound according to Claim 1 wherein R^3 is selected from the group consisting of:

H, methyl, ethyl, n-propyl, prop-2-yl, n-butyl, isobutyl, but-2-yl, cyclopropylmethyl, cyclohexylmethyl, 2-methanesulfinyl-ethyl, 1-hydroxyethyl, toluyl, naphthalen-2-ylmethyl, benzyloxymethyl, and hydroxymethyl.

4. A compound according to Claim 3 wherein R^3 is selected from the group consisting of: toluyl, isobutyl and cyclohexylmethyl.

5. A compound according to Claim 4 wherein R^3 is isobutyl.

6. A compound according to Claim 1 wherein R^4 is selected from the group consisting of: $R^5OC(O)$-,$R^5C(O)$- or R^5SO_2-.

7. A compound according to Claim 6 wherein R^4 is $R^5C(O)$-.

8. A compound according to Claim 7 wherein R^5 is selected from the group consisting of: C_{1-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl.

9. A compound according to Claim 8 wherein R^5 is selected from the group consisting of:

methyl, halogenated methyl, alkoxy substituted methyl, heterocycle substituted methyl;

butyl, aryl substituted butyl;

isopentyl;

cyclohexyl;

butenyl, aryl substituted butenyl;

acetyl;

phenyl, phenyl substituted with one or more halogens, phenyl substituted with one or more alkoxy groups, phenyl substituted with one or more sulfonyl groups;

benzyl;

naphthylenyl;

benzo[1,3]dioxolyl;

furanyl, halogen substituted furanyl, aryl substituted furanyl;

tetrahydrofuran-2-yl;

benzofuranyl, alkoxy substituted benzofuranyl, halogen substituted benzofuranyl, alkyl substituted benzofuranyl;

benzo[*b*]thiophenyl, alkoxy substituted benzo[*b*]thiophenyl;

quinolinyl;

quinoxalinyl;

1,8 naphthyridinyl;

indolyl, alkyl substituted indolyl;

pyridinyl, alkyl substituted pyridinyl, 1-oxy-pyridinyl;

thiophenyl, alkyl substituted thiophenyl, halogen substituted thiophenyl;

thieno[3,2-*b*]thiophenyl;

isoxazolyl, alkyl substituted isoxazolyl; and

oxazolyl.

10. A compound according to Claim 8 wherein R^5 is selected from the group consisting of:

pentanonyl;

naphthylen-2-yl;

benzo[1,3]dioxol-5-yl,

furan-2-yl;

benzofuran-2-yl;

benzo[*b*]thiophen-2-yl;

quinolin-2-yl, quinolin-3-yl, quinolin-4-yl, quinolin-6-yl, and quinolin-8-yl;

quinoxalin-2-yl;

1,8 naphthyridin-2-yl;

indol-3-yl, indol-5-yl;

pyridin-2-yl , pyridin-5-yl,

thiophen-3-yl;

thieno[3,2-*b*]thiophene-2-yl;

isoxazol-4-yl; and

oxazol-4-yl.

11. A compound according to Claim 8 wherein R^5 is selected from the group consisting of:

trifluoromethyl, phenoxy-methyl, 4-fluoro-phenoxy-methyl, 2-thiophenyl-methyl;

4-(4-methoxy)phenyl-butyl;

4-pentanonyl;

4,4-bis(4-methoxyphenyl)-but-3-enyl;

3,4-dichlorophenyl, 4-fluorophenyl, 3,4-dimethoxy-phenyl, 3-benzyloxy-4-methoxy-phenyl, 4-methanesulfonyl-phenyl;

5-nitro-furan-2-yl, 5-(4-nitrophenyl)-furan-2-yl, 5-(3-triflouromethyl-phenyl)-furan-2-yl, 5-bromo-furan-2-yl, 5-(4-chloro-phenyl)-furan-2-yl;

5-(2-piperazin-4-carboxylic acid *tert*-butyl ester- ethoxy) benzofuran-2-yl, 5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-yl, 5-(2-piperazin-1-yl-ethoxy)benzofuran-2-yl, 5-(2-cyclohexyl-ethoxy)-benzofuran-2-yl, 7-methoxy-benzofuran-2-yl, 5-methoxy-benzofura-2-yl, 5,6-dimethoxy-benzofuran-2-yl, 5-fluoro-benzofuran-2-yl, 5,6-difluoro-benzofuran-2-yl, 3-methyl-benzofuran-2-yl;

5,6-dimethoxy- benzo[*b*]thiophen-2-yl;

N-methyl-indol-2-yl;

1-oxy-pyridin-2-yl, 2-methyl-pyridin-5-yl;

5-methyl-thiophen-2-yl, 4,5-dibromo-thiophen-2-yl;

5-*tert*-butyl-3-methyl thieno[3,2-*b*]thiophen-2-yl;

3,5-dimethyl- isoxazol-4-yl; and

5-methyl-2-phenyl oxazol-4-yl, and 2-phenyl-5-trifluoromethyl-oxazol-4-yl.

12. A compound according to Claim 8 wherein R^5 is selected from the group consisting of: 3-methyl-benzofuran-2-yl, thieno[3,2-b]thiophen-2-yl, 5-methoxybenzofuran-2-yl, quinoxalin-2-yl, and quinolin-2-yl.

13. A compound according to Claim 1 wherein R' is selected from the group consisting of H and naphthalen-2-yl-methyl.

14. A compound according to Claim 13 wherein R' is H.

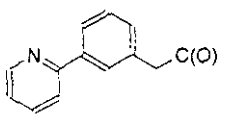
15. A compound according to Claim 1 wherein R" is H.

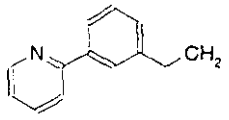
16. A compound according to Claim 1 wherein R"' is selected from the group consisting of H and 6,6-dimethyl.

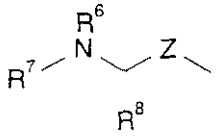
17. A compound according to Claim 16 wherein R"' is H.

