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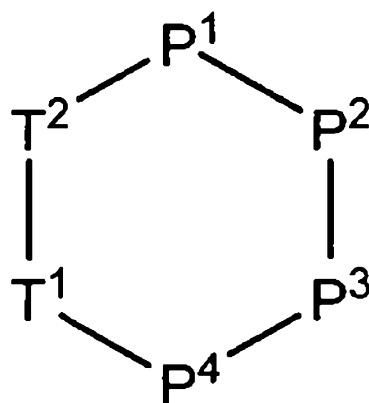
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(54) Title: TEMPLATE-FIXED PEPTIDOMIMETICS WITH CCR10 ANTAGONISTIC ACTIVITY



(I)

(57) Abstract: Novel template-fixed β -hairpin peptidomimetics of the general formula (I) wherein the single elements T or P are α -amino acid residues connected in either direction which, depending on their positions in the chain, are as defined in the description and the claims, and salts thereof, have the property to antagonize the receptor CCR10. They can be used as medicaments to treat or prevent diseases or conditions in the area of dermatological and cutaneous disorders, inflammation, allergic disorders, respiratory diseases, diseases of the gastro-intestinal tract, ophthalmic diseases, haematology and cancer. These β -hairpin peptidomimetics can be manufactured by a process which is based on a mixed solid- and solution phase synthetic strategy.

WO 2011/060937 A1

Template - fixed peptidomimetics with CCR10 antagonistic activity

The present invention provides peptidomimetics incorporating a chain of 4 α -amino acid residues as defined below attached to a template which provides specific structural constraints for a β -hairpin like conformation. These template-fixed β -hairpin mimetics have an antagonizing activity against the CCR10 receptor and are thus useful in the treatment of a variety of diseases and disorders such as inflammatory skin diseases, allergic asthma, gastro-intestinal/colon diseases, certain melanomas, cutaneous lymphoma, or other conditions mediated or sustained through the activity of CCR10. The present invention also relates to methods of using these compounds in the treatment of the various diseases and disorders stated above, to pharmaceutical compositions and forms comprising these compounds and efficient processes for the preparation and production of these compounds and their intermediates.

Many medically relevant biological processes are mediated by signal transduction that involves chemokines and their receptors, for instance the tissue specific recruitment of leukocytes to sites of inflammation. Within the blood there is a subset of memory T cells, morphologically characterized by the expression of the cutaneous lymphocyte antigen (CLA), which homes preferentially to dermal endothelial cells and associated tissue. There are recent studies showing that CLA⁺ memory T cells as well express the chemokine receptor CCR10 and in addition that a specific ligand for this receptor, CCL27, is markedly up-regulated in tissue where an enrichment of these CCR10 expressing cells could be detected. This suggests, that the CCR10/CCL27 interaction plays a significant role in the tissue specific trafficking of CLA⁺ memory T cells to e.g. inflammatory skin lesions. Besides on CLA⁺ T cells, expression of CCR10 has been shown on melanocytes, dermal fibroblasts, skin keratinocytes, microvascular endothelial cells, Langerhans cells, and certain tissue types, e.g. human heart or colon. Abundant expression of CCL27, tightly regulated by proinflammatory mediators, such as TNF- α and IL-1 β , was observed in the epidermis, predominantly by keratinocytes. While expressed in keratinocytes, CCL27 has a high affinity to extracellular matrix

proteins, therefore, after extracellular diffusion, being as well presented on cutaneous vascular epithelium cells to participate in the leukocyte arrest.

An increasing number of studies are providing evidence that the CCR10/CCL27 interaction is instrumental for the migration and localization of T cell subsets during physiological responses in inflamed or infected skin or mucosal tissue (J. Morales et al., *Proc. Nat. Acad. Sci.*, **1999**, 96, 14470-14475; B. Homey et al., *J. Immunol.*, **2000**, 164, 3465-3470; B. Homey et al., *Nature Medicine*, **2002**, 8, 157-165; B. Eksteen et al., *J. Immunol.*, **2006**, 177, 593-603). Under pathological conditions such as psoriatic, atopic dermatitis or graft versus host disease the expression of CCL27 was found dramatically up-regulated in comparison to normal skin or tissue biopsy. Consequently a marked accumulation of recruited CCR10⁺ lymphocytes could be observed (B. Homey, *Current Drug Targets – Inflammation & Allergy*, 2004, 3, 169-174; B. Homey et al., *J. Allergy Clin. Immunol.*, 2006, 118, 178-189; N. Annels et al., *Brit. J. of Haematology*, **2006**, 133, 538-549). The same effect was noted in nickel-allergic humans after cutaneous challenge with nickel. In two separate in vivo proof of concept studies using a DNFB-induction and an ovalbumin DTH model in wild-type mice, respectively, the same authors could show a significant reduction in leukocyte recruitment along with lower swelling upon treatment with a function blocking antibody against CCL27.

More recent findings strongly suggest the significant contribution of a second ligand/receptor interaction of CCR10, in this case with the mucosa-associated epithelial chemokine CCL28, to the pathogenesis of inflammatory respiratory tract and skin diseases as demonstrated for allergic asthma in murine models and atopic dermatitis in human children (B. P. Mahon, *Immunology Letters*, **2006**, 103, 92-100; M. H. M. Ezzat et al., *Int. J. of Dermatology*, **2009**, 48, 822-829; A. Zlotnik et al., *J. of Biological Chem.*, **2000**, 275, 22313-22323).

Other studies in the field are indicating an increased expression of CCR10 in melanoma specimen up to 800-fold based on RNA quantification when compared with healthy skin. This resulted in mouse B16 melanoma cells not only in growth advantage, but also in a striking increase in metastasis to the draining lymph node in comparison to

B16 cells without CCR10 expression. *In vitro*, activation of CCR10 by CCL27 leads to the activation of PI3K with the overall downstream effect of protection of CCR10-expressing B16 cells from tumor-specific cytotoxic T cells (T. Murakami et al., *J. Exp. Med.*, **2003**, *198*, 1337-1347; X. Wu et al., *Curr. Pharm. Design*, **2009**, *15*, 742-757; O. Simonetti et al., *Eur. J. of Cancer*, **2006**, *42*, 1181-1187).

Proof of concept studies, such as those described above, highly recommend the transmembrane G-protein coupled receptor (GPCR) CCR10 as an attractive target for the treatment of various disease conditions. Although over the past 15 years, nearly 350 therapeutic agents targeting GPCR receptors have been successfully introduced into the market (Th. Klabunde, G. Hessler, *ChemBioChem* **2002**, *3*, 928-44; G. Vauquelin et al. *Fundam. Clin. Pharmacol.* **2005**, *19*, 45-56), several toxicological problems, which arose from mainly lack of selectivity of some of those drugs, need to be further addressed. Clearly there is a need for a different concept in the design of these agents to solve the current issues and lead to effective and save drugs for treating or preventing the target associated diseases or disorders.

The present invention provides now new chemical entities for a potential use as potent, selective and drugable ligands for the GPC receptor CCR10. In the compounds described below, a new strategy is utilized to stabilize β -hairpin conformations in backbone-cyclic peptidomimetics exhibiting selective antagonizing activity against the CCR10 receptor. This involves transplanting a loop sequence of a natural or unnatural biopolymer onto a template, whose function is to restrain the peptide loop backbone into a hairpin geometry.

Template-bound hairpin mimetic peptides have been described in the literature (D. Obrecht, M. Altorfer, J. A. Robinson, *Adv. Med. Chem.* **1999**, *4*, 1-68; J. A. Robinson, *Syn. Lett.* **2000**, *4*, 429-441) and the ability to generate β -hairpin peptidomimetics using combinatorial and parallel synthesis methods has now been established (L. Jiang, K. Moehle, B. Dhanapal, D. Obrecht, J. A. Robinson, *Helv. Chim. Acta.* **2000**, *83*, 3097-

3112). These methods allow the synthesis and screening of large hairpin mimetic libraries, which in turn considerably facilitates structure-activity studies and hence the discovery of new molecules with potent and, especially, selective agonizing or antagonizing activity.

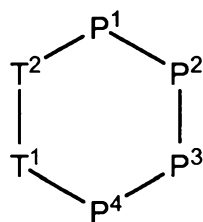
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There are few studies in the field describing tetrameric peptides linked to a template as agonist and/or antagonists of GPCR's and, among others, as well for CCR10 (WO2008092281). The present invention is now providing, as an alternative, novel compounds which differ significantly in structure and, surprisingly, exhibit a substantial
10 improvement of key pharmaceutical parameters, e.g. biological potency, stability or selectivity.

β -Hairpin peptidomimetics obtained by the approach described here are useful as antagonist of CCR10 and therefore as agents in the chemotherapy of e.g. psoriasis,
15 atopic dermatitis, contact sensitivity and allergic dermatitis, Stevens-Johnson syndrome, bullous cutaneous diseases, systemic lupus erythematosus, systemic and multiple sclerosis, allergic asthma, arthritis, graft versus host disease, certain melanoma and cutaneous lymphoma, thyroiditis, as well as inflammatory processes of the gastro-intestinal tract and the eye.

20

The present invention relates to novel β -hairpin peptidomimetics of formula (I),



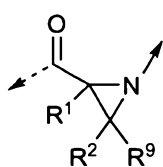
(I)

- 5 wherein the single elements T or P are connected in either direction from the carbonyl (C=O) point of attachment to the nitrogen (N) of the next element and wherein

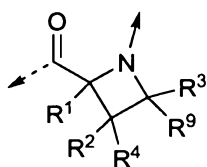
T^1 and T^2 are independently

an L or D α -amino acid of one of the formulae

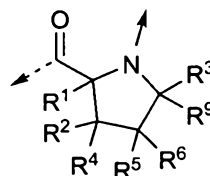
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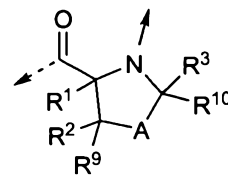
AA1



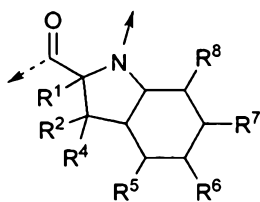
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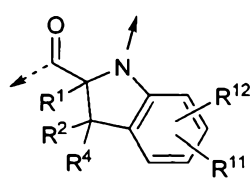
AA3



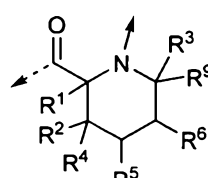
AA4



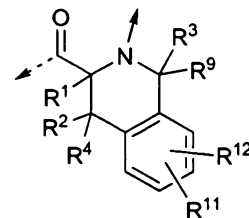
AA5



AA6



AA7



AA8

15

P^1 and P^3 are independently

$-NR^1CH(R^{19})CO-$;

P^2 is $-NR^1C(R^{20})(R^{21})CO-$; or $-NR^1C(Z)CO-$;

P^4 is $-NR^1CH(R^{24})CO-$;

A is O; NR^9 ; S; SO ; or SO_2

5 R^1 , R^2 and R^3 are independently

H; CF_3 ; lower alkyl; lower alkenyl; aryl-lower alkyl; or heteroaryl-lower alkyl;

R^4 , R^5 , R^6 , R^7 and R^8 are independently

H; F; CF_3 ; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl; aryl;

heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; $-(CHR^{13})_oOR^{15}$;

10 $-(CHR^{13})_oSR^{15}$; $-(CHR^{13})_oNR^{15}R^{16}$; $-(CHR^{13})_oCONR^{15}R^{16}$;

$-(CHR^{13})_oNR^1CONR^{15}R^{16}$; $-(CHR^{13})_oNR^1COR^{15}$; $-(CHR^{13})_oCOOR^{15}$;

$-(CHR^{13})_oCONR^{15}R^{16}$; $-(CHR^{13})_oPO(OR^1)_2$; $-(CHR^{13})_oSO_2R^{15}$;

$-(CHR^{13})_oNR^1SO_2R^{15}$; $-(CHR^{13})_oSO_2NR^{15}R^{16}$; $-(CR^1R^{13})_oR^{30}$; or

$-(CHR^1)_nO(CHR^2)_mR^{30}$; or

15 R^4 and R^2 taken together can form:

$=O$; $-(CHR^{19})_p-$; $-(CH_2)_nO(CH_2)_m-$; $-(CH_2)_nS(CH_2)_m-$; or $-(CH_2)_nNR^1(CH_2)_m-$; or

R^4 and R^5 ; R^5 and R^6 ; R^6 and R^7 ; R^7 and R^8 ; or R^6 and R^9 taken together can form:

$-(CHR^{19})_p-$; $-(CH_2)_nO(CH_2)_m-$; $-(CH_2)_nS(CH_2)_m-$; or $-(CH_2)_nNR^1(CH_2)_m-$;

R^9 and R^{10} are independently

20 H; F; CF_3 ; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl; aryl;

heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; $-(CHR^{13})_rOR^{15}$;

$-(CHR^{13})_rSR^{15}$; $-(CHR^{10})_rNR^{15}R^{16}$; $-(CHR^{13})_rCONR^{15}R^{16}$;

$-(CHR^{13})_rNR^1CONR^{15}R^{16}$; $-(CHR^{13})_rNR^1COR^{15}$; $-(CHR^{13})_oCOOR^{15}$;

$-(CHR^{13})_oCONR^{15}R^{16}$; $-(CHR^{13})_rPO(OR^1)_2$; $-(CHR^{13})_rSO_2R^{15}$;

25 $-(CHR^{13})_rNR^1SO_2R^{15}$; $-(CHR^{13})_rSO_2NR^{15}R^{16}$; $-(CR^1R^{13})_oR^{30}$; or

$-(CHR^1)_rO(CHR^1)_oR^{30}$;

R^{11} and R^{12} are independently

H; F; Cl; Br; CF_3 ; OCF_3 ; $OCHF_2$; CN; NO_2 ; lower alkyl; lower alkenyl; aryl;

heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; $-(CHR^{13})_oOR^{15}$;

30 $-(CHR^{13})_oSR^{15}$; $-(CHR^{13})_oNR^{15}R^{16}$; $-(CHR^{13})_oCONR^{15}R^{16}$;

$-(CHR^{13})_oNR^1CONR^{15}R^{16}$; $-(CHR^{13})_oNR^1COR^{15}$; $-(CHR^{13})_oCOOR^{15}$;

$-(\text{CHR}^{13})_o\text{CONR}^{15}\text{R}^{16}$; $-(\text{CHR}^{13})_o\text{PO}(\text{OR}^1)_2$; $-(\text{CHR}^{13})_o\text{SO}_2\text{R}^{15}$;
 $-(\text{CHR}^{13})_o\text{NR}^{15}\text{SO}_2\text{R}^{15}$; $-(\text{CHR}^{13})_o\text{SO}_2\text{NR}^{15}\text{R}^{16}$; or $-(\text{CR}^1\text{R}^{13})_o\text{R}^{30}$;

R^{13} is H; F; CF_3 ; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl;
 cycloalkyl-lower alkyl; heterocycloalkyl-lower alkyl; aryl; heteroaryl;

5 aryl-lower alkyl; heteroaryl-lower alkyl; $-(\text{CHR}^1)_o\text{OR}^{15}$; $-(\text{CHR}^1)_o\text{SR}^{15}$;
 $-(\text{CHR}^1)_o\text{NR}^{15}\text{R}^{16}$; $-(\text{CHR}^1)_o\text{NC}(=\text{NR}^{17})\text{NR}^{15}\text{R}^{16}$; $-(\text{CHR}^1)_o\text{COOR}^{15}$;
 $-(\text{CHR}^1)_o\text{CONR}^{15}\text{R}^{16}$; $-(\text{CHR}^1)_o\text{SO}_2\text{R}^{15}$; or $-(\text{CHR}^1)_o\text{SO}_2\text{NR}^{15}\text{R}^{16}$;

R^{14} is H; CF_3 ; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl;
 cycloalkyl-lower alkyl; heterocycloalkyl-lower alkyl; aryl; heteroaryl;

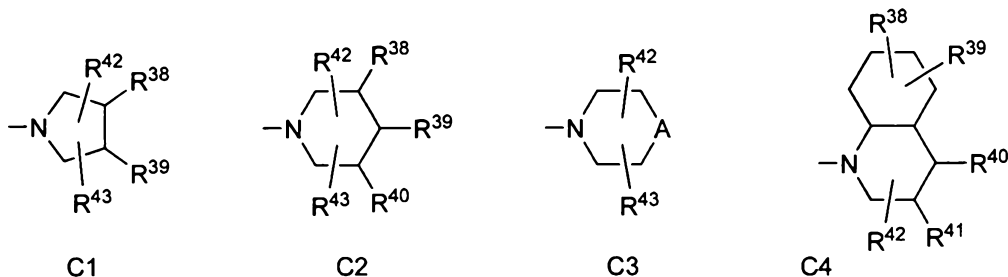
10 aryl-lower alkyl; heteroaryl-lower alkyl; cycloalkyl-aryl; heterocycloalkyl-aryl;
 cycloalkyl-heteroaryl; heterocycloalkyl-heteroaryl; aryl-cycloalkyl;
 aryl-heterocycloalkyl; heteroaryl-cycloalkyl; heteroaryl-heterocycloalkyl;
 $-(\text{CHR}^1)_o\text{OR}^{15}$; $-(\text{CHR}^1)_o\text{SR}^{15}$; $-(\text{CHR}^1)_o\text{NR}^{15}\text{R}^{16}$; $-(\text{CHR}^1)_o\text{COOR}^{15}$;
 $-(\text{CHR}^1)_o\text{CONR}^{15}\text{R}^{16}$; or $-(\text{CHR}^1)_o\text{SO}_2\text{R}^{15}$;

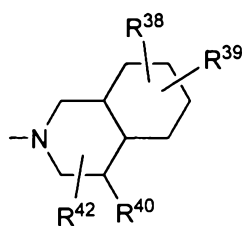
15 R^{15} , R^{16} , R^{17} and R^{18} are independently

H; lower alkyl; lower alkenyl; lower alkoxy; cycloalkyl; heterocycloalkyl;
 cycloalkyl-lower alkyl; heterocycloalkyl-lower alkyl; aryl; heteroaryl;
 aryl-lower alkyl; heteroaryl-lower alkyl; cycloalkyl-aryl; heterocycloalkyl-aryl;
 cycloalkyl-heteroaryl; heterocycloalkyl-heteroaryl; aryl-cycloalkyl;

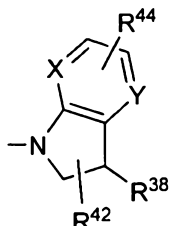
20 aryl-heterocycloalkyl; heteroaryl-cycloalkyl; or heteroaryl-heterocycloalkyl; or
 the structural elements $-\text{NR}^{15}\text{R}^{16}$ and $-\text{NR}^{17}\text{R}^{18}$ can independently form:

heterocycloalkyl; aryl-heterocycloalkyl; or heteroaryl-heterocycloalkyl;
 or a group of one of the following formulae

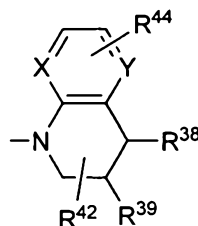




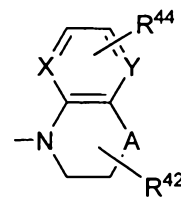
C5



C6



C7



C8

X and Y are independently

-CR⁴⁵; or N;

5

R¹⁹ is alkyl; alkenyl; cycloalkyl-lower alkyl; heterocycloalkyl-lower alkyl;

-(CR¹R⁴)_nR³⁰; -(CH₂)_nO(CH₂)_mR³⁰; -(CH₂)_nS(CH₂)_mR³⁰; or

-(CH₂)_nNR¹⁴(CH₂)_mR³⁰;

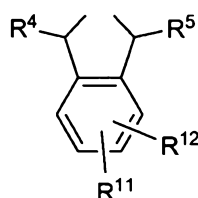
10 R²⁰ and R²¹ are independently

alkyl; alkenyl; -(CHR⁴)_oOR¹⁵; -(CHR⁴)_oSR¹⁵; or -(CHR⁴)_rNR¹⁵R¹⁶;

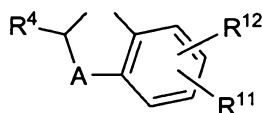
Z is -(CR²²R²³)_(n+m+1)-; -(CR²²R²³)_nNR¹⁵(CR²²R²³)_m-; -(CR²²R²³)_nO(CR²²R²³)_m-;

-(CR²²R²³)_nS(CR²²R²³)_m-; -O(CR²²R²³)_rO-;

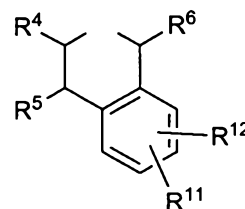
15 or a group of one of the formulae



Z1



Z2



Z3

R²² and R²³ are independently

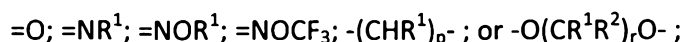
H; F; CF₃; alkyl; alkenyl; cycloalkyl; heterocycloalkyl; aryl; heteroaryl;

20 aryl-lower alkyl; or heteroaryl-lower alkyl; -(CR¹R¹³)_oOR¹⁵; -(CR¹R¹³)_oSR¹⁵;

-(CR¹R¹³)_oNR¹⁵R¹⁶; -(CR¹R¹³)_oCOOR¹⁵; -(CR¹R¹³)_oCONR¹⁵R¹⁶; or

-(CR¹R¹³)_oSO₂R¹⁵; or

R²² and R²³ taken together can form:



R²⁴ is alkyl; alkenyl; $-(CR^1R^{13})_qNR^{15}R^{16}$; $-(CR^1R^{13})_qNR^{25}R^{26}$; $-(CR^1R^{13})_qNR^{14}R^{27}$;
 5 $-(CH_2)_qC(=NR^{13})NR^{15}R^{16}$; $-(CH_2)_qC(=NOR^{17})NR^{15}R^{16}$;
 $-(CH_2)_qC(=NNR^{15}R^{16})NR^{17}R^{18}$; $-(CR^1R^{13})_qNR^2C(=NR^{17})NR^{15}R^{16}$;
 $-(CR^1R^{13})_qN=C(NR^{15}R^{16})NR^{17}R^{18}$; $-(CR^1R^{13})_qOR^{14}$; $-(CR^1R^{13})_qOR^{25}$;
 $-(CR^1R^{13})_qOR^{27}$; $-(CR^1R^{13})_qSR^{15}$; $-(CR^1R^{13})_qSO_2R^{15}$; $-(CR^1R^{13})_qNR^{14}SO_2R^{15}$;
 $-(CR^1R^{13})_qSO_2NR^{14}R^{18}$; $-(CR^1R^{13})_qNR^{14}SO_2NR^{15}R^{16}$; $-(CR^1R^{13})_qSO_2NR^{15}R^{16}$;
 10 $-(CR^1R^{13})_qPO(OR^1)_2$; $-(CH_2)_nO(CH_2)_mNR^{15}R^{16}$;
 $-(CH_2)_nO(CH_2)_mC(=NR^{17})NR^{15}R^{16}$; $-(CH_2)_nO(CH_2)_mC(=NOR^{17})NR^{15}R^{16}$;
 $-(CH_2)_nO(CH_2)_mC(=NNR^{15}R^{16})NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mNR^1C(=NR^{17})NR^{15}R^{16}$;
 $-(CH_2)_nO(CH_2)_mN=C(NR^{15}R^{16})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mNR^{15}R^{16}$;
 $-(CH_2)_nS(CH_2)_mC(=NR^{17})NR^{15}R^{16}$; $-(CH_2)_nS(CH_2)_mC(=NOR^{17})NR^{15}R^{16}$;
 15 $-(CH_2)_nS(CH_2)_mC(=NNR^{15}R^{16})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mNR^1C(=NR^{17})NR^{15}R^{16}$;
 $-(CH_2)_nS(CH_2)_mN=C(NR^{15}R^{16})NR^{17}R^{18}$; $-(CR^1R^{13})_qCOOR^{15}$; $-(CR^1R^{13})_qCOOR^{25}$;
 $-(CR^1R^{13})_qCOOR^{28}$; $-(CR^1R^{13})_qCONR^{15}R^{16}$; or $-(CR^1R^{13})_qCONR^{25}R^{26}$;
 or alternatively heteroaryl; or heteroarylalkyl;

R²⁵ and R²⁶ are independently

20 H; -CH₃; $-[(CH_2)_2O]_rCH_3$; or $-[(CH_2)_2O]_rCF_3$;

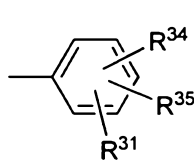
R²⁷ is $-COR^{19}$; $-CO(CR^1R^{13})_oR^{15}$; $-CO(CR^1R^{13})_oOR^{14}$; $-CO(CR^1R^{13})_oNR^{15}R^{16}$;
 $-CO(CR^1R^{13})_oNR^{24}R^{14}$; $-CO(CR^1R^{19})NR^{15}R^{16}$; $-CO(CR^1R^{29})NR^{15}R^{16}$;
 $-CO(CHR^1)_oCONR^{15}R^{16}$; $-CO(CHR^1)_oCONR^2SO_2R^{15}$; $-CO(CR^1R^{13})_oNR^2SO_2R^{15}$;
 $-CONR^1(CHR^{15})_nNR^2(CHR^{13})_mR^{14}$; $-CO(CHR^{15})_nO(CHR^{13})_mR^{14}$;
 25 $-CONR^1(CHR^{15})_nO(CHR^{13})_mR^{14}$; $-SO_2R^{19}$; $-SO_2(CR^1R^{13})_oR^{15}$;
 $-SO_2(CR^1R^{13})_oNR^{15}R^{16}$; or $-SO_2(CR^1R^{13})_oNR^{14}R^{25}$;

R²⁸ is $-NR^1C(R^2)(R^{19})COOR^{15}$; $-NR^1C(R^2)(R^{19})CONR^{15}R^{16}$; $-NR^1C(R^2)(R^{29})COOR^{15}$;
 $-NR^1C(R^2)(R^{29})CONR^{15}R^{16}$;

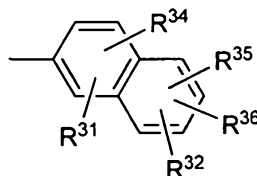
R²⁹ is $-(CR^1R^{13})_qNR^{15}R^{16}$; $-(CH_2)_qC(=NR^{17})NR^{15}R^{16}$; $-(CH_2)_qC(=NOR^{17})NR^{15}R^{16}$;
 30 $-(CH_2)_qC(=NNR^{15}R^{16})NR^{17}R^{18}$; $-(CR^1R^{13})_qNR^2C(=NR^{16})NR^{14}R^{15}$;
 $-(CR^1R^{13})_qN=C(NR^{15}R^{16})NR^{17}R^{18}$; $-(CR^1R^{13})_qOR^{14}$; $-(CR^1R^{13})_qSR^{15}$;

- $-(\text{CR}^1\text{R}^{13})_q\text{SO}_2\text{R}^{15}$; $-(\text{CR}^1\text{R}^{13})_q\text{NR}^{14}\text{SO}_2\text{R}^{15}$; $-(\text{CR}^1\text{R}^{13})_q\text{SO}_2\text{NR}^{14}\text{R}^{14}$;
 $-(\text{CR}^1\text{R}^{13})_q\text{SO}_2\text{NR}^{15}\text{R}^{16}$; $-(\text{CR}^1\text{R}^{13})_q\text{NR}^2\text{SO}_2\text{NR}^{15}\text{R}^{16}$; $-(\text{CR}^1\text{R}^{13})_q\text{PO}(\text{OR}^1)_2$;
 $-(\text{CH}_2)_n\text{O}(\text{CH}_2)_m\text{NR}^{15}\text{R}^{16}$; $-(\text{CH}_2)_n\text{O}(\text{CH}_2)_m\text{C}(=\text{NR}^{17})\text{NR}^{15}\text{R}^{16}$;
 $-(\text{CH}_2)_n\text{O}(\text{CH}_2)_m\text{C}(=\text{NOR}^{17})\text{NR}^{15}\text{R}^{16}$; $-(\text{CH}_2)_n\text{O}(\text{CH}_2)_m\text{C}(=\text{NNR}^{15}\text{R}^{16})\text{NR}^{17}\text{R}^{18}$;
5 $-(\text{CH}_2)_n\text{O}(\text{CH}_2)_m\text{NR}^{14}\text{C}(=\text{NR}^{17})\text{NR}^{15}\text{R}^{16}$; $-(\text{CH}_2)_n\text{O}(\text{CH}_2)_m\text{N}=\text{C}(\text{NR}^{15}\text{R}^{16})\text{NR}^{17}\text{R}^{18}$;
 $-(\text{CH}_2)_n\text{S}(\text{CH}_2)_m\text{NR}^{15}\text{R}^{16}$; $-(\text{CH}_2)_n\text{S}(\text{CH}_2)_m\text{NR}^{15}\text{R}^{16}$;
 $-(\text{CH}_2)_n\text{S}(\text{CH}_2)_m\text{C}(=\text{NR}^{17})\text{NR}^{15}\text{R}^{16}$; $-(\text{CH}_2)_n\text{S}(\text{CH}_2)_m\text{C}(=\text{NOR}^{17})\text{NR}^{15}\text{R}^{16}$;
 $-(\text{CH}_2)_n\text{S}(\text{CH}_2)_m\text{C}(=\text{NNR}^{15}\text{R}^{16})\text{NR}^{17}\text{R}^{18}$; $-(\text{CH}_2)_n\text{S}(\text{CH}_2)_m\text{NR}^{14}\text{C}(=\text{NR}^{17})\text{NR}^{15}\text{R}^{16}$;
 $-(\text{CH}_2)_n\text{S}(\text{CH}_2)_m\text{N}=\text{C}(\text{NR}^{15}\text{R}^{16})\text{NR}^{17}\text{R}^{18}$; $-(\text{CR}^1\text{R}^{13})_q\text{COOR}^{15}$; or
10 $-(\text{CR}^1\text{R}^{13})_q\text{CONR}^{15}\text{R}^{16}$;

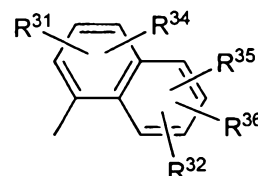
R^{30} is an aryl group of one of the formulae



AR1

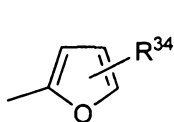


AR2

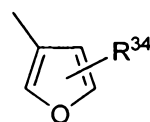


AR3

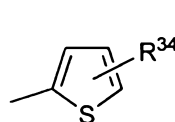
or a heteroaryl group of one of the formulae



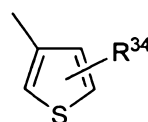
H1



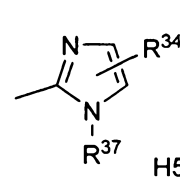
H2



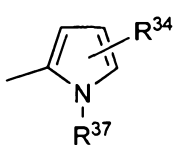
H3



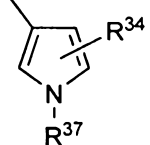
H4



H5



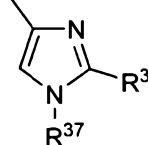
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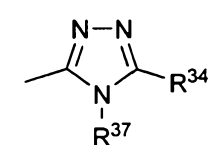
H7



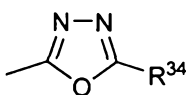
H8



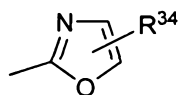
H9



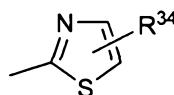
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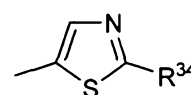
H11



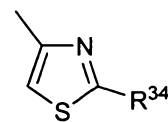
H12



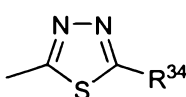
H13



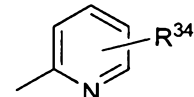
H14



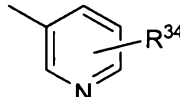
H15



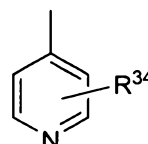
H16



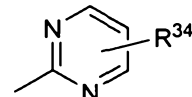
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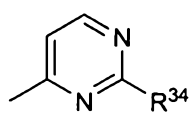
H18



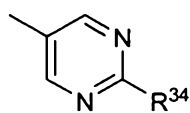
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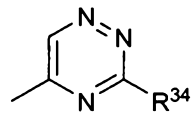
H20



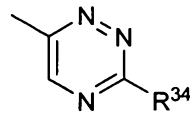
H21



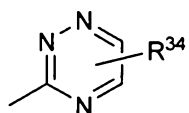
H22



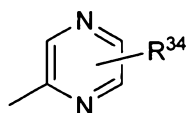
H23



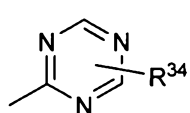
H24



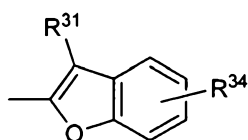
H25



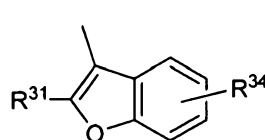
H26



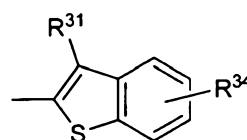
H27



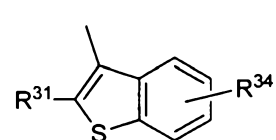
H28



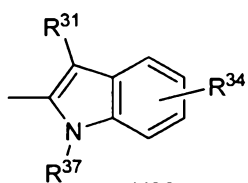
H29



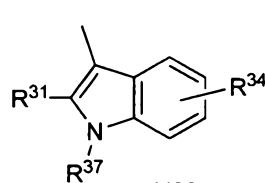
H30



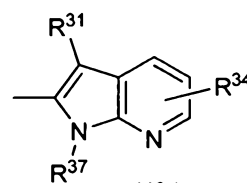
H31



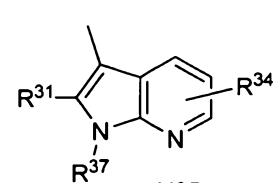
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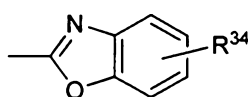
H33



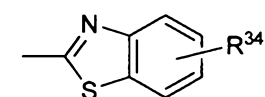
H34



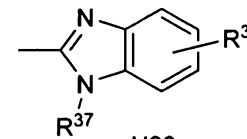
H35



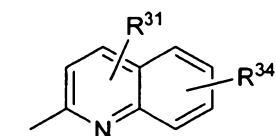
H36



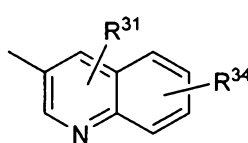
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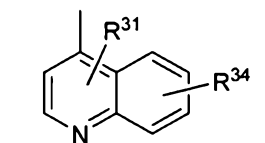
H38