18. A compound according to Claim 1 wherein R" and R"' are both H.

19. A compound according to Claim 1 wherein:

R^2 is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $R^9C(O)$-, $R^9C(S)$-, R^9SO_2-, $R^9OC(O)$-, $R^9R^{11}NC(O)$-, $R^9R^{11}NC(S)$-, $R^9R^{11}NSO_2$-, 

, 

and 

;

R^6 is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

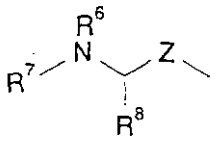
R^7 is selected from the group consisting of: : H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $R^{10}C(O)$-, $R^{10}C(S)$-, $R^{10}SO_2$-, $R^{10}OC(O)$-, $R^{10}R^{14}NC(O)$-, and $R^{10}R^{14}NC(S)$;

R^8 is selected from the group consisting of: H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, HetC_{0-6}alkyl and ArC_{0-6}alkyl;

R^9 is selected from the group consisting of: C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R^{10} is selected from the group consisting of: C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl or Het-C_{0-6}alkyl; and

Z is selected from the group consisting of: C(O) and CH_2.

20. A compound according to Claim 19 wherein R^2 is selected from the group consisting of: Ar-C_{0-6}alkyl, $R^9C(O)$-, R^9SO_2, $R^9R^{11}NC(O)$-, and  .

21. A compound according to Claim 20 wherein R^2 is selected from the group consisting of: Ar-C_{0-6}alkyl, $R^9C(O)$-, and R^9SO_2.

22. A compound according to Claim 21 wherein R^2 is R^9SO_2.

23. A compound according to Claim 19 wherein R^6 is H.

24. A compound according to Claim 19 wherein R^7 is $R^{10}OC(O)$.

25. A compound according to Claim 19 wherein R^8 is C_{1-6}alkyl.

26. A compound according to Claim 25 wherein R^8 is isobutyl.

27. A compound according to Claim 19 wherein R^9 is selected from the group consisting of: C_{1-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl.

28. A compound according to Claim 27 wherein R^9 is selected from the group consisting of:

methyl;

ethyl, and C_{1-6}alkyl -substituted ethyl;

butyl, C_{1-6}alkyl-substituted butyl;

tert-butyl;

isopentyl;

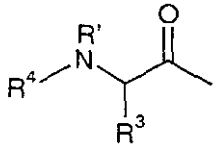
phenyl, halogen substituted phenyl,C_{1-6}alkoxy phenyl, cyanophenyl;

toluyl, Het-substituted toluyl;
benzoic acid;
naphthylenyl;
benzo[1,3]dioxolyl;
benzo[1,2,5]oxadiazolyl;
pyridinyl, 1-oxy-pyridinyl, C_{1-6}alkyl pyridinyl;
thiophene;
thiazolyl;
1H-imidazolyl, C_{1-6}alkyl substituted imidazolyl;
1H-[1,2,4]triazolyl, C_{1-6}alkyl substituted 1H-[1,2,4]triazolyl; and
quinolinyl.

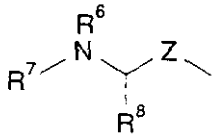
29. A compound according to Claim 27 wherein R^9 is selected from the group consisting of:

2-cyclohexyl-ethyl;
3-methylbutyl;
3,4-dichlorophenyl, 4-bromophenyl, 2-fluorophenyl, 4-fluorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3-methoxyphenyl, 4-methoxyphenyl, 3,4-dimethoxyphenyl, 2-cyanophenyl;
2-benzoic acid;
naphthylen-2-yl;
benzo[1,3]dioxol-5-yl;
benzo[1,2,5]oxadiazol-4-yl;
pyridin-2-yl, pyridin-3-yl , 1-oxy-pyridin-2-yl, 1-oxy-pyridin-3-yl, 3-methyl-pyridin-2-yl, 6-methyl-pyridin-2-yl;
thiophene-2-yl;
thiazol-2-yl;
1H-imidazol-2-yl, 1H-imidazol-4-yl, 1-methyl-1H-imidazol-2-yl, 1-methyl-1H-imidazol-4-yl;
1H-[1,2,4]triazol-3-yl, 5-methyl-1H-[1,2,4]triazol-3-yl; and
quinolin-2-yl.

30. A compound according to Claim 1 wherein:

R^1 is  ;

R^2 is selected from the group consisting of:

Ar-C_{0-6}alkyl, $R^9C(O)$-, R^9SO_2, $R^9R^{11}NC(O)$-, and  ;

R^3 is selected from the group H, C_{1-6}alkyl and Ar C_{0-6}alkyl;

R^4 is selected from the group consisting of: $R^5OC(O)$-, $R^5C(O)$- or R^5SO_2-;

R^5 is selected from the group consisting of: C_{1-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl;

R^6 is H;

R^7 is $R^{10}OC(O)$;

R^8 is C_{1-6}alkyl;

$R^9$is selected from the group consisting of: C_{1-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl;

R^{10} is selected from the group consisting of: C_{1-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl;

R' is H;

R" is H;and

R"' is H.

31. A compound according to Claim 30 wherein:

R^2 is selected from the group consisting of: Ar-C_{0-6}alkyl, $R^9C(O)$- and R^9SO_2;

R^3 is selected from the group consisting of: H, methyl, ethyl, n-propyl, prop-2-yl, n-butyl, isobutyl, but-2-yl, cyclopropylmethyl, cyclohexylmethyl, 2-methanesulfinyl-ethyl, 1-hydroxyethyl, toluyl, naphthalen-2-ylmethyl, benzyloxymethyl, and hydroxymethyl;

R^4 is $R^5C(O)$-;

R^5 is selected from the group consisting of:

methyl, halogenated methyl, alkoxy substituted methyl, heterocycle substituted methyl;

butyl, aryl substituted butyl;

isopentyl;

cyclohexyl;

butenyl, aryl substituted butenyl;

acetyl;

phenyl, phenyl substituted with one or more halogens, phenyl substituted with one or more alkoxy groups, phenyl substituted with one or more sulfonyl groups;

benzyl;

naphthylenyl;

benzo[1,3]dioxolyl;

furanyl, halogen substituted furanyl, aryl substituted furanyl;

tetrahydrofuran-2-yl;

benzofuranyl, alkoxy substituted benzofuranyl, halogen substituted benzofuranyl, alkyl substituted benzofuranyl;

benzo[*b*]thiophenyl, alkoxy substituted benzo[*b*]thiophenyl;

quinolinyl;

quinoxalinyl;

1,8 naphthyridinyl;

indolyl (22), alkyl substituted indolyl;

pyridinyl, alkyl substituted pyridinyl, 1-oxy pyridinyl;

thiophenyl, alkyl substituted thiophenyl, halogen substituted thiophenyl;

thieno[3,2-*b*]thiophenyl;

isoxazolyl, alkyl substituted isoxazolyl; and

oxazolyl;

R^9 is selected from the group consisting of:

methyl;

ethyl, C_{1-6}alkyl -substituted ethyl;

butyl, C_{1-6}alkyl-substituted butyl;

tert-butyl;

isopentyl;

phenyl, halogen substituted phenyl,C_{1-6}alkoxy phenyl, cyanophenyl;

toluyl, Het-substituted toluyl;

benzoic acid;

naphthylenyl;

benzo[1,3]dioxolyl;

benzo[1,2,5]oxadiazolyl;

pyridinyl, 1-oxy-pyridinyl, C_{1-6}alkyl pyridinyl;

thiophene;

thiazolyl;

1H-imidazolyl, C_{1-6}alkyl substituted imidazolyl;

1H-[1,2,4]triazolyl, C_{1-6}alkyl substituted 1H-[1,2,4]triazolyl; and

quinolinyl.

32. A compound according to Claim 30 wherein: R^5 is selected from the group consisting of:

pentanonyl;

naphthylen-2-yl;

benzo[1,3]dioxol-5-yl,

furan-2-yl;

benzofuran-2-yl;

benzo[*b*]thiophen-2-yl;

quinolin-2-yl, quinolin-3-yl, quinolin-4-yl, quinolin-6-yl, and quinolin-8-yl;

quinoxalin-2-yl;

1,8 naphthyridin-2-yl;

indol-3-yl, indol-5-yl;

pyridin-2-yl , pyridin-5-yl,

thiophen-3-yl;

thieno[3,2-*b*]thiophene-2-yl;

isoxazol-4-yl; and

oxazol-4-yl.

33. A compound according to Claim 30 wherein R^5 is selected from the group consisting of:

trifluoromethyl, phenoxy-methyl, 4-fluoro-phenoxy-methyl , 2-thiophenyl-methyl;

4-(4-methoxy)phenyl-butyl;

4-pentanonyl;

4,4-bis(4-methoxyphenyl)-but-3-enyl;

3,4-dichlorophenyl, 4-fluorophenyl, 3,4-dimethoxy-phenyl, 3-benzyloxy-4-methoxy-phenyl, 4-methanesulfonyl-phenyl;

5-nitro-furan-2-yl, 5-(4-nitrophenyl)-furan-2-yl, 5-(3-triflouromethyl-phenyl)-furan-2-yl, 5-bromo-furan-2-yl, 5-(4-chloro-phenyl)-furan-2-yl;

5-(2-piperazin-4-carboxylic acid *tert*-butyl ester- ethoxy) benzofuran-2-yl, 5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-yl(44), 5-(2-piperazin-1-yl-ethoxy)benzofuran-2-yl, 5-(2-cyclohexyl-ethoxy)-benzofuran-2-yl, 7-methoxy-benzofuran-2-yl, 5-methoxy-benzofura-2-yl, 5,6-dimethoxy-benzofuran-2-yl, 5-fluoro-benzofuran-2-yl, 5,6-difluoro-benzofuran-2-yl, 3-methyl-benzofuran-2-yl;

5,6-dimethoxy- benzo[*b*]thiophen-2-yl;

N-methyl-indol-2-yl;

1-oxy-pyridin-2-yl, 2-methyl-pyridin-5-yl;

5-methyl-thiophen-2-yl, 4,5-dibromo-thiophen-2-yl;

5-*tert*-butyl-3-methyl thieno[3,2-*b*]thiophen-2-yl;

3,5-dimethyl- isoxazol-4-yl;

5-methyl-2-phenyl oxazol-4-yl, and 2-phenyl-5-trifluoromethyl-oxazol-4-yl.

34. A compound according to Claim 30 wherein R^9 is selected from the group consisting of:

2-cyclohexyl-ethyl;

3-methylbutyl;

3,4-dichlorophenyl, 4-bromophenyl, 2-fluorophenyl, 4-fluorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3-methoxyphenyl, 4-methoxyphenyl, 3,4-dimethoxyphenyl, 2-cyanophenyl;

2-benzoic acid;

naphthylen-2-yl;

benzo[1,3]dioxol-5-yl;

benzo[1,2,5]oxadiazol-4-yl;

pyridin-2-yl, pyridin-3-yl, 1-oxy-pyridin-2-yl, 1-oxy-pyridin-3-yl , 3-methyl-pyridin-2-yl, 6-methyl-pyridin-2-yl;

thiophene-2-yl;

thiazol-2-yl;

1H-imidazol-2-yl, 1H-imidazol-4-yl, 1-methyl-1H-imidazol-2-yl, 1-methyl-1H-imidazol-4-yl;

1H-[1,2,4]triazol-3-yl, 5-methyl-1H-[1,2,4]triazol-3-yl; and

quinolin-2-yl.

35. A compound according to Claim 30 wherein:

R^2 is R^9SO_2;

R^3 is isobutyl;

R^4 is $R^5C(O)$;

R^5 is selected from the group consisting of: 3-methyl-benzofuran-2-yl, thieno[3,2-b]thiophen-2-yl, 5-methoxybenzofuran-2-yl, quinoxalin-2-yl, or quinolin-2-yl; and

R^9 is selected from the group consisting of: pyridin-2-yl and 1-oxy-pyridin-2-yl.