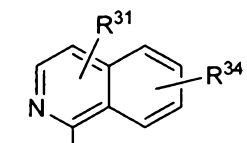
H39



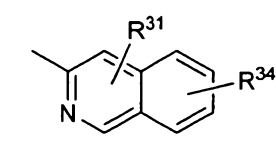
H40



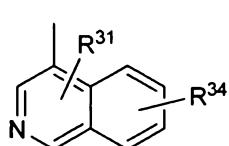
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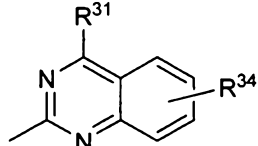
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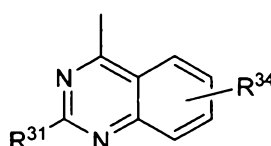
H43



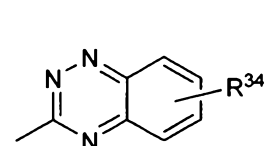
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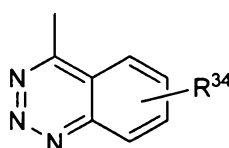
H45



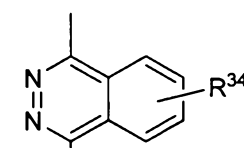
H46



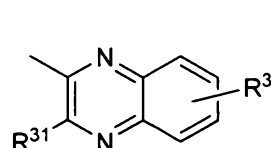
H47



H48



H49

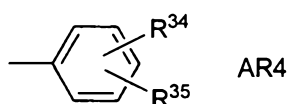


H50

R^{31} and R^{32} are independently

- H; F; Cl; Br; NO_2 ; CN; CF_3 ; OCHF_2 ; OCF_3 ; lower alkyl; lower alkenyl;
 aryl-lower alkyl; aryl; heteroaryl; $-(\text{CH}_2)_o\text{R}^{33}$; $-(\text{CH}_2)_o\text{OR}^{15}$; $-\text{O}(\text{CH}_2)_o\text{R}^{33}$;
 $-(\text{CH}_2)_o\text{SR}^{15}$; $-(\text{CH}_2)_o\text{NR}^{15}\text{R}^{16}$; $-(\text{CH}_2)_o\text{OCONR}^{15}\text{R}^{16}$; $-(\text{CH}_2)_o\text{NR}^1\text{CONR}^{15}\text{R}^{16}$;
 5 $-(\text{CH}_2)_o\text{NR}^1\text{COR}^{15}$; $-(\text{CH}_2)_o\text{COOR}^{15}$; $-(\text{CH}_2)_o\text{CONR}^{15}\text{R}^{16}$; $-(\text{CH}_2)_o\text{PO}(\text{OR}^1)_2$;
 $-(\text{CH}_2)_o\text{SO}_2\text{R}^{14}$; or $-(\text{CH}_2)_o\text{COR}^{15}$;

R^{33} is an aryl group of the formula



R^{34} , R^{35} and R^{36} are independently

- 10 H; F; Cl; Br; OH; NH_2 ; NO_2 ; CN; CF_3 ; OCHF_2 ; OCF_3 ; $-\text{NR}^1\text{R}^{15}$; $-(\text{CH}_2)_o\text{COOR}^{15}$;
 $-(\text{CH}_2)_o\text{CONR}^1\text{R}^{15}$; lower alkyl; lower alkoxy; or lower alkenyl;

R^{37} is H; lower alkyl; or aryl-lower alkyl;

R^{38} , R^{39} , R^{40} and R^{41} are independently

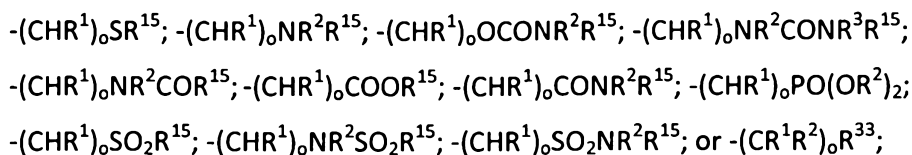
- H; F; CF_3 ; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl; aryl;
 15 heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; $-(\text{CHR}^1)_o\text{OR}^{15}$;
 $-(\text{CHR}^1)_o\text{SR}^{15}$; $-(\text{CHR}^1)_o\text{NR}^2\text{R}^{15}$; $-(\text{CHR}^1)_o\text{OCONR}^2\text{R}^{15}$; $-(\text{CHR}^1)_o\text{NR}^2\text{CONR}^3\text{R}^{15}$;
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 $-(\text{CHR}^1)_o\text{PO}(\text{OR}^2)_2$; $-(\text{CHR}^1)_o\text{SO}_2\text{R}^{15}$; $-(\text{CHR}^1)_o\text{NR}^2\text{SO}_2\text{R}^{15}$; $-(\text{CHR}^1)_o\text{SO}_2\text{NR}^2\text{R}^{15}$;
 $(\text{CR}^1\text{R}^2)_o\text{R}^{33}$; or $-(\text{CHR}^1)_n\text{O}(\text{CHR}^2)_m\text{R}^{33}$;

20 R^{42} and R^{43} are independently

- H; F; CF_3 ; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl; aryl; heteroaryl;
 aryl-lower alkyl; heteroaryl-lower alkyl; $-(\text{CHR}^1)_r\text{OR}^{15}$; $-(\text{CHR}^1)_r\text{SR}^{15}$; -
 $(\text{CHR}^1)_r\text{NR}^2\text{R}^{15}$; $-(\text{CHR}^1)_r\text{OCONR}^2\text{R}^{15}$; $-(\text{CHR}^1)_r\text{NR}^2\text{CONR}^3\text{R}^{15}$;
 $-(\text{CHR}^1)_r\text{NR}^2\text{COR}^{15}$; $-(\text{CHR}^1)_o\text{COOR}^{15}$; $-(\text{CHR}^1)_o\text{CONR}^2\text{R}^{15}$; $-(\text{CHR}^1)_r\text{PO}(\text{OR}^2)_2$; -
 25 $(\text{CHR}^1)_r\text{SO}_2\text{R}^{15}$; $-(\text{CHR}^1)_r\text{NR}^2\text{SO}_2\text{R}^{15}$; $-(\text{CHR}^1)_r\text{SO}_2\text{NR}^2\text{R}^{15}$; $-(\text{CR}^1\text{R}^2)_o\text{R}^{33}$; or
 $-(\text{CHR}^1)_r\text{O}(\text{CHR}^2)_o\text{R}^{33}$;

R^{44} and R^{45} are independently

- H; F; Cl; Br; CF_3 ; OCF_3 ; OCHF_2 ; CN; NO_2 ; lower alkyl; lower alkenyl; aryl;
 heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; $-(\text{CHR}^1)_o\text{OR}^{15}$;



5 n and m are independently an integer of 0-5 with the proviso that $n+m \leq 6$;

o is 0-4; p is 2-6; q is 1-6; r is 1-3;

or pharmaceutically acceptable salts thereof.

Each single group "R^x", with the same index-number x for $x = 1 - 45$ in a specific
 10 formula, is independently selected and, therefore, they are the same or different.

As used in this description, the term "alkyl", taken alone or in combinations (i.e. as part of another group, such as "arylalkyl") designates saturated, straight-chain or branched hydrocarbon radicals having up to 12, preferably up to 8, carbon atoms and may be
 15 optionally substituted. In accordance with a preferred embodiment of the present invention "alkyl" is "lower alkyl" which designated alkyl groups having up to 6 carbon atoms.

The term "alkenyl", taken alone or in combinations, designates straight chain or
 20 branched hydrocarbon radicals having up to 12, preferably up to 8, carbon atoms and containing at least one or, depending on the chain length, up to four olefinic double bonds. Such alkenyl moieties are optionally substituted and can exist as *E* or *Z* configurations, both of which are part of the invention.

25 The term "cycloalkyl", taken alone or in combinations, refers to a saturated or partially unsaturated alicyclic moiety having from three to ten carbon atoms and may be optionally substituted. Examples of this moiety include, but are not limited to, cyclohexyl, norbonyl, decaliny and the like.

30 The term "heterocycloalkyl", taken alone or in combinations, describes a saturated or partially unsaturated mono- or bicyclic moiety having from three to nine ring carbon

atoms and one or more ring heteroatoms selected from nitrogen, oxygen or sulphur. This term includes, for example, morpholino, piperazino, azetidiny, pyrrolidiny, tetrahydrofuranyl, piperidiny, octahydro-1*H*-indolyl, 1,7-diazaspiro[4.4]nonane and the like. Said heterocycloalkyl ring(s) might be optionally substituted.

5

The term "aryl", taken alone or in combinations, designates aromatic carbocyclic hydrocarbon radicals containing one or two six-membered rings, such as phenyl or naphthyl, which may be optionally substituted by up to three substituents such as Br, Cl, F, CF₃, OCF₃, OCHF₂, N(CH₃)₂, NO₂, lower alkyl, lower alkenyl, phenyl or phenoxy.

10

The term "heteroaryl", taken alone or in combinations, designates aromatic heterocyclic radicals containing one or two five- and/or six-membered rings, at least one of them containing up to three heteroatoms selected from the group consisting of O, S and N and whereby the heteroaryl radicals or tautomeric forms thereof may be
15 attached via any suitable atom. Said heteroaryl ring(s) are optionally substituted, e.g. as indicated above for "aryl".

The term "arylalkyl", as used herein, refers to an alkyl group as defined above, substituted by an aryl group, as defined above. Examples of arylalkyl moieties include,
20 but are not limited to, benzyl, 1-phenylethyl, 2-phenylethyl, 3-phenylpropyl, 2-phenylpropyl and the like. Similarly, the term "aryl-lower alkyl", refers to the above moiety but wherein the alkyl group is a "lower alkyl" group.

The term "heteroarylalkyl", as used herein, refers to an alkyl group as defined above,
25 substituted by a heteroaryl group, as defined above. Analogously the term "heteroaryl-lower alkyl", refers to the above moiety but wherein the alkyl group is a "lower alkyl" group.

The term "aryl-cycloalkyl", as used herein, refers to a cycloalkyl group as defined
30 above, substituted or annelated by an aryl group, as defined above. Examples of aryl-

cycloalkyl moieties include, but are not limited to, phenylcyclopentyl, 2,3-dihydro-1*H*-indenyl, 1,2,3,4-tetrahydronaphthalenyl and the like.

The term "aryl-heterocycloalkyl", as used herein, refers to a heterocycloalkyl group as defined above, substituted or annelated by an aryl group, as defined above. Examples of aryl-heterocycloalkyl moieties include, but are not limited to, indolinyl, 1,2,3,4-tetrahydroquinolinyl and the like.

The term "heteroaryl-cycloalkyl", as used herein, refers to a cycloalkyl group as defined above, substituted or annelated by a heteroaryl group, as defined above. Examples of heteroaryl-cycloalkyl moieties include, but are not limited to, 5,6,7,8-tetrahydroquinolinyl and the like.

The term "heteroaryl-heterocycloalkyl", as used herein, refers to a heterocycloalkyl group as defined above, substituted or annelated by a heteroaryl group, as defined above. Examples of heteroaryl-heterocycloalkyl moieties include, but are not limited to, 4-(thiazol-2-yl)piperazinyl, 5,6,7,8-tetrahydro-1,6-naphthyridinyl and the like.

The terms "cycloalkyl-aryl", "heterocycloalkyl-aryl", "cycloalkyl-heteroaryl", and "heterocycloalkyl-heteroaryl", as used herein, are defined analog to the terms "aryl-cycloalkyl", "aryl-heterocycloalkyl", "heteroaryl-cycloalkyl" and "heteroaryl-heterocycloalkyl", as defined above, but connected in the opposite direction, e.g. instead of 4-(thiazol-2-yl)piperazinyl the term refers to 2-(piperazin-1-yl)thiazolyl and the like.

The terms "alkoxy" and "aryloxy", taken alone or in combinations, refer to the groups of -O-Alkyl and -O-Aryl respectively, wherein an alkyl group or an aryl group is as defined above.

The term "optionally substituted" is intended to mean that a group, such as but not limited to alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocycloalkyl, alkoxy and aryl-oxy may be substituted with one or more substituents independently selected from

but not limited to, e.g., amino (-NH₂), dimethylamino, nitro (-NO₂), halogen (F, Cl, Br, I), CF₃, cyano (-CN), hydroxy, methoxy, oxo (=O), carboxy, phenyl, phenyloxy, benzyl, sulfonic acid, sulfate, phosphonic acid, phosphate, or phosphonate etc.

- 5 The term "lower" designates radicals and compounds having up to 6 atoms. Thus, for example, the term "lower alkyl" designates saturated, straight-chain, or branched hydrocarbon radicals having up to 6 carbon atoms, such as methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, *s*-butyl, isobutyl, *t*-butyl, and the like and may be optionally substituted.

10

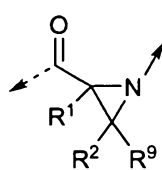
The peptidomimetics of the present invention can also be diastereomers (e.g. epimers) or enantiomers of the compounds of formula (I). These stereoisomers can be prepared by a modification of the process described below in which epimers or enantiomers of chiral starting materials are used. In case of ambiguous stereochemistry in the above
 15 description each single epimer is part of the present invention as well as a mixture of both.

A further embodiment of the present invention may also include compounds, which are identical to the compounds of formula (I), except that one or more atoms are
 20 replaced by an atom having an atomic mass number or mass different from the atomic mass number or mass usually found in nature, e.g. compounds enriched in ²H (D), ³H, ¹¹C, ¹⁴C, ¹²⁷I etc. These isotopic analogs and their pharmaceutical salts and formulations are considered useful agents in the therapy and/or diagnostic, for example, but not limited to, where a fine-tuning of *in vivo* half-life time could lead to an optimized
 25 dosage regimen.

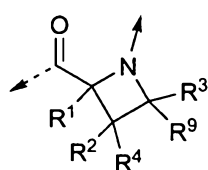
A particular embodiment of the invention relates to derivatives of general formula (I), wherein specifically

T¹ is ^DPro; ^DPip; or ^DAze;

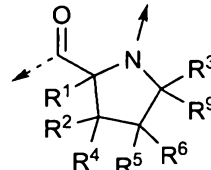
30 T² is an L or D α-amino acid of one of the formulae



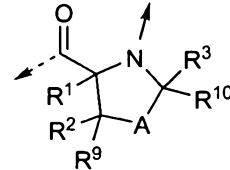
AA1



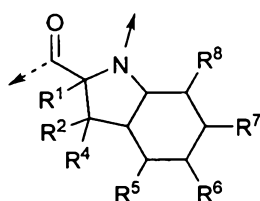
AA2



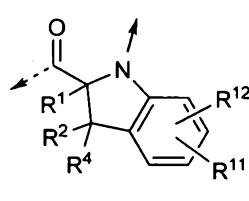
AA3



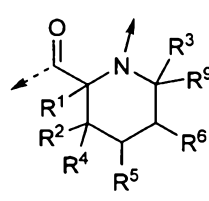
AA4



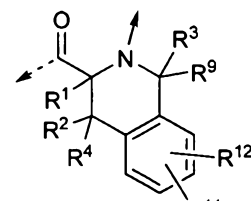
AA5



AA6



AA7



AA8

5

R^{14} is H; CF_3 ; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl;

cycloalkyl-lower alkyl; heterocycloalkyl-lower alkyl; aryl; heteroaryl;

aryl-lower alkyl; heteroaryl-lower alkyl; $-(CHR^1)_3OR^{15}$; $-(CHR^1)_3SR^{15}$;

10 $-(CHR^1)_3NR^{15}R^{16}$; $-(CHR^1)_3COOR^{15}$; $-(CHR^1)_3CONR^{15}R^{16}$; or $-(CHR^1)_3SO_2R^{15}$;

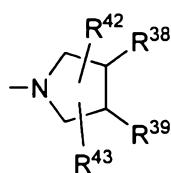
R^{15} , R^{16} , R^{17} and R^{18} are independently

H; lower alkyl; lower alkenyl; lower alkoxy; cycloalkyl; heterocycloalkyl;

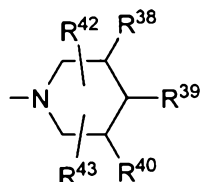
cycloalkyl-lower alkyl; heterocycloalkyl-lower alkyl; aryl; heteroaryl;

aryl-lower alkyl; or heteroaryl-lower alkyl; or

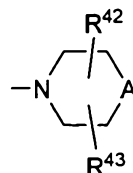
15 the structural elements $-NR^{15}R^{16}$ and $-NR^{17}R^{18}$ can independently form a group of one of the formulae



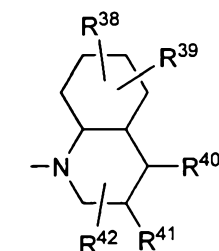
C1



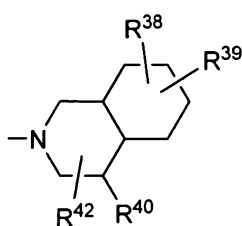
C2



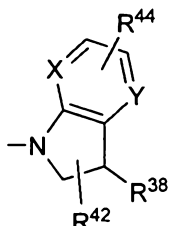
C3



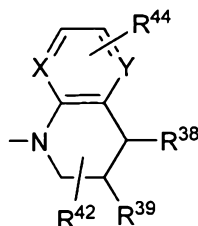
C4



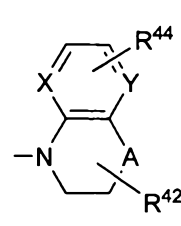
C5



C6



C7



C8

- R^{24} is alkyl; alkenyl; $-(CR^{1R^{13}})_qNR^{15R^{16}}$; $-(CR^{1R^{13}})_qNR^{25R^{26}}$; $-(CR^{1R^{13}})_qNR^{14R^{27}}$;
 $-(CH_2)_qC(=NR^{17})NR^{15R^{16}}$; $-(CR^{1R^{13}})_qNR^2C(=NR^{17})NR^{15R^{16}}$; $-(CR^{1R^{13}})_qOR^{15}$;
 $-(CR^{1R^{13}})_qOR^{25}$; $-(CR^{1R^{13}})_qOR^{27}$; $-(CR^{1R^{13}})_qSR^{15}$; $-(CR^{1R^{13}})_qSO_2R^{15}$;
 $-(CR^{1R^{13}})_qNR^{15}SO_2R^{16}$; $-(CR^{1R^{13}})_qSO_2NR^{1R^{14}}$; $-(CR^{1R^{13}})_qSO_2NR^{15R^{16}}$;
 $-(CH_2)_nO(CH_2)_mNR^{15R^{16}}$; $-(CH_2)_nO(CH_2)_mC(=NR^{17})NR^{15R^{16}}$;
 $-(CH_2)_nO(CH_2)_mNR^1C(=NR^{17})NR^{15R^{16}}$; $-(CH_2)_nO(CH_2)_mN=C(NR^{15R^{16}})NR^{17R^{18}}$;
 $-(CH_2)_nS(CH_2)_mNR^{15R^{16}}$; $-(CR^{1R^{13}})_qCOOR^{15}$; $-(CR^{1R^{13}})_qCOOR^{25}$;
 $-(CR^{1R^{13}})_qCOOR^{28}$; $-(CR^{1R^{13}})_qCONR^{15R^{16}}$; or $-(CR^{1R^{13}})_qCONR^{25R^{26}}$;
 or alternatively heteroaryl; or heteroarylalkyl;

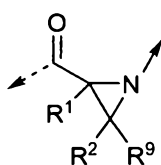
s is 2-4

with all other elements of formula (I) being as described above.

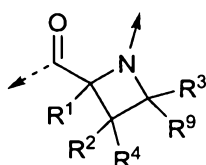
- 15 In another particular embodiment of the invention the elements of general formula (II) are defined as follows

T^1 is ^DPro ; ^DPip ; or ^DAze ;

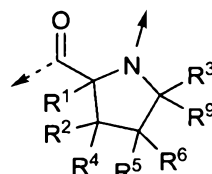
T^2 is an L or D α -amino acid of one of the formulae



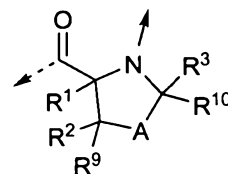
AA1



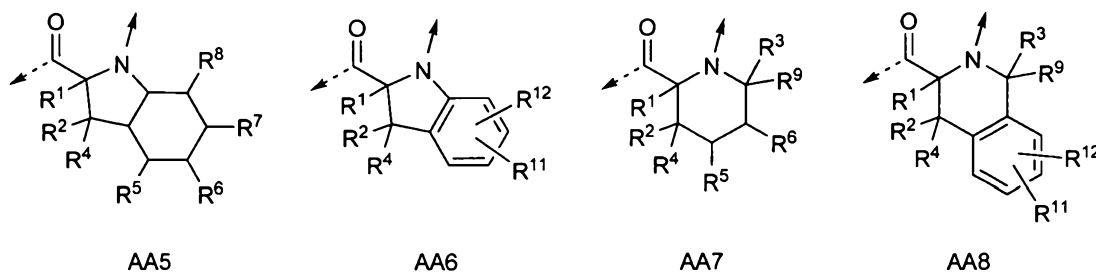
AA2



AA3



AA4



P^1 and P^3 are independently

- 5 His; His(Me); His(Bn); hHis; Phe; Phe(2Cl); Phe(3Cl); Phe(4Cl); Phe(3,4Cl₂);
 Phe(2F); Phe(3F); Phe(4F); Phe(3,4F₂); Phe(3CN); Phe(4CN); Phe(2CF₃);
 Phe(3CF₃); Phe(4CF₃); Phe(3,4(CF₃)₂); Phe(4COOMe); hPhe; Thi; Tza; Trp;
 Trp(5OH); Trp(5Cl); Trp(6Cl); Trp(5,6Cl₂); Trp(5Br); Trp(6Br); Trp(6CF₃);
 Trp(7Aza); hTrp; Tyr; Tyr(Me); Tyr(Ph); Tyr(Bn); Tyr(4OHPh); Tyr(4MeOCOBn);
 10 hTyr; Thr(Bn); Ser(Bn); 2Pal; 3Pal; 4Pal; Phg; Ala(2Furyl); Ala(3Furyl); Ala(2Quin);
 Ala(3Quin); Ala(4Quin); Ala(*t*Bu); Gly(*t*Bu); 1Nal; 2Nal; Nle(6OBn); Cha; hCha;
 Bip; Bbta; or OctG;
- P^2 is Aib; Ac3c; Ac4c; Cyp; Chx; Chx(4oxo); Ac7c; Ac8c; ^DAtc; ^LAtc; ^{DL}Atc; Deg; or 4,4-
 AC-ThioTHP;
- 15 P^4 is Arg; hArg; Ala(Ppz); Thr; *allo*Thr; Gln; Gln(Me); Gln(Me₂); Gln(*i*Pr); Gln(*c*Pr);
 Gln(*i*Bu); Glu(Ala); Glu(^DAla); Glu(Arg); Glu(^DArg); Glu(Glu); Glu(Gly); Glu(His);
 Glu(Leu); Glu(^DLeu); Glu(2Nal); Glu(Sar); Glu(Trp); Glu(^DTrp); Cys; hCys; Ser;
 hSer; Ser(Me); hSer(Me); Thr; Met; Met(O₂); Lys; hLys; Lys(Ac); Lys(Me); Lys(Bz);
 Lys(Nic); Lys(4Oxa); Lys((5*R*)OH); Orn; Dap; Dap(MeO(CH₂)₂); Dap(CONH₂);
 20 Dap((MeO(CH₂)₂)₂); Dab(Sar); Dab; Dab(Ac); Dab(Ala); Dab(^DAla); Dab(Arg);
 Dab(^DArg); Dab(Dab); Dab(Glu); Dab(Gly); Dab(His); Dab(Leu); Dab(^DLeu);
 Dab(MEMCO); Dab(4Me₂NPhSO₂); Dab(MeO(CH₂)₂NHCO);
 Dab((MeO(CH₂)₂)(Me)NCO); Dab(MePpzCO); Dab(MeSO₂); Dab(morphCO);
 Dab(2Nal); Dab(Trp); Dab(^DTrp); Dab(Sar); Gln(Alk1); Gln(Alk2); Gln(Alk3);
 25 Gln(Alk4); Gln(Alk5); Gln(Alk6); Gln(Alk7); Gln(Alk8); Gln(Alk9); Gln(Alk10);
 Gln(Alk11); Gln(Alk12); Gln(Alk13); Gln(Alk14); Gln(Alk15); Gln(Alk16);
 Gln(Alk17); Gln(Alk18); Gln(Alk19); Gln(Alk20); Gln(Alk21); Gln(Alk22);

Gln(Alk23); Gln(Alk24); Gln(Alk25); Gln(Alk26); Gln(Alk27); Gln(Alk28);
Gln(Alk29); Gln(Alk30); Gln(Alk31); Gln(Alk32); Gln(Alk33); Gln(Alk34); Glu(cN1);
Glu(cN2); Glu(cN3); Glu(cN4); Glu(cN5); Glu(cN6); Glu(cN7); Glu(cN8); Glu(cN9);
Glu(cN10); Glu(cN11); Glu(cN12); Glu(cN13); Glu(cN14); Glu(cN15); Glu(cN16);
5 Glu(cN17); Sab(N1); Sab(N2); Sab(N3); Sab(N4); Sab(N5); Sab(N6); Sab(N7);
Sab(N8); Sab(N9); Sab(N10); Sab(N11); Sab(N12); Sab(N13); Sab(N14);
Sab(N15); Sab(N16); Sab(N17); Sab(N18); Sab(N19); Sab(N20); Sab(N21);
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10 Sab(N36); Sab(N37); Sab(N38); Sab(N39); Sab(N40); Sab(N41); Sab(N42);
Sab(N43); Sab(N44); Sab(N45); Sab(N46); Sab(N47); Sab(N48); Sab(N49);
Sab(N50); Sab(N51); Sab(N52); Sab(N53); Sab(N54); Sab(N55); Sab(N56);
Sab(N57); Sab(N58); Sab(N59); Sab(N60); Sab(N61); Dab(SN1); Dab(SN2);
Dab(SN3); Dab(SN4); Dab(SN5); Dab(SN6); Dab(SN7); Dab(SN8); Dab(SN9);
15 Dab(SN10); Dab(SN11); Dab(SN12); Dab(SN13); Dab(SN14); Dab(SN15);
Dab(SN16); Dab(SN17); Dab(SN18); Dab(SN19); Dab(SN20); Dab(SN21);
Dab(SN22); Dab(SN23); Dab(SN24); Dab(SN25); Dab(SN26); Dab(SN27);
Dab(SN28); Dab(SN29); Dab(SN30); Dab(SN31); Dab(SN32); Dab(SN33);
Dab(SN34); Dab(SN35); Dab(SN36); Dab(SN37); Dab(SN38); Dab(SN39);
20 Dab(SN40); Dab(SN41); Dab(SN42); Dab(SN43); Dab(SN44); Dab(SN45);
Dab(SN46); Dab(SN47); Dab(SN48); Dab(SN49); Dab(SN50); Dab(SN51);
Dab(SN52); Dab(SN53); Dab(SN54); Dab(SN55); Dab(SN56); Dab(SN57);
Dab(SN58); Dab(SN59); Dab(SN60); Dab(SN61); Dab(UN1); Dab(UN2);
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Dap(SN10); Dap(SN11); Dap(SN12); Dap(SN13); Dap(SN14); Dap(SN15);
Dap(SN16); Dap(SN17); Dap(SN18); Dap(SN19); Dap(SN20); Dap(SN21);
Dap(SN22); Dap(SN23); Dap(SN24); Dap(SN25); Dap(SN26); Dap(SN27);
Dap(SN28); Dap(SN29); Dap(SN30); Dap(SN31); Dap(SN32); Dap(SN33);
5 Dap(SN34); Dap(SN35); Dap(SN36); Dap(SN37); Dap(SN38); Dap(SN39);
Dap(SN40); Dap(SN41); Dap(SN42); Dap(SN43); Dap(SN44); Dap(SN45);
Dap(SN46); Dap(SN47); Dap(SN48); Dap(SN49); Dap(SN50); Dap(SN51);
Dap(SN52); Dap(SN53); Dap(SN54); Dap(SN55); Dap(SN56); Dap(SN57);
Dap(SN58); Dap(SN59); Dap(SN60); Dap(SN61); Dap(UN1); Dap(UN2);
10 Dap(UN3); Dap(UN4); Dap(UN5); Dap(UN6); Dap(UN7); Dap(UN8); Dap(UN9);
Dap(UN10); Dap(UN11); Dap(UN12); Dap(UN13); Dap(UN14); Dap(UN15);
Dap(UN16); Dap(UN17); Dap(UN18); Dap(UN19); Dap(UN20); Dap(UN21);
Dap(UN22); Dap(UN23); Dap(UN24); Dap(UN25); Dap(UN26); Dap(UN27);
Dap(UN28); Dap(UN29); Dap(UN30); Dap(UN31); Dap(UN32); Dap(UN33);
15 Dap(UN34); Dap(UN35); Dap(UN36); Dap(UN37); Dap(UN38); Dap(UN39);
Dap(UN40); Dap(UN41); Dap(UN42); Dap(UN43); Dap(UN44); Dap(UN45);
Dap(UN46); Dap(UN47); Dap(UN48); Dap(UN49); Dap(UN50); Dap(UN51);
Dap(UN52); Dap(UN53); Dap(UN54); Dap(UN55); Dap(UN56); Dap(UN57);
Dap(UN58); Dap(UN59); Dap(UN60); Dap(UN61); Dap(S1); Dap(S2); Dap(S3);
20 Dap(S4); Dap(S5); Dap(S6); Dap(S7); Dap(S8); Dap(S9); Dap(S10); Dap(S11);
Dap(S12); Dap(S13); Dap(S14); Dap(S15); Dap(S16); Dap(S17); Dap(S18);
Dap(A1); Dap(A2); Dap(A3); Dap(A4); Dap(A5); Dap(A6); Dap(A7); Dap(A8);
Dap(A9); Dap(A10); Dap(A11); Dap(A12); Dap(A13); Dap(A14); Dap(A15);
Dap(A16); Dap(A17); Dap(A18); Dap(A19); Dap(A20); Dap(A21); Dap(A22);
25 Dap(A23); Dap(A24); Dap(A25); Dap(A26); Dap(A27); Dap(A28); Dap(A29);
Dap(A30); Dap(A31); Dap(A32); Dap(A33); Dap(A34); Dap(A35); Dap(A36);
Dap(A37); Dap(A38); Dap(A39); Dap(A40); Dap(A41); Dap(A42); Dap(A43);
Dap(A44); Dap(A45); Dap(A46); Dap(A47); Dap(A48); Dap(A49); Dap(A50);
Dap(A51); Dap(A52); Dap(A53); Dap(A54); Dap(Suc1); Dap(Suc2); Dap(Suc3);
30 Dap(Suc4); Dap(Suc5); Dap(Suc6); Dap(Suc7); Dap(Suc8); Dap(Suc9); or
Dap(Suc10);

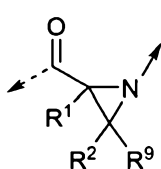
- or alternatively His; His(Me); His(Bn); hHis; Lat; Trp; Trp(5OH); Trp(5Cl); Trp(6Cl);
 Trp(5,6Cl₂); Trp(5Br); Trp(6Br); Trp(6CF₃); Trp(7Aza); hTrp; Tza; 2Pal; 3Pal; 4Pal;
 h2Pal; h3Pal; h4Pal; Ala(1Im); Ala(2Im); hAla(1Im); hAla(2Im); Ala(Pyrazinyl);
 Ala(1Pyrazolyl); Ala(3Pyrazolyl); Ala(2Pyrimidin); Ala(4Pyrimidin); Ala(5Pyrimidin);
 5 Ala(2Quin); Ala(3Quin); or Ala(4Quin);
 or pharmaceutically acceptable salts thereof.

In a further particular embodiment of the invention the elements of general formula (I)

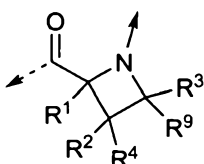
- 10 are defined as follows

T¹ is ^DPro; ^DPip; or ^DAze;

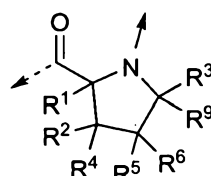
T² is an L or D α-amino acid of one of the formulae



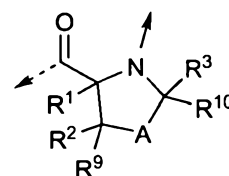
AA1



AA2

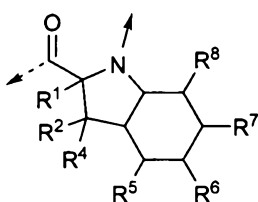


AA3

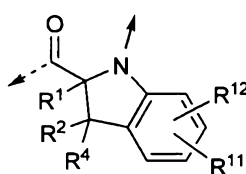


AA4

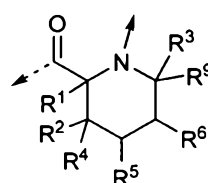
15



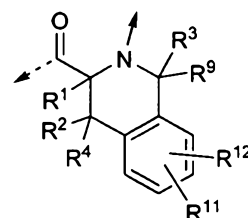
AA5



AA6



AA7



AA8

- 20 P¹ and P³ are independently

His; His(Me); His(Bn); hHis; Phe; Phe(2Cl); Phe(3Cl); Phe(4Cl); Phe(3,4Cl₂);
 Phe(2F); Phe(3F); Phe(4F); Phe(3,4F₂); Phe(3CN); Phe(4CN); Phe(2CF₃);
 Phe(3CF₃); Phe(4CF₃); Phe(3,4(CF₃)₂); Phe(4COOMe); hPhe; Thi; Tza; Trp;
 Trp(5OH); Trp(5Cl); Trp(6Cl); Trp(5,6Cl₂); Trp(5Br); Trp(6Br); Trp(6CF₃);

- Trp(7Aza); hTrp; Tyr; Tyr(Me); Tyr(Ph); Tyr(Bn); Tyr(4OHPh); Tyr(4MeOCOBn);
 hTyr; Thr(Bn); Ser(Bn); 2Pal; 3Pal; 4Pal; Phg; Ala(2Furyl); Ala(3Furyl); Ala(2Quin);
 Ala(3Quin); Ala(4Quin); Ala(tBu); Gly(tBu); 1Nal; 2Nal; Nle(6OBn); Cha; hCha;
 Bip; Bbta; or OctG;
- 5 P² is Aib; Ac3c; Ac4c; Cyp; Chx; Chx(4oxo); Ac7c; Ac8c; ^DAtc; ^LAtc; ^{DL}Atc; Deg; or 4,4-
 AC-ThioTHP;
- P⁴ is Arg; hArg; Ala(Ppz); Thr; *allo*Thr; Gln; Gln(Me); Gln(Me₂); Gln(*i*Pr); Gln(*c*Pr);
 Gln(*i*Bu); Glu(Ala); Glu(^DAla); Glu(Arg); Glu(^DArg); Glu(Glu); Glu(Gly); Glu(His);
 Glu(Leu); Glu(^DLeu); Glu(2Nal); Glu(Sar); Glu(Trp); Glu(^DTrp); Cys; hCys; Ser; hSer;
- 10 Ser(Me); hSer(Me); Thr; Met; Met(O₂); Lys; hLys; Lys(Ac); Lys(Me); Lys(Bz);
 Lys(Nic); Lys(4Oxa); Lys((5*R*)OH); Orn; Dap; Dap(MeO(CH₂)₂); Dap(CONH₂);
 Dap((MeO(CH₂)₂)₂); Dab(Sar); Dab; Dab(Ac); Dab(Ala); Dab(^DAla); Dab(Arg);
 Dab(^DArg); Dab(Dab); Dab(Glu); Dab(Gly); Dab(His); Dab(Leu); Dab(^DLeu);
 Dab(MEMCO); Dab(4Me₂NPhSO₂); Dab(MeO(CH₂)₂NHCO);
- 15 Dab((MeO(CH₂)₂)(Me)NCO); Dab(MePpzCO); Dab(MeSO₂); Dab(morphCO);
 Dab(2Nal); Dab(Trp); Dab(^DTrp); Dab(Sar); or Dab(SN13);
 or alternatively His; His(Me); hHis; 2Pal; 3Pal; 4Pal; h2Pal; h3Pal; h4Pal; Trp;
 Ala(1Im); Ala(2Im); hAla(1Im); hAla(2Im); or Ala(2Pyrimidin);
- or pharmaceutically acceptable salts thereof.

20

In an even further particular embodiment of the invention the elements of general formula (I) are defined as follows

- T¹ is ^DPro; ^DPip; or ^DAze;
- 25 T² is Pro; ^DPro; Oic; Pip; Tic; Tic(7OH); Thz; Thz(5,5Me₂); Pro((4*S*)F); Pro(5,5Me₂);
 Pro((4*S*)cHex); Pro((4*R*)Ph); Pro((4*R*)Bn); Pro((4*R*)4BrBn); Pro((4*R*)3CNBn);
 Hyp(Ph); Hyp(Bn); Hyp(4BrBn); Hyp(3CNBn); Hyp(4CNBn); Hyp(CONHPh); or
 (4*S*)-Hyp(Bn);
- P¹ and P³ are independently
- 30 Phe; Phe(4Cl); Phe(4F); Phe(4CN); Phe(3CF₃); Phe(4CF₃); Phe(4COOMe); Trp;

- Trp(5OH); Trp(6Cl); Tyr; Tyr(Me) Tyr(Ph); Tyr(4OHPh); Tyr(4MeOCOBn); hTyr;
 Ala(2Furyl); Ala(2Quin); 2Nal; Nle(6OBn); ^{DL}Trp(7Aza); Cha; Bip; Bbta; or OctG;
 P² is Aib; Ac3c; Ac4c; Cyp; Chx; Chx(4oxo); Ac7c; Ac8c; ^{DL}Atc; Deg;
 or 4,4-AC-ThioTHP;
 5 P⁴ is Arg; hArg; Ala(Ppz); Thr; *allo*Thr; Gln; Gln(*i*Pr); Gln(*c*Pr); Glu(Ala); Glu(^DAla);
 Glu(Arg); Glu(^DArg); Glu(Glu); Glu(Gly); Glu(His); Glu(Leu); Glu(^DLeu); Glu(2Nal);
 Glu(Sar); Glu(Trp); Glu(^DTrp); Cys; hCys; Ser; hSer; Ser(Me); hSer(Me); Thr; Met;
 Met(O₂); Lys; hLys; Lys(Ac); Lys(Me); Lys(Bz); Lys(Nic); Lys(4Oxa); Lys((5*R*)OH);
 Dap; Dap(MeO(CH₂)₂); Dap(CONH₂); Dap((MeO(CH₂)₂)₂); Dab; Dab(Ac);
 10 Dab(morphCO); Dab(MePpzCO); Dab(MEMCO); Dab(MeO(CH₂)₂NHCO);
 Dab((MeO(CH₂)₂)(Me)NCO); Dab(MeSO₂); Dab(4Me₂NPhSO₂); Dab(Dab); or
 Dab(SN13) ;
 or alternatively His; hHis; 2Pal; 3Pal; or 4Pal;
 or pharmaceutically acceptable salts thereof.

15

Hereinafter follows a list of abbreviations, corresponding to generally adopted usual practice, of amino acids which, or the residues of which, are suitable for the purposes of the present invention and referred to in this document.

- In spite of this specific determination of amino acids, it is noted that, for a person
 20 skilled in the art, it is obvious that derivatives of these amino acids, resembling alike structural and physico-chemical properties, lead to functional analogs with similar biological activity, and therefore still form part of the gist of this invention.

Ala	L-Alanine
Arg	L-Arginine
25 Asn	L-Asparagine
Asp	L-Aspartic acid
Cit	L-Citrulline
Cys	L-Cysteine
Glu	L-Glutamic acid
30 Gln	L-Glutamine
Gly	Glycine

	His	L-Histidine
	Ile	L-Isoleucine
	Leu	L-Leucine
	Lys	L-Lysine
5	Met	L-Methionine
	Orn	L-Ornithine
	Phe	L-Phenylalanine
	Pro	L-Proline
	Ser	L-Serine
10	Thr	L-Threonine
	Trp	L-Tryptophan
	Tyr	L-Tyrosine
	Val	L-Valine
	Ac3c	1-aminocyclopropane carboxylic acid
15	Ac4c	1-aminocyclobutane carboxylic acid
	Ac7c	1-aminocycloheptane carboxylic acid
	Ac8c	1-aminocyclooctane carboxylic acid
	Ala(<i>t</i> Bu)	(<i>S</i>)-2-amino-4,4-dimethylpentanoic acid
	Ala(2Furyl)	(<i>S</i>)-2-amino-3-(furan-2-yl)propanoic acid
20	Ala(3Furyl)	(<i>S</i>)-2-amino-3-(furan-3-yl)propanoic acid
	Ala(1Im)	(<i>S</i>)-2-amino-3-(1H-imidazol-1-yl)propanoic acid
	Ala(2Im)	(<i>S</i>)-2-amino-3-(1H-imidazol-2-yl)propanoic acid
	Ala(Ppz)	(<i>S</i>)-2-amino-3-(piperazin-1-yl)propanoic acid
	Ala(Pyrazinyl)	(<i>S</i>)-2-amino-3-(pyrazin-2-yl)propanoic acid
25	Ala(1Pyrazolyl)	(<i>S</i>)-2-amino-3-(1H-pyrazol-1-yl)propanoic acid
	Ala(3Pyrazolyl)	(<i>S</i>)-2-amino-3-(1H-pyrazol-3-yl)propanoic acid
	Ala(2Pyrimidin)	(<i>S</i>)-2-amino-3-(pyrimidin-2-yl)propanoic acid
	Ala(4Pyrimidin)	(<i>S</i>)-2-amino-3-(pyrimidin-4-yl)propanoic acid
	Ala(5Pyrimidin)	(<i>S</i>)-2-amino-3-(pyrimidin-5-yl)propanoic acid
30	Ala(2Quin)	(<i>S</i>)-2-amino-3-(quinolin-2-yl)propanoic acid
	Ala(3Quin)	(<i>S</i>)-2-amino-3-(quinolin-3-yl)propanoic acid

	Ala(4Quin)	(S)-2-amino-3-(quinolin-4-yl)propanoic acid
	Aib	2-methyl-2-aminopropanoic acid
	^{DL} Atc	(R,S)-2-amino-1,2,3,4-tetrahydronaphthalene-2-carboxylic acid
	Aze	(S)-azetidine-2-carboxylic acid
5	4,4-AC-ThioTHP	4-aminotetrahydro-2H-thiopyran-4-carboxylic acid
	Bbta	(S)-2-amino-3-(1-benzothiophen-3-yl)propanoic acid
	Bip	(S)-2-amino-3-(4-biphenyl)propanoic acid
	Cha	(S)-2-amino-3-cyclohexylpropanoic acid
	Chx	1-aminocyclohexane carboxylic acid
10	Chx(4oxo)	1-amino-4-oxo-cyclohexane carboxylic acid
	Cyp	1-aminocyclopentane carboxylic acid
	Dab	(S)-2,4-diaminobutanoic acid
	Dab(Ac)	(S)-4-acetamido-2-aminobutanoic acid
	Dab(Ala)	(S)-2-amino-4-((S)-2-aminopropanamido)butanoic acid
15	Dab(^D Ala)	(S)-2-amino-4-((R)-2-aminopropanamido)butanoic acid
	Dab(Arg)	(S)-2-amino-4-((S)-2-amino-5-guanidinopentanamido)butanoic acid
	Dab(^D Arg)	(S)-2-amino-4-((R)-2-amino-5-guanidinopentanamido)butanoic acid
	Dab(Dab)	(S)-2-amino-4-((S)-2,4-diaminobutanamido)butanoic acid
20	Dab(Glu)	(S)-4-amino-5-((S)-3-amino-3-carboxypropylamino)-5-oxopentanoic acid
	Dab(Gly)	(S)-2-amino-4-(2-aminoacetamido)butanoic acid
	Dab(His)	(S)-2-amino-4-((S)-2-amino-3-(1H-imidazol-5-yl)-propanamido)butanoic acid
25	Dab(Leu)	(S)-2-amino-4-((S)-2-amino-4-methylpentanamido)butanoic acid
	Dab(^D Leu)	(S)-2-amino-4-((R)-2-amino-4-methylpentanamido)butanoic acid
	Dab(MEMCO)	(S)-2-amino-4-(2-(2-methoxyethoxy)acetamido)butanoic acid
	Dab(4Me ₂ NPhSO ₂)	(S)-2-amino-4-(4-(dimethylamino)phenylsulfonamido)butanoic acid
	Dab(MeO(CH ₂) ₂ NHCO)	(S)-2-amino-4-(3-(2-methoxyethyl)ureido)butanoic acid
30	Dab((MeO(CH ₂) ₂)(Me)NCO)	(S)-2-amino-4-(3-(2-methoxyethyl)-3-methylureido)-butanoic acid

	Dab(MePpzCO)	(S)-2-amino-4-(4-methylpiperazine-1-carboxamido)butanoic acid
	Dab(MeSO ₂)	(S)-2-amino-4-(methylsulfonamido)butanoic acid
	Dab(morphCO)	(S)-2-amino-4-(morpholine-4-carboxamido)butanoic acid
	Dab(2Nal)	(S)-2-amino-4-((S)-2-amino-3-(naphthalen-2-yl)-
5		propanamido)butanoic acid
	Dab(Trp)	(S)-2-amino-4-((S)-2-amino-3-(1 <i>H</i> -indol-3-yl)propanamido)-
		butanoic acid
	Dab(^D Trp)	(S)-2-amino-4-((<i>R</i>)-2-amino-3-(1 <i>H</i> -indol-3-yl)propanamido)-
		butanoic acid
10	Dab(Sar)	(S)-2-amino-4-(2-(methylamino)acetamido)butanoic acid
	Dap	(S)-2,4-diaminopropanoic acid
	Dap(CONH ₂)	(S)-2-amino-3-ureidopropanoic acid
	Dap(MeO(CH ₂) ₂)	(S)-2-amino-3-(2-methoxyethylamino)propanoic acid
	Dap((MeO(CH ₂) ₂) ₂)	(S)-2-amino-3-(bis(2-methoxyethyl)amino)propanoic acid
15	Dab(Sar)	(S)-2-amino-3-(2-(methylamino)acetamido)propanoic acid
	Deg	2-amino-2-ethylbutanoic acid
	Gly(<i>t</i> Bu)	(S)-2-amino-3,3-dimethylbutanoic acid
	Gln(<i>i</i> Bu)	(S)-2-amino-5-(isobutylamino)-5-oxopentanoic acid
	Gln(Me)	(S)-2-amino-5-(methylamino)-5-oxopentanoic acid
20	Gln(Me ₂)	(S)-2-amino-5-(dimethylamino)-5-oxopentanoic acid
	Gln(<i>i</i> Pr)	(S)-2-amino-5-(isopropylamino)-5-oxopentanoic acid
	Gln(<i>c</i> Pr)	(S)-2-amino-5-(cyclopropylamino)-5-oxopentanoic acid
	Glu(Ala)	(S)-2-amino-5-((S)-1-carboxyethylamino)-5-oxopentanoic acid
	Glu(^D Ala)	(S)-2-amino-5-((<i>R</i>)-1-carboxyethylamino)-5-oxopentanoic acid
25	Glu(Arg)	(S)-2-amino-5-((S)-1-carboxy-4-guanidinobutylamino)-5-
		oxopentanoic acid
	Glu(^D Arg)	(S)-2-amino-5-((<i>R</i>)-1-carboxy-4-guanidinobutylamino)-5-
		oxopentanoic acid
	Glu(Glu)	(S)-2-((S)-4-amino-4-carboxybutanamido)pentanedioic acid
30	Glu(Gly)	(S)-2-amino-5-(carboxymethylamino)-5-oxopentanoic acid

	Glu(His)	(S)-2-amino-5-((S)-1-carboxy-2-(1 <i>H</i> -imidazol-5-yl)ethylamino)-5-oxopentanoic acid
	Glu(Leu)	(S)-2-amino-5-((S)-1-carboxy-3-methylbutylamino)-5-oxopentanoic acid
5	Glu(^D Leu)	(S)-2-amino-5-((R)-1-carboxy-3-methylbutylamino)-5-oxopentanoic acid
	Glu(2Nal)	(S)-2-amino-5-((S)-1-carboxy-2-(naphthalen-2-yl)ethylamino)-5-oxopentanoic acid
	Glu(Sar)	(S)-2-amino-5-((carboxymethyl)(methyl)amino)-5-oxopentanoic acid
10	Glu(Trp)	(S)-2-amino-5-((S)-1-carboxy-2-(1 <i>H</i> -indol-3-yl)ethylamino)-5-oxopentanoic acid
	Glu(^D Trp)	(S)-2-amino-5-((R)-1-carboxy-2-(1 <i>H</i> -indol-3-yl)ethylamino)-5-oxopentanoic acid
	hAla(1Im)	(S)-2-amino-3-(1 <i>H</i> -imidazol-1-yl)-butanoic acid
15	hAla(2Im)	(S)-2-amino-3-(1 <i>H</i> -imidazol-2-yl)-butanoic acid
	hArg	(S)-2-amino-6-guanidinohexanoic acid
	hCha	(S)-2-amino-4-cyclohexylbutanoic acid
	hCys	(S)-2-amino-4-mercaptopbutanoic acid
	hHis	(S)-2-amino-4-(1 <i>H</i> -imidazol-5-yl)butanoic acid
20	hLys	(S)-2,7-diaminoheptanoic acid
	h2Pal	(S)-2-amino-4-(pyridin-2-yl)-butanoic acid
	h3Pal	(S)-2-amino-3-(pyridine-3-yl)-butanoic acid
	h4Pal	(S)-2-amino-3-(pyridine-4-yl)-butanoic acid
	hPhe	(S)-2-amino-4-phenylbutanoic acid
25	hSer	(S)-2-amino-4-hydroxybutanoic acid
	hSer(Me)	(S)-2-amino-4-methoxybutanoic acid
	hTrp	(S)-2-amino-4-(1 <i>H</i> -indol-3-yl)butanoic acid
	hTyr	(S)-2-amino-4-(4-hydroxyphenyl)butanoic acid
	His(Me)	(S)-2-amino-3-(1-methyl-1 <i>H</i> -imidazol-5-yl)propanoic acid
30	His(Bn)	(S)-2-amino-3-(1-benzyl-1 <i>H</i> -imidazol-5-yl)propanoic acid
	Hyp(Bn)	(2 <i>S</i> ,4 <i>R</i>)-4-(benzyloxy)pyrrolidine-2-carboxylic acid

	(4 <i>S</i>)-Hyp(Bn)	(2 <i>S</i> ,4 <i>S</i>)-4-(benzyloxy)pyrrolidine-2-carboxylic acid
	Hyp(4BrBn)	(2 <i>S</i> ,4 <i>R</i>)-4-(4-bromobenzyloxy)pyrrolidine-2-carboxylic acid
	Hyp(3CNBn)	(2 <i>S</i> ,4 <i>R</i>)-4-(3-cyanobenzyloxy)pyrrolidine-2-carboxylic acid
	Hyp(4CNBn)	(2 <i>S</i> ,4 <i>R</i>)-4-(4-cyanobenzyloxy)pyrrolidine-2-carboxylic acid
5	Hyp(CONHPh)	(2 <i>S</i> ,4 <i>R</i>)-4-(phenylcarbamoyloxy)pyrrolidine-2-carboxylic acid
	Hyp(Ph)	(2 <i>S</i> ,4 <i>R</i>)-4-phenoxy-pyrrolidine-2-carboxylic acid
	Lat	(<i>S</i>)-2-amino-3-(2-aminopyrimidin-4-yl)propanoic acid
	Lys(Ac)	(<i>S</i>)-6-acetamido-2-amino-hexanoic acid
	Lys(Bz)	(<i>S</i>)-2-amino-6-benzamido-hexanoic acid
10	Lys(Me)	(<i>S</i>)-2-amino-6-(methylamino)hexanoic acid
	Lys(Nic)	(<i>S</i>)-2-amino-6-(nicotinamido)hexanoic acid
	Lys((5 <i>R</i>)OH)	(2 <i>S</i> ,5 <i>R</i>)-2,6-diamino-5-hydroxyhexanoic acid
	Lys(4Oxa)	(<i>S</i>)-2-amino-3-(2-aminoethoxy)propanoic acid
	Met(O ₂)	(<i>S</i>)-2-amino-4-(methylsulfonyl)butanoic acid
15	1Nal	(<i>S</i>)-2-amino-3-naphthalen-1-ylpropanoic acid
	2Nal	(<i>S</i>)-2-amino-3-naphthalen-2-ylpropanoic acid
	Nle	(<i>S</i>)-2-amino-hexanoic acid
	Nle(6OBn)	(<i>S</i>)-2-amino-6-(benzyloxy)hexanoic acid
	OctG	(<i>S</i>)-2-aminodecanoic acid
20	Oic	(2 <i>S</i> ,3 <i>aS</i> ,7 <i>aS</i>)-octahydro-1 <i>H</i> -indole-2-carboxylic acid
	2Pal	(<i>S</i>)-2-amino-3-(pyridine-2-yl) propionic acid
	3Pal	(<i>S</i>)-2-amino-3-(pyridine-3-yl)propionic acid
	4Pal	(<i>S</i>)-2-amino-3-(pyridine-4-yl)propionic acid
	Phe(2Cl)	(<i>S</i>)-2-amino-3-(2-chlorophenyl)propanoic acid
25	Phe(3Cl)	(<i>S</i>)-2-amino-3-(3-chlorophenyl)propanoic acid
	Phe(4Cl)	(<i>S</i>)-2-amino-3-(4-chlorophenyl)propanoic acid
	Phe(3,4Cl ₂)	(<i>S</i>)-2-amino-3-(3,4-dichlorophenyl)propanoic acid
	Phe(2F)	(<i>S</i>)-2-amino-3-(2-fluorophenyl)propanoic acid
	Phe(3F)	(<i>S</i>)-2-amino-3-(3-fluorophenyl)propanoic acid
30	Phe(4F)	(<i>S</i>)-2-amino-3-(4-fluorophenyl)propanoic acid
	Phe(4CN)	(<i>S</i>)-2-amino-3-(4-cyanophenyl)propanoic acid

	Phe(4CF ₃)	(S)-2-amino-3-(4-(trifluoromethyl))propanoic acid
	Phe(4COOMe)	(S)-2-amino-3-(4-(methoxycarbonyl)phenyl)propanoic acid
	Phg	(S)-2-amino-2-phenylacetic acid
	Pip	(S)-piperidine-2-carboxylic acid
5	Pro((4R)4BrBn)	(2S,4R)-4-(4-bromobenzyl)pyrrolidine-2-carboxylic acid
	Pro((4R)Bn)	(2S,4R)-4-benzylpyrrolidine-2-carboxylic acid
	Pro((4R)3CNBn)	(2S,4R)-4-(3-cyanobenzyl)pyrrolidine-2-carboxylic acid
	Pro((4S)F)	(2S,4S)-4-fluoropyrrolidine-2-carboxylic acid
	Pro((4S)cHex)	(2S,4S)-4-cyclohexylpyrrolidine-2-carboxylic acid
10	Pro(5,5Me ₂)	(S)-3,3-dimethylpyrrolidine-2-carboxylic acid
	Pro((4R)Ph)	(2S,4R)-4-phenylpyrrolidine-2-carboxylic acid
	Ser(Bn)	(S)-2-amino-3-(benzyloxy)propanoic acid
	Ser(Me)	(S)-2-amino-3-methoxy-propanoic acid
	Thi	(S)-2-amino-3-(thiophen-2-yl)propanoic acid
15	alloThr	(2S,3S)-2-amino-3-hydroxybutanoic acid
	Thr(Bn)	(2S,3R)-2-amino-3-(benzyloxy)butanoic acid
	Thz	(4R)-1,3-thiazolidine-4-carboxylic acid
	Thz(5,5Me ₂)	(4R)-5,5-dimethyl-1,3-thiazolidine-4-carboxylic acid
	Tic	(3S)-1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid
20	Tic(7OH)	(3S)-7-hydroxy-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid
	^{DL} Trp(7Aza)	(RS)-2-amino-3-(1H-pyrrolo[2,3-b]pyridin-3-yl)propanoic acid
	Trp(5Br)	(S)-2-amino-3-(5-bromo-1H-indol-3-yl)propanoic acid
	Trp(6Br)	(S)-2-amino-3-(6-bromo-1H-indol-3-yl)propanoic acid
	Trp(6CF ₃)	(S)-2-amino-3-(6-(trifluoromethyl)-1H-indol-3-yl)propanoic acid
25	Trp(5Cl)	(S)-2-amino-3-(5-chloro-1H-indol-3-yl)propanoic acid
	Trp(6Cl)	(S)-2-amino-3-(6-chloro-1H-indol-3-yl)propanoic acid
	Trp(5,6Cl)	(S)-2-amino-3-(5,6-dichloro-1H-indol-3-yl)propanoic acid
	Trp(5OH)	(S)-2-amino-3-(5-hydroxy-1H-indol-3-yl)propanoic acid
	Tyr(Bn)	(S)-2-amino-3-(4-(benzyloxy)phenyl)propanoic acid
30	Tyr(Me)	(S)-2-amino-3-(4-methoxyphenyl)propanoic acid

	Tyr(4MeOCOBn)	(S)-2-amino-3-(4-(4-(methoxycarbonyl)benzyloxy)phenyl)-propanoic acid
	Tyr(Ph)	(S)-2-amino-3-(4-phenoxyphenyl)propanoic acid
	Tyr(4OHPh)	(S)-2-amino-3-[4-(4-hydroxyphenoxy)phenyl]propanoic acid
5	Tza	(S)-2-amino-3-(thiazol-4-yl)propanoic acid
	Gln(Alk1)	(S)-2-amino-5-oxo-5-(2,2,2-trifluoroethylamino)pentanoic acid
	Gln(Alk2)	(S)-2-amino-5-(cyclopentylamino)-5-oxopentanoic acid
	Gln(Alk3)	(S)-2-amino-5-(cyclohexylamino)-5-oxopentanoic acid
10	Gln(Alk4)	(S)-2-amino-5-oxo-5-(tetrahydro-2H-pyran-4-ylamino)pentanoic acid
	Gln(Alk5)	(S)-2-amino-5-(2-hydroxyethylamino)-5-oxopentanoic acid
	Gln(Alk6)	(S)-2-amino-5-(2-methoxyethylamino)-5-oxopentanoic acid
	Gln(Alk7)	(S)-2-amino-5-(2-aminoethylamino)-5-oxopentanoic acid
	Gln(Alk8)	(S)-2-amino-5-(2-(dimethylamino)ethylamino)-5-oxopentanoic acid
15	Gln(Alk9)	(S)-2-amino-5-((2-methoxyethyl)(methyl)amino)-5-oxopentanoic acid
	Gln(Alk10)	(S)-2-amino-5-((2-(dimethylamino)ethyl)(methyl)amino)-5-oxopentanoic acid
	Gln(Alk11)	(S)-2-amino-5-(3-aminopropylamino)-5-oxopentanoic acid
	Gln(Alk12)	(S)-2-amino-5-(3-(dimethylamino)propylamino)-5-oxopentanoic acid
20	Gln(Alk13)	(S)-2-amino-5-((3-(dimethylamino)propyl)(methyl)amino)-5-oxopentanoic acid
	Gln(Alk14)	(S)-5-(3-acetamidopropylamino)-2-amino-5-oxopentanoic acid
	Gln(Alk15)	(S)-2-amino-5-oxo-5-(2-(pyrrolidin-1-yl)ethylamino)pentanoic acid
	Gln(Alk16)	(S)-2-amino-5-(2-morpholinoethylamino)-5-oxopentanoic acid
25	Gln(Alk17)	(S)-2-amino-5-(3-morpholinopropylamino)-5-oxopentanoic acid
	Gln(Alk18)	(S)-2-amino-5-(1,3-dihydroxypropan-2-ylamino)-5-oxopentanoic acid
	Gln(Alk19)	(S)-2-amino-5-(4-hydroxy-3-(hydroxymethyl)butylamino)-5-oxopentanoic acid
	Gln(Alk20)	(S)-2-amino-5-oxo-5-(piperidin-4-ylmethylamino)pentanoic acid
30	Gln(Alk21)	(S)-2-amino-5-(methyl((tetrahydro-2H-pyran-4-yl)methyl)amino)-5-oxopentanoic acid

- Gln(Alk22) (2S)-2-amino-5-(methyl(2-(1-methylpyrrolidin-2-yl)ethyl)amino)-5-oxopentanoic acid
- Gln(Alk23) (S)-2-amino-5-oxo-5-(thiazol-2-ylmethylamino)pentanoic acid
- Gln(Alk24) (S)-2-amino-5-((1-methyl-1H-imidazol-4-yl)methylamino)-5-oxopentanoic acid
- 5 Gln(Alk25) (S)-2-amino-5-(benzylamino)-5-oxopentanoic acid
- Gln(Alk26) (S)-2-amino-5-(4-(methylsulfonyl)benzylamino)-5-oxopentanoic acid
- Gln(Alk27) (S)-2-amino-5-oxo-5-(pyridin-3-ylmethylamino)pentanoic acid
- Gln(Alk28) (S)-2-amino-5-oxo-5-(4-(trifluoromethyl)benzylamino)pentanoic acid
- 10 Gln(Alk29) (S)-2-amino-5-(2-methoxybenzylamino)-5-oxopentanoic acid
- Gln(Alk30) (S)-2-amino-5-((1-methyl-1H-benzo[d]imidazol-2-yl)methylamino)-5-oxopentanoic acid
- Gln(Alk31) (S)-2-amino-5-((4-methyl-6-(trifluoromethyl)pyrimidin-2-yl)methylamino)-5-oxopentanoic acid
- 15 Gln(Alk32) (S)-5-(2-(1H-indol-3-yl)ethylamino)-2-amino-5-oxopentanoic acid
- Gln(Alk33) (2S)-2-amino-5-(2,3-dihydro-1H-inden-1-ylamino)-5-oxopentanoic acid
- Gln(Alk34) (2S)-2-amino-5-oxo-5-(1,2,3,4-tetrahydronaphthalen-1-ylamino)-pentanoic acid
- 20 Glu(cN1) (S)-2-amino-5-(azetidin-1-yl)-5-oxopentanoic acid
- Glu(cN2) (S)-2-amino-5-oxo-5-(pyrrolidin-1-yl)pentanoic acid
- Glu(cN3) (S)-2-amino-5-oxo-5-(piperidin-1-yl)pentanoic acid
- Glu(cN4) (S)-2-amino-5-morpholino-5-oxopentanoic acid
- Glu(cN5) (S)-2-amino-5-oxo-5-(piperazin-1-yl)pentanoic acid
- 25 Glu(cN6) (S)-2-amino-5-(4-methylpiperazin-1-yl)-5-oxopentanoic acid
- Glu(cN7) (S)-2-amino-5-(4-hydroxypiperidin-1-yl)-5-oxopentanoic acid
- Glu(cN8) (S)-2-amino-5-(4-(dimethylamino)piperidin-1-yl)-5-oxopentanoic acid
- Glu(cN9) (2S)-2-amino-5-(7-methyl-1,7-diazaspiro[4.4]nonan-1-yl)-5-oxopentanoic acid
- 30 Glu(cN10) (S)-2-amino-5-(indolin-1-yl)-5-oxopentanoic acid
- Glu(cN11) (S)-2-amino-5-(5,6-dihydro-1,7-naphthyridin-7(8H)-yl)-5-oxopentanoic acid

- Glu(cN12) (S)-2-amino-5-(3,4-dihydro-1,5-naphthyridin-1(2H)-yl)-5-oxopentanoic acid
- Glu(cN13) (S)-2-amino-5-(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)-5-oxopentanoic acid
- 5 Glu(cN14) (S)-5-(4-(1H-imidazol-1-yl)piperidin-1-yl)-2-amino-5-oxopentanoic acid
- Glu(cN15) (S)-5-(4-(1H-imidazol-2-yl)piperidin-1-yl)-2-amino-5-oxopentanoic acid
- Glu(cN16) (S)-2-amino-5-(1,4-oxazepan-4-yl)-5-oxopentanoic acid
- Glu(cN17) (S)-2-amino-5-(4-methyl-1,4-diazepan-1-yl)-5-oxopentanoic acid
- 10 Sab(N1) (S)-2-amino-4-sulfamoylbutanoic acid
- Sab(N2) (S)-2-amino-4-(N-methylsulfamoyl)butanoic acid
- Sab(N3) (S)-2-amino-4-(N,N-dimethylsulfamoyl)butanoic acid
- Sab(N4) (S)-2-amino-4-(N-isopropylsulfamoyl)butanoic acid
- Sab(N5) (S)-2-amino-4-(N-cyclopropylsulfamoyl)butanoic acid
- 15 Sab(N6) (S)-2-amino-4-(N-isobutylsulfamoyl)butanoic acid
- Sab(N7) (S)-2-amino-4-(N-(2,2,2-trifluoroethyl)sulfamoyl)butanoic acid
- Sab(N8) (S)-2-amino-4-(azetidin-1-ylsulfonyl)butanoic acid
- Sab(N9) (S)-2-amino-4-(pyrrolidin-1-ylsulfonyl)butanoic acid
- Sab(N10) (S)-2-amino-4-(piperidin-1-ylsulfonyl)butanoic acid
- 20 Sab(N11) (S)-2-amino-4-(morpholinosulfonyl)butanoic acid
- Sab(N12) (S)-2-amino-4-(piperazin-1-ylsulfonyl)butanoic acid
- Sab(N13) (S)-2-amino-4-(4-methylpiperazin-1-ylsulfonyl)butanoic acid
- Sab(N14) (S)-4-(4-acetylpiperazin-1-ylsulfonyl)-2-aminobutanoic acid
- Sab(N15) (S)-2-amino-4-(4-hydroxypiperidin-1-ylsulfonyl)butanoic acid
- 25 Sab(N16) (2S)-2-amino-4-(2-methyl-1-oxo-2,6-diazaspiro[4.5]decan-6-ylsulfonyl)-butanoic acid
- Sab(N17) (S)-2-amino-4-(4-(dimethylamino)piperidin-1-ylsulfonyl)butanoic acid
- Sab(N18) (2S)-2-amino-4-(7-methyl-1,7-diazaspiro[4.4]nonan-1-ylsulfonyl)-butanoic acid
- 30 Sab(N19) (S)-2-amino-4-(2,2-dimethylpyrrolidin-1-ylsulfonyl)butanoic acid
- Sab(N20) (S)-2-amino-4-(N-cyclopentylsulfamoyl)butanoic acid

- Sab(N21) (S)-2-amino-4-(*N*-cyclohexylsulfamoyl)butanoic acid
- Sab(N22) (S)-2-amino-4-(*N*-(tetrahydro-2*H*-pyran-4-yl)sulfamoyl)butanoic acid
- Sab(N23) (S)-2-amino-4-(*N*-(2-hydroxyethyl)sulfamoyl)butanoic acid
- Sab(N24) (S)-2-amino-4-(*N*-(2-methoxyethyl)sulfamoyl)butanoic acid
- 5 Sab(N25) (S)-2-amino-4-(*N*-(2-aminoethyl)sulfamoyl)butanoic acid
- Sab(N26) (S)-2-amino-4-(*N*-(2-(dimethylamino)ethyl)sulfamoyl)butanoic acid
- Sab(N27) (S)-2-amino-4-(*N*-(2-methoxyethyl)-*N*-methylsulfamoyl)butanoic acid
- Sab(N28) (S)-2-amino-4-(*N*-(2-(dimethylamino)ethyl)-*N*-methylsulfamoyl)-
butanoic acid
- 10 Sab(N29) (S)-2-amino-4-(*N*-(3-aminopropyl)sulfamoyl)butanoic acid
- Sab(N30) (S)-2-amino-4-(*N*-(3-(dimethylamino)propyl)sulfamoyl)butanoic acid
- Sab(N31) (S)-2-amino-4-(*N*-(3-(dimethylamino)propyl)-*N*-methylsulfamoyl)-
butanoic acid
- Sab(N32) (S)-4-(*N*-(2-acetamidoethyl)sulfamoyl)-2-aminobutanoic acid
- 15 Sab(N33) (S)-2-amino-4-(*N*-(2-(pyrrolidin-1-yl)ethyl)sulfamoyl)butanoic acid
- Sab(N34) (S)-2-amino-4-(*N*-(2-morpholinoethyl)sulfamoyl)butanoic acid
- Sab(N35) (S)-2-amino-4-(*N*-(3-morpholinopropyl)sulfamoyl)butanoic acid
- Sab(N36) (S)-2-amino-4-(*N*-(1,3-dihydroxypropan-2-yl)sulfamoyl)butanoic acid
- Sab(N37) (S)-2-amino-4-(*N*-(4-hydroxy-3-(hydroxymethyl)butyl)sulfamoyl)-
20 butanoic acid
- Sab(N38) (S)-2-amino-4-(*N*-(piperidin-4-ylmethyl)sulfamoyl)butanoic acid
- Sab(N39) (S)-2-amino-4-(*N*-methyl-*N*-((tetrahydro-2*H*-pyran-4-yl)methyl)-
sulfamoyl)butanoic acid
- Sab(N40) (2*S*)-2-amino-4-(*N*-methyl-*N*-(2-(1-methylpyrrolidin-2-yl)ethyl)-
25 sulfamoyl)-butanoic acid
- Sab(N41) (S)-2-amino-4-(*N*-(thiazol-2-ylmethyl)sulfamoyl)butanoic acid
- Sab(N42) (S)-2-amino-4-(*N*-((1-methyl-1*H*-imidazol-4-yl)methyl)-
sulfamoyl)butanoic acid
- Sab(N43) (S)-2-amino-4-(*N*-benzylsulfamoyl)butanoic acid
- 30 Sab(N44) (S)-2-amino-4-(*N*-(4-(methylsulfonyl)benzyl)sulfamoyl)butanoic acid
- Sab(N45) (S)-2-amino-4-(*N*-(pyridin-3-ylmethyl)sulfamoyl)butanoic acid