36. A compound according to Claim 35 wherein R^5 is 3-methyl-benzofuran-2-yl.

37. A compound according to Claim 35 wherein R^9 is 1-oxy-pyridin-2-yl.

38. A compound according to Claim 1 selected from the group consisting of:

{(S)-1-[1-((S)-2-Benzyloxycarbonylamino-4-methyl-pentanoyl)-3-oxo-azepan-4-ylcarbamoyl}carbamic acid benzyl ester;

Naphthylene-2-carboxylic acid[(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide;

Benzo[1,3]dioxole-5-carboxylic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide;

Benzofuran-2-carboxylic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide;

Benzo[b]thiophene-2-carboxylic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide;

Naphthylene-2-sulphonyl [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide;

Quinoline-2-carboxylic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide;

3,4-dichlorobenzoic acid [(S)-1-(1-benzyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide;

4-{(S)-Methyl-2-[(quinoline-2-carbonyl)-amino]pentanoylamino}-3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]azepanium;

1-((S)-2-Benzyloxycarbonylamino-4-methyl-pentyl)-4-{(S)-4-methyl-2-[(2-quinoiline-2-carbonyl)-amino]-pentanoylamino)-3-oxo-azepanium;

1-Benzoyl-4-((S)-2-(benzo[1,3]dioxole-carbonylamino)-4-methyl-pentanoylamino)-3-oxo-azepanium;

1-Benzoyl-4-((S)-2-(4-fluoro-benzoylamino)-4-methyl-pentanoylamino)-3-oxo-azepanium;

3-Oxo-4-((S)-4-methyl-2-{[5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]amino}-pentanoylamino)-1-(4-methyl-pentanoyl)-azepanium;

5-(2-Morpholin-4-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide;

4-((S)-4-Methyl-2-{[5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]amino}-pentanoylamino)-3-oxo-azepane-1-carboxylic acid phenylamide;

5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)acetyl]-azepan-4-ylcarbamoyl}-butyl)amide;

5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-1-(benzoyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide;

5-(2-Pyrrolidin-1-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide;

5-(2-Piperidin-1-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide;

5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide;

Naphthlene-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide;

1H_Indole-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide;

1H-Indole-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide;

Benzofuran-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]amide;

Benzofuran-2-carboxylic acid [(S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide;

5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-3-methyl-1-(3-oxo-1-phenethyl-azepan-4-ylcarbamoyl]-butyl}amide;

Naphthylene-2-carboxylic acid [(S)-3-methyl-1-(3-oxo-1-phenethyl-azepan-4-ylcarbamoyl]-butyl}amide;

Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

Naphthylene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

4-((S)-4-Methyl-2-{[(5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carbonyl]-amino}-pentanoylamino)-3-oxo-azepane-1-carboxylic acid tert-butyl ester;

4-((S)-4-Methyl-2-{[(5-(2-morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid [(S)-3-methyl-1-(3-oxo-azepan-4-ylcarbamoyl]-butyl}amide;

4-Methyl-pentanoic acid {3-oxo-1-[2-(3-pyridin-2-yl-phenyl-acetyl]-azepan-4-yl}-amide;

((S)-3-Methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-ylcarbamoyl}-butyl)-naphthylene-2-methyl-carbamic acid tert-butyl ester;

(S)-4-Methyl-2-[(naphthylen-2-ylmethyl)-amino]-pentenoic acid [3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-yl}-amide;

4-[2-(2-{(S)-3-Methyl-1-[3-oxo-1-(pyidine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butylcarbamoyl}-benzofuran-5-yloxy)-ethyl]-piperazine-1-carboxylic acid tert-butyl ester;

5-(2-Piperizin-1-yl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-3-butyl}-amide;

5-(2-Cyclohexyl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

5-(2-Cyclohexyl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide;

4-[2-(2-{(S)-3-Methyl-1-[3-oxo-1-(3-pyridin-2-yl-phenyl)-ethyl [azepan-4-ylcarbamoyl]-butylcarbamoyl}-benzofuran-5-yloxy)-ethyl]-piperazine-1-carboxylic acid *tert*-butyl ester;

5-(2-piperizin-1-yl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)ethyl]-azepan-4-ylcarbamoyl}-butyl)amide;

(S)-4-Methyl-2-(methyl-naphthalen-2-ylmethyl-amino)pentanoic acid [3-oxo-1-(pyridine-2-sulphonyl)-azepan-4-yl]-amide;

(S)-4-Methyl-2-(methyl-naphthalen-2-ylmethyl-amino)pentanoic acid {3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-yl}-amide;

5-(2-Morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid methyl ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)acetyl]-azepan-4-ylcarbamoyl}-butyl)amide;

Benzofuran-2-carboxylic acid methyl {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide;

2,2,2-Trifluoro-N-((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-ylcarbamoyl}-butyl)-N-naphthylen-2-ylmethyl-acetamide;

4-[(S)-(Methanesulphonyl-naphthylen-2-ylmethyl-amino)-4-methyl-pentanoylamino]-3-oxo-azepane-1-carboxylic acid benzyl ester;

Quinoline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Quinoline-8-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Quinoline-6-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Quinoline-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Quinoline-3-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Isoquinoline-3-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Isoquinoline-1-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Quinoxaline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

1,8-Naphthyridine-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

1H-Indole-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

5-Methoxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

5-Bromo-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

5-Nitro-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

5-(4-Nitro-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Tetrahydro-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

(S)-4-Methyl-2-(2-phenoxy-acetylamino)-pentanoic acid [3-oxo-(pyridine-2-sulfonyl)-azepan-4-yl]-amide;

(S)-2-[2-(4-Fluoro-phenoxy)-acetylamino]-4-methyl-pentanoic acid [3-oxo-(pyridine-2-sulfonyl)-azepan-4-yl]-amide;

Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-carbonyl)-azepan-4-ylcarbamoyl)-3- butyl]-amide;

Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-carbonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

4-((S)-2-tert-Butylcarbonylamino-4-methyl-pentanoylamino)-3-oxo-azepane-1-carboxylic acid benzyl ester;

5,6-Dimethoxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-methyl-1H-imidazole-4-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(5-methyl-1H-[1,2,4]triazole-3-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide;

Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1-methyl-1H-imidazole-3-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide;

Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1H-imidazole-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide;

Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1-methyl-1H-imidazole-4-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide;

5-(4-Oxy-morpholino-4-yl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-3-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-3-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Quinoline-3-carboxylic acid {(S)-1-(3,4-dichloro-benzene-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl)]-3-methyl-butyl}-amide;

5-Hydroxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(1-methyl-1H-imidazole-4-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide;

Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)]-3-methyl-butyl}-amide;

2-(4-{(S)-2-{(Benzofuran-2-carbonyl)-amino}-4-methyl-pentanoylamino}-3-oxo-azepane-1-sulfonyl)-benzoic acid;

3-(4-{(S)-2-{(Benzofuran-2-carbonyl)-amino}-4-methyl-pentanoylamino}-3-oxo-azepane-1-sulfonyl)-benzoic acid;

Benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

5-Bromo-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

5,6-Dimethoxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

1-Oxy-pyridine-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

(S)-4-Methyl-2-(pyridine-2-sulfonylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide;

(S)-2-(3-Benzyl-ureido)-4-methyl-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide;

(S)-4-Methyl-2-(3-phenyl-uriedo)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide;

Benzofuran-2-carboxylic acid {(S)-1-[6,6-dimethyl-3-oxo-1(pyridine-sulphonyl)-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide;

5-Methoxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Quinoxaline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Quinoline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Thiophene-3-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

1H-Indole-5-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Benzo[1,3]dioxole-5-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

(S)-4-Methyl-2-(2-thiophen-2-yl-acetylamino)-pentanoic acid [3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-yl]-amide;

1H-Indole-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

4-Fluoro-{(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulphonyl)-azepan-4-carbamoyl]-butyl}-benzamide;

5-(2-Morpholin-4-yl-ethoxy)-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-(1-oxy-pyridine2-sulphonyl)-azepan-4-ylcarbamoyl]- -buty}-amide;

Thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

3-Methyl-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

6-Methyl-N-{(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-nicotinamide;

(S)-4-Methyl-2-(2-thiophen-yl-acetylamino)-pentanoic acid-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-butyl}amide;

1H-Indole-6-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Benzo[1,3]dioxole-5-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

3,4-Dihydro-2H-benzo[b][1,4]dioxepine-7-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]butyl}amide;

5-Methyl-thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

4,5-Dibromo-thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

3,5-Dimethyl-isoxazole-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

(S)-2-(2-Benzyloxy-acetylamino)-4-methyl-pentanoic acid[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-yl]-amide;

5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

5-Methyl-2 –phenyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Benzofuran-2-carboxylic acid {(S)-1-[1-(3,4-dimethoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}-amide;

Benzofuran-2-carboxylic acid {(S)-1-[1-(4-bromo-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide;

Benzofuran-2-carboxylic acid {(S)-1-[1-(benzo[1,2,5]oxadiazole-4-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide;

Benzofuran-2-carboxylic acid {(S)-1-[1-(3,5-dimethyl-oxazole-4 -sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl–butyl}-amide;

3-Methyl-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

5-*tert*-Butyl-3-methyl-thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

5-Methyl-2-phenyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

2-Phenyl-5-trifluoromethyl-oxazole-4-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Quinoline-2-carboxylic acid [(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide;

1-Methyl-1H-indole-2-carboxylic acid [(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide;

Furan-2-carboxylic acid {[(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butylcarbamoyl]-methyl}-amide;

5-Methoxy-benzofuran-2-carboxylic acid [(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide;

Quinoxaline-2-carboxylic acid [(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide;

5-(4-Chloro-phenyl)-furan-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

(S)-2-[2-(4-Methoxy-phenyl)-acetylamino)-4-methyl-pentanoic acid (1-methanesulfonyl-3-oxo-azepan-4-yl)-amide;

Quinoline-2-carboxylic acid {[(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

1-Methyl-1H-indole -2-carboxylic acid {[(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

Furan-2-carboxylic acid ({(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butylcarbamoyl}-methyl)-amide;

5-Methoxy-benzofuran-2-carboxylic acid {(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

Quinoxaline-2-carboxylic acid {(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

(S)-2-[2-(4-Methoxy-phenyl)-acetylamino)-4-methyl-pentanoic acid [1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-yl]-amide;

Quinoline-2-carboxylic acid {[(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

1-Methyl-1H-indole-2-carboxylic acid {[(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

Furan-2-carboxylic acid ({(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butylcarbamoyl}-methyl)-amide;

5-Methoxy-benzofuran-2-carboxylic acid {[(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

Quinoxaline-2-carboxylic acid {[(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

(S)-2-[2-(4-Methoxy-phenyl)-acetylamino)-4-methyl-pentanoic acid [1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-yl]-amide;

1-Methyl-1H-indole-2-carboxylic acid {[(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

Furan-2-carboxylic acid ({(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butylcarbamoyl}-methyl)-amide;

5-Methoxy-benzofuran-2-carboxylic acid {[(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

Quinoxaline-2-carboxylic acid {[(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

(S)-2-[2-(4-Methoxy-phenyl)-acetylamino)-4-methyl-pentanoic acid [1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-yl]-amide;

Benzofuran-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

5-Methoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

7-Methoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

5,6-Dimethoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

3-Methyl-benzofuran-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

1-Methyl-1H-indole-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

Quinoxaline-2-carboxylic acid-{(S)-1-[1-(3-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

Benzofuran-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

5-Methoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

7-Methoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

5,6-Dimethoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

5-Methyl-benzofuran-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

1-Methyl-1H-indole-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

(S)-4-Methyl-2-(1-oxy-pyridine-2-sulfonylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide;