	Sab(N46)	(S)-2-amino-4-(N-(4-(trifluoromethyl)benzyl)sulfamoyl)butanoic acid
	Sab(N47)	(S)-2-amino-4-(N-(2-methoxybenzyl)-N-methylsulfamoyl)butanoic acid
	Sab(N48)	(S)-2-amino-4-(N-((1-methyl-1H-benzo[d]imidazol-2-yl)methyl)-sulfamoyl)butanoic acid
5	Sab(N49)	(S)-2-amino-4-(N-((4-methyl-6-(trifluoromethyl)pyrimidin-2-yl)methyl)-sulfamoyl)butanoic acid
	Sab(N50)	(S)-4-(N-(2-(1H-indol-2-yl)ethyl)sulfamoyl)-2-aminobutanoic acid
	Sab(N51)	(S)-2-amino-4-(indolin-1-ylsulfonyl)butanoic acid
	Sab(N52)	(S)-2-amino-4-(5,6-dihydro-1,7-naphthyridin-7(8H)-ylsulfonyl)-
10		butanoic acid
	Sab(N53)	(S)-2-amino-4-(3,4-dihydro-1,5-naphthyridin-1(2H)-ylsulfonyl)-
		butanoic acid
	Sab(N54)	(S)-2-amino-4-(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-ylsulfonyl)-
		butanoic acid
15	Sab(N55)	(S)-4-(4-(1H-imidazol-1-yl)piperidin-1-ylsulfonyl)-2-aminobutanoic acid
	Sab(N56)	(S)-4-(4-(1H-imidazol-2-yl)piperidin-1-ylsulfonyl)-2-aminobutanoic acid
	Sab(N57)	(S)-4-(1,4-oxazepan-4-ylsulfonyl)-2-aminobutanoic acid
	Sab(N58)	(S)-2-amino-4-(4-methyl-1,4-diazepan-1-ylsulfonyl)butanoic acid
	Sab(N59)	(2S)-2-amino-4-(N-(2,3-dihydro-1H-inden-1-yl)sulfamoyl)butanoic acid
20	Sab(N60)	(2S)-2-amino-4-(N-(1,2,3,4-tetrahydronaphthalen-1-yl)sulfamoyl)-
		butanoic acid
	Sab(N61)	(S)-2-amino-4-(4-(2-hydroxyethyl)piperazin-1-ylsulfonyl)butanoic acid
	Dab(SN1)	(S)-2-amino-4-(sulfamoylamino)butanoic acid
25	Dab(SN2)	(S)-2-amino-4-(N-methylsulfamoylamino)butanoic acid
	Dab(SN3)	(S)-2-amino-4-(N,N-dimethylsulfamoylamino)butanoic acid
	Dab(SN4)	(S)-2-amino-4-(N-isopropylsulfamoylamino)butanoic acid
	Dab(SN5)	(S)-2-amino-4-(N-cyclopropylsulfamoylamino)butanoic acid
	Dab(SN6)	(S)-2-amino-4-(N-isobutylsulfamoylamino)butanoic acid
30	Dab(SN7)	(S)-2-amino-4-(N-(2,2,2-trifluoroethyl)sulfamoylamino)butanoic acid
	Dab(SN8)	(S)-2-amino-4-(azetidin-1-ylsulfonylamino)butanoic acid

	Dab(SN9)	(S)-2-amino-4-(pyrrolidin-1-ylsulfonylamino)butanoic acid
	Dab(SN10)	(S)-2-amino-4-(piperidin-1-ylsulfonylamino)butanoic acid
	Dab(SN11)	(S)-2-amino-4-(morpholinosulfonylamino)butanoic acid
	Dab(SN12)	(S)-2-amino-4-(piperazin-1-ylsulfonylamino)butanoic acid
5	Dab(SN13)	(S)-2-amino-4-(4-methylpiperazin-1-ylsulfonylamino)butanoic acid
	Dab(SN14)	(S)-4-(4-acetylpiperazin-1-ylsulfonylamino)-2-aminobutanoic acid
	Dab(SN15)	(S)-2-amino-4-(4-hydroxypiperidin-1-ylsulfonylamino)butanoic acid
	Dab(SN16)	(2S)-2-amino-4-(2-methyl-1-oxo-2,6-diazaspiro[4.5]decan-6-yl-sulfonylamino)butanoic acid
10	Dab(SN17)	(S)-2-amino-4-(4-(dimethylamino)piperidin-1-ylsulfonylamino)-butanoic acid
	Dab(SN18)	(2S)-2-amino-4-(7-methyl-1,7-diazaspiro[4.4]nonan-1-ylsulfonylamino)-butanoic acid
	Dab(SN19)	(S)-2-amino-4-(2,2-dimethylpyrrolidin-1-ylsulfonylamino)butanoic acid
15	Dab(SN20)	(S)-2-amino-4-(<i>N</i> -cyclopentylsulfamoylamino)butanoic acid
	Dab(SN21)	(S)-2-amino-4-(<i>N</i> -cyclohexylsulfamoylamino)butanoic acid
	Dab(SN22)	(S)-2-amino-4-(<i>N</i> -(tetrahydro-2 <i>H</i> -pyran-4-yl)sulfamoylamino)butanoic acid
	Dab(SN23)	(S)-2-amino-4-(<i>N</i> -(2-hydroxyethyl)sulfamoylamino)butanoic acid
	Dab(SN24)	(S)-2-amino-4-(<i>N</i> -(2-methoxyethyl)sulfamoylamino)butanoic acid
20	Dab(SN25)	(S)-2-amino-4-(<i>N</i> -(2-aminoethyl)sulfamoylamino)butanoic acid
	Dab(SN26)	(S)-2-amino-4-(<i>N</i> -(2-(dimethylamino)ethyl)sulfamoylamino)butanoic acid
	Dab(SN27)	(S)-2-amino-4-(<i>N</i> -(2-methoxyethyl)- <i>N</i> -methylsulfamoylamino)-butanoic acid
	Dab(SN28)	(S)-2-amino-4-(<i>N</i> -(2-(dimethylamino)ethyl)- <i>N</i> -methylsulfamoylamino)-butanoic acid
25		
	Dab(SN29)	(S)-2-amino-4-(<i>N</i> -(3-aminopropyl)sulfamoylamino)butanoic acid
	Dab(SN30)	(S)-2-amino-4-(<i>N</i> -(3-(dimethylamino)propyl)sulfamoylamino)butanoic acid
	Dab(SN31)	(S)-2-amino-4-(<i>N</i> -(3-(dimethylamino)propyl)- <i>N</i> -methylsulfamoylamino)-butanoic acid
30	Dab(SN32)	(S)-4-(<i>N</i> -(2-acetamidoethyl)sulfamoylamino)-2-aminobutanoic acid
	Dab(SN33)	(S)-2-amino-4-(<i>N</i> -(2-(pyrrolidin-1-yl)ethyl)sulfamoylamino)butanoic acid

- Dab(SN34) (S)-2-amino-4-(*N*-(2-morpholinoethyl)sulfamoylamino)butanoic acid
- Dab(SN35) (S)-2-amino-4-(*N*-(3-morpholinopropyl)sulfamoylamino)butanoic acid
- Dab(SN36) (S)-2-amino-4-(*N*-(1,3-dihydroxypropan-2-yl)sulfamoylamino)-
butanoic acid
- 5 Dab(SN37) (S)-2-amino-4-(*N*-(4-hydroxy-3-(hydroxymethyl)butyl)-
sulfamoylamino)butanoic acid
- Dab(SN38) (S)-2-amino-4-(*N*-(piperidin-4-ylmethyl)sulfamoylamino)butanoic acid
- Dab(SN39) (S)-2-amino-4-(*N*-methyl-*N*-((tetrahydro-2*H*-pyran-4-yl)methyl)-
sulfamoylamino)butanoic acid
- 10 Dab(SN40) (2*S*)-2-amino-4-(*N*-methyl-*N*-(2-(1-methylpyrrolidin-2-yl)ethyl)-
sulfamoylamino)butanoic acid
- Dab(SN41) (S)-2-amino-4-(*N*-(thiazol-2-ylmethyl)sulfamoylamino)butanoic acid
- Dab(SN42) (S)-2-amino-4-(*N*-((1-methyl-1*H*-imidazol-4-yl)methyl)-
sulfamoylamino)butanoic acid
- 15 Dab(SN43) (S)-2-amino-4-(*N*-benzylsulfamoylamino)butanoic acid
- Dab(SN44) (S)-2-amino-4-(*N*-(4-(methylsulfonyl)benzyl)sulfamoylamino)butanoic acid
- Dab(SN45) (S)-2-amino-4-(*N*-(pyridin-3-ylmethyl)sulfamoylamino)butanoic acid
- Dab(SN46) (S)-2-amino-4-(*N*-(4-(trifluoromethyl)benzyl)sulfamoylamino)butanoic acid
- Dab(SN47) (S)-2-amino-4-(*N*-(2-methoxybenzyl)-*N*-methylsulfamoylamino)-
20 butanoic acid
- Dab(SN48) (S)-2-amino-4-(*N*-((1-methyl-1*H*-benzo[*d*]imidazol-2-yl)methyl)-
sulfamoylamino)butanoic acid
- Dab(SN49) (S)-2-amino-4-(*N*-((4-methyl-6-(trifluoromethyl)pyrimidin-2-yl)methyl)-
sulfamoylamino)butanoic acid
- 25 Dab(SN50) (S)-4-(*N*-(2-(1*H*-indol-2-yl)ethyl)sulfamoylamino)-2-aminobutanoic acid
- Dab(SN51) (S)-2-amino-4-(indolin-1-ylsulfonylamino)butanoic acid
- Dab(SN52) (S)-2-amino-4-(5,6,7,8-tetrahydro-1,7-naphthyridine-7-sulfonamido)-
butanoic acid
- Dab(SN53) (S)-2-amino-4-(1,2,3,4-tetrahydro-1,5-naphthyridine-1-sulfonamido)-
30 butanoic acid

- Dab(SN54) (S)-2-amino-4-(5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrazine-7-sulfonamido)-butanoic acid
- Dab(SN55) (S)-4-(4-(1*H*-imidazol-1-yl)piperidin-1-ylsulfonylamino)-2-aminobutanoic acid
- 5 Dab(SN56) (S)-4-(4-(1*H*-imidazol-2-yl)piperidin-1-ylsulfonylamino)-2-aminobutanoic acid
- Dab(SN57) (S)-4-(1,4-oxazepan-4-ylsulfonylamino)-2-aminobutanoic acid
- Dab(SN58) (S)-2-amino-4-(4-methyl-1,4-diazepan-1-ylsulfonylamino)butanoic acid
- Dab(SN59) (2*S*)-2-amino-4-(*N*-(2,3-dihydro-1*H*-inden-1-ylamino)sulfamoyl)-
- 10 butanoic acid
- Dab(SN60) (2*S*)-2-amino-4-(*N*-(1,2,3,4-tetrahydronaphthalen-1-yl)sulfamoylamino)-butanoic acid
- Dab(SN61) (S)-2-amino-4-(4-(2-hydroxyethyl)piperazine-1-sulfonamido)butanoic acid
- 15 Dab(UN1) (S)-2-amino-4-ureidobutanoic acid
- Dab(UN2) (S)-2-amino-4-(3-methylureido)butanoic acid
- Dab(UN3) (S)-2-amino-4-(3,3-dimethylureido)butanoic acid
- Dab(UN4) (S)-2-amino-4-(3-isopropylureido)butanoic acid
- Dab(UN5) (S)-2-amino-4-(3-cyclopropylureido)butanoic acid
- 20 Dab(UN6) (S)-2-amino-4-(3-isobutylureido)butanoic acid
- Dab(UN7) (S)-2-amino-4-(3-(2,2,2-trifluoroethyl)ureido)butanoic acid
- Dab(UN8) (S)-2-amino-4-(azetidine-1-carboxamido)butanoic acid
- Dab(UN9) (S)-2-amino-4-(pyrrolidine-1-carboxamido)butanoic acid
- Dab(UN10) (S)-2-amino-4-(piperidine-1-carboxamido)butanoic acid
- 25 Dab(UN11) (S)-2-amino-4-(morpholine-4-carboxamido)butanoic acid
- Dab(UN12) (S)-2-amino-4-(piperazine-1-carboxamido)butanoic acid
- Dab(UN13) (S)-2-amino-4-(4-methylpiperazine-1-carboxamido)butanoic acid
- Dab(UN14) (S)-4-(4-acetylpiperazine-1-carboxamido)-2-aminobutanoic acid
- Dab(UN15) (S)-2-amino-4-(4-hydroxypiperidine-1-carboxamido)butanoic acid
- 30 Dab(UN16) (2*S*)-2-amino-4-(2-methyl-1-oxo-2,6-diazaspiro[4.5]decane-6-carboxamido)butanoic acid

- Dab(UN17) (S)-2-amino-4-(4-(dimethylamino)piperidine-1-carboxamido)butanoic acid
- Dab(UN18) (2S)-2-amino-4-(7-methyl-1,7-diazaspiro[4.4]nonane-1-carboxamido)-
butanoic acid
- Dab(UN19) (S)-2-amino-4-(2,2-dimethylpyrrolidine-1-carboxamido)butanoic acid
- 5 Dab(UN20) (S)-2-amino-4-(3-cyclopentylureido)butanoic acid
- Dab(UN21) (S)-2-amino-4-(3-cyclohexylureido)butanoic acid
- Dab(UN22) (S)-2-amino-4-(3-(tetrahydro-2H-pyran-4-yl)ureido)butanoic acid
- Dab(UN23) (S)-2-amino-4-(3-(2-hydroxyethyl)ureido)butanoic acid
- Dab(UN24) (S)-2-amino-4-(3-(2-methoxyethyl)ureido)butanoic acid
- 10 Dab(UN25) (S)-2-amino-4-(3-(2-aminoethyl)ureido)butanoic acid
- Dab(UN26) (S)-2-amino-4-(3-(2-(dimethylamino)ethyl)ureido)butanoic acid
- Dab(UN27) (S)-2-amino-4-(3-(2-methoxyethyl)-N-methylureido)butanoic acid
- Dab(UN28) (S)-2-amino-4-(3-(2-(dimethylamino)ethyl)-N-methylureido)butanoic acid
- Dab(UN29) (S)-2-amino-4-(3-(3-aminopropyl)ureido)butanoic acid
- 15 Dab(UN30) (S)-2-amino-4-(3-(3-(dimethylamino)propyl)ureido)butanoic acid
- Dab(UN31) (S)-2-amino-4-(3-(3-(dimethylamino)propyl)-N-methylureido)butanoic acid
- Dab(UN32) (S)-4-(3-(2-acetamidoethyl)ureido)-2-aminobutanoic acid
- Dab(UN33) (S)-2-amino-4-(3-(2-(pyrrolidin-1-yl)ethyl)ureido)butanoic acid
- Dab(UN34) (S)-2-amino-4-(3-(2-morpholinoethyl)ureido)butanoic acid
- 20 Dab(UN35) (S)-2-amino-4-(3-(3-morpholinopropyl)ureido)butanoic acid
- Dab(UN36) (S)-2-amino-4-(3-(1,3-dihydroxypropan-2-yl)ureido)butanoic acid
- Dab(UN37) (S)-2-amino-4-(3-(4-hydroxy-3-(hydroxymethyl)butyl)ureido)butanoic acid
- Dab(UN38) (S)-2-amino-4-(3-(piperidin-4-ylmethyl)ureido)butanoic acid
- Dab(UN39) (S)-2-amino-4-(3-methyl-3-((tetrahydro-2H-pyran-4-yl)methyl)ureido)-
25 butanoic acid
- Dab(UN40) (2S)-2-amino-4-(3-methyl-3-(2-(1-methylpyrrolidin-2-yl)ethyl)ureido)-
butanoic acid
- Dab(UN41) (S)-2-amino-4-(3-(thiazol-2-ylmethyl)ureido)butanoic acid
- Dab(UN42) (S)-2-amino-4-(3-((1-methyl-1H-imidazol-4-yl)methyl)ureido)butanoic acid
- 30 Dab(UN43) (S)-2-amino-4-(3-benzylureido)butanoic acid
- Dab(UN44) (S)-2-amino-4-(3-(4-(methylsulfonyl)benzyl)ureido)butanoic acid

- Dab(UN45) (S)-2-amino-4-(3-(pyridin-3-ylmethyl)ureido)butanoic acid
- Dab(UN46) (S)-2-amino-4-(3-(4-(trifluoromethyl)benzyl)ureido)butanoic acid
- Dab(UN47) (S)-2-amino-4-(3-(2-methoxybenzyl)-3-methylureido)butanoic acid
- Dab(UN48) (S)-2-amino-4-(3-((1-methyl-1*H*-benzo[*d*]imidazol-2-yl)methyl)ureido)-
5 butanoic acid
- Dab(UN49) (S)-2-amino-4-(3-((4-methyl-6-(trifluoromethyl)pyrimidin-2-yl)methyl)-
ureido)butanoic acid
- Dab(UN50) (S)-4-(3-(2-(1*H*-indol-2-yl)ethyl)ureido)-2-aminobutanoic acid
- Dab(UN51) (S)-2-amino-4-(indoline-1-carboxamido)butanoic acid
- 10 Dab(UN52) (S)-2-amino-4-(5,6,7,8-tetrahydro-1,7-naphthyridine-7-carboxamido)-
butanoic acid
- Dab(UN53) (S)-2-amino-4-(1,2,3,4-tetrahydro-1,5-naphthyridine-1-carboxamido)-
butanoic acid
- Dab(UN54) (S)-2-amino-4-(5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrazine-7-
15 carboxamido)-butanoic acid
- Dab(UN55) (S)-4-(4-(1*H*-imidazol-1-yl)piperidine-1-carboxamido)-2-
aminobutanoic acid
- Dab(UN56) (S)-4-(4-(1*H*-imidazol-2-yl)piperidine-1-carboxamido)-2-
aminobutanoic acid
- 20 Dab(UN57) (S)-4-(1,4-oxazepane-4-carboxamido)-2-aminobutanoic acid
- Dab(UN58) (S)-2-amino-4-(4-methyl-1,4-diazepane-1-carboxamido)butanoic acid
- Dab(UN59) (2*S*)-2-amino-4-(3-(2,3-dihydro-1*H*-inden-1-yl)ureido)butanoic acid
- Dab(UN60) (2*S*)-2-amino-4-(3-(1,2,3,4-tetrahydronaphthalen-1-yl)ureido)-
butanoic acid
- 25 Dab(UN61) (S)-2-amino-4-(4-(2-hydroxyethyl)piperazine-1-carboxamido)butanoic acid
- Dab(S1) (S)-2-amino-4-(methylsulfonamido)butanoic acid
- Dab(S2) (S)-2-amino-4-(ethylsulfonamido)butanoic acid
- Dab(S3) (S)-2-amino-4-(1-methylethylsulfonamido)butanoic acid
- 30 Dab(S4) (S)-2-amino-4-(cyclopropanesulfonamido)butanoic acid
- Dab(S5) (S)-2-amino-4-(2-methylpropylsulfonamido)butanoic acid

	Dab(S6)	(S)-2-amino-4-(2,2,2-trifluoroethylsulfonamido)butanoic acid
	Dab(S7)	(S)-2-amino-4-(cyclopentanesulfonamido)butanoic acid
	Dab(S8)	(S)-2-amino-4-(cyclohexanesulfonamido)butanoic acid
	Dab(S9)	(S)-2-amino-4-(tetrahydro-2H-pyran-4-sulfonamido)butanoic acid
5	Dab(S10)	(S)-2-amino-4-(phenylsulfonamido)butanoic acid
	Dab(S11)	(S)-2-amino-4-(4-aminophenylsulfonamido)butanoic acid
	Dab(S12)	(S)-2-amino-4-(4-(dimethylamino)phenylsulfonamido)butanoic acid
	Dab(S13)	(S)-2-amino-4-(4-morpholinophenylsulfonamido)butanoic acid
	Dab(S14)	(S)-2-amino-4-(4-cyanophenylsulfonamido)butanoic acid
10	Dab(S15)	(S)-2-amino-4-(5-cyanopyridine-2-sulfonamido)butanoic acid
	Dab(S16)	(S)-2-amino-4-(1H-pyrazole-4-sulfonamido)butanoic acid
	Dab(S17)	(S)-2-amino-4-(1H-1,2,4-triazole-5-sulfonamido)butanoic acid
	Dab(S18)	(S)-2-amino-4-(1,1-dimethylethylsulfonamido)butanoic acid
15	Dab(A1)	(S)-4-acetamido-2-aminobutanoic acid
	Dab(A2)	(S)-2-amino-4-propionamidobutanoic acid
	Dab(A3)	(S)-2-amino-4-isobutyramidobutanoic acid
	Dab(A4)	(S)-2-amino-4-(cyclopropanecarboxamido)butanoic acid
	Dab(A5)	(S)-2-amino-4-(3,3,3-trifluoropropanamido)butanoic acid
20	Dab(A6)	(S)-2-amino-4-(4,4,4-trifluorobutanamido)butanoic acid
	Dab(A7)	(S)-2-amino-4-(3-aminopropanamido)butanoic acid
	Dab(A8)	(S)-2-amino-4-(4-aminobutanamido)butanoic acid
	Dab(A9)	(S)-2-amino-4-(5-aminopentanamido)butanoic acid
	Dab(A10)	(S)-2-amino-4-(3-methoxypropanamido)butanoic acid
25	Dab(A11)	(S)-2-amino-4-(3-(methylamino)propanamido)butanoic acid
	Dab(A12)	(S)-2-amino-4-(3-(dimethylamino)propanamido)butanoic acid
	Dab(A13)	(S)-2-amino-4-(3-(phenylamino)propanamido)butanoic acid
	Dab(A14)	(2S)-2-amino-4-(3-aminobutanamido)butanoic acid
	Dab(A15)	(S)-2-amino-4-(3-amino-3-methylbutanamido)butanoic acid
30	Dab(A16)	(S)-2-amino-4-(3-(methylsulfonyl)propanamido)butanoic acid
	Dab(A17)	(S)-2-amino-4-(2-cyclopropylacetamido)butanoic acid

	Dab(A18)	(2S)-2-amino-4-(2-(pyrrolidin-3-yl)acetamido)butanoic acid
	Dab(A19)	(2S)-2-amino-4-(2-(pyrrolidin-2-yl)acetamido)butanoic acid
	Dab(A20)	(S)-2-amino-4-(2-(piperidin-4-yl)acetamido)butanoic acid
	Dab(A21)	(2S)-2-amino-4-(2-(piperidin-3-yl)acetamido)butanoic acid
5	Dab(A22)	(2S)-2-amino-4-(2-(piperidin-2-yl)acetamido)butanoic acid
	Dab(A23)	(S)-2-amino-4-(3-(piperidin-1-yl)propanamido)butanoic acid
	Dab(A24)	(S)-2-amino-4-(3-(piperazin-1-yl)propanamido)butanoic acid
	Dab(A25)	(S)-2-amino-4-(3-(4-methylpiperazin-1-yl)propanamido)butanoic acid
	Dab(A26)	(S)-2-amino-4-(3-morpholinopropanamido)butanoic acid
10	Dab(A27)	(S)-2-amino-4-(2-(1-aminocyclohexyl)acetamido)butanoic acid
	Dab(A28)	(S)-2-amino-4-(2-(4-aminotetrahydro-2H-pyran-4-yl)acetamido)- butanoic acid
	Dab(A29)	(2S)-2-amino-4-(2,2-dimethyl-1,3-dioxolane-4-carboxamido)butanoic acid
	Dab(A30)	(S)-2-amino-4-benzamidobutanoic acid
15	Dab(A31)	(S)-2-amino-4-(isonicotinamido)butanoic acid
	Dab(A32)	(S)-2-amino-4-(nicotinamido)butanoic acid
	Dab(A33)	(S)-2-amino-4-(picolinamido)butanoic acid
	Dab(A34)	(S)-2-amino-4-(6-(trifluoromethyl)nicotinamido)butanoic acid
	Dab(A35)	(S)-2-amino-4-(3-methoxybenzamido)butanoic acid
20	Dab(A36)	(S)-2-amino-4-(3-(difluoromethoxy)benzamido)butanoic acid
	Dab(A37)	(S)-2-amino-4-(4-(methylsulfonyl)benzamido)butanoic acid
	Dab(A38)	(S)-2-amino-4-(benzo[d][1,3]dioxole-5-carboxamido)butanoic acid
	Dab(A39)	(S)-2-amino-4-(2-(pyridin-3-yl)acetamido)butanoic acid
	Dab(A40)	(S)-2-amino-4-(pyrimidine-4-carboxamido)butanoic acid
25	Dab(A41)	(S)-2-amino-4-(3-cyanobenzamido)butanoic acid
	Dab(A42)	(S)-2-amino-4-(thiophene-2-carboxamido)butanoic acid
	Dab(A43)	(S)-2-amino-4-(1-methyl-1H-pyrrole-2-carboxamido)butanoic acid
	Dab(A44)	(S)-2-amino-4-(thiazole-2-carboxamido)butanoic acid
	Dab(A45)	(S)-2-amino-4-(thiazole-4-carboxamido)butanoic acid
30	Dab(A46)	(S)-2-amino-4-(1-methyl-1H-imidazole-2-carboxamido)butanoic acid
	Dab(A47)	(S)-2-amino-4-(1-methyl-1H-imidazole-5-carboxamido)butanoic acid

- Dab(A48) (S)-2-amino-4-(1-methyl-1*H*-indole-2-carboxamido)butanoic acid
- Dab(A49) (S)-2-amino-4-(benzo[*d*]thiazole-2-carboxamido)butanoic acid
- Dab(A50) (S)-2-amino-4-(quinoxaline-2-carboxamido)butanoic acid
- Dab(A51) (S)-4-(3-(1*H*-indol-3-yl)propanamido)-2-aminobutanoic acid
- 5 Dab(A52) (S)-2-amino-4-(2-aminothiazole-4-carboxamido)butanoic acid
- Dab(A53) (S)-2-amino-4-(2-(2-aminothiazol-4-yl)acetamido)butanoic acid
- Dab(A54) (S)-2-amino-4-(4-guanidinobutanamido)butanoic acid
- Dab(A55) (S)-2-amino-4-((1*H*-imidazol-4-yl)methylamino)butanoic acid
- Dab(A56) (S)-2-amino-4-(3-(1-methyl-1*H*-imidazol-5-yl)propanamido)butanoic acid
- 10
- Dab(Suc1) (S)-2-amino-4-(4-(methylamino)-4-oxobutanamido)butanoic acid
- Dab(Suc2) (S)-2-amino-4-(4-(dimethylamino)-4-oxobutanamido)butanoic acid
- Dab(Suc3) (S)-2-amino-4-(4-morpholino-4-oxobutanamido)butanoic acid
- Dab(Suc4) (S)-2-amino-4-(4-oxo-4-(piperazin-1-yl)butanamido)butanoic acid
- 15 Dab(Suc5) (S)-2-amino-4-(4-(4-methylpiperazin-1-yl)-4-oxobutanamido)butanoic acid
- Dab(Suc6) (S)-2-amino-4-(4-(methylsulfonamido)-4-oxobutanamido)butanoic acid
- Dab(Suc7) (S)-2-amino-4-(4-(1,1-dimethylethylsulfonamido)-4-oxobutanamido)-
butanoic acid
- Dab(Suc8) (S)-2-amino-4-(4-oxo-4-(phenylsulfonamido)butanamido)butanoic acid
- 20 Dab(Suc9) (S)-2-amino-4-(4-(4-chloropyridine-3-sulfonamido)-4-oxobutanamido)-
butanoic acid
- Dab(Suc10) (S)-2-amino-4-(4-(naphthalene-2-sulfonamido)-4-oxobutanamido)-
butanoic acid
- 25 Asn(Alk1) (S)-2-amino-4-oxo-4-(2,2,2-trifluoroethylamino)butanoic acid
- Asn(Alk2) (S)-2-amino-4-(cyclopentylamino)-4-oxobutanoic acid
- Asn(Alk3) (S)-2-amino-4-(cyclohexylamino)-4-oxobutanoic acid
- Asn(Alk4) (S)-2-amino-4-oxo-4-(tetrahydro-2*H*-pyran-4-ylamino)butanoic acid
- Asn(Alk5) (S)-2-amino-4-(2-hydroxyethylamino)-4-oxobutanoic acid
- 30 Asn(Alk6) (S)-2-amino-4-(2-methoxyethylamino)-4-oxobutanoic acid
- Asn(Alk7) (S)-2-amino-4-(2-aminoethylamino)-4-oxobutanoic acid

	Asn(Alk8)	(S)-2-amino-4-(2-(dimethylamino)ethylamino)-4-oxobutanoic acid
	Asn(Alk9)	(S)-2-amino-4-((2-methoxyethyl)(methyl)amino)-4-oxobutanoic acid
	Asn(Alk10)	(S)-2-amino-4-((2-(dimethylamino)ethyl)(methyl)amino)-4-oxobutanoic acid
5	Asn(Alk11)	(S)-2-amino-4-(3-aminopropylamino)-4-oxobutanoic acid
	Asn(Alk12)	(S)-2-amino-4-(3-(dimethylamino)propylamino)-4-oxobutanoic acid
	Asn(Alk13)	(S)-2-amino-4-((3-(dimethylamino)propyl)(methyl)amino)-4-oxobutanoic acid
	Asn(Alk14)	(S)-4-(3-acetamidopropylamino)-2-amino-4-oxobutanoic acid
10	Asn(Alk15)	(S)-2-amino-4-oxo-4-(2-(pyrrolidin-1-yl)ethylamino)butanoic acid
	Asn(Alk16)	(S)-2-amino-4-(2-morpholinoethylamino)-4-oxobutanoic acid
	Asn(Alk17)	(S)-2-amino-4-(3-morpholinopropylamino)-4-oxobutanoic acid
	Asn(Alk18)	(S)-2-amino-4-(1,3-dihydroxypropan-2-ylamino)-4-oxobutanoic acid
	Asn(Alk19)	(S)-2-amino-4-(4-hydroxy-3-(hydroxymethyl)butylamino)-4-oxobutanoic acid
15		
	Asn(Alk20)	(S)-2-amino-4-oxo-4-(piperidin-4-ylmethylamino)butanoic acid
	Asn(Alk21)	(S)-2-amino-4-(methyl((tetrahydro-2H-pyran-4-yl)methyl)amino)-4-oxobutanoic acid
	Asn(Alk22)	(2S)-2-amino-4-(methyl(2-(1-methylpyrrolidin-2-yl)ethyl)amino)-4-oxobutanoic acid
20		
	Asn(Alk23)	(S)-2-amino-4-oxo-4-(thiazol-2-ylmethylamino)butanoic acid
	Asn(Alk24)	(S)-2-amino-4-((1-methyl-1H-imidazol-4-yl)methylamino)-4-oxobutanoic acid
	Asn(Alk25)	(S)-2-amino-4-(benzylamino)-4-oxobutanoic acid
25	Asn(Alk26)	(S)-2-amino-4-(4-(methylsulfonyl)benzylamino)-4-oxobutanoic acid
	Asn(Alk27)	(S)-2-amino-4-oxo-4-(pyridin-3-ylmethylamino)butanoic acid
	Asn(Alk28)	(S)-2-amino-4-oxo-4-(4-(trifluoromethyl)benzylamino)butanoic acid
	Asn(Alk29)	(S)-2-amino-4-(2-methoxybenzylamino)-4-oxobutanoic acid
	Asn(Alk30)	(S)-2-amino-4-((1-methyl-1H-benzo[d]imidazol-2-yl)methylamino)-4-oxobutanoic acid
30		

- Asn(Alk31) (S)-2-amino-4-((4-methyl-6-(trifluoromethyl)pyrimidin-2-yl)-methylamino)-4-oxobutanoic acid
- Asn(Alk32) (S)-4-(2-(1*H*-indol-3-yl)ethylamino)-2-amino-4-oxobutanoic acid
- Asn(Alk33) (2*S*)-2-amino-4-(2,3-dihydro-1*H*-inden-1-ylamino)-4-oxobutanoic acid
- 5 Asn(Alk34) (2*S*)-2-amino-4-oxo-4-(1,2,3,4-tetrahydronaphthalen-1-ylamino)-butanoic acid
- Asp(cN1) (S)-2-amino-4-(azetidin-1-yl)-4-oxobutanoic acid
- Asp(cN2) (S)-2-amino-4-oxo-4-(pyrrolidin-1-yl)butanoic acid
- 10 Asp(cN3) (S)-2-amino-4-oxo-4-(piperidin-1-yl)butanoic acid
- Asp(cN4) (S)-2-amino-4-morpholino-4-oxobutanoic acid
- Asp(cN5) (S)-2-amino-4-oxo-4-(piperazin-1-yl)butanoic acid
- Asp(cN6) (S)-2-amino-4-(4-methylpiperazin-1-yl)-4-oxobutanoic acid
- Asp(cN7) (S)-2-amino-4-(4-hydroxypiperidin-1-yl)-4-oxobutanoic acid
- 15 Asp(cN8) (S)-2-amino-4-(4-(dimethylamino)piperidin-1-yl)-4-oxobutanoic acid
- Asp(cN9) (2*S*)-2-amino-4-(7-methyl-1,7-diazaspiro[4.4]nonan-1-yl)-4-oxobutanoic acid
- Asp(cN10) (S)-2-amino-4-(indolin-1-yl)-4-oxobutanoic acid
- Asp(cN11) (S)-2-amino-4-(5,6-dihydro-1,7-naphthyridin-7(8*H*)-yl)-4-oxobutanoic acid
- 20 Asp(cN12) (S)-2-amino-4-(3,4-dihydro-1,5-naphthyridin-1(2*H*)-yl)-4-oxobutanoic acid
- Asp(cN13) (S)-2-amino-4-(5,6-dihydroimidazo[1,2-*a*]pyrazin-7(8*H*)-yl)-4-oxobutanoic acid
- Asp(cN14) (S)-4-(4-(1*H*-imidazol-1-yl)piperidin-1-yl)-2-amino-4-oxobutanoic acid
- Asp(cN15) (S)-4-(4-(1*H*-imidazol-2-yl)piperidin-1-yl)-2-amino-4-oxobutanoic acid
- 25 Asp(cN16) (S)-2-amino-4-(1,4-oxazepan-4-yl)-4-oxobutanoic acid
- Asp(cN17) (S)-2-amino-4-(4-methyl-1,4-diazepan-1-yl)-4-oxobutanoic acid
- Sap(N1) (*R*)-2-amino-3-sulfamoylpropanoic acid
- Sap(N2) (*R*)-2-amino-3-(*N*-methylsulfamoyl)propanoic acid
- 30 Sap(N3) (*R*)-2-amino-3-(*N,N*-dimethylsulfamoyl)propanoic acid
- Sap(N4) (*R*)-2-amino-3-(*N*-isopropylsulfamoyl)propanoic acid

- Sap(N5) (R)-2-amino-3-(N-cyclopropylsulfamoyl)propanoic acid
- Sap(N6) (R)-2-amino-3-(N-isobutylsulfamoyl)propanoic acid
- Sap(N7) (R)-2-amino-3-(N-(2,2,2-trifluoroethyl)sulfamoyl)propanoic acid
- Sap(N8) (R)-2-amino-3-(azetidin-1-ylsulfonyl)propanoic acid
- 5 Sap(N9) (R)-2-amino-3-(pyrrolidin-1-ylsulfonyl)propanoic acid
- Sap(N10) (R)-2-amino-3-(piperidin-1-ylsulfonyl)propanoic acid
- Sap(N11) (R)-2-amino-3-(morpholinosulfonyl)propanoic acid
- Sap(N12) (R)-2-amino-3-(piperazin-1-ylsulfonyl)propanoic acid
- Sap(N13) (R)-2-amino-3-(4-methylpiperazin-1-ylsulfonyl)propanoic acid
- 10 Sap(N14) (R)-3-(4-acetyl piperazin-1-ylsulfonyl)-2-aminopropanoic acid
- Sap(N15) (R)-2-amino-3-(4-hydroxypiperidin-1-ylsulfonyl)propanoic acid
- Sap(N16) (2R)-2-amino-3-(2-methyl-1-oxo-2,6-diazaspiro[4.5]decan-6-ylsulfonyl)-propanoic acid
- Sap(N17) (R)-2-amino-3-(4-(dimethylamino)piperidin-1-ylsulfonyl)propanoic acid
- 15 Sap(N18) (2R)-2-amino-3-(7-methyl-1,7-diazaspiro[4.4]nonan-1-ylsulfonyl)-propanoic acid
- Sap(N19) (R)-2-amino-3-(2,2-dimethylpyrrolidin-1-ylsulfonyl)propanoic acid
- Sap(N20) (R)-2-amino-3-(N-cyclopentylsulfamoyl)propanoic acid
- Sap(N21) (R)-2-amino-3-(N-cyclohexylsulfamoyl)propanoic acid
- 20 Sap(N22) (R)-2-amino-3-(N-(tetrahydro-2H-pyran-4-yl)sulfamoyl)propanoic acid
- Sap(N23) (R)-2-amino-3-(N-(2-hydroxyethyl)sulfamoyl)propanoic acid
- Sap(N24) (R)-2-amino-3-(N-(2-methoxyethyl)sulfamoyl)propanoic acid
- Sap(N25) (R)-2-amino-3-(N-(2-aminoethyl)sulfamoyl)propanoic acid
- Sap(N26) (R)-2-amino-3-(N-(2-(dimethylamino)ethyl)sulfamoyl)propanoic acid
- 25 Sap(N27) (R)-2-amino-3-(N-(2-methoxyethyl)-N-methylsulfamoyl)propanoic acid
- Sap(N28) (R)-2-amino-3-(N-(2-(dimethylamino)ethyl)-N-methylsulfamoyl)-propanoic acid
- Sap(N29) (R)-2-amino-3-(N-(3-aminopropyl)sulfamoyl)propanoic acid
- Sap(N30) (R)-2-amino-3-(N-(3-(dimethylamino)propyl)sulfamoyl)propanoic acid
- 30 Sap(N31) (R)-2-amino-3-(N-(3-(dimethylamino)propyl)-N-methylsulfamoyl)-propanoic acid

	Sap(N32)	(<i>R</i>)-3-(<i>N</i> -(2-acetamidoethyl)sulfamoyl)-2-aminopropanoic acid
	Sap(N33)	(<i>R</i>)-2-amino-3-(<i>N</i> -(2-(pyrrolidin-1-yl)ethyl)sulfamoyl)propanoic acid
	Sap(N34)	(<i>R</i>)-2-amino-3-(<i>N</i> -(2-morpholinoethyl)sulfamoyl)propanoic acid
	Sap(N35)	(<i>R</i>)-2-amino-3-(<i>N</i> -(3-morpholinopropyl)sulfamoyl)propanoic acid
5	Sap(N36)	(<i>R</i>)-2-amino-3-(<i>N</i> -(1,3-dihydroxypropan-2-yl)sulfamoyl)propanoic acid
	Sap(N37)	(<i>R</i>)-2-amino-3-(<i>N</i> -(4-hydroxy-3-(hydroxymethyl)butyl)sulfamoyl)- propanoic acid
	Sap(N38)	(<i>R</i>)-2-amino-3-(<i>N</i> -(piperidin-4-ylmethyl)sulfamoyl)propanoic acid
	Sap(N39)	(<i>R</i>)-2-amino-3-(<i>N</i> -methyl- <i>N</i> -((tetrahydro-2 <i>H</i> -pyran-4-yl)methyl)- sulfamoyl)propanoic acid
10		
	Sap(N40)	(2 <i>R</i>)-2-amino-3-(<i>N</i> -methyl- <i>N</i> -(2-(1-methylpyrrolidin-2-yl)ethyl)- sulfamoyl)propanoic acid
	Sap(N41)	(<i>R</i>)-2-amino-3-(<i>N</i> -(thiazol-2-ylmethyl)sulfamoyl)propanoic acid
	Sap(N42)	(<i>R</i>)-2-amino-3-(<i>N</i> -((1-methyl-1 <i>H</i> -imidazol-4-yl)methyl)sulfamoyl)- propanoic acid
15		
	Sap(N43)	(<i>R</i>)-2-amino-3-(<i>N</i> -benzylsulfamoyl)propanoic acid
	Sap(N44)	(<i>R</i>)-2-amino-3-(<i>N</i> -(4-(methylsulfonyl)benzyl)sulfamoyl)propanoic acid
	Sap(N45)	(<i>R</i>)-2-amino-3-(<i>N</i> -(pyridin-3-ylmethyl)sulfamoyl)propanoic acid
	Sap(N46)	(<i>R</i>)-2-amino-3-(<i>N</i> -(4-(trifluoromethyl)benzyl)sulfamoyl)propanoic acid
20	Sap(N47)	(<i>R</i>)-2-amino-3-(<i>N</i> -(2-methoxybenzyl)- <i>N</i> -methylsulfamoyl)propanoic acid
	Sap(N48)	(<i>R</i>)-2-amino-3-(<i>N</i> -((1-methyl-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-yl)methyl)- sulfamoyl)propanoic acid
	Sap(N49)	(<i>R</i>)-2-amino-3-(<i>N</i> -((4-methyl-6-(trifluoromethyl)pyrimidin-2-yl)methyl)- sulfamoyl)propanoic acid
25	Sap(N50)	(<i>R</i>)-3-(<i>N</i> -(2-(1 <i>H</i> -indol-2-yl)ethyl)sulfamoyl)-2-aminopropanoic acid
	Sap(N51)	(<i>R</i>)-2-amino-3-(indolin-1-ylsulfonyl)propanoic acid
	Sap(N52)	(<i>R</i>)-2-amino-3-(5,6-dihydro-1,7-naphthyridin-7(8 <i>H</i>)-ylsulfonyl)- propanoic acid
	Sap(N53)	(<i>R</i>)-2-amino-3-(3,4-dihydro-1,5-naphthyridin-1(2 <i>H</i>)-ylsulfonyl)- propanoic acid
30		

- Sap(N54) (R)-2-amino-3-(5,6-dihydroimidazo[1,2-*a*]pyrazin-7(8*H*)-ylsulfonyl)-propanoic acid
- Sap(N55) (R)-3-(4-(1*H*-imidazol-1-yl)piperidin-1-ylsulfonyl)-2-aminopropanoic acid
- Sap(N56) (R)-3-(4-(1*H*-imidazol-2-yl)piperidin-1-ylsulfonyl)-2-aminopropanoic acid
- 5 Sap(N57) (R)-3-(1,4-oxazepan-4-ylsulfonyl)-2-aminopropanoic acid
- Sap(N58) (R)-2-amino-3-(4-methyl-1,4-diazepan-1-ylsulfonyl)propanoic acid
- Sap(N59) (2*R*)-2-amino-3-(*N*-(2,3-dihydro-1*H*-inden-1-yl)sulfamoyl)propanoic acid
- Sap(N60) (2*R*)-2-amino-3-(*N*-(1,2,3,4-tetrahydronaphthalen-1-yl)sulfamoyl)-propanoic acid
- 10 Sap(N61) (R)-2-amino-3-(4-(2-hydroxyethyl)piperazin-1-ylsulfonyl)propanoic acid
- Dap(SN1) (S)-2-amino-3-(sulfamoylamino)propanoic acid
- Dap(SN2) (S)-2-amino-3-(*N*-methylsulfamoylamino)propanoic acid
- Dap(SN3) (S)-2-amino-3-(*N,N*-dimethylsulfamoylamino)propanoic acid
- 15 Dap(SN4) (S)-2-amino-3-(*N*-isopropylsulfamoylamino)propanoic acid
- Dap(SN5) (S)-2-amino-3-(*N*-cyclopropylsulfamoylamino)propanoic acid
- Dap(SN6) (S)-2-amino-3-(*N*-isobutylsulfamoylamino)propanoic acid
- Dap(SN7) (S)-2-amino-3-(*N*-(2,2,2-trifluoroethyl)sulfamoylamino)propanoic acid
- Dap(SN8) (S)-2-amino-3-(azetidin-1-ylsulfonylamino)propanoic acid
- 20 Dap(SN9) (S)-2-amino-3-(pyrrolidin-1-ylsulfonylamino)propanoic acid
- Dap(SN10) (S)-2-amino-3-(piperidin-1-ylsulfonylamino)propanoic acid
- Dap(SN11) (S)-2-amino-3-(morpholinosulfonylamino)propanoic acid
- Dap(SN12) (S)-2-amino-3-(piperazin-1-ylsulfonylamino)propanoic acid
- Dap(SN13) (S)-2-amino-3-(4-methylpiperazin-1-ylsulfonylamino)propanoic acid
- 25 Dap(SN14) (S)-3-(4-acetyl piperazin-1-ylsulfonylamino)-2-aminopropanoic acid
- Dap(SN15) (S)-2-amino-3-(4-hydroxypiperidin-1-ylsulfonylamino)propanoic acid
- Dap(SN16) (2*S*)-2-amino-3-(2-methyl-1-oxo-2,6-diazaspiro[4.5]decan-6-yl-sulfonylamino)propanoic acid
- Dap(SN17) (S)-2-amino-3-(4-(dimethylamino)piperidin-1-ylsulfonylamino)-propanoic acid
- 30

- Dap(SN18) (2S)-2-amino-3-(7-methyl-1,7-diazaspiro[4.4]nonan-1-ylsulfonylamino)-propanoic acid
- Dap(SN19) (S)-2-amino-3-(2,2-dimethylpyrrolidin-1-ylsulfonylamino)propanoic acid
- Dap(SN20) (S)-2-amino-3-(N-cyclopentylsulfamoylamino)propanoic acid
- 5 Dap(SN21) (S)-2-amino-3-(N-cyclohexylsulfamoylamino)propanoic acid
- Dap(SN22) (S)-2-amino-3-(N-(tetrahydro-2H-pyran-4-yl)sulfamoylamino)-propanoic acid
- Dap(SN23) (S)-2-amino-3-(N-(2-hydroxyethyl)sulfamoylamino)propanoic acid
- Dap(SN24) (S)-2-amino-3-(N-(2-methoxyethyl)sulfamoylamino)propanoic acid
- 10 Dap(SN25) (S)-2-amino-3-(N-(2-aminoethyl)sulfamoylamino)propanoic acid
- Dap(SN26) (S)-2-amino-3-(N-(2-(dimethylamino)ethyl)sulfamoylamino)propanoic acid
- Dap(SN27) (S)-2-amino-3-(N-(2-methoxyethyl)-N-methylsulfamoylamino)-propanoic acid
- Dap(SN28) (S)-2-amino-3-(N-(2-(dimethylamino)ethyl)-N-methylsulfamoylamino)-propanoic acid
- 15 Dap(SN29) (S)-2-amino-3-(N-(3-aminopropyl)sulfamoylamino)propanoic acid
- Dap(SN30) (S)-2-amino-3-(N-(3-(dimethylamino)propyl)sulfamoylamino)-propanoic acid
- Dap(SN31) (S)-2-amino-3-(N-(3-(dimethylamino)propyl)-N-methylsulfamoylamino)-propanoic acid
- 20 Dap(SN32) (S)-3-(N-(2-acetamidoethyl)sulfamoylamino)-2-aminopropanoic acid
- Dap(SN33) (S)-2-amino-3-(N-(2-(pyrrolidin-1-yl)ethyl)sulfamoylamino)propanoic acid
- Dap(SN34) (S)-2-amino-3-(N-(2-morpholinoethyl)sulfamoylamino)propanoic acid
- Dap(SN35) (S)-2-amino-3-(N-(3-morpholinopropyl)sulfamoylamino)propanoic acid
- 25 Dap(SN36) (S)-2-amino-3-(N-(1,3-dihydroxypropan-2-yl)sulfamoylamino)-propanoic acid
- Dap(SN37) (S)-2-amino-3-(N-(4-hydroxy-3-(hydroxymethyl)butyl)sulfamoylamino)-propanoic acid
- Dap(SN38) (S)-2-amino-3-(N-(piperidin-4-ylmethyl)sulfamoylamino)propanoic acid
- 30 Dap(SN39) (S)-2-amino-3-(N-methyl-N-((tetrahydro-2H-pyran-4-yl)methyl)-sulfamoylamino)propanoic acid

- Dap(SN40) (2*S*)-2-amino-3-(*N*-methyl-*N*-(2-(1-methylpyrrolidin-2-yl)ethyl)-sulfamoylamino)propanoic acid
- Dap(SN41) (*S*)-2-amino-3-(*N*-(thiazol-2-ylmethyl)sulfamoylamino)propanoic acid
- Dap(SN42) (*S*)-2-amino-3-(*N*-((1-methyl-1*H*-imidazol-4-yl)methyl)-sulfamoylamino)propanoic acid
- 5 Dap(SN43) (*S*)-2-amino-3-(*N*-benzylsulfamoylamino)propanoic acid
- Dap(SN44) (*S*)-2-amino-3-(*N*-(4-(methylsulfonyl)benzyl)sulfamoylamino)-propanoic acid
- Dap(SN45) (*S*)-2-amino-3-(*N*-(pyridin-3-ylmethyl)sulfamoylamino)propanoic acid
- 10 Dap(SN46) (*S*)-2-amino-3-(*N*-(4-(trifluoromethyl)benzyl)sulfamoylamino)-propanoic acid
- Dap(SN47) (*S*)-2-amino-3-(*N*-(2-methoxybenzyl)-*N*-methylsulfamoylamino)-propanoic acid
- Dap(SN48) (*S*)-2-amino-3-(*N*-((1-methyl-1*H*-benzo[*d*]imidazol-2-yl)methyl)-sulfamoylamino)propanoic acid
- 15 Dap(SN49) (*S*)-2-amino-3-(*N*-((4-methyl-6-(trifluoromethyl)pyrimidin-2-yl)methyl)-sulfamoylamino)propanoic acid
- Dap(SN50) (*S*)-3-(*N*-(2-(1*H*-indol-2-yl)ethyl)sulfamoylamino)-2-aminopropanoic acid
- Dap(SN51) (*S*)-2-amino-3-(indolin-1-ylsulfonylamino)propanoic acid
- 20 Dap(SN52) (*S*)-2-amino-3-(5,6,7,8-tetrahydro-1,7-naphthyridine-7-sulfonamido)-propanoic acid
- Dap(SN53) (*S*)-2-amino-3-(1,2,3,4-tetrahydro-1,5-naphthyridine-1-sulfonamido)-propanoic acid
- Dap(SN54) (*S*)-2-amino-3-(5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrazine-7-sulfonamido)-propanoic acid
- 25 Dap(SN55) (*S*)-3-(4-(1*H*-imidazol-1-yl)piperidin-1-ylsulfonylamino)-2-amino-propanoic acid
- Dap(SN56) (*S*)-3-(4-(1*H*-imidazol-2-yl)piperidin-1-ylsulfonylamino)-2-amino-propanoic acid
- 30 Dap(SN57) (*S*)-3-(1,4-oxazepan-4-ylsulfonylamino)-2-aminopropanoic acid
- Dap(SN58) (*S*)-2-amino-3-(4-methyl-1,4-diazepan-1-ylsulfonylamino)propanoic acid

- Dap(SN59) (2S)-2-amino-3-(*N*-(2,3-dihydro-1*H*-inden-1-ylamino)sulfamoyl)-propanoic acid
- Dap(SN60) (2S)-2-amino-3-(*N*-(1,2,3,4-tetrahydronaphthalen-1-yl)sulfamoylamino)-propanoic acid
- 5 Dap(SN61) (S)-2-amino-3-(4-(2-hydroxyethyl)piperazine-1-sulfonamido)propanoic acid
- Dap(UN1) (S)-2-amino-3-ureidopropanoic acid
- Dap(UN2) (S)-2-amino-3-(3-methylureido)propanoic acid
- Dap(UN3) (S)-2-amino-3-(3,3-dimethylureido)propanoic acid
- 10 Dap(UN4) (S)-2-amino-3-(3-isopropylureido)propanoic acid
- Dap(UN5) (S)-2-amino-3-(3-cyclopropylureido)propanoic acid
- Dap(UN6) (S)-2-amino-3-(3-isobutylureido)propanoic acid
- Dap(UN7) (S)-2-amino-3-(3-(2,2,2-trifluoroethyl)ureido)propanoic acid
- Dap(UN8) (S)-2-amino-3-(azetidine-1-carboxamido)propanoic acid
- 15 Dap(UN9) (S)-2-amino-3-(pyrrolidine-1-carboxamido)propanoic acid
- Dap(UN10) (S)-2-amino-3-(piperidine-1-carboxamido)propanoic acid
- Dap(UN11) (S)-2-amino-3-(morpholine-4-carboxamido)propanoic acid
- Dap(UN12) (S)-2-amino-3-(piperazine-1-carboxamido)propanoic acid
- Dap(UN13) (S)-2-amino-3-(4-methylpiperazine-1-carboxamido)propanoic acid
- 20 Dap(UN14) (S)-3-(4-acetylpiperazine-1-carboxamido)-2-aminopropanoic acid
- Dap(UN15) (S)-2-amino-3-(4-hydroxypiperidine-1-carboxamido)propanoic acid
- Dap(UN16) (2S)-2-amino-3-(2-methyl-1-oxo-2,6-diazaspiro[4.5]decane-6-carboxamido)propanoic acid
- Dap(UN17) (S)-2-amino-3-(4-(dimethylamino)piperidine-1-carboxamido)-propanoic acid
- 25 Dap(UN18) (2S)-2-amino-3-(7-methyl-1,7-diazaspiro[4.4]nonane-1-carboxamido)-propanoic acid
- Dap(UN19) (S)-2-amino-3-(2,2-dimethylpyrrolidine-1-carboxamido)propanoic acid
- Dap(UN20) (S)-2-amino-3-(3-cyclopentylureido)propanoic acid
- 30 Dap(UN21) (S)-2-amino-3-(3-cyclohexylureido)propanoic acid
- Dap(UN22) (S)-2-amino-3-(3-(tetrahydro-2*H*-pyran-4-yl)ureido)propanoic acid

- Dap(UN23) (S)-2-amino-3-(3-(2-hydroxyethyl)ureido)propanoic acid
- Dap(UN24) (S)-2-amino-3-(3-(2-methoxyethyl)ureido)propanoic acid
- Dap(UN25) (S)-2-amino-3-(3-(2-aminoethyl)ureido)propanoic acid
- Dap(UN26) (S)-2-amino-3-(3-(2-(dimethylamino)ethyl)ureido)propanoic acid
- 5 Dap(UN27) (S)-2-amino-3-(3-(2-methoxyethyl)-3-methylureido)propanoic acid
- Dap(UN28) (S)-2-amino-3-(3-(2-(dimethylamino)ethyl)-3-methylureido)propanoic acid
- Dap(UN29) (S)-2-amino-3-(3-(3-aminopropyl)ureido)propanoic acid
- Dap(UN30) (S)-2-amino-3-(3-(3-(dimethylamino)propyl)ureido)propanoic acid
- Dap(UN31) (S)-2-amino-3-(3-(3-(dimethylamino)propyl)-3-methylureido)-
- 10 propanoic acid
- Dap(UN32) (S)-3-(3-(2-acetamidoethyl)ureido)-2-aminopropanoic acid
- Dap(UN33) (S)-2-amino-3-(3-(2-(pyrrolidin-1-yl)ethyl)ureido)propanoic acid
- Dap(UN34) (S)-2-amino-3-(3-(2-morpholinoethyl)ureido)propanoic acid
- Dap(UN35) (S)-2-amino-3-(3-(3-morpholinopropyl)ureido)propanoic acid
- 15 Dap(UN36) (S)-2-amino-3-(3-(1,3-dihydroxypropan-2-yl)ureido)propanoic acid
- Dap(UN37) (S)-2-amino-3-(3-(4-hydroxy-3-(hydroxymethyl)butyl)ureido)-
- propanoic acid
- Dap(UN38) (S)-2-amino-3-(3-(piperidin-4-ylmethyl)ureido)propanoic acid
- Dap(UN39) (S)-2-amino-3-(3-methyl-3-((tetrahydro-2H-pyran-4-yl)methyl)ureido)-
- 20 propanoic acid
- Dap(UN40) (2S)-2-amino-3-(3-methyl-3-(2-(1-methylpyrrolidin-2-yl)ethyl)ureido)-
- propanoic acid
- Dap(UN41) (S)-2-amino-3-(3-(thiazol-2-ylmethyl)ureido)propanoic acid
- Dap(UN42) (S)-2-amino-3-(3-((1-methyl-1H-imidazol-4-yl)methyl)ureido)-
- 25 propanoic acid
- Dap(UN43) (S)-2-amino-3-(3-benzylureido)propanoic acid
- Dap(UN44) (S)-2-amino-3-(3-(4-(methylsulfonyl)benzyl)ureido)propanoic acid
- Dap(UN45) (S)-2-amino-3-(3-(pyridin-3-ylmethyl)ureido)propanoic acid
- Dap(UN46) (S)-2-amino-3-(3-(4-(trifluoromethyl)benzyl)ureido)propanoic acid
- 30 Dap(UN47) (S)-2-amino-3-(3-(2-methoxybenzyl)-3-methylureido)propanoic acid

- Dap(UN48) (S)-2-amino-3-(3-((1-methyl-1*H*-benzo[*d*]imidazol-2-yl)methyl)ureido)-propanoic acid
- Dap(UN49) (S)-2-amino-3-(3-((4-methyl-6-(trifluoromethyl)pyrimidin-2-yl)methyl)ureido)propanoic acid
- 5 Dap(UN50) (S)-3-(3-(2-(1*H*-indol-2-yl)ethyl)ureido)-2-aminopropanoic acid
- Dap(UN51) (S)-2-amino-3-(indoline-1-carboxamido)propanoic acid
- Dap(UN52) (S)-2-amino-3-(5,6,7,8-tetrahydro-1,7-naphthyridine-7-carboxamido)-propanoic acid
- Dap(UN53) (S)-2-amino-3-(1,2,3,4-tetrahydro-1,5-naphthyridine-1-carboxamido)-propanoic acid
- 10 Dap(UN54) (S)-2-amino-3-(5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrazine-7-carboxamido)-propanoic acid
- Dap(UN55) (S)-3-(4-(1*H*-imidazol-1-yl)piperidine-1-carboxamido)-2-aminopropanoic acid
- 15 Dap(UN56) (S)-3-(4-(1*H*-imidazol-2-yl)piperidine-1-carboxamido)-2-aminopropanoic acid
- Dap(UN57) (S)-3-(1,4-oxazepane-4-carboxamido)-2-aminopropanoic acid
- Dap(UN58) (S)-2-amino-3-(4-methyl-1,4-diazepane-1-carboxamido)propanoic acid
- Dap(UN59) (2*S*)-2-amino-3-(3-(2,3-dihydro-1*H*-inden-1-yl)ureido)propanoic acid
- 20 Dap(UN60) (2*S*)-2-amino-3-(3-(1,2,3,4-tetrahydronaphthalen-1-yl)ureido)-propanoic acid
- Dap(UN61) (S)-2-amino-3-(4-(2-hydroxyethyl)piperazine-1-carboxamido)-propanoic acid
- 25 Dap(S1) (S)-2-amino-3-(methylsulfonamido)propanoic acid
- Dap(S2) (S)-2-amino-3-(ethylsulfonamido)propanoic acid
- Dap(S3) (S)-2-amino-3-(1-methylethylsulfonamido)propanoic acid
- Dap(S4) (S)-2-amino-3-(cyclopropanesulfonamido)propanoic acid
- Dap(S5) (S)-2-amino-3-(2-methylpropylsulfonamido)propanoic acid
- 30 Dap(S6) (S)-2-amino-3-(2,2,2-trifluoroethylsulfonamido)propanoic acid
- Dap(S7) (S)-2-amino-3-(cyclopentanesulfonamido)propanoic acid

	Dap(S8)	(S)-2-amino-3-(cyclohexanesulfonamido)propanoic acid
	Dap(S9)	(S)-2-amino-3-(tetrahydro-2H-pyran-4-sulfonamido)propanoic acid
	Dap(S10)	(S)-2-amino-3-(phenylsulfonamido)propanoic acid
	Dap(S11)	(S)-2-amino-3-(4-aminophenylsulfonamido)propanoic acid
5	Dap(S12)	(S)-2-amino-3-(4-(dimethylamino)phenylsulfonamido)propanoic acid
	Dap(S13)	(S)-2-amino-3-(4-morpholinophenylsulfonamido)propanoic acid
	Dap(S14)	(S)-2-amino-3-(4-cyanophenylsulfonamido)propanoic acid
	Dap(S15)	(S)-2-amino-3-(5-cyanopyridine-2-sulfonamido)propanoic acid
	Dap(S16)	(S)-2-amino-3-(1H-pyrazole-4-sulfonamido)propanoic acid
10	Dap(S17)	(S)-2-amino-3-(1H-1,2,4-triazole-5-sulfonamido)propanoic acid
	Dap(S18)	(S)-2-amino-3-(1,1-dimethylethylsulfonamido)propanoic acid
	Dap(A1)	(S)-3-acetamido-2-aminopropanoic acid
	Dap(A2)	(S)-2-amino-3-propionamidopropanoic acid
15	Dap(A3)	(S)-2-amino-3-isobutyramidopropanoic acid
	Dap(A4)	(S)-2-amino-3-(cyclopropanecarboxamido)propanoic acid
	Dap(A5)	(S)-2-amino-3-(3,3,3-trifluoropropanamido)propanoic acid
	Dap(A6)	(S)-2-amino-3-(4,4,4-trifluorobutanamido)propanoic acid
	Dap(A7)	(S)-2-amino-3-(3-aminopropanamido)propanoic acid
20	Dap(A8)	(S)-2-amino-3-(4-aminobutanamido)propanoic acid
	Dap(A9)	(S)-2-amino-3-(5-aminopentanamido)propanoic acid
	Dap(A10)	(S)-2-amino-3-(3-methoxypropanamido)propanoic acid
	Dap(A11)	(S)-2-amino-3-(3-(methylamino)propanamido)propanoic acid
	Dap(A12)	(S)-2-amino-3-(3-(dimethylamino)propanamido)propanoic acid
25	Dap(A13)	(S)-2-amino-3-(3-(phenylamino)propanamido)propanoic acid
	Dap(A14)	(2S)-2-amino-3-(3-aminobutanamido)propanoic acid
	Dap(A15)	(S)-2-amino-3-(3-amino-3-methylbutanamido)propanoic acid
	Dap(A16)	(S)-2-amino-3-(3-(methylsulfonyl)propanamido)propanoic acid
	Dap(A17)	(S)-2-amino-3-(2-cyclopropylacetamido)propanoic acid
30	Dap(A18)	(2S)-2-amino-3-(2-(pyrrolidin-3-yl)acetamido)propanoic acid
	Dap(A19)	(2S)-2-amino-3-(2-(pyrrolidin-2-yl)acetamido)propanoic acid

	Dap(A20)	(S)-2-amino-3-(2-(piperidin-4-yl)acetamido)propanoic acid
	Dap(A21)	(2S)-2-amino-3-(2-(piperidin-3-yl)acetamido)propanoic acid
	Dap(A22)	(2S)-2-amino-3-(2-(piperidin-2-yl)acetamido)propanoic acid
	Dap(A23)	(S)-2-amino-3-(3-(piperidin-1-yl)propanamido)propanoic acid
5	Dap(A24)	(S)-2-amino-3-(3-(piperazin-1-yl)propanamido)propanoic acid
	Dap(A25)	(S)-2-amino-3-(3-(4-methylpiperazin-1-yl)propanamido)propanoic acid
	Dap(A26)	(S)-2-amino-3-(3-morpholinopropanamido)propanoic acid
	Dap(A27)	(S)-2-amino-3-(2-(1-aminocyclohexyl)acetamido)propanoic acid
	Dap(A28)	(S)-2-amino-3-(2-(4-aminotetrahydro-2H-pyran-4-yl)acetamido)-
10		propanoic acid
	Dap(A29)	(2S)-2-amino-3-(2,2-dimethyl-1,3-dioxolane-4-carboxamido)-
		propanoic acid
	Dap(A30)	(S)-2-amino-3-benzamidopropanoic acid
	Dap(A31)	(S)-2-amino-3-(isonicotinamido)propanoic acid
15	Dap(A32)	(S)-2-amino-3-(nicotinamido)propanoic acid
	Dap(A33)	(S)-2-amino-3-(picolinamido)propanoic acid
	Dap(A34)	(S)-2-amino-3-(6-(trifluoromethyl)nicotinamido)propanoic acid
	Dap(A35)	(S)-2-amino-3-(3-methoxybenzamido)propanoic acid
	Dap(A36)	(S)-2-amino-3-(3-(difluoromethoxy)benzamido)propanoic acid
20	Dap(A37)	(S)-2-amino-3-(4-(methylsulfonyl)benzamido)propanoic acid
	Dap(A38)	(S)-2-amino-3-(benzo[d][1,3]dioxole-5-carboxamido)propanoic acid
	Dap(A39)	(S)-2-amino-3-(2-(pyridin-3-yl)acetamido)propanoic acid
	Dap(A40)	(S)-2-amino-3-(pyrimidine-4-carboxamido)propanoic acid
	Dap(A41)	(S)-2-amino-3-(3-cyanobenzamido)propanoic acid
25	Dap(A42)	(S)-2-amino-3-(thiophene-2-carboxamido)propanoic acid
	Dap(A43)	(S)-2-amino-3-(1-methyl-1H-pyrrole-2-carboxamido)propanoic acid
	Dap(A44)	(S)-2-amino-3-(thiazole-2-carboxamido)propanoic acid
	Dap(A45)	(S)-2-amino-3-(thiazole-4-carboxamido)propanoic acid
	Dap(A46)	(S)-2-amino-3-(1-methyl-1H-imidazole-2-carboxamido)propanoic acid
30	Dap(A47)	(S)-2-amino-3-(1-methyl-1H-imidazole-5-carboxamido)propanoic acid
	Dap(A48)	(S)-2-amino-3-(1-methyl-1H-indole-2-carboxamido)propanoic acid

- Dap(A49) (S)-2-amino-3-(benzo[d]thiazole-2-carboxamido)propanoic acid
- Dap(A50) (S)-2-amino-3-(quinoxaline-2-carboxamido)propanoic acid
- Dap(A51) (S)-3-(3-(1*H*-indol-3-yl)propanamido)-2-aminopropanoic acid
- Dap(A52) (S)-2-amino-3-(2-aminothiazole-4-carboxamido)propanoic acid
- 5 Dap(A53) (S)-2-amino-3-(2-(2-aminothiazol-4-yl)acetamido)propanoic acid
- Dap(A54) (S)-2-amino-3-(4-guanidinobutanamido)propanoic acid
-
- Dap(Suc1) (S)-2-amino-3-(4-(methylamino)-4-oxobutanamido)propanoic acid
- Dap(Suc2) (S)-2-amino-3-(4-(dimethylamino)-4-oxobutanamido)propanoic acid
- 10 Dap(Suc3) (S)-2-amino-3-(4-morpholino-4-oxobutanamido)propanoic acid
- Dap(Suc4) (S)-2-amino-3-(4-oxo-4-(piperazin-1-yl)butanamido)propanoic acid
- Dap(Suc5) (S)-2-amino-3-(4-(4-methylpiperazin-1-yl)-4-oxobutanamido)-
propanoic acid
- Dap(Suc6) (S)-2-amino-3-(4-(methylsulfonamido)-4-oxobutanamido)propanoic acid
- 15 Dap(Suc7) (S)-2-amino-3-(4-(1,1-dimethylethylsulfonamido)-4-oxobutanamido)-
propanoic acid
- Dap(Suc8) (S)-2-amino-3-(4-oxo-4-(phenylsulfonamido)butanamido)propanoic acid
- Dap(Suc9) (S)-2-amino-3-(4-(4-chloropyridine-3-sulfonamido)-4-oxobutanamido)-
propanoic acid
- 20 Dap(Suc10) (S)-2-amino-3-(4-(naphthalene-2-sulfonamido)-4-oxobutanamido)-
propanoic acid

In a preferred embodiment of the invention the β -hairpin peptidomimetics of general
 25 formula (I) are selected from the group consisting of:

- cyclo(-Trp-Aib-Trp-Arg-^DPro-Tic-);
- cyclo(-Trp-Aib-Trp-Dab-^DPro-Tic-);
- cyclo(-Trp-Cyp-Trp-Arg-^DPro-Tic(7OH)-);
- 30 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Pro((4*S*)F)-);
- cyclo(-Trp-Cyp-Trp-Arg-^DPro-Thz-);

- cyclo(-Trp-Cyp-Trp-Dab-^DPro-Thz-);
 cyclo(-Trp(5OH)-Cyp-Trp-Gln-^DPro-Thz-);
 cyclo(-Trp(5OH)-Cyp-Trp-Arg-^DPro-Tic-);
 cyclo(-2Nal-Cyp-Trp-Gln-^DPro-Tic-);
 5 cyclo(-2Nal-Cyp-Trp-Dab-^DPip-Pip-);
 cyclo(-Trp(5OH)-Chx-Trp(5OH)-Arg-^DPro-Oic-);
 cyclo(-Trp(5OH)-Cyp-Trp(5OH)-Dap-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPip-Oic-);
 cyclo(-Trp-Cyp-2Nal-Dab-^DPip-Oic-);
 10 cyclo(-Trp-Cyp-2Nal-Gln-^DPro-Oic-);
 cyclo(-OctG-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Gln-^DPro-Oic-);
 cyclo(-Trp-Chx-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Ac3c-Trp-Dab-^DPro-Oic-);
 15 cyclo(-Trp-Ac4c-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-4,4-AC-ThioTHP-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Phe(4F)-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Tyr(Me)-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Ala(2Quin)-Dab-^DPro-Oic-);
 20 cyclo(-Trp-Cyp-Trp-Arg-^DAze-Tic-);
 cyclo(-Trp-Cyp-Trp-Dab-^DAze-Tic-);
 cyclo(-Cha-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp(5OH)-Cyp-Trp-Arg-^DPro-Thz(5,5Me₂)-);
 25 cyclo(-Trp-Atc-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Ala(2Furyl)-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Phe(4F)-Ser-^DPro-Oic-);
 cyclo(-Trp-Cyp-Phe(4Cl)-Ser-^DPro-Oic-);
 cyclo(-Trp-Cyp-Phe(4CF₃)-Dab-^DPro-Oic-);
 30 cyclo(-Trp-Cyp-DLTrp(7Aza)-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Tyr(Ph)-Dab-^DPro-Oic-);