Quinoxaline-2-carboxylic acid-{(S)-1-[1-(2-fluoro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

5-Methoxy-benzofuran-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

7-Methoxy-benzofuran-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

5,6-Dimethoxy-benzofuran-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

3-Methyl-benzofuran-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

Benzo[b]thiophene-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

1-Methyl-1-H-indole-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

Quinoxaline-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

Benzofuran-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

5-Methoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

7-Methoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

5,6-Dimethoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

3-Methyl-benzofuran-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

1-Methyl-1H-indole-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

Quinoxaline-2-carboxylic acid-{(S)-1-[1-(4-chloro-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

Benzofuran-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

5-Methoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

7-Methoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

5,6-Dimethoxy-benzofuran-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

3-Methyl-benzofuran-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

1-Methyl-1H-indole-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

Quinoxaline-2-carboxylic acid-{(S)-1-[1-(3-methoxy-benzenesulphonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

Benzofuran-2-carboxylic acid-{(S)-3-methyl-1-[3-oxo-1-(thiophene-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[(2,2',4-tridueterio)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Benzofuran-2-carboxylic acid {(S)-2-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

Benzofuran-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-propyl}-amide;

Benzofuran-2-carboxylic acid {(S)-2-cyclohexyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

Benzofuran-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

Benzofuran-2-carboxylic acid {(S)-3-methanesulfinyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-propyl}-amide;

Benzofuran-2-carboxylic acid {[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-methyl}-amide;

Benzofuran-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-pentyl}-amide;

Benzofuran-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

Benzofuran-2-carboxylic acid {(S)-2-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-propyl}-amide;

Benzofuran-2-carboxylic acid {(S)-2-hydroxy-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-propyl}-amide;

Benzofuran-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-2-phenyl-ethyl}-amide;

1-(Benzofuran-2-carbonyl)-pyrrolidine-2-carboxylic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide;

3,4-Dimethoxy-N-{(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-benzamide;

Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(4-imethoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

Benzo[1,3]dioxole-5-carboxylic acid {(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3methyl-butyl}-amide;

(S)-2-(2-Benzyloxy-acetylamino)-4-methyl-pentanoic acid[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-yl]-amide;

Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-yl carbamoyl]-3-methyl-butyl}-amide;

Benzofuran-2-carboxylic acid {(S)-1-[1-benzoyl-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide;

(S)-4-Methyl-2-(quinoline-8-sulfonylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide;

(S)-4-Methyl-2-(naphthylene-2-sulfonylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide;

Benzofuran-2-carboxylic acid-{(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-yl carbamoyl]-3-methyl-butyl}-amide;

N-{(S)-1-[1-(4-Fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl}-3-methyl-butyl}-3,4-dimethoxy-benzamide;

Cyclohexanecarboxylic acid {(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl}-3-methyl-butyl}-amide;

(S)-2-(2-Benzyloxy-acetylamino)-4-methyl-pentanoic acid[1-(methanesulfonyl)-3-oxo-azepan-4-yl]-amide;

Benzo[b]thiophene-2-carboxylic acid-{(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-yl carbamoyl)-3-methyl-butyl]-amide;

Benzo[1,3]dioxole-5-carboxylic acid-{(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-yl carbamoyl)-3-methyl-butyl]-amide;

Benzofuran-2-carboxylic acid-{(S)-1-(1-methanesulfonyl-3-oxo-azepan-4-yl carbamoyl)-3-methyl-butyl]-amide;

N-[(S)-1-(1-Methanesulfonyl)-3-oxo-azepan-4-ylcarbamoyl}-3-methyl-butyl}-3,4-dimethoxy-benzamide;

(S)-2-(2-Benzyloxy-acetylamino)-4-methyl-pentanoic acid[1-(2-cyano-benzensulfonyl)-3-oxo-azepan-4-yl]-amide;

N-{(S)-1-[1-(2-Cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl}-3-methyl-butyl}-4-methanesulfonyl-1-benzamide;

Benzo[b]thiophene-2-carboxylic acid-{(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-yl carbamoyl)-3-methyl-butyl]-amide;

Benzo[1,3]dioxole-5-carboxylic acid-{(S)-1-[1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl)-3-methyl-butyl]-amide;

(S)-4-Methyl-2-[4-oxo-4-((4-phenoxy-phenyl)-butyrylamino}-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide;

N-{(S)-1-[(1-(2-cyano-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl}-3-methyl-butyl}-3,4-dimethoxy-benzamide;

Cyclohexanecarboxylic acid {(S)-1-[1-(4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl}-3-methyl-butyl}-amide;

4-Methansulfonyl-N-{(S)-1-[4-methoxy-benzenesulfonyl)-3-oxo-azepan-4-carbamoyl]-3-methyl-butyl-benzamide;

4-Methansulfonyl-N-{(S)-1-[4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-carbamoyl]-3-methyl-butyl-benzamide;

({(S)-3-Methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butylcarbamoyl}-carbamic acid benzyl ester;

(S)-2-[5-(4-Methoxy-phenyl)-pentanoylamnio]-4-methyl-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide;

(S)-2-[2-(3-Benzyloxy-4-methoxy-phenyl)-acetylamnio]-4-methylpentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide;

5,6-Difluoro-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide;

(S)-4-Methyl-2-(5-oxo-hexanoylamino)-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-amide;

Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide;

5-Methoxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide;

3-Methyl-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide;

7-Methoxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide;

5,6-Dimethoxy-benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide;

(R)-1-Benzyl-5-oxo-pyrrolidine-2-carboxylic acid {(S)-3-methyl-1-{3-oxo-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

(S)-1-Benzyl-5-oxo-pyrrolidine-2-carboxylic acid {(S)-3-methyl-1-{3-oxo-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Benzofuran-2-carboxylic acid {(S)-2-cyclopropyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-ethyl]-amide;

Benzofuran-2-carboxylic acid {(S)-3-methylsulfanyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-propyl]-amide;

Benzofuran-2-carboxylic acid {(S)-2-naphthylen-2-yl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-ethyl]-amide;

Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(6-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide;

Thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide;

3-Methyl-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide;

5-Methoxy-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[1-(3-methyl-pyridine-2-sulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-butyl}amide;

5,6-Difluoro-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid{(S)-2-cyclohexyl-1-{3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-(4-Chloro-phenyl)-furan-2-carboxylic acid{(S)-2-cyclohexyl-1-{3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[6-methyl-3-oxo-1-(pyridine-sulphonyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

5-(4-Chloro-phenyl)-furan-2-carboxylic acid{(S)-2-cyclohexyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-(3-Trifluoromethyl-phenyl)-furan-2-carboxylic acid{(S)-2-cyclohexyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-Fluoro-benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

5,6-Dimethoxy-benzofuran-2-carboxylic acid{(S)-2-cyclohexyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5,5-Bis-(4-methoxy-phenyl)-pent-4-enoic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]}-butyl}-amide;

Quinoline-8-carboxylic acid {(S)-2-naphthylen-2-yl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-ethyl]-amide;

Naphthylene-1-carboxylic acid {(S)-2-naphthylen-2-yl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl)-ethyl]-amide;

Quinoline-8-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-2-phenyl-ethyl}-amide;

Naphthyridine-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

Naphthylene-1-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-2-phenyl-ethyl}-amide;

3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(cyclohexyl-proprionyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(4-methyl-pentanoyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(1-oxy-pyridine-2-carbonyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

(S)-Acetylamino-4-methyl-pentanoic acid [3-oxo-1-(pyridine-2-sulfonyl)-

azepan-4-yl]-amide;

Quinoline-2-carboxylic acid {1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-pentyl}-amide;

Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo -1-(cyclohexyl-proprionyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

Benzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(4-methyl-pentanoyl)-azepan-4-ylcarbamoyl]-butyl}-amide;

Quinoline-2-carboxylic acid {(S)-1-[3-oxo-1-(pyridine-2 -sulfonyl)-azepan-4-ylcarbamoyl]-2-phenyl-ethyl}-amide;

Benzofuran-2-carboxylic acid{(S)-2-benzyloxy-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepane-4-ylcarbamoyl]-ethyl}-amide;

Benzofuran-2-carboxylic acid{(S)-2-hydroxy-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepane-4-ylcarbamoyl]-ethyl}-amide;

5-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

7-Methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

3-Methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Benzo[b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

1-Methyl-1H-indole-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

Quinoxaline-2-carboxylic acid {(S)-3-methyl-1-[3-oxo-1-(thiazole-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide; and

Quinoline-2-carboxylic acid {[(S)-1-[1-(4-fluoro-benzenesulfonyl)-3-oxo-azepan-4-ylcarbamoyl]-3-methyl-butyl}-amide.

39. A pharmaceutical composition comprising a compound according to Claims 1 to 38 and a pharmaceutically acceptable carrier, diluent or excipient.

40. A method of inhibiting a protease, comprising administering to a patient in need thereof an effective amount of a compound according to Claims 1 to 38.

41. A method according to Claim 40 wherein said protease is selected from the group consisting of a cysteine protease and a serine protease.

42. A method according to Claim 41 wherein said protease is a cysteine protease.

43. A method according to Claim 42 wherein said cysteine protease is cathepsin K.

44. A method of treating a disease characterized by bone loss comprising inhibiting said bone loss by administering to a patient in need thereof an effective amount of a compound according to Claims 1 to 38.

45. A method according to Claim 44 wherein said disease is osteoporosis.

46. A method according to Claim 44 wherein said disease is periodontitis.

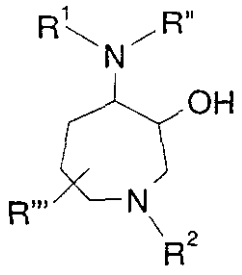
47. A method according to Claim 44 wherein said disease is gingivitis.

48. A method of treating a disease characterized by excessive cartilage or matrix degradation comprising inhibiting said excessive cartilage or matrix degradation by administering to a patient in need thereof an effective amount of a compound according to Claims 1 to 38.

49. A method according to Claim 48 wherein said disease is osteoarthritis.

50. A method according to Claim 48 wherein said disease is rheumatoid arthritis.

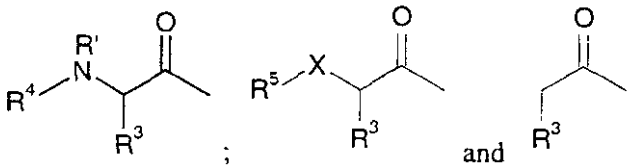
51. A compound of Formula II:



II

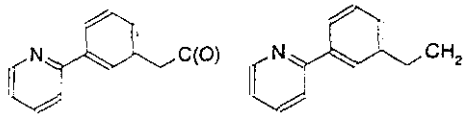
wherein:

R^1 is selected from the group consisting of:

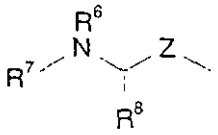


; and

R^2 is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $R^9C(O)$-, $R^9C(S)$-, R^9SO_2-, $R^9OC(O)$-, $R^9R^{11}NC(O)$-, $R^9R^{11}NC(S)$-, $R^9(R^{11})NSO_2$-



and



;

R^3 is selected from the group consisting of: H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, HetC_{0-6}alkyl and ArC_{0-6}alkyl;

R^3 and R' may be connected to form a pyrrolidine, piperidine or morpholine ring;

R^4 is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $R^5C(O)$-, $R^5C(S)$-, R^5SO_2-, $R^5OC(O)$-, $R^5R^{13}NC(O)$-, and $R^5R^{13}NC(S)$-;

R^5 is selected from the group consisting of: H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl;

R^6 is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, or Het-C_{0-6}alkyl;

R^7 is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $R^{10}C(O)$-, $R^{10}C(S)$-, $R^{10}SO_2$-, $R^{10}OC(O)$-, $R^{10}R^{14}NC(O)$-, and $R^{10}R^{14}NC(S)$-;