- cyclo(-Phe(4CF₃)-Cyp-Trp-Dab-^DPip-Pro((4*R*)Ph)-);
cyclo(-Trp-Cyp-Trp-Dab-^DPro-Pro((4*R*)Bn)-);
cyclo(-Trp-Cyp-Trp-Dab-^DPro-Pro((4*R*)4BrBn)-);
cyclo(-Trp-Cyp-Trp-Dab-^DPro-Pro((4*R*)3CNBn)-);
5 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Pro((4*S*)cHex)-);
cyclo(-Trp-Cyp-Trp-Dab-^DPro-Pro(5,5Me₂)-);
cyclo(-Trp-Cyp-Phe(4Cl)-Dab-^DPro-Hyp(Bn)-);
cyclo(-Phe(4CN)-Cyp-Phe(4F)-Ser-^DPro-Hyp(Bn)-);
cyclo(-Trp-Cyp-Trp-Dab-^DPro-Hyp(Bn)-);
10 cyclo(-Trp-Cyp-Trp-Ser-^DPro-Hyp(Bn)-);
cyclo(-Phe(4CN)-Cyp-Trp-Gln-^DPro-Hyp(Bn)-);
cyclo(-Trp(6Cl)-Cyp-Trp-Dab-^DPro-Hyp(Bn)-);
cyclo(-Phe(4CN)-Cyp-Trp-Dab-^DPro-Hyp(Bn)-);
cyclo(-Phe(4CN)-Cyp-Trp-Ser-^DPip-Hyp(Bn)-);
15 cyclo(-Trp-Cyp-Trp-Dab-^DPro-(4*S*)-Hyp(Bn)-);
cyclo(-Trp-Cyp-Trp-Dab-^DPro-Hyp(Ph)-);
cyclo(-Trp-Cyp-Trp-Dab-^DPro-Hyp(4CNBn)-);
cyclo(-Phe(4CF₃)-Cyp-Trp-Dab-^DPro-Hyp(4BrBn)-);
cyclo(-Phe(4CN)-Cyp-Trp-Ser-^DPro-Hyp(4BrBn)-);
20 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Hyp(4BrBn)-);
cyclo(-Trp-Cyp-Trp-Dab-^DPro-Hyp(CONHPh)-);
cyclo(-Trp-Cyp-Trp-alloThr-^DPro-Oic-);
cyclo(-Trp-Cyp-Trp-hArg-^DPro-Oic-);
cyclo(-Trp-Cyp-Trp-hCys-^DPro-Oic-);
25 cyclo(-Trp-Cyp-Trp-Gln(*i*Pr)-^DPro-Oic-);
cyclo(-Trp-Cyp-Trp-hSer(Me)-^DPro-Oic-);
cyclo(-Trp-Cyp-Trp-Lys(Ac)-^DPro-Oic-);
cyclo(-Trp-Cyp-Trp-Lys(Bz)-^DPro-Oic-);
cyclo(-Trp-Cyp-Trp-Lys(Me)-^DPro-Oic-);
30 cyclo(-Trp-Cyp-Trp-Lys((5*R*)OH)-^DPro-Oic-);
cyclo(-Trp-Cyp-Trp-Lys(Nic)-^DPro-Oic-);

- cyclo(-Trp-Cyp-Trp-Met(O₂)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Ala(Ppz)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dap(CONH₂)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab(Dab)-^DPro-Oic-);
 5 cyclo(-Trp-Cyp-Trp-Dab(MEMCO)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab(MeO(CH₂)₂NHCO)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dap(MeO(CH₂)₂)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dap((MeO(CH₂)₂)₂)-^DPro-Oic-);
 cyclo(-Ph(4COOMe)-Cyp-Trp-Dab-^DPro-Oic-);
 10 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Hyp(3CNBn)-);
 cyclo(-Phe(4CN)-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Ser-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Ser-^DPip-Oic-);
 cyclo(-Trp(6Cl)-Cyp-Trp-Ser-^DPro-Oic-);
 15 cyclo(-Phe(4CN)-Cyp-Trp-Ser-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Lys(4Oxa)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Ser(Me)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Thr-^DPro-Oic-);
 cyclo(-Bip-Cyp-Trp-Dab-^DPro-Oic-);
 20 cyclo(-hTyr-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Bbta-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Nle(6OBn)-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Tyr(4OHPh)-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Tyr(Ph)-Cyp-Trp-Dab-^DPro-Oic-);
 25 cyclo(-Tyr(4MeOCOBn)-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Deg-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Ac7c-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Chx(4oxo)-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Ac8c-Trp-Dab-^DPro-Oic-);
 30 cyclo(-Trp-Cyp-Trp-Dab((MeO(CH₂)₂)(Me)NCO)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab(morphCO)-^DPro-Oic-);

- cyclo(-Trp-Cyp-Trp-Dab(MePpzCO)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab(MeSO₂)-^DPro-Oic-)
 cyclo(-Trp-Cyp-Trp-Dab(4Me₂NPhSO₂)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab(Ac)-^DPro-Oic-);
 5 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Hyp-);
 cyclo(-Trp-Cyp-Trp-Dap-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab(SN13)-^DPro-Oic-);
 or pharmaceutically acceptable salts thereof.

- 10 In a most preferred embodiment of the invention the β-hairpin peptidomimetics of general formula (I) are selected from the group consisting of:

- cyclo(-Cha-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Oic-);
 15 cyclo(-Phe(4CF₃)-Cyp-Trp-Dab-^DPip-Pro((4*R*)Ph)-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Pro(5,5Me₂)-);
 cyclo(-Phe(4CN)-Cyp-Trp-Dab-^DPro-Hyp(Bn)-);
 cyclo(-Trp-Cyp-Trp-Met(O₂)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dap(CONH₂)-^DPro-Oic-);
 20 cyclo(-Phe(4CN)-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Lys(4Oxa)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab(MePpzCO)-^DPro-Oic-);
 or pharmaceutically acceptable salts thereof.

- 25 In an alternatively preferred embodiment of the invention the β-hairpin peptidomimetics of general formula (I) are selected from the group consisting of:

- cyclo(-Trp-Cyp-Trp-Dab(A55)-^DPro-Oic-);
 cyclo(-Phe(4CF₃)-Cyp-Trp-Dab-^DPro-Oic-);
 30 cyclo(-Phe(4CF₃)-Cyp-Trp-Dab(A56)-^DPro-Oic-);
 cyclo(-Phe(3CF₃)-Cyp-Trp-Dab-^DPro-Oic-);

cyclo(-Phe(4CF₃)-Cyp-Trp-3Pal-^DPic-Oic-);
or pharmaceutically acceptable salts thereof.

A further embodiment of the invention relates to the preparation of present β -hairpin
5 peptidomimetics by a process which comprises the steps of

- (a) coupling an appropriately functionalized solid support with an appropriately N-protected derivative of that amino acid which in the desired end-product is in position T¹ or T² or P¹ to P⁴ as defined above; any functional group which may
10 be present in said N-protected amino acid derivative being likewise appropriately protected;
- (b) removing the N-protecting group from the product obtained in step (a);
- (c) coupling the product thus obtained with an appropriately N-protected derivative of that amino acid which in the desired end-product is in the position
15 of the next element (T or P), following counterclockwise or clockwise the sequence according to general formula (I) in -COOH to -NH₂ orientation; any functional group which may be present in said N-protected amino acid derivative being likewise appropriately protected;
- (d) removing the N-protecting group from the product thus obtained;
- 20 (e) repeating steps (c) and (d) until all amino acid residues have been introduced;
- (f) if desired, selectively deprotecting one or several protected functional group(s) present in the molecule and chemically transforming the reactive group(s) thus liberated;
- (g) detaching the product thus obtained from the solid support;
- 25 (h) cyclizing the product cleaved from the solid support;
- (i) removing any protecting groups present on functional groups of any members of the chain of amino acid residues and, if desired, any protecting group(s) which may in addition be present in the molecule; and
- (j) if desired, implementing additional chemical transformations of one or more
30 reactive group(s) present in the molecule;

- (k) if desired, converting the product thus obtained into a pharmaceutically acceptable salt or converting a pharmaceutically acceptable, or unacceptable, salt thus obtained into the corresponding free compound of formula (I) or into a different, pharmaceutically acceptable salt.

5

The process of the invention can advantageously be carried out as parallel array synthesis to yield libraries of template-fixed β -hairpin peptidomimetics of the above general formula (I). Such parallel synthesis allows one to obtain arrays of numerous (normally 24 to 192, typically 96) compounds of general formula (I) in high yields and
10 defined purities, minimizing the formation of dimeric and polymeric by-products. The proper choice of the functionalized solid-support (i.e. solid support plus linker molecule), templates and site of cyclization play thereby key roles.

The functionalized solid support is conveniently derived from polystyrene crosslinked
15 with, preferably 1-5%, divinylbenzene; polystyrene coated with polyethyleneglycol spacers (Tentagel®); and polyacrylamide resins (see also Obrecht, D.; Villalgordo, J.-M, "Solid-Supported Combinatorial and Parallel Synthesis of Small-Molecular-Weight Compound Libraries", *Tetrahedron Organic Chemistry Series*, Vol. 17, Pergamon, Elsevier Science, 1998).

20

The solid support is functionalized by means of a linker, i.e. a bifunctional spacer molecule which contains on one end an anchoring group for attachment to the solid support and on the other end a selectively cleavable functional group used for the subsequent chemical transformations and cleavage procedures. For the purposes of
25 the present invention two types of linkers are used:

Type 1 linkers are designed to release the amide group under acidic conditions (Rink H, *Tetrahedron Lett.* 1987, 28, 3783-3790). Linkers of this kind form amides of the carboxyl group of the amino acids; examples of resins functionalized by such linker
30 structures include 4-((((2,4-dimethoxyphenyl)Fmoc-aminomethyl)phenoxyacetamido)-aminomethyl] PS resin, 4-((((2,4-dimethoxyphenyl)Fmoc-aminomethyl)phenoxyacet-

amido)aminomethyl]-4-methylbenzhydrylamine PS resin (Rink amide MBHA PS Resin), and 4-((((2,4-dimethoxyphenyl)Fmoc-aminomethyl)phenoxyacetamido)aminomethyl)-benzhydrylamine PS-resin (Rink amide BHA PS resin). Preferably, the support is derived from polystyrene crosslinked with, most preferably 1-5%, divinylbenzene and
5 functionalized by means of the 4-((((2,4-dimethoxyphenyl)Fmoc-aminomethyl)phenoxyacetamido) linker.

Type 2 linkers are designed to eventually release the carboxyl group under acidic conditions. Linkers of this kind form acid-labile esters with the carboxyl group of the
10 amino acids, usually acid-labile benzyl, benzhydryl and trityl esters; examples of such linker structures include 2-methoxy-4-hydroxymethylphenoxy (Sasrin® linker), 4-(2,4-dimethoxyphenyl-hydroxymethyl)-phenoxy (Rink linker), 4-(4-hydroxymethyl-3-methoxyphenoxy)butyric acid (HMPB linker), trityl and 2-chlorotrityl. Preferably, the support is derived from polystyrene crosslinked with, most preferably 1-5%, divinylbenzene
15 and functionalized by means of the 2-chlorotrityl linker.

When carried out as parallel array syntheses the processes of the invention can be advantageously carried out as described herein below but it will be immediately apparent to those skilled in the art how these procedures will have to be modified in
20 case it is desired to synthesize one single compound of the above formula (I).

A number of reaction vessels (normally 24 to 192, typically 96) equal to the total number of compounds to be synthesized by the parallel method are loaded with 25 to 1000 mg, preferably 100 mg, of the appropriate functionalized solid support which is
25 preferably derived from polystyrene cross-linked with 1 to 3% of divinylbenzene, or from Tentagel resin.

The solvent to be used must be capable of swelling the resin and includes, but is not limited to, dichloromethane (DCM), dimethylformamide (DMF), N-methylpyrrolidone
30 (NMP), dioxane, toluene, tetrahydrofuran (THF), ethanol (EtOH), trifluoroethanol (TFE), isopropylalcohol and the like. Solvent mixtures containing as at least one component a

polar solvent (e. g. 20% TFE/DCM, 35% THF/NMP) are beneficial for ensuring high reactivity and solvation of the resin-bound peptide chains (Fields, G. B., Fields, C. G., *J. Am. Chem. Soc.* **1991**, *113*, 4202-4207).

- 5 With the development of various linkers that release the C-terminal carboxylic acid group under mild acidic conditions, not affecting acid-labile groups protecting functional groups in the side chain(s), considerable progresses have been made in the synthesis of protected peptide fragments. The 2-methoxy-4-hydroxybenzylalcohol-derived linker (Sasrin® linker, Mergler et al., *Tetrahedron Lett.* **1988**, *29* 4005-4008) is
- 10 cleavable with diluted trifluoroacetic acid (0.5-1% TFA in DCM) and is stable to Fmoc deprotection conditions during the peptide synthesis, Boc/tBu-based additional protecting groups being compatible with this protection scheme. Other linkers which are suitable for the processes of the invention include the super acid labile 4-(2,4-dimethoxyphenyl-hydroxymethyl)-phenoxy linker (Rink linker, Rink, H. *Tetrahedron*
- 15 *Lett.* **1987**, *28*, 3787-3790), where the removal of the peptide requires 10% acetic acid in DCM or 0.2% trifluoroacetic acid in DCM; the 4-(4-hydroxymethyl-3-methoxy-phenoxy)butyric acid-derived linker (HMPB-linker, Flörsheimer & Riniker, *Peptides* **1991**, *1990* 131) which is also cleaved with 1% TFA/DCM in order to yield a peptide fragment containing all acid labile side-chain protective groups; and, in addition, the 2-
- 20 chlorotriylchloride linker (Barlos et al., *Tetrahedron Lett.* **1989**, *30*, 3943-3946), which allows the peptide detachment using a mixture of glacial acetic acid/trifluoro-ethanol/DCM (1:2:7) for about 30 min.

Suitable protecting groups for amino acids and, respectively, for their residues are, for

25 example,

- for the amino group (as is present e.g. also in the side-chain of lysine)
 - Cbz benzyloxycarbonyl
 - Boc *tert.*-butyloxycarbonyl
 - 30 Fmoc 9-fluorenylmethoxycarbonyl
 - Alloc allyloxycarbonyl

Teoc	trimethylsilylethoxycarbonyl
Tcc	trichloroethoxycarbonyl
Nps	<i>o</i> -nitrophenylsulfonyl
Trt	triphenylmethyl or trityl

5

- for the carboxyl group (as is present e.g. also in the side-chain of aspartic and glutamic acid) by conversion into esters with the alcohol components

tBu *tert.*-butyl

Bn benzyl

10 Me methyl

Ph phenyl

Pac phenacyl

allyl

Tse trimethylsilylethyl

15 Tce trichloroethyl

- for the guanidino group (as is present e.g. in the side-chain of arginine)

Pmc 2,2,5,7,8-pentamethylchroman-6-sulfonyl

Ts tosyl (i.e. *p*-toluenesulfonyl)

20 Cbz benzyloxycarbonyl

Pbf 2,2,4,6,7-pentamethyldihydrobenzofuran-5-sulfonyl

- for the hydroxy group (as is present e.g. in the side-chain of threonine and serine)

25 tBu *tert.*-butyl

Bn benzyl

Trt trityl

- and for the mercapto group (as is present e.g. in the side-chain of cysteine)

30 Acm acetamidomethyl

tBu *tert.*-butyl

Bn	benzyl
Trt	trityl
Mtr	4-methoxytrityl.

- 5 The 9-fluorenylmethoxycarbonyl- (Fmoc)-protected amino acid derivatives are preferably used as the building blocks for the construction of the template-fixed β -hairpin loop mimetics of formula (I). For the deprotection, i. e. cleaving off of the Fmoc group, 20% piperidine in DMF or 2% DBU/2% piperidine in DMF can be used.
- 10 The quantity of the reactant, i. e. of the amino acid derivative, is usually 1 to 20 equivalents based on the milliequivalents per gram (meq/g) loading of the functionalized solid support (typically 0.1 to 2.85 meq/g for polystyrene resins) originally weighed into the reaction tube. Additional equivalents of reactants can be used, if required, to drive the reaction to completion in a reasonable time. The reaction tubes, in
15 combination with the holder block and the manifold, are reinserted into the reservoir block and the apparatus is fastened together. Gas flow through the manifold is initiated to provide a controlled environment, for example, nitrogen, argon, air and the like. The gas flow may also be heated or chilled prior to flow through the manifold. Heating or cooling of the reaction wells is achieved by heating the reaction block or
20 cooling externally with isopropanol/dry ice and the like to bring about the desired synthetic reactions. Agitation is achieved by shaking or magnetic stirring (within the reaction tube). The preferred workstations (without, however, being limited thereto) are Labsource's Combi-chem station and MultiSyn Tech's-Syro synthesizer.
- 25 Amide bond formation requires the activation of the α -carboxyl group for the acylation step. If this activation is being carried out by means of the commonly used carbodiimides, such as dicyclohexylcarbodiimide (DCC, Sheehan & Hess, *J. Am. Chem. Soc.* **1955**, 77, 1067-1068) or diisopropylcarbodiimide (DIC, Sarantakis et al *Biochem. Biophys. Res. Commun.* **1976**, 73, 336-342), the resulting dicyclohexylurea and
30 diisopropylurea is insoluble and, respectively, soluble in the solvents generally used. In a variation of the carbodiimide method 1-hydroxybenzotriazole (HOBt, König & Geiger,

Chem. Ber **1970**, *103*, 788-798) is included as an additive to the coupling mixture. HOBt prevents dehydration, suppresses racemization of the activated amino acids and acts as a catalyst to improve the sluggish coupling reactions. Certain phosphonium reagents have been used as direct coupling reagents, such as benzotriazol-1-yl-oxy-tris-(dimethylamino)-phosphonium hexafluorophosphate (BOP, Castro et al., *Tetrahedron Lett.* **1975**, *14*, 1219-1222; *Synthesis*, **1976**, 751-752), or benzotriazol-1-yl-oxy-tris-pyrrolidino-phosphonium hexafluorophosphate (Py-BOP, Coste et al., *Tetrahedron Lett.* **1990**, *31*, 205-208), or 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TBTU), or hexafluorophosphate (HBTU, Knorr et al., *Tetrahedron Lett.* **1989**, *30*, 1927-1930); these phosphonium and uronium reagents are also suitable for in situ formation of HOBt esters with the protected amino acid derivatives. More recently diphenoxyphosphoryl azide (DPPA) or O-(7-aza-benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium tetrafluoroborate (TATU) or O-(7-aza-benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (HATU)/7-aza-1-hydroxy benzotriazole (HOAt, Carpino et al., *Tetrahedron Lett.* **1994**, *35*, 2279-2281) have also been used as coupling reagents.

Due to the fact that near-quantitative coupling reactions are essential, it is desirable to have experimental evidence for completion of the reactions. The ninhydrin test (Kaiser et al., *Anal. Biochemistry* **1970**, *34*, 595), where a positive colorimetric response to an aliquot of resin-bound peptide indicates qualitatively the presence of the primary amine, can easily and quickly be performed after each coupling step. Fmoc chemistry allows the spectrophotometric detection of the Fmoc chromophore when it is released with the base (Meienhofer et al., *Int. J. Peptide Protein Res.* **1979**, *13*, 35-42).

25

The resin-bound intermediate within each reaction tube is washed free of excess of retained reagents, of solvents, and of by-products by repetitive exposure to pure solvent(s).

Washing procedures are repeated up to about 30 times (preferably about 5 times), monitoring the efficiency of reagent, solvent, and by-product removal by methods such as TLC, GC, LC-MS or inspection of the washings.

- 5 The above described procedure of reacting the resin-bound compound with reagents within the reaction wells followed by removal of excess reagents, by-products, and solvents is repeated with each successive transformation until the final resin-bound fully protected linear peptide has been obtained.
- 10 Before this fully protected linear peptide is detached from the solid support, it is possible, if desired, to selectively deprotect one or several protected functional group(s) present in the molecule and to appropriately substitute the reactive group(s) thus liberated. To this effect, the functional group(s) in question must initially be protected by a protecting group which can be selectively removed without affecting
- 15 the remaining protecting groups present. Alloc (allyloxycarbonyl) is an example for such an amino protecting group which can be selectively removed, e.g. by means of Pd⁰ and phenylsilane in CH₂Cl₂, without affecting the remaining protecting groups, such as Fmoc, present in the molecule. The reactive group thus liberated can then be treated with an agent suitable for introducing the desired substituent. Thus, for
- 20 example, an amino group can be acylated by means of an acylating agent corresponding to the acyl substituent to be introduced.

After detachment of the fully protected linear peptide from the solid support the individual solutions/extracts are then manipulated as needed to isolate the final

25 compounds. Typical manipulations include, but are not limited to, evaporation, concentration, liquid/liquid extraction, acidification, basification, neutralization or additional reactions in solution.

The solutions containing fully protected linear peptide derivatives which have been

30 cleaved off from the solid support and neutralized with a base, are evaporated. Cyclization is then effected in solution using solvents such as DCM, DMF, dioxane, THF

and the like. Various coupling reagents which were mentioned earlier as activators for the amide bond formation can be used for the cyclization. The duration of the cyclization is about 6-48 hours, preferably about 16 hours. The progress of the reaction is followed, e.g. by RP-HPLC (Reverse Phase High Performance Liquid Chromatography). Then the solvent is removed by evaporation, the fully protected cyclic peptide derivative is dissolved in a solvent which is not miscible with water, such as DCM, and the solution is extracted with water or a mixture of water-miscible solvents, in order to remove any excess of the coupling reagent.

10 Finally, the fully protected peptide derivative is treated with 95% TFA, 2.5% H₂O, 2.5% TIS or another combination of scavengers for effecting the cleavage of protecting groups. The cleavage reaction time is commonly 30 minutes to 12 hours, preferably about 2.5 hours. The volatiles are evaporated to dryness and the crude peptide is dissolved in 20% AcOH in water and extracted with isopropyl ether or other solvents
15 which are suitable therefore. The aqueous layer is collected and evaporated to dryness, and the fully deprotected cyclic peptide derivative of formula (I) is obtained as end-product.

For some compounds of the present invention according general formula (I) additional
20 synthetic steps are required. These transformations can be applied either on a partially deprotected cyclic or linear peptide, attached or already released from the solid support or on the final deprotected molecule as exemplified below.

Depending on its purity, this peptide derivative can be used directly for biological
25 assays, or it has to be further purified, for example by preparative HPLC.

As mentioned earlier, it is thereafter possible, if desired, to convert a fully deprotected product of formula (I) thus obtained into a pharmaceutically acceptable salt or to convert a pharmaceutically acceptable, or unacceptable, salt thus obtained into the
30 corresponding free compound of formula (I) or into a different, pharmaceutically

acceptable, salt. Any of these operations can be carried out by methods well known in the art.

5 In general the building blocks for the peptidomimetics of the present invention can be synthesized according to the literature methods (example described below), are known to a person skilled in the art or are commercially available. A few additional new syntheses were carried out for this invention and are described in the examples. All other corresponding amino acids have been described either as unprotected or as
10 Boc- or Fmoc-protected racemates, (D)- or (L)-isomers. It will be appreciated that unprotected amino acid building blocks can be easily transformed into the corresponding Fmoc-protected amino acid building blocks required for the present invention by standard protecting group manipulations. Reviews describing general methods for the synthesis of α -amino acids include: R. Duthaler, *Tetrahedron (Report)*
15 **1994**, 349, 1540-1650; R. M. Williams, "Synthesis of optically active α -amino acids", *Tetrahedron Organic Chemistry Series*, Vol.7, J. E. Baldwin, P. D. Magnus (Eds.), Pergamon Press., Oxford **1989**. An especially useful method for the synthesis of optically active α -amino acids relevant for this invention includes kinetic resolution using hydrolytic enzymes (M. A. Verhovskaya, I. A. Yamskov, *Russian Chem. Rev.* **1991**,
20 **60**, 1163-1179; R. M. Williams, "Synthesis of optically active α -amino acids", *Tetrahedron Organic Chemistry Series*, Vol.7, J. E. Baldwin, P. D. Magnus (Eds.), Pergamon Press., Oxford **1989**, Chapter 7, p.257-279). Kinetic resolution using hydrolytic enzymes involves hydrolysis of amides and nitriles by aminopeptidases or nitrilases, cleavage of N-acyl groups by acylases, and ester hydrolysis by lipases or
25 proteases. It is well documented that certain enzymes will lead specifically to pure (L)-enantiomers whereas others yield the corresponding (D)-enantiomers (e.g.: R. Duthaler, *Tetrahedron Report* **1994**, 349, 1540-1650; R. M. Williams, "Synthesis of optically active α -amino acids", *Tetrahedron Organic Chemistry Series*, Vol.7, J. E. Baldwin, P. D. Magnus (Eds.), Pergamon Press., Oxford **1989**).

The β -hairpin peptidomimetics of the invention can be used in a wide range of applications in order to antagonize the CCR10 receptor activity leading to the desired therapeutic effect in man or, due to their similar etiology, in other mammals. Especially they can be used as agents for treating and/or preventing diseases or
5 conditions associated with the immune response in the area of inflammation, cutaneous disorders or cancer, such as, but not limited to, psoriasis, atopic dermatitis, contact sensitivity and allergic dermatitis, Stevens-Johnson syndrome, bullous cutaneous diseases, systemic lupus erythematosus, systemic and multiple sclerosis, allergic asthma, arthritis, graft versus host disease, certain melanoma and cutaneous
10 lymphoma, thyroiditis, as well as inflammatory processes of the gastro-intestinal tract and the eye.

For use as medicaments the β -hairpin peptidomimetics of the invention can be administered singly, as mixtures of several β -hairpin peptidomimetics of the invention
15 or in combination with other pharmaceutically active agents. The β -hairpin peptidomimetics of the invention may be administered per se or applied as a pharmaceutical preparation, e.g. an appropriate formulation together with carriers, diluents or excipients well known in the art.

20 Pharmaceutical compositions comprising β -hairpin peptidomimetics of the invention may be manufactured by means of conventional mixing, dissolving, granulating, coated tablet-making, levigating, emulsifying, encapsulating, entrapping or lyophilizing processes. Pharmaceutical compositions may be formulated in conventional manner using one or more physiologically acceptable carriers, diluents, excipients or auxiliaries
25 which facilitate processing of the active β -hairpin peptidomimetics into preparations which can be used pharmaceutically. Proper formulation depends upon the method of administration chosen.

For topical administration the β -hairpin peptidomimetics of the invention may be
30 formulated as solutions, gels, ointments, creams, suspensions, etc. as are well-known in the art.

Systemic formulations include those designed for administration by injection, e.g. subcutaneous, intravenous, intramuscular, intrathecal or intraperitoneal injection, as well as those designed for transdermal, transmucosal, oral or pulmonary administration.

5

For injections, the β -hairpin peptidomimetics of the invention may be formulated in adequate solutions, preferably in physiologically compatible buffers such as Hink's solution, Ringer's solution, or physiological saline buffer. The solution may contain formulatory agents such as suspending, stabilizing and/or dispersing agents.

10 Alternatively, the β -hairpin peptidomimetics of the invention may be in powder form for combination with a suitable vehicle, e.g., sterile pyrogen-free water, before use.

For transmucosal administration, penetrants appropriate to the barrier to be permeated are used in the formulation as known in the art.

15

For oral administration, the compounds of the invention can be readily formulated by combining the active β -hairpin peptidomimetics with pharmaceutically acceptable carriers well known in the art. Such carriers enable the β -hairpin peptidomimetics of the invention to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions etc., for oral ingestion of a patient to be treated. For oral formulations such as, for example, powders, capsules and tablets, suitable excipients include fillers such as sugars, such as lactose, sucrose, mannitol and sorbitol; cellulose preparations such as maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP); granulating agents; and binding agents. If desired, disintegrating agents may be added, such as cross-linked polyvinylpyrrolidones, agar, or alginic acid or a salt thereof, such as sodium alginate. If desired, solid dosage forms may be sugar-coated or enteric-coated using standard techniques.

30

For oral liquid preparations such as, for example, suspensions, elixirs and solutions, suitable carriers, excipients or diluents include water, glycols, oils, alcohols, etc. In addition, flavoring agents, preservatives, coloring agents and the like may be added.

- 5 For buccal administration, the composition may take the form of tablets, lozenges, etc. formulated as usual.

For administration by inhalation, the β -hairpin peptidomimetics of the invention are conveniently delivered in form of an aerosol spray from pressurized packs or a nebulizer, with the use of a suitable propellant, e.g. dichlorodifluoromethane, trichlorofluoromethane, carbon dioxide or another suitable gas. In the case of a pressurized aerosol the dose unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of e.g. gelatin for use in an inhaler or insufflator may be formulated containing a powder mix of the β -hairpin peptidomimetics of the invention and a suitable powder base such as lactose or starch.

The compounds may also be formulated in rectal or vaginal compositions such as solutions for enema or suppositories together with appropriate suppository bases such as cocoa butter or other glycerides.

20

In addition to the formulations described previously, the β -hairpin peptidomimetics of the invention may also be formulated as depot preparations. Such long acting formulations may be administered by implantation (e.g. subcutaneously or intramuscularly) or by intramuscular injection. For the manufacture of such depot preparations the β -hairpin peptidomimetics of the invention may be formulated with suitable polymeric or hydrophobic materials (e.g. as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble salts.

In addition, other pharmaceutical delivery systems may be employed such as liposomes and emulsions well known in the art. Certain organic solvents such as dimethylsulfoxide also may be employed. Additionally, the β -hairpin peptidomimetics

30

of the invention may be delivered using a sustained-release system, such as semipermeable matrices of solid polymers containing the therapeutic agent. Various sustained-release materials have been established and are well known by those skilled in the art. Sustained-release capsules may, depending on their chemical nature, 5 release the compounds for a few weeks up to over 3 years. Depending on the chemical nature and the biological stability of the therapeutic agent, additional strategies for protein stabilization may be employed.

As the β -hairpin peptidomimetics of the invention may contain charged residues, they 10 may be included in any of the above-described formulations as such or as pharmaceutically acceptable salts. Pharmaceutically acceptable salts tend to be more soluble in aqueous and other protic solvents than are the corresponding free base forms.

In addition, the compounds of the present invention and their pharmaceutical 15 acceptable salts may be used per se or in any appropriate formulation in morphological different solid state forms, which may or may not contain different amounts of solvent, e.g. hydrate remaining from the crystallization process.

The β -hairpin peptidomimetics of the invention, or compositions thereof, will generally 20 be used in an amount effective to achieve the intended purpose. It is to be understood that the amount used will depend on a particular application.

For the use of treating or preventing diseases or disorders with an etiology comprising, or associated with, an increased activity of the CCR10 receptor and its ligands (e.g. 25 CCL27 or CCL28), the β -hairpin peptidomimetics of the invention or compositions thereof, are administered or applied in a therapeutically effective amount. Determination of a therapeutically effective amount is well within the capacities of those skilled in the art, especially in view of the detailed disclosure provided herein.

30 The effective dosage of the active ingredients employed may vary depending on the particular compound or pharmaceutical preparation employed, the mode of adminis-

tration and the severity and type of the condition treated. Thus, the dosage regimen is selected in accordance with factors including the route of administration and the clearance pathway, e.g. the renal and hepatic function of the patient. A physician, clinician or veterinarian skilled in the art can readily determine and prescribe the
5 amount of the single active ingredients required to prevent, ameliorate or arrest the progress of the condition or disease. Optimal precision in achieving concentration of active ingredients without toxicity requires a regimen based on the kinetics of the active ingredients' availability to the target sites. This involves a consideration of the distribution, equilibrium, and elimination of the active ingredients.

10

In cases of local administration or selective uptake, the effective local concentration of the β -hairpin peptidomimetics of the invention may not be related to plasma concentration. One having the skills in the art will be able to optimize therapeutically effective local dosages without undue experimentation.

15

The invention will now be further described in the Examples below, which are intended as an illustration only and not to be construed as limiting the scope of the invention in any way.

The following abbreviations are used in these Examples:

5		
	Boc	<i>tert</i> -Butyloxycarbonyl;
	DCHA	Dicyclohexylamine;
	DEAD	Diethyl azodicarboxylate;
	DIPEA	Diisopropylethylamine;
10	Fmoc	Fluorenylmethyloxycarbonyl;
	HATU	O-(7-Aza-benzotriazole-1-yl)-N,N,N',N'-tetramethyluronoium hexafluorophosphate.
	HBTU	O-(Benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate;
15	HCTU	O-(6-Chlorobenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate
	PyBop®	(Benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate;
	TIS	Triisopropylsilane;
20	TPP	Triphenylphosphine;
	rt	Room temperature

Examples

1. Peptide synthesis

5 1.1 General synthetic procedures

Two general methods, Method A and Method B, for the synthesis of the peptide-mimetics of the present invention are exemplified here. This is to demonstrate the principal concept and does not limit or restrict the present invention in any way. A
10 person skilled in the art is easily able to modify these procedures, especially, but not limited to, choosing a different starting position within the ring system, to still achieve the preparation of the claimed cyclic peptidomimetic compounds of the present invention.

15 *Coupling of the first protected amino acid residue to the resin*

Method A:

0.5 g of 2-chlorotritylchloride resin (Barlos et al. *Tetrahedron Lett.* **1989**, 30, 3943-3946) (1.4 mmol/g, 0.7 mmol) was filled into a dried flask. The resin was suspended in
20 CH₂Cl₂ (2.5 ml) and allowed to swell at room temperature for 30 min. The resin was treated with 0.43 mmol (0.6 eq) of the first suitably protected amino acid residue or building block (see below) and 488 µl (4eq) of diisopropylethylamine (DIPEA) in CH₂Cl₂ (2.5 ml) and the mixture was shaken at rt for 4 hours. The resin was washed with CH₂Cl₂ (1x), DMF (1x), CH₂Cl₂ (1x), DMF(1x) and CH₂Cl₂ (2x). The resin was shaken in 30
25 ml CH₂Cl₂/MeOH/DIPEA (17:2:1) for 30 min; then washed in the following order with CH₂Cl₂ (1x), DMF (1x), CH₂Cl₂ (1x), MeOH (1x), CH₂Cl₂ (1x), MeOH (1x), CH₂Cl₂ (2x), Et₂O (2x) and dried under vacuum for 6 hours.

Method B:

30 In a dried flask, 2-chlorotritylchloride resin (loading: 1.4 mmol/g) was swollen in dry CH₂Cl₂ for 30 min (7 ml CH₂Cl₂ per g resin). A solution of 0.8 eq of Fmoc-AA-OH and 6

eq of DIPEA in dry CH₂Cl₂/DMF (4/1) (10 ml per g resin) was added. After shaking for 2-4 h at rt the resin was filtered and washed successively with CH₂Cl₂, DMF, CH₂Cl₂, DMF and CH₂Cl₂. Then a solution of dry CH₂Cl₂/MeOH/DIPEA (17:2:1) was added (10 ml per g resin). After shaking for 3 x 30 min the resin was filtered in a pre-weighed sinter funnel and washed successively with CH₂Cl₂, DMF, CH₂Cl₂, MeOH, CH₂Cl₂, MeOH, CH₂Cl₂ (2x) and Et₂O (2x). The resin was dried under high vacuum overnight. The final mass of resin was calculated before the qualitative control.

The following preloaded resins were prepared: Fmoc-Tic-2-chlorotrityl resin, Fmoc-Oic-2-chlorotrityl resin, Fmoc-^DPro-2-chlorotrityl resin, Fmoc-Arg-2-chlorotrityl resin, Fmoc-^DAze-2-chlorotrityl resin, Fmoc-Trp-2-chlorotrityl resin, Fmoc-Hyp-2-chlorotrityl resin, Fmoc-Hyp(Bn)-2-chlorotrityl resin, Fmoc-(4S)-Hyp(Bn)-2-chlorotrityl resin, Hyp(4BrBn)-2-chlorotrityl resin, Fmoc-Dab-2-chlorotrityl resin, Fmoc-Thz-2-chlorotrityl resin, Fmoc-Pip-2-chlorotrityl resin, Fmoc-Phe(4CN)-2-chlorotrityl resin, Fmoc-Pro((4R)Ph)-2-chlorotrityl resin, Fmoc-^{DL}Atc-2-chlorotrityl resin, Fmoc-Bbta-2-chlorotrityl resin and Fmoc-^{DL}Trp (7Aza)-2-chlorotrityl resin.

Synthesis of the fully protected peptide fragment

The synthesis was carried out on a Syro-peptide synthesizer (MultiSynTech GmbH) using 24 to 96 reaction vessels. In each vessel were placed approximately 60 mg (Method A) or 80 mg (Method B) of the above resin (weight of the resin before loading). The following reaction cycles were programmed and carried out:

25 Method A:

Step	Reagent	Time
1	CH ₂ Cl ₂ , wash and swell (manual)	1 x 3 min
2	DMF, wash and swell	1 x 60 min
30 3	40 % piperidine/DMF	1 x 5 min and 1 x 15 min
4	DMF, wash	5 x 1 min

5	5 eq. Fmoc amino acid/DMF	
	+ 5 eq. HCTU	
	+ 10 eq. DIPEA	2 x 60 min
6	DMF, wash	5 x 1 min
5 7	CH ₂ Cl ₂ , wash (at the end of the synthesis)	3 x 1 min

Steps 3 to 6 are repeated to add each amino-acid residue.

Method B:

10

Step	Reagent	Time
1	CH ₂ Cl ₂ , wash and swell (manual)	1 x 3 min
2	DMF, wash and swell	1 x 60 min
3	40 % piperidine/DMF	1 x 5 min and 1 x 15 min
15 4	DMF, wash	5 x 1 min
5	3.5 eq. Fmoc amino acid/DMF	
	+ 3.5 eq. HCTU	
	+ 7 eq. DIPEA	2 x 60 min
6	DMF, wash	5 x 1 min
20 7	CH ₂ Cl ₂ , wash (at the end of the synthesis)	3 x 1 min

Steps 3 to 6 are repeated to add each amino-acid residue.

After the synthesis of the fully protected peptide fragment had been terminated, the
 25 cleavage, cyclization and work up procedures, as described herein below, were used
 for the preparation of the final compounds.

Cleavage, backbone cyclization and deprotection of the peptide

30 After assembly of the linear peptide, the resin was suspended in 1 ml of 1% TFA in
 CH₂Cl₂ (v/v; 0.14 mmol) for 3 minutes and filtered, and the filtrate was neutralized with

1 ml of 20% DIPEA in CH₂Cl₂ (v/v; 1.15 mmol). This procedure was repeated four times to ensure completion of the cleavage. The resin was washed three times with 1 ml of CH₂Cl₂. The CH₂Cl₂ layers containing product were evaporated to dryness.

- 5 The fully protected linear peptide was solubilised in 8 ml of dry DMF. Then 2 eq. of HATU in dry DMF (1-2 ml) and 4 eq. of DIPEA in dry DMF (1-2 ml) were added to the peptide, followed by stirring for 16 h. The volatiles were removed by evaporation. The crude cyclic peptide was dissolved in 7 ml of CH₂Cl₂ and extracted three times with 4.5 ml 10% acetonitrile in water (v/v). The CH₂Cl₂ layers were evaporated to dryness.

10

To fully deprotect the peptide, 4-7 ml of cleavage cocktail TFA/TIS/H₂O (95:2.5:2.5) was added, and the mixture was kept for 2.5-4 h at room temperature until the reaction was completed. The reaction mixture was evaporated to dryness and the crude peptide was dissolved in 7 ml 20% AcOH in water (v/v) and extracted three times with
15 4 ml diisopropyl ether. The aqueous layer was collected and evaporated to dryness, and the residue was purified by preparative reverse phase LC-MS.

Purification procedure (preparative reverse phase LC-MS)

- 20 Compounds were purified by reverse phase chromatography using a Vydac 218MS column, 30 x 150 mm (Cat No. 218MS103015), 10 µm or a Waters XBridge C18, 30 x 150 mm, 5 µm (Cat No. 186002982).

Mobile phases used were:

A: 0.1% TFA in Water/Acetonitrile 95/5 v/v

- 25 B: 0.1 % TFA in Acetonitrile

Gradient slopes in the preparative runs were adapted each time based on analytical LC-MS analysis of the crude product. As an example, a typical run (purification of **Ex. 94**) was executed with a flow rate of 35 ml/min running a gradient from 0-2 min. 0% B, 9 min. 55% B to a final of 9.1-12.5 min. 100% B (retention time: 7.38 min in this case).

- 30 Detection: MS and UV @ 220 nm

Fractions collected were evaporated using a Genevac HT4 evaporator or a Büchi system.

Alternatively for larger amounts the following LC-purification system was used:

5 Column: Vydac 218MS, 10 µm, 50 x 150 mm

Mobile phase A: 0.1% TFA in Water

Mobile phase B: 0.1% TFA in Acetonitrile

Flow rate: 150 ml/min

Detection: UV @ 220 nm

10 After lyophilisation the products were obtained typically as white to off-white powders and analysed by HPLC-ESI-MS methods as described below. Analytical data after preparative HPLC purification are shown in *Table 1*.

1.2 Analytical Methods

15

Analytical method A:

Analytical HPLC retention times (RT, in minutes) were determined using a Gemini NX column, 50 x 2.0 mm, (cod. 00B-4453-B0 - Phenomenex) with the following solvents **A** (H₂O + 0.1% TFA) and **B** (CH₃CN + 0.1% TFA) and the gradient: 0-0.1 min: 97% A, 3% B;

20 2.7 min: 3% A 97% B; 2.7-3 min: 3% A, 97% B; 3.05-3.3 min: 97% A, 3% B. Flow rate = 0.8 ml/min

Analytical method B:

Analytical HPLC retention times (RT, in minutes) were determined using a XBridge C18
25 column, 50 x 2.0 mm, (cod. 186003084 - Waters) with the following solvents **A** (H₂O + 0.1% TFA) and **B** (CH₃CN + 0.1% TFA) and the gradient: 0-0.05 min: 97% A, 3% B; 3 min: 3% A 97% B; 3-3.6 min: 3% A, 97% B; 3.6-4.3 min: 97% A, 3% B. Flow rate = 0.5 ml/min

Analytical method C:

30 Analytical HPLC retention times (RT, in minutes) were determined using an UPLC BEH C18 column, 100 x 2.1 mm, (cod. 186002352 - Waters) with the following solvents **A**

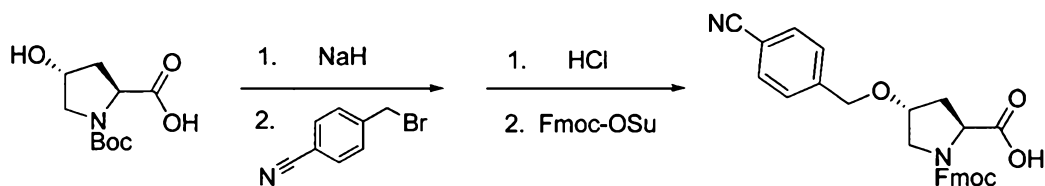
(H₂O + 0.1% TFA) and **B** (CH₃CN + 0.1% TFA) and the gradient: 0-0.2 min: 99% A, 1% B; 4 min: 35% A 65% B; 4.05-4.2 min: 5% A, 95% B; 4.2-4.5 min: 99% A, 1% B. Flow rate = 0.6 ml/min

5 Analytical method D:

Analytical HPLC retention times (RT, in minutes) were determined using an HPLC Agilent HP1100 Ascentis Express C18 column, 50 x 3 mm, (cod. 53811-U-Supelco) with the following solvents **A** (H₂O + 0.1% TFA) and **B** (CH₃CN + 0.1% TFA) and the gradient: 0-0.05 min: 97% A, 3% B; 3.35 min: 67% A, 33% B; 3.4-3.65 min: 3% A, 97% B; 3.67-3.7 min: 97% A, 3% B. Flow rate = 1.3 ml/min

1.3 Synthesis of special building blocks

(2S, 4R)-4-(4-cyanobenzoyloxy)-1-(tert-butoxycarbonyl)pyrrolidine-2-carboxylic acid

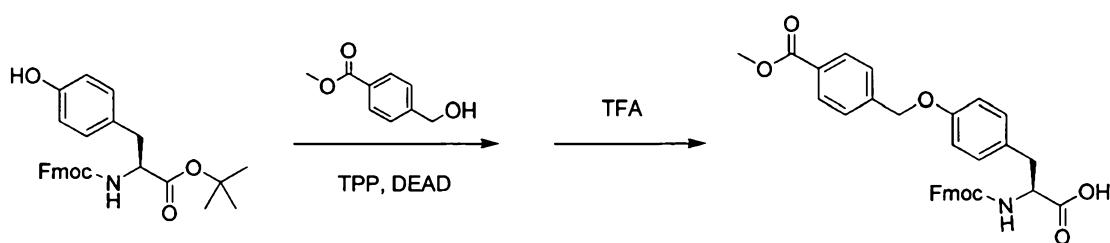


(2S,4R)-1-(tert-Butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid (1.0 g; 4.3 mmol) in dry THF (5 ml) was carefully combined at 0 °C with a suspension of sodium hydride (60% in paraffin oil, a total of 420 mg; 5.2 mmol; 2.4 eq) in dry THF (9 ml). The mixture was stirred at 0 °C before a solution of 4-(bromomethyl)benzonitrile (1.5 g; 7.8 mmol; 1.8 eq) in dry THF (5 ml) was added in several tranches. Then the mixture was stirred for 45 min at 0 °C and at rt until progress of reaction was ceased. The crude reaction mixture was diluted with 5% aqueous citric acid (50 ml) and extracted twice with ethyl acetate, dried over MgSO₄ and concentrated *in vacuo* to yield 3.2 g crude product.

Flash chromatography on silica gel ($\text{CH}_2\text{Cl}_2/\text{MeOH}$ 98:2 to 9:1) afforded 580 mg (2*S*,4*R*)-4-(4-cyanobenzyloxy)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid.

(2*S*,4*R*)-4-(4-Cyanobenzyloxy)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid (250 mg, 722 μmol) was dissolved in 4M HCl in dioxane (3 ml, 12 mmol) and the solution was stirred for 1 h at rt. The product was concentrated and washed with Et_2O . A clear solution was obtained by addition of 120 mg potassium carbonate (866 μmol) to the residue suspended in 5 ml water and 15 ml acetonitrile. At 0 °C 9-fluorenylmethyl *N*-succinimidyl carbonate (292 mg, 866 μmol) was added in portions to the solution. The reaction mixture was stirred at rt overnight, diluted in water and treated twice with Et_2O (pH around 9-10). The organic layers are washed twice with sat. aq. NaHCO_3 , which were combined, acidified to pH = 1-2 with 5N HCl and re-extracted twice with EtOAc . All combined organic layers were dried (MgSO_4) and concentrated to afford 229 mg (2*S*,4*R*)-4-(4-cyanobenzyloxy)-1-(((9*H*-fluoren-9-yl)methoxy)carbonyl)pyrrolidine-2-carboxylic acid.

(*S*)-2-(((9*H*-fluoren-9-yl)methoxy)carbonylamino)-3-(4-(4-(methoxycarbonyl)benzyloxy)phenyl)propanoic acid



20

(*S*)-*tert*-Butyl 2-(((9*H*-fluoren-9-yl)methoxy)carbonylamino)-3-(4-hydroxyphenyl)propanoate (100 mg, 218 μmol), triphenylphosphine (TPP, 171 mg, 653 μmol) and methyl 4-(hydroxymethyl)benzoate (80 mg, 479 μmol) were combined in 4 ml of dry benzene under nitrogen. A solution of DEAD (40% in toluene, 299 μl , 653 μmol), diluted with 3 ml of dry benzene, was added dropwise over 20 min at 4 °C. The mixture was stirred 20 min at 4 °C, then at rt overnight. The addition of TPP (57 mg, 218 μmol) and DEAD

(100 μ l, 218 μ mol) was repeated twice to drive the reaction to completion. Volatiles were removed *in vacuo* and the crude material was purified by flash chromatography on silica gel (hexane/ethylacetate 95/5 to 1/1) afforded 60 mg (S)-2-(Fmoc-amino)-((4-methoxycarbonyl)benzyl)tyrosine *tert*-butyl ester.

5

The purified *tert*-butyl-tyrosine derivative (55 mg, 91 μ mol) was dissolved in 600 μ l dichloromethane and cooled to 0 °C. 600 μ l of TFA were added slowly and the reaction mixture was stirred for 3 h at rt. After the reaction was completed, solvents were removed and co-evaporated once with dichloromethane and 3 times with toluene to
10 yield 46 mg of the final building block (S)-2-(((9H-fluoren-9-yl)methoxy)carbonyl-amino)-3-(4-(4-(methoxycarbonyl)-benzyloxy)phenyl)propanoic acid.

15 1.4 Synthesis of peptide sequences

Examples 1, 2 and 9 are shown in Table 1.

The peptides were synthesized according general Method A starting with the amino acid (S)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid which was grafted to the resin
20 (Fmoc-Tic-2-chlorotrityl resin). The linear peptides were synthesized on the solid support according to the procedure described above in the following sequence: Resin-Tic-^DPro-P⁴-P³-P²-P¹. The products were cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above.

After lyophilisation the products were obtained as white powders and characterised by
25 HPLC-MS, analytical method A as described above. For analytical data, see Ex. 1, 2, 9 in Table 1.

Examples 3 and 8 are shown in Table 1.

The peptides were synthesized according general Method A starting with the amino
30 acid L-arginine which was grafted to the resin (Fmoc-Arg-2-chlorotrityl resin). The linear peptides were synthesized on the solid support according to the procedure

described above in the following sequence: Resin-Arg-Trp-Cyp-P¹-T²-T¹. The products were cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above.

After lyophilisation the products were obtained as white powders and characterised by
5 HPLC-MS, analytical method A as described above. For analytical data, see Ex. 3, 8 in Table 1.

Examples 4 - 6 are shown in Table 1.

The peptides were synthesized according general Method A starting with the amino
10 acid D-proline which was grafted to the resin (Fmoc-^DPro-2-chlorotrityl resin). The linear peptides were synthesized on the solid support according to the procedure described above in the following sequence: Resin-^DPro-P⁴-P³-P²-P¹-T². The products were cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above.

15 After lyophilisation the products were obtained as white powders and characterised by HPLC-MS, analytical method A as described above. For analytical data, see Ex. 4, 5, 6 in Table 1.

Example 7 is shown in Table 1.

20 The peptide was synthesized according general Method A starting with the amino acid (S)-thiazolidine-4-carboxylic acid which was grafted to the resin (Fmoc-Thz-2-chlorotrityl resin). The linear peptide was synthesized on the solid support according to the procedure described above in the following sequence: Resin-Thz-^DPro-Gln-Trp-Cyp-P¹. The product was cleaved from the resin, cyclized, deprotected and purified by
25 preparative reverse phase LC-MS as described above.

After lyophilisation the product was obtained as a white powder and characterised by HPLC-MS, analytical method A as described above. For analytical data, see Ex. 7 in Table 1.

Example 10 is shown in *Table 1*.

The peptide was synthesized according general Method A starting with the amino acid L-pipecolic acid which was grafted to the resin (Fmoc-Pip-2-chlorotrityl resin). The linear peptide was synthesized on the solid support according to the procedure
5 described above in the following sequence: Resin-Pip-^DPip-Dab-Trp-Cyp-P¹. The product was cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above.

After lyophilisation the product was obtained as a white powder and characterised by HPLC-MS, analytical method A as described above. For analytical data, see **Ex. 10** in
10 *Table 1*.

Examples 11 – 24 and 104 are shown in *Table 1*.

The peptides were synthesized according general Method A starting with the amino acid (S)-(2S,3aS,7aS)-1-octahydro-1H-indole-2-carboxylic acid which was grafted to the
15 resin (Fmoc-Oic-2-chlorotrityl resin). The linear peptides were synthesized on the solid support according to the procedure described above in the following sequence: Resin-Oic-T¹-P⁴-P³-P²-P¹. The products were cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above.

After lyophilisation the products were obtained as white powders and characterised by
20 HPLC-MS, analytical method A as described above. For analytical data, see **Ex. 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 104** in *Table 1*.

Examples 25 and 26 are shown in *Table 1*.

The peptides were synthesized according general Method A starting with the amino
25 acid D-azetidine-2-carboxylic acid which was grafted to the resin (Fmoc-^DAze-2-chlorotrityl resin). The linear peptides were synthesized on the solid support according to the procedure described above in the following sequence: Resin-^DAze-P⁴-P³-P²-P¹-T²-. The products were cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above.

After lyophilisation the products were obtained as white powders and characterised by HPLC-MS, analytical method A for **Ex. 25** and analytical method C for **Ex. 26** as described above. For analytical data, see **Ex. 25, 26** in *Table 1*.

5 Examples 27 and 28 are shown in *Table 1*.

The peptides were synthesized according general Method A starting with the amino acid (S)-(2S,3aS,7aS)-1-octahydro-1H-indole-2-carboxylic acid which was grafted to the resin (Fmoc-Oic-2-chlorotrityl resin). The linear peptides were synthesized on the solid support according to the procedure described above in the following sequence: Resin-
10 Oic-^DPro-Dab-Trp-Cyp-P¹. The products were cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above.

After lyophilisation the products were obtained as white powders and characterised by HPLC-MS, analytical method C as described above. For analytical data, see **Ex. 27, 28** in *Table 1*.

15

Example 29 is shown in *Table 1*.

The peptide was synthesized according general Method A starting with the amino acid D-proline which was grafted to the resin (Fmoc-^DPro-2-chlorotrityl resin). The linear peptide was synthesized on the solid support according to the procedure described
20 above in the following sequence: Resin-^DPro-Arg-Trp-Cyp-P1-T². The product was cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above.

After lyophilisation the product was obtained as a white powder and characterised by HPLC-MS, analytical method A as described above. For analytical data, see **Ex. 29** in
25 *Table 1*.

Example 30 is shown in *Table 1*.

The peptide was synthesized according general Method A starting with the amino acid (R,S)-2-amino-1,2,3,4-tetrahydronaphthalene-2-carboxylic acid which was grafted to
30 the resin (Fmoc-^{DL}Atc-2-chlorotrityl resin). The linear peptide was synthesized on the solid support according to the procedure described above in the following sequence:

Resin-^{DL}Atc-Trp-Oic-^DPro-Dab-Trp. The product was cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above.

After lyophilisation the product was obtained as a white powder and characterised by HPLC-MS, analytical method C as described above. For analytical data, see **Ex. 30** in

5 *Table 1*.

Example 31 is shown in *Table 1*.

The peptide was synthesized according general Method B starting with the amino acid (S)-(2S,3aS,7aS)-1-octahydro-1H-indole-2-carboxylic acid which was grafted to the
10 resin (Fmoc-Oic-2-chlorotrityl resin). The linear peptide was synthesized on the solid support according to the procedure described above in the following sequence: Resin-Oic-^DPro-Dab-P³-P²-P¹. The product was cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above.

After lyophilisation the product was obtained as a white powder and characterised by
15 HPLC-MS, analytical method B as described above. For analytical data, see **Ex. 31** in *Table 1*.

Examples 32 - 34, 36, 58 - 70, 76, 79 - 87, 89 - 96, 107, 109 and 110 are shown in *Table 1*.

20 The peptides were synthesized according general Method B starting with the amino acid (S)-(2S,3aS,7aS)-1-octahydro-1H-indole-2-carboxylic acid which was grafted to the resin (Fmoc-Oic-2-chlorotrityl resin). The linear peptides were synthesized on the solid support according to the procedure described above in the following sequence: Resin-Oic-T¹-P⁴-P³-P²-P¹. The products were cleaved from the resin, cyclized, deprotected
25 and purified by preparative reverse phase LC-MS as described above.

For **Ex. 76** saponification at the side-chain of P¹ occurred. Therefore esterification with MeOH applying standard synthesis procedures was accomplished before purification.

After lyophilisation the products were obtained as white to off-white powders and characterised by HPLC-MS, analytical method A or D as described above and indicated
30 in *Table 1*. For analytical data, see **Ex. 32, 33, 34, 36, 58, 59, 60, 61, 62, 63, 64, 65, 66,**

67, 68, 69, 70, 76, 79, 80, 81, 82, 83, 84, 85, 86, 87, 89, 90, 91, 92, 93, 94, 95, 96, 107, 109, 110 in *Table 1*.

Example 35 is shown in *Table 1*.

- 5 The peptide was synthesized according general Method A starting with the amino acid 2-amino-3-(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)propanoic acid which was grafted to the resin (Fmoc-^{DL}Trp(7Aza)-2-chlorotrityl resin). The linear peptide was synthesized on the solid support according to the procedure described above in the following sequence: Resin-^{DL}Trp(7Aza)-Cyp-Trp-Oic-^DPro-Dab. The product was cleaved from the resin, cyclized, 10 deprotected and purified by preparative reverse phase LC-MS as described above. After lyophilisation the product was obtained as a white powder and characterised by HPLC-MS, analytical method A as described above. For analytical data, see **Ex. 35** in *Table 1*.

- 15 **Example 37** is shown in *Table 1*.

The peptide was synthesized according general Method B starting with the amino acid 4*R*-phenyl-L-proline which was grafted to the resin (Fmoc-Pro((4*R*)Ph)-2-chlorotrityl resin). The linear peptide was synthesized on the solid support according to the procedure described above in the following sequence: Resin-Pro((4*R*)Ph)-^DPip-Dab-Trp- 20 Cyp-P¹. The product was cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above. After lyophilisation the product was obtained as a white powder and characterised by HPLC-MS, analytical method A as described above. For analytical data, see **Ex. 37** in *Table 1*.

25

Examples 38 - 42, 52 - 53 and 57 are shown in *Table 1*.

The peptides were synthesized according general Method B starting with the amino acid D-proline which was grafted to the resin (Fmoc-^DPro-2-chlorotrityl resin). The linear peptides were synthesized on the solid support according to the procedure 30 described above in the following sequence: Resin-^DPro-Dab-Trp-Cyp-P¹-T². The

products were cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above.

After lyophilisation the products were obtained as white powders and characterised by HPLC-MS, analytical method A as described above. For analytical data, see Ex. 38, 39,
5 40, 41, 42, 52, 53, 57 in Table 1.

Examples 43 - 50 are shown in Table 1.

The peptides were synthesized according general Method B starting with the amino acid (2*S*,4*R*)-4-benzyloxypyrrolidine-2-carboxylic acid which was grafted to the resin
10 (Fmoc-Hyp(Bn)-2-chlorotrityl resin). The linear peptides were synthesized on the solid support according to the procedure described above in the following sequence: Resin-Hyp(Bn)-T¹-P⁴-P³-P²-P¹. The products were cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above.

After lyophilisation the products were obtained as white powders and characterised by
15 HPLC-MS, analytical method A as described above. For analytical data, see Ex. 43, 44, 45, 46, 47, 48, 49, 50 in Table 1.

Example 51 is shown in Table 1.

The peptide was synthesized according general Method B starting with the amino acid
20 (2*S*,4*S*)-4-benzyloxypyrrolidine-2-carboxylic acid which was grafted to the resin (Fmoc-(4*S*)-Hyp(Bn)-2-chlorotrityl resin). The linear peptides was synthesized on the solid support according to the procedure described above in the following sequence: Resin-Hyp(Bn)-T¹-P⁴-P³-P²-P¹. The products was cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above.

25 After lyophilisation the product was obtained as a white powder and characterised by HPLC-MS, analytical method A as described above. For analytical data, see Ex. 51 in Table 1.

Examples 54 - 56 are shown in Table 1.

30 The peptides were synthesized according general Method B starting with the amino acid (2*S*,4*R*)-4-(4-bromobenzyl)-pyrrolidine-2-carboxylic acid which was grafted to the

resin (Fmoc-Hyp(4BrBn)-2-chlorotrityl resin). The linear peptides were synthesized on the solid support according to the procedure described above in the following sequence: Resin-Hyp(4BrBn)-^DPro-P⁴-P³-P²-P¹. The products were cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above.

After lyophilisation the products were obtained as white powders and characterised by HPLC-MS, analytical method A as described above.

For analytical data, see **Ex. 54, 55, 56** in *Table 1*.

Example 78 is shown in *Table 1*.

The peptide was synthesized according general Method A starting with the amino acid (2S)-3-(4-cyanophenyl)-2-amino)propanoic acid which was grafted to the resin (Fmoc-Phe(4CN)-2-chlorotrityl resin). The linear peptide was synthesized on the solid support according to the procedure described above in the following sequence: Resin-Phe(4CN)-Oic-^DPro-Dab-Trp-Cyp. The product was cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above.

After lyophilisation the product was obtained as a white powder and characterised by HPLC-MS, analytical method A as described above. For analytical data, see **Ex. 78** in *Table 1*.

20

Example 88 is shown in *Table 1*.

The peptide was synthesized according general Method A starting with the amino acid (2S)-3-(1-benzothiophen-3-yl)-2-amino propanoic acid which was grafted to the resin (Fmoc-Bbta-2-chlorotrityl resin). The linear peptide was synthesized on the solid support according to the procedure described above in the following sequence: Resin-Bbta-Oic-^DPro-Dab-Trp-Cyp. The product was cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above.

After lyophilisation the product was obtained as a white powder and characterised by HPLC-MS, analytical method A as described above. For analytical data, see **Ex. 88** in *Table 1*.

30

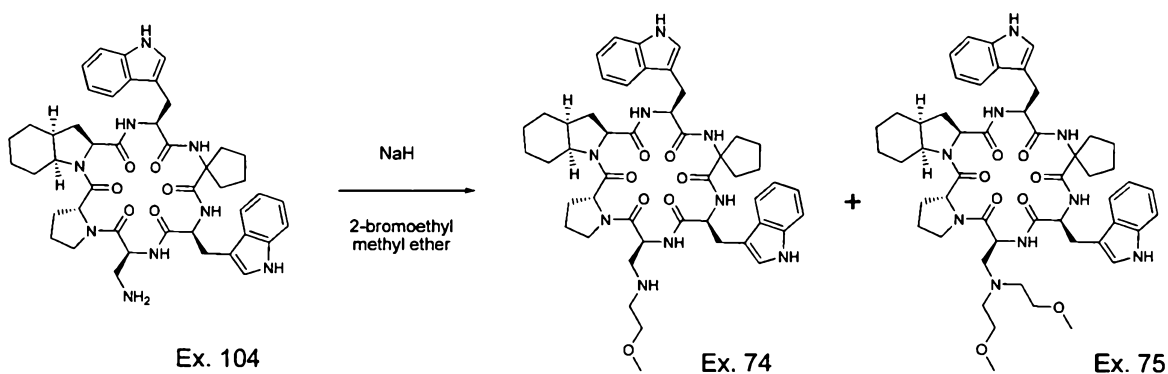
Example 103 is shown in *Table 1*.

The peptides were synthesized according general Method A starting with the amino acid (*S*)-2,4-diaminobutanoic acid which was grafted to the resin (Fmoc-Dab-2-chlorotrityl resin). The linear peptide was synthesized on the solid support according to
5 the procedure described above in the following sequence: Resin-Dab-Trp-Cyp-Trp-Trp-T²-T¹. The product was cleaved from the resin, cyclized, deprotected and purified by preparative reverse phase LC-MS as described above.

After lyophilisation the product was obtained as white powders and characterised by HPLC-MS, analytical method A as described above. For analytical data, see **Ex. 103** in
10 *Table 1*.

1.5 Post peptide sequence modifications

15 **Examples 74 and 75** as shown in *Table 1*.



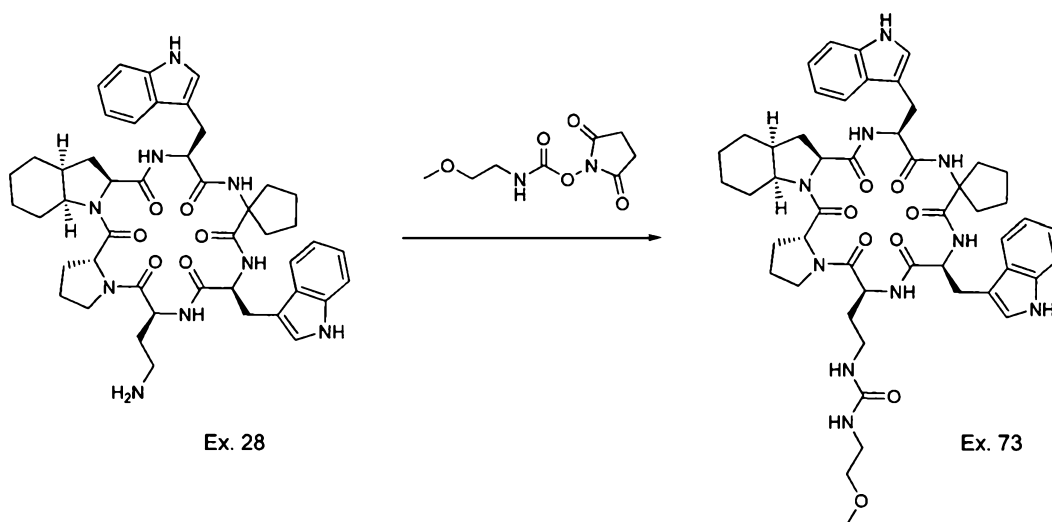
To a solution of 40 mg **Ex. 104** (44 μ mol) in 0.5 ml dry DMF was added 4 mg sodium
20 hydride (55% in mineral oil, 87 μ mol) at 0°C. The suspension was stirred at 0°C for 10 min, then sodium iodide (3.3 mg, 22 μ mol) and 2-bromoethyl methyl ether (6 μ l, 66 μ mol) were added. The reaction mixture was stirred overnight at rt. To complete the reaction the above addition sequence was repeated involving another 9 mg sodium hydride and 20 μ l 2-bromoethyl methyl ether. Then some drops of water were added,
25 the reaction mixture was concentrated and purified by preparative reverse phase LC-

MS as described above. After lyophilisation 1.7 mg of **Ex. 74** and 1.8 mg of **Ex. 75** was obtained as off-white powders and characterised by HPLC-MS, analytical method A as described above.

For analytical data, see **Ex. 74** and **Ex. 75** in *Table 1*.

5

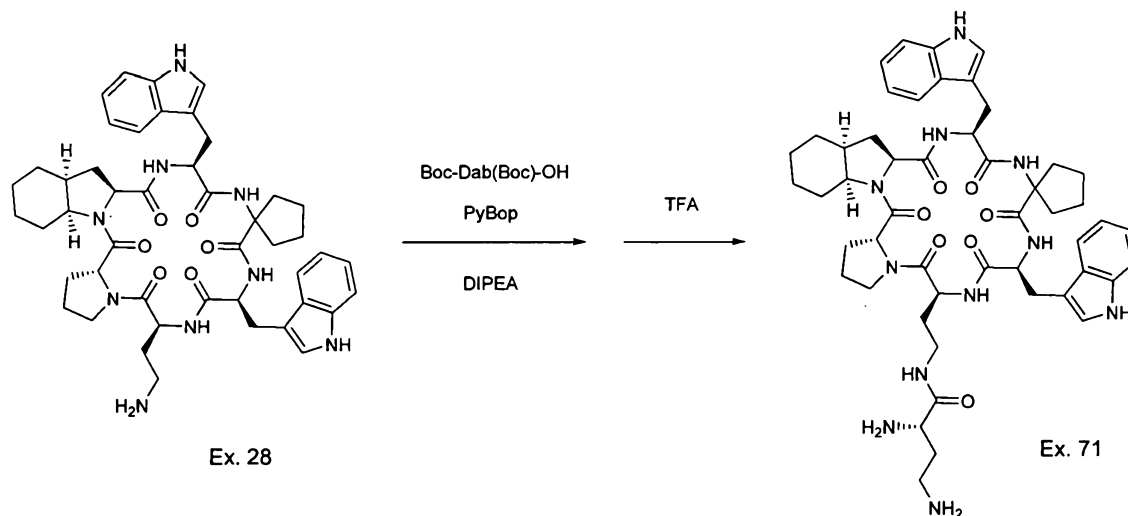
Example 73 as shown in *Table 1*.



- 10 To a solution of 15 mg **Ex. 28** (18 μmol) and 9 μl DIPEA (54 μmol) in 0.5 ml dry THF was added 8 mg of *N*-succinimidyl-*N*-(2-methoxyethyl)carbamate (36 μmol) and the mixture was stirred overnight at rt. The reaction mixture was concentrated and purified by preparative reverse phase LC-MS as described above. After lyophilisation 2 mg of **Ex. 73** was obtained and characterised by HPLC-MS, analytical method A as
- 15 described above.

For analytical data, see **Ex. 73** in *Table 1*.