R^8 is selected from the group consisting of: H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, HetC_{0-6}alkyl and ArC_{0-6}alkyl;

R^9 is selected from the group consisting of: C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl;

R^{10} is selected from the group consisting of: C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl and Het-C_{0-6}alkyl;

R^{11} is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R^{12} is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R^{13} is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R^{14} is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R' is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

R" is selected from the group consisting of: H, C_{1-6}alkyl, Ar-C_{0-6}alkyl, or Het-C_{0-6}alkyl;

R'" is selected from the group consisting of: H, C_{1-6}alkyl, C_{3-6}cycloalkyl-C_{0-6}alkyl, Ar-C_{0-6}alkyl, and Het-C_{0-6}alkyl;

X is selected from the group consisting of: CH_2, S, and O;

Z is selected from the group consisting of: C(O) and CH_2;

and pharmaceutically acceptable salts, hydrates and solvates thereof.

52. A compound according to Claim 51 selected from the group consisting of:

[(S)-1(3-Hydroxy-azepan-4-ylcarbamoyl)-3-methyl-butyl]-carbamic acid benzyl ester;

(S)-2-Amino-4-methyl-pentanoic acid (1-benzyl-3-hydroxy-azepan-4-yl)-amide;

(S)-2-Amino-4-methyl-pentanoic acid{3-hydroxy-1-[2-(3-pyridin-2-yl-phenyl)-acetyl]-azepan-4-yl}-amide;

{(S)-1-[4-((S)-2-Amino-4-methyl-pentanoylamino)-3-hydroxy-azepan-1-ylmethyl]-3-methyl-butyl}-carbamic acid benzyl ester;

(S)-2-Amino-4-methyl-pentanoic acid-(1-benzoyl-3-hydroxy-azepan-4-yl)-amide;

(S)-2-Amino-4-methyl-pentanoic acid [3-hydroxy-1-(4-methyl-pentanoyl)-azepan-4-yl]-amide;

(S)-2-Amino-4-methyl-pentanoic acid (1-benzenesulfonyl-3-hydroxy-azepan-4-yl)-amide;

thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

5-methoxybenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

thieno[3,2-b]thiophene-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

3-methylbenzofuran-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide;

quinoline-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide; and

quinoxaline-2-carboxylic acid {(S)-3-methyl-1-[3-hydroxy-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-butyl}amide.

53. A process for the synthesis of a compound according to Claim 1 comprising the step of oxidizing a corresponding compound of Claim 51 with an oxidant to provide the compound of Formula (I) as a mixture of diastereomers.

54. The process of Claim 53 wherein the oxidant is sulfur trioxide pyridine complex in DMSO and triethylamine.

55. The process of Claim 54 further comprising the step of separating the diasteromers by separating means.

56. The process of Claim 55 wherein said separating means is high presssure liquid chromatography (HPLC).

57. The process of Claim 53 further comprising the step of deuterating said diastereomers with a deuterating agent.

58. The process of Claim 57 wherein said deuterating agent is CD_3OD: D_2O (10:1) in triethylamine.

59. Use of a compound according to any one of Claims 1 to 38 in the manufacture of a medicament for use in inhibiting a protease selected from the group consisting of a cysteine protease and a serine protease.

60. A use according to Claim 59 wherein said protease is a cysteine protease.

61. A use according to Claim 60 wherein said cysteine protease is cathepsin K.

62. Use of a compound according to any one of Claims 1 to 38 in the manufacture of a medicament for use in treating a disease characterized by bone loss.

63. A use according to Claim 62 wherein said disease is osteoporosis.

64. A use according to Claim 62 wherein said disease is periodontitis.

65. A use according to Claim 62 wherein said disease is gingivitis.

66. Use of a compound according to any one of Claims 1 to 38 in the manufacture of a medicament for use in treating a disease characterized by excessive cartilage or matrix degradation.

67. A use according to Claim 66 wherein said disease is osteoarthritis.

68. A use according to Claim 66 wherein said disease is rheumatoid arthritis.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/30730

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 31/55; C07D 223/08, 401/02, 403/02, 405/02, 409/02, 411/02, 413/02, 417/02, 419/02
US CL : 514/212; 540/596, 597, 598, 599, 600, 601, 602, 603, 604

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)
U.S. : 514/212; 540/596, 597, 598, 599, 600, 601, 602, 603, 604

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 practicable, search terms used)
EAST, CAS ONLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A,P	US 5,902,882 A (MATZINGER et al) 11 May 1999 (19.05.1999), column 5, lines 52-62.	51-68
A	WINKLER, D.A., Molecular Modeling Studies of "Flap Up" Mannosyl Cation Mimics. Journal of Medicinal Chemistry. October 1996, Vol. 39, No. 21, pages 4332-4334, especially page 4332.	51-68
A	TANNER, D. et al., Total synthesis of Balanol. Part 1. Enantioselective Synthesis of the Hexahydroazepine Ring via Chiral Epoxides and Aziridines. Tetrahedron. May 1995, Vol. 51, No. 21, pages 6061-6070, especially page 6062.	51-68

☐ Further documents are listed in the continuation of Box C. ☐ 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

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"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
28 February 2000 (28.02.2000)	20 MAR 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer Brenda Coleman Telephone No. 703-308-1235

Form PCT/ISA/210 (second sheet) (July 1998)

蛋白酶抑制劑

撮　錄

本發明描述了4-氨基-氮雜-3-酮蛋白酶抑制劑和藥學上可接受的鹽，水合物和其溶劑合物，本物質抑制蛋白酶包括組織蛋白酶 K；這种化合物的藥物組合物；藥物組合物新的中間体；以及有關骨丟失過量或軟骨或基質的降解，包括骨質疏松；牙齦的病變如牙齦炎和牙周炎；關節炎尤其是骨關節炎和類風濕性關節炎；培吉特氏病；惡性高鈣血症；和骨代謝疾病的治療方法，包括通過給予急症病人本發明化合物抑制所述的骨丟失或過量的軟骨或基質降解。