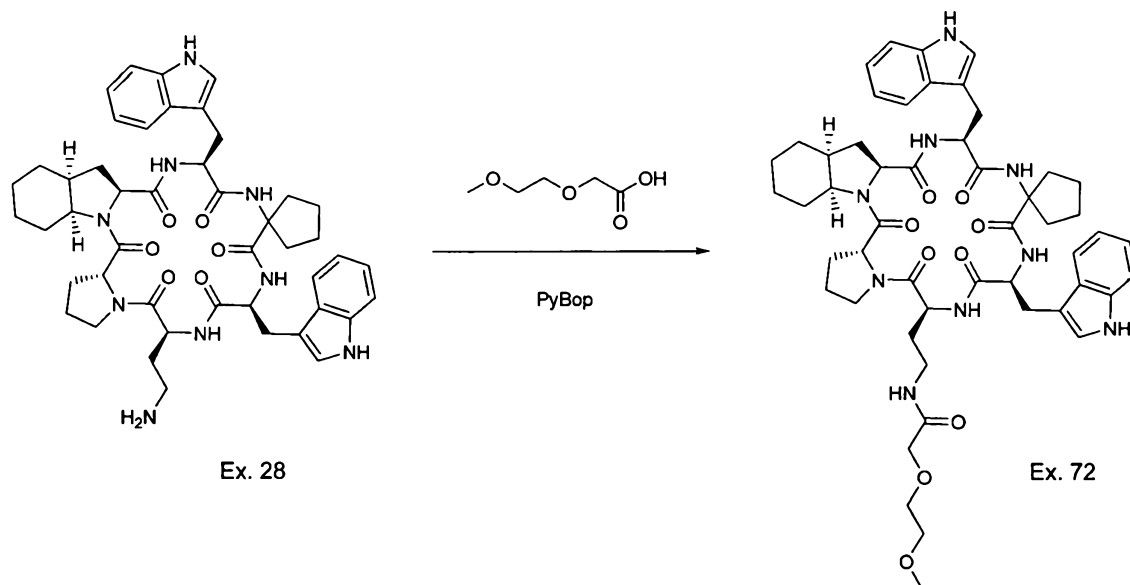
Example 71 as shown in Table 1.



A solution of 20 mg Ex. 28 (24 μ mol), 36 mg Boc-Dab(Boc)-OH-DCHA (72 μ mol), 38 mg
5 PyBOP (72 μ mol) and 25 μ l DIPEA (144 μ mol) in 0.5 ml dry DMF was stirred overnight
at rt. The reaction mixture was concentrated, resuspended in CH_2Cl_2 , washed with
water and concentrated again. The crude material was dissolved in 3 ml TFA containing
0.1 ml of water. After 2 h at rt the solution was concentrated and then purified by
preparative reverse phase LC-MS as described above. After lyophilisation 2.5 mg of Ex.
10 71 was obtained and characterised by HPLC-MS, analytical method A as described
above.

For analytical data, see Ex. 71 in Table 1.

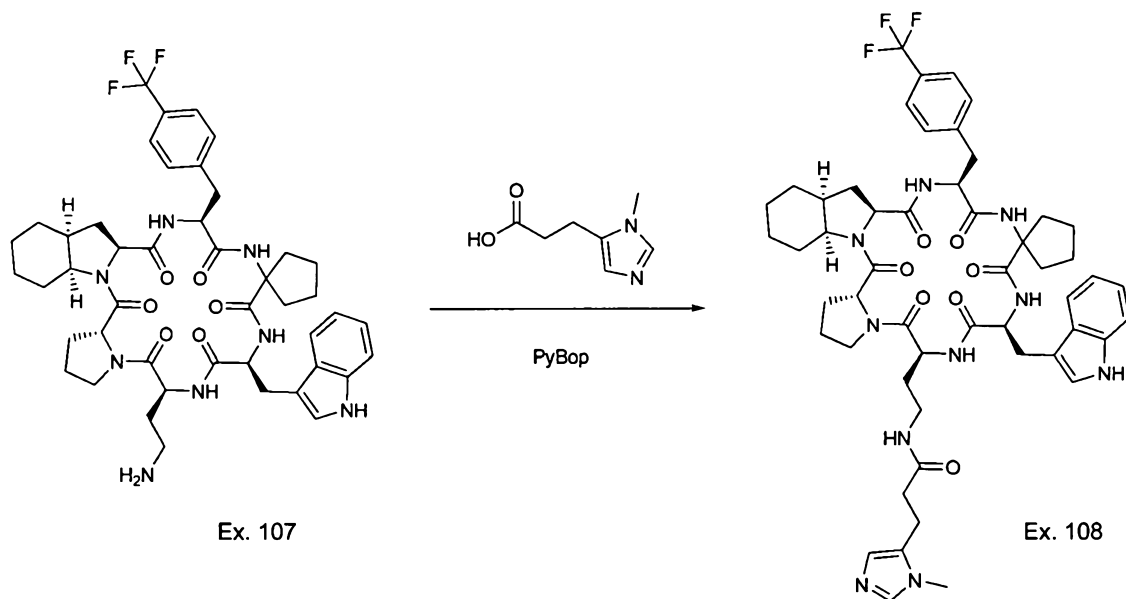
Example 72 as shown in *Table 1*.



- 5 To a solution of 42 mg **Ex. 28** (50 μmol) and 26 μl DIPEA (150 μmol) in 1 ml dry DMF was added 14 mg of 2-(2-methoxyethoxy)acetic acid (100 μmol) and 53 mg of PyBOP (100 μmol). The reaction mixture was stirred for 1h at rt, concentrated and purified by preparative reverse phase LC-MS as described above. After lyophilisation 7 mg of **Ex. 72** was obtained and characterised by HPLC-MS, analytical method A as described
- 10 above.

For analytical data, see **Ex. 72** in *Table 1*.

Example 108 as shown in *Table 1*.

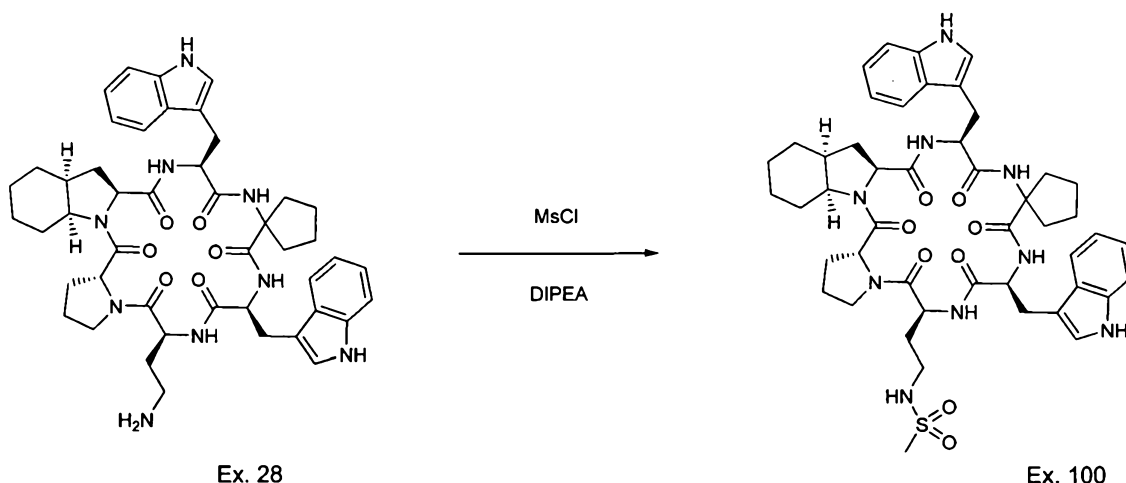


5

To a solution of 59 mg **Ex. 107** (61 μmol) and 41 μl DIPEA (242 μmol) in 1.2 ml dry DMF was added 19 mg of 3-(1-methyl-1H-imidazol-5-yl)propanoic acid (121 μmol) and 63 mg of PyBOP (121 μmol). The reaction mixture was stirred for 1h at rt, concentrated and purified by preparative reverse phase LC-MS as described above. After lyophilisation 30 mg of **Ex. 108** was obtained and characterised by HPLC-MS, analytical method D as described above.

For analytical data, see **Ex. 108** in *Table 1*.

Example 100 as shown in *Table 1*.



- 5 To a solution of 25 mg **Ex. 28** (free base; 28 μmol) and 19 μl DIPEA (112 μmol) in 1 ml dry THF/ CHCl_3 / CH_2Cl_2 (1:1:2) was added 6.5 μl methanesulfonyl chloride (84 μmol) and a catalytic amount of DMAP and the reaction mixture was stirred overnight at rt. Then additional 6.5 μl methanesulfonyl chloride (84 μmol) and 19 μl DIPEA (112 μmol) were added, stirred for 4 h at rt, finally concentrated and purified by preparative reverse
- 10 phase LC-MS as described above. After lyophilisation 3 mg of **Ex. 100** was obtained and characterised by HPLC-MS, analytical method A as described above.
- For analytical data, see **Ex. 100** in *Table 1*.

Example 101 as shown in *Table 1*.

- 15 Analogue to the procedure for **Ex. 100** but employing 2x 18.5 μl of 4-(dimethylamino)-benzene-1-sulfonyl chloride (2x 84 μmol). After purification by preparative reverse phase LC-MS and lyophilisation, 10 mg of **Ex. 101** was obtained and characterised by HPLC-MS, analytical method A as described above.
- For analytical data, see **Ex. 101** in *Table 1*.

20

Example 105 as shown in *Table 1*.

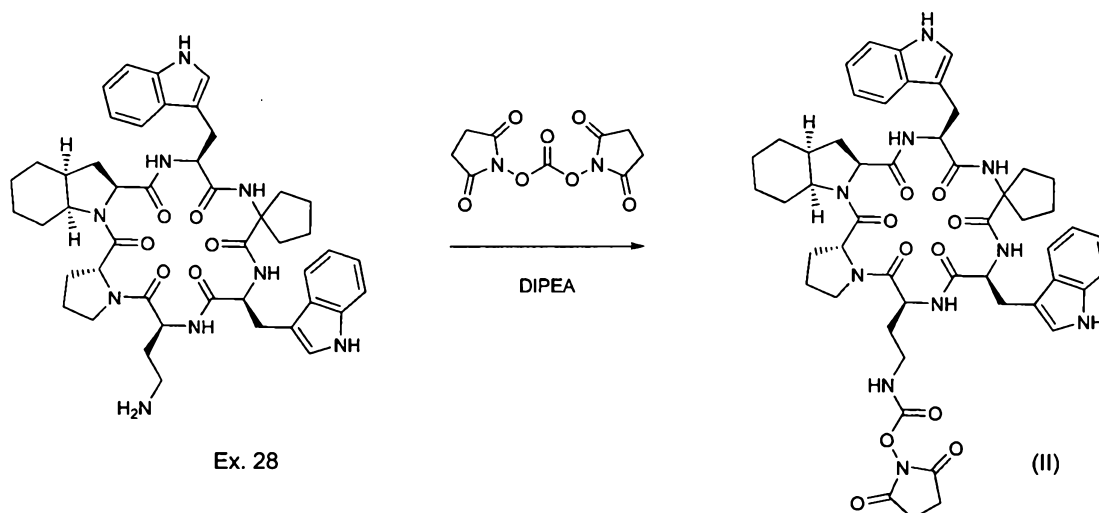
Analogue to the procedure for **Ex. 100** but employing 22 mg of **Ex. 28** (free base; 25 μmol), 16 mg of sodium carbonate (144 μmol) and 34 mg of 4-methylpiperazine-1-

sulfonyl chloride (144 μmol) in THF. After purification by preparative reverse phase LC-MS and lyophilisation, 5 mg of **Ex. 105** was obtained and characterised by HPLC-MS, analytical method A as described above.

For analytical data, see **Ex. 105** in Table 1.

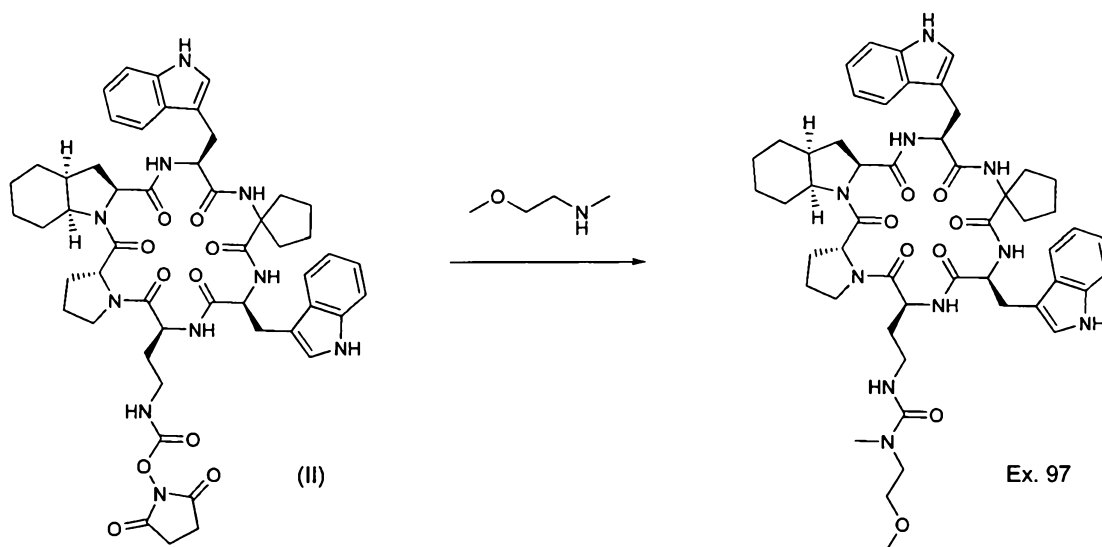
5

Preparation of intermediate **(II)**.



52 mg of *N,N'*-disuccinimidyl carbonate (free base; 202 μmol) was suspended in 2 ml
10 dry CH_2Cl_2 , cooled to 0°C and 32 μl DIPEA (185 μmol) was added. Then a solution of
150 mg **Ex. 28** (168 μmol) in 2.5 ml dry acetonitrile/ CH_2Cl_2 (1:1) was added dropwise
over 10 min. The reaction mixture was stirred at rt for 7 h before additional 15 μl
DIPEA (84 μmol) and 22 mg of *N,N'*-disuccinimidyl carbonate (84 μmol) was added.
The suspension was stirred overnight at rt, then concentrated, precipitated and
15 washed twice with diethylether to yield 177 mg crude **(II)** as a white solid.

Example 97 as shown in *Table 1*.



25 mg of succinimidyl carbamate (II) (26 μ mol) and 9 μ l 2-methoxy-N-methylethylamine (77 μ mol) were combined in 1 ml dry THF. The reaction mixture was stirred for 2 h at rt, concentrated and purified by preparative reverse phase LC-MS as described above. After lyophilisation 8 mg of Ex. 97 was obtained and characterised by HPLC-MS, analytical method A as described above. For analytical data, see Ex. 97 in *Table 1*.

10

Example 98 as shown in *Table 1*.

Analogue to the procedure for Ex. 97 but employing 20 mg of (II) (21 μ mol) and 6 μ l morpholine (62 μ mol). After purification by preparative reverse phase LC-MS and lyophilisation, 3 mg of Ex. 98 was obtained and characterised by HPLC-MS, analytical method A as described above. For analytical data, see Ex. 98 in *Table 1*.

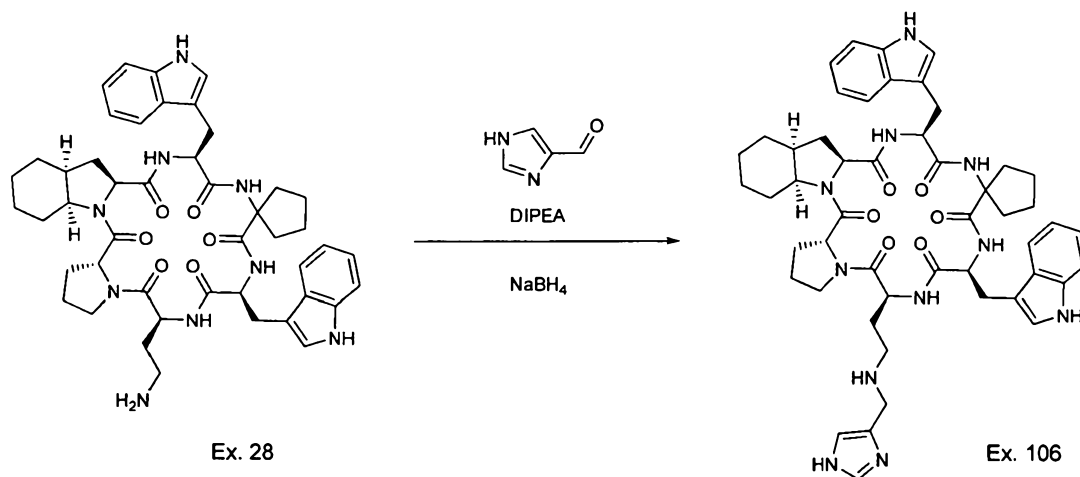
15

Example 99 as shown in *Table 1*.

Analogue to the procedure for Ex. 97 but employing 20 mg of (II) (21 μ mol) and 7 μ l N-methylpiperazine (62 μ mol). After purification by preparative reverse phase LC-MS and lyophilisation, 7 mg of Ex. 99 was obtained and characterised by HPLC-MS, analytical method A as described above. For analytical data, see Ex. 99 in *Table 1*.

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Example 106 as shown in *Table 1*.



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To a solution of 40 mg **Ex. 28** (42 μmol) and 22 μl DIPEA (127 μmol) in 1.0 ml dry THF was added 6.1 mg $1H\text{-imidazole-4-carbaldehyde}$ (63 μmol). After 5 h at rt, 3.2 mg sodium borohydride (85 μmol) was added and the reaction mixture monitored for completion (ca. 15 min). A few drops of water were added and the mixture was concentrated and purified by preparative reverse phase LC-MS as described above. After lyophilisation 13 mg of **Ex. 106** was obtained as a white solid and characterised by HPLC-MS, analytical method D as described above.

For analytical data, see **Ex. 106** in *Table 1*.

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1.6 Sequence data

Table 1: Examples

Ex.	Sequence ID	P1 ^{a)}	P2 ^{a)}	P3 ^{a)}	P4 ^{a)}	T1 ^{a)}	T2 ^{a)}	Synth. Method	Purity % ^{b)}	[M+H] ⁺	RT [min]	Anal. Method
1	SEQ ID NO:1	Trp	Aib	Trp	Arg	⁰ Pro	Tic	A	94	870.3	1.79	A
2	SEQ ID NO:2	Trp	Aib	Trp	Dab	⁰ Pro	Tic	A	96	814.3	1.78	A
3	SEQ ID NO:3	Trp	Cyp	Trp	Arg	⁰ Pro	Tic(7OH)	A	98	912.7	1.75	A
4	SEQ ID NO:4	Trp	Cyp	Trp	Dab	⁰ Pro	Pro((4S)F)	A	>98	796.3	1.66	A
5	SEQ ID NO:5	Trp	Cyp	Trp	Arg	⁰ Pro	Thz	A	95	852.4	1.74	A
6	SEQ ID NO:6	Trp	Cyp	Trp	Dab	⁰ Pro	Thz	A	>98	796.3	1.71	A
7	SEQ ID NO:7	Trp(5OH)	Cyp	Trp	Gln	⁰ Pro	Thz	A	95	840.2	1.71	A
8	SEQ ID NO:8	Trp(5OH)	Cyp	Trp	Arg	⁰ Pro	Tic	A	93	912.7	1.71	A
9	SEQ ID NO:9	2Nal	Cyp	Trp	Gln	⁰ Pro	Tic	A	92	879.5	2.14	A
10	SEQ ID NO:10	2Nal	Cyp	Trp	Dab	⁰ Pip	Pip	A	91	817.4	1.92	A
11	SEQ ID NO:11	Trp(5OH)	Chx	Trp(5OH)	Arg	⁰ Pro	Oic	A	88	934.7	1.64	A
12	SEQ ID NO:12	Trp(5OH)	Cyp	Trp(5OH)	Dap	⁰ Pro	Oic	A	96	850.3	1.56	A
13	SEQ ID NO:13	Trp	Cyp	Trp	Dab	⁰ Pip	Oic	A	>98	846.4	1.88	A
14	SEQ ID NO:14	Trp	Cyp	2Nal	Dab	⁰ Pip	Oic	A	94	857.3	1.99	A
15	SEQ ID NO:15	Trp	Cyp	2Nal	Gln	⁰ Pro	Oic	A	79	871.3	2.13	A
16	SEQ ID NO:16	OctG	Cyp	Trp	Dab	⁰ Pro	Oic	A	98	815.4	2.08	A
17	SEQ ID NO:17	Trp	Cyp	Trp	Gln	⁰ Pro	Oic	A	91	860.5	1.99	A
18	SEQ ID NO:18	Trp	Chx	Trp	Dab	⁰ Pro	Oic	A	96	846.3	1.86	A

Table 1: Examples (continued)

Ex.	Sequence ID	P1 ^{a)}	P2 ^{a)}	P3 ^{a)}	P4 ^{a)}	T1 ^{a)}	T2 ^{a)}	Synth. Method	Purity % ^{b)}	[M+H] ⁺	RT [min]	Anal. Method
19	SEQ ID NO:19	Trp	Ac3c	Trp	Dab	^b Pro	Oic	A	97	804.4	1.75	A
20	SEQ ID NO:20	Trp	Ac4c	Trp	Dab	^b Pro	Oic	A	96	818.3	1.79	A
21	SEQ ID NO:21	Trp	4,4-AC-ThioTHP	Trp	Dab	^b Pro	Oic	A	97	864.3	1.82	A
22	SEQ ID NO:22	Trp	Cyp	Phe(4F)	Dab	^b Pro	Oic	A	72	811.4	1.86	A
23	SEQ ID NO:23	Trp	Cyp	Tyr(Me)	Dab	^b Pro	Oic	A	88	823.3	1.83	A
24	SEQ ID NO:24	Trp	Cyp	Ala(2Quin)	Dab	^b Pro	Oic	A	97	844.5	1.61	A
25	SEQ ID NO:25	Trp	Cyp	Trp	Arg	^b Aze	Tic	A	97	882.4	1.84	A
26	SEQ ID NO:26	Trp	Cyp	Trp	Dab	^b Aze	Tic	A	95	826.8	3.23	C
27	SEQ ID NO:27	Cha	Cyp	Trp	Dab	^b Pro	Oic	A	95	799.2	3.66	C
28	SEQ ID NO:28	Trp	Cyp	Trp	Dab	^b Pro	Oic	A	90	832.2	3.38	C
29	SEQ ID NO:29	Trp(SOH)	Cyp	Trp	Arg	^b Pro	Thz(5,5Me ₂)	A	92	896.3	1.69	A
30	SEQ ID NO:30	Trp	^b LAtc	Trp	Dab	^b Pro	Oic	A	>98	894.4	3.77; 3.82 ^{c)}	C
31	SEQ ID NO:31	Trp	Cyp	Ala(2Furyl)	Dab	^b Pro	Oic	B	84	783.4	2.17	B
32	SEQ ID NO:32	Trp	Cyp	Phe(4F)	Ser	^b Pro	Oic	B	>98	798.4	2.10	A
33	SEQ ID NO:33	Trp	Cyp	Phe(4Cl)	Ser	^b Pro	Oic	B	98	814.4	2.17	A
34	SEQ ID NO:34	Trp	Cyp	Phe(4CF ₃)	Dab	^b Pro	Oic	B	91	861.4	1.97	A
35	SEQ ID NO:35	Trp	Cyp	^b LTrp(7Aza)	Dab	^b Pro	Oic	A	93	833.3	1.58	A
36	SEQ ID NO:36	Trp	Cyp	Tyr(Ph)	Dab	^b Pro	Oic	B	93	885.3	2.02	A
37	SEQ ID NO:37	Phe(4CF ₃)	Cyp	Trp	Dab	^b Pip	Pro((4R)Ph)	B	92	897.3	2.02	A
38	SEQ ID NO:38	Trp	Cyp	Trp	Dab	^b Pro	Pro((4R)Bn)	B	89	868.4	1.91	A

Table 1: Examples (continued)

Ex.	Sequence ID	P1 ^{a)}	P2 ^{a)}	P3 ^{a)}	P4 ^{a)}	T1 ^{a)}	T2 ^{a)}	Synth. Method	Purity % ^{b)}	[M+H] ⁺	RT [min]	Anal. Method
39	SEQ ID NO:39	Trp	Cyp	Trp	Dab	^D Pro	Pro((4R)4BrBn)	B	90	948.4	1.99	A
40	SEQ ID NO:40	Trp	Cyp	Trp	Dab	^D Pro	Pro((4R)3CNBn)	B	96	893.5	1.86	A
41	SEQ ID NO:41	Trp	Cyp	Trp	Dab	^D Pro	Pro((4S)cHex)	B	93	860.4	1.98	A
42	SEQ ID NO:42	Trp	Cyp	Trp	Dab	^D Pro	Pro(5,5Me ₂)	B	98	806.3	1.76	A
43	SEQ ID NO:43	Trp	Cyp	Phe(4Cl)	Dab	^D Pro	Hyp(Bn)	B	96	879.4	1.98	A
44	SEQ ID NO:44	Phe(4CN)	Cyp	Phe(4F)	Ser	^D Pro	Hyp(Bn)	B	92	836.4	2.16	A
45	SEQ ID NO:45	Trp	Cyp	Trp	Dab	^D Pro	Hyp(Bn)	B	>98	884.7	1.87	A
46	SEQ ID NO:46	Trp	Cyp	Trp	Ser	^D Pro	Hyp(Bn)	B	98	871.5	2.10	A
47	SEQ ID NO:47	Phe(4CN)	Cyp	Trp	Gln	^D Pro	Hyp(Bn)	B	93	898.3	2.02	A
48	SEQ ID NO:48	Trp(6Cl)	Cyp	Trp	Dab	^D Pro	Hyp(Bn)	B	97	918.4	1.96	A
49	SEQ ID NO:49	Phe(4CN)	Cyp	Trp	Dab	^D Pro	Hyp(Bn)	B	96	870.3	1.84	A
50	SEQ ID NO:50	Phe(4CN)	Cyp	Trp	Ser	^D Pip	Hyp(Bn)	B	93	871.5	2.19	A
51	SEQ ID NO:51	Trp	Cyp	Trp	Dab	^D Pro	(4S)-Hyp(Bn)	B	96	884.3	1.84	A
52	SEQ ID NO:52	Trp	Cyp	Trp	Dab	^D Pro	Hyp(Ph)	B	95	870.4	1.88	A
53	SEQ ID NO:53	Trp	Cyp	Trp	Dab	^D Pro	Hyp(4CNBn)	B	95	909.5	1.85	A
54	SEQ ID NO:54	Phe(4CF ₃)	Cyp	Trp	Dab	^D Pro	Hyp(4BrBn)	B	97	991.5	2.09	A
55	SEQ ID NO:55	Phe(4CN)	Cyp	Trp	Ser	^D Pro	Hyp(4BrBn)	B	93	937.4	2.22	A
56	SEQ ID NO:56	Trp	Cyp	Trp	Dab	^D Pro	Hyp(4BrBn)	B	93	962.5	1.99	A
57	SEQ ID NO:57	Trp	Cyp	Trp	Dab	^D Pro	Hyp(CONHPh)	B	98	913.4	1.87	A
58	SEQ ID NO:58	Trp	Cyp	Trp	alloThr	^D Pro	Oic	B	95	833.3	2.11	A
59	SEQ ID NO:59	Trp	Cyp	Trp	hArg	^D Pro	Oic	B	94	902.4	1.86	A

Table 1: Examples (continued)

Ex.	Sequence ID	P1 ^{a)}	P2 ^{a)}	P3 ^{a)}	P4 ^{a)}	T1 ^{a)}	T2 ^{a)}	Synth. Method	Purity % ^{b)}	[M+H] ⁺	RT [min]	Anal. Method
60	SEQ ID NO:60	Trp	Cyp	Trp	hCis	^D Pro	Oic	B	96	903.4	2.00	A
61	SEQ ID NO:61	Trp	Cyp	Trp	Gln(iPr)	^D Pro	Oic	B	97	902.4	2.17	A
62	SEQ ID NO:62	Trp	Cyp	Trp	hSer(Me)	^D Pro	Oic	B	97	847.3	2.19	A
63	SEQ ID NO:63	Trp	Cyp	Trp	Lys(Ac)	^D Pro	Oic	B	93	902.4	2.06	A
64	SEQ ID NO:64	Trp	Cyp	Trp	Lys(Bz)	^D Pro	Oic	B	94	964.4	2.27	A
65	SEQ ID NO:65	Trp	Cyp	Trp	Lys(Me)	^D Pro	Oic	B	90	874.3	1.83	A
66	SEQ ID NO:66	Trp	Cyp	Trp	Lys((SR)OH)	^D Pro	Oic	B	89	876.4	1.78	A
67	SEQ ID NO:67	Trp	Cyp	Trp	Lys(Nic)	^D Pro	Oic	B	95	965.4	1.91	A
68	SEQ ID NO:68	Trp	Cyp	Trp	Met(O ₂)	^D Pro	Oic	B	98	895.3	2.10	A
69	SEQ ID NO:69	Trp	Cyp	Trp	Ala(Ppz)	^D Pro	Oic	B	85	887.3	1.74	A
70	SEQ ID NO:70	Trp	Cyp	Trp	Dap(CONH ₂)	^D Pro	Oic	B	95	861.3	1.97	A
71	SEQ ID NO:71	Trp	Cyp	Trp	Dab(Dab)	^D Pro	Oic	d)	83	932.4	1.69	A
72	SEQ ID NO:72	Trp	Cyp	Trp	Dab(MEMCO)	^D Pro	Oic	d)	>98	948.7	2.10	A
73	SEQ ID NO:73	Trp	Cyp	Trp	Dab(MeO(CH ₂) ₂ NCO)	^D Pro	Oic	d)	81	933.4	2.08	A
74	SEQ ID NO:74	Trp	Cyp	Trp	Dap(MeO(CH ₂) ₂)	^D Pro	Oic	d)	98	876.4	1.93	A
75	SEQ ID NO:75	Trp	Cyp	Trp	Dap((MeO (CH ₂) ₂) ₂)	^D Pro	Oic	d)	98	934.5	2.02	A
76	SEQ ID NO:76	Phe(4CO OMe)	Cyp	Trp	Dab	^D Pro	Oic	B/d)	96	851.3	1.81	A
77	SEQ ID NO:77	Trp	Cyp	Trp	Dab	^D Pro	Hyp(3CNBn)	d)	90	909.4	1.83	A
78	SEQ ID NO:78	Phe(4CN)	Cyp	Trp	Dab	^D Pro	Oic	A	86	818.4	1.76	A

Table 1: Examples (continued)

Ex.	Sequence ID	P1 ^{a)}	P2 ^{a)}	P3 ^{a)}	P4 ^{a)}	T1 ^{a)}	T2 ^{a)}	Synth. Method	Purity % ^{b)}	[M+H] ⁺	RT [min]	Anal. Method
79	SEQ ID NO:79	Trp	Cyp	Trp	Ser	^b Pro	Oic	B	>98	819.5	2.07	A
80	SEQ ID NO:80	Trp	Cyp	Trp	Ser	^b Pip	Oic	B	96	833.4	2.16	A
81	SEQ ID NO:81	Trp(6Cl)	Cyp	Trp	Ser	^b Pro	Oic	B	>98	853.0	2.13	A
82	SEQ ID NO:82	Phe(4CN)	Cyp	Trp	Ser	^b Pro	Oic	B	97	805.3	2.00	A
83	SEQ ID NO:83	Trp	Cyp	Trp	Lys(4Oxa)	^b Pro	Oic	B	94	862.3	1.79	A
84	SEQ ID NO:84	Trp	Cyp	Trp	Ser(Me)	^b Pro	Oic	B	98	833.3	2.19	A
85	SEQ ID NO:85	Trp	Cyp	Trp	Thr	^b Pro	Oic	B	97	833.4	2.13	A
86	SEQ ID NO:86	Bip	Cyp	Trp	Dab	^b Pro	Oic	B	98	869.3	2.02	A
87	SEQ ID NO:87	hTyr	Cyp	Trp	Dab	^b Pro	Oic	B	>98	823.3	1.74	A
88	SEQ ID NO:88	Bbta	Cyp	Trp	Dab	^b Pro	Oic	A	95	849.3	1.93	A
89	SEQ ID NO:89	Nle(6OBn)	Cyp	Trp	Dab	^b Pro	Oic	B	93	865.3	1.96	A
90	SEQ ID NO:90	Phe(4OHPh)	Cyp	Trp	Dab	^b Pro	Oic	B	94	901.3	1.85	A
91	SEQ ID NO:91	Tyr(Ph)	Cyp	Trp	Dab	^b Pro	Oic	B	98	885.3	2.03	A
92	SEQ ID NO:92	Tyr(4MeO COBn)	Cyp	Trp	Dab	^b Pro	Oic	B	94	957.4	2.00	A
93	SEQ ID NO:93	Trp	Deg	Trp	Dab	^b Pro	Oic	B	>98	834.3	1.82	A
94	SEQ ID NO:94	Trp	Ac7c	Trp	Dab	^b Pro	Oic	B	95	860.3	1.90	A
95	SEQ ID NO:95	Trp	Chx(4oxo)	Trp	Dab	^b Pro	Oic	B	95	860.3	1.90	A
96	SEQ ID NO:96	Trp	Ac8c	Trp	Dab	^b Pro	Oic	B	94	874.4	1.92	A
97	SEQ ID NO:97	Trp	Cyp	Trp	Dab((MeO(CH ₂) ₂) ₂ (Me)NCO)	^b Pro	Oic	d)	96	947.4	2.12	A

Table 1: Examples (continued)

Ex.	Sequence ID	P1 ^{a)}	P2 ^{a)}	P3 ^{a)}	P4 ^{a)}	T1 ^{a)}	T2 ^{a)}	Synth. Method	Purity % ^{b)}	[M+H] ⁺	RT [min]	Anal. Method
98	SEQ ID NO:98	Trp	Cyp	Trp	Dab(morphCO)	^D Pro	Oic	d)	98	945.4	2.08	A
99	SEQ ID NO:99	Trp	Cyp	Trp	Dab(MePpzCO)	^D Pro	Oic	d)	98	958.4	1.81	A
100	SEQ ID NO:100	Trp	Cyp	Trp	Dab(MeSO ₂)	^D Pro	Oic	d)	91	910.3	2.08	A
101	SEQ ID NO:101	Trp	Cyp	Trp	Dab(4Me ₂ N PhSO ₂)	^D Pro	Oic	d)	95	1015.4	2.28	A
102	SEQ ID NO:102	Trp	Cyp	Trp	Dab(Ac)	^D Pro	Oic	d)	95	874.3	2.04	A
103	SEQ ID NO:103	Trp	Cyp	Trp	Dab	^D Pro	Hyp	A	97	794.4	1.59	A
104	SEQ ID NO:104	Trp	Cyp	Trp	Dap	^D Pro	Oic	A	98	818.4	1.84	A
105	SEQ ID NO:105	Trp	Cyp	Trp	Dab(SN13)	^D Pro	Oic	d)	90	994.5	1.86	A
106	SEQ ID NO:106	Trp	Cyp	Trp	Dab(A55)	^D Pro	Oic	d)	97	912.4	2.17	D
107	SEQ ID NO:107	Phe(4CF ₃)	Cyp	Trp	Dab	^D Pro	Oic	B	94	861.4	1.95	A
108	SEQ ID NO:108	Phe(4CF ₃)	Cyp	Trp	Dab(A56)	^D Pro	Oic	d)	91	997.3	2.69	D
109	SEQ ID NO:109	Phe(3CF ₃)	Cyp	Trp	Dab	^D Pro	Oic	B	99	861.3	2.65	D
110	SEQ ID NO:110	Phe(4CF ₃)	Cyp	Trp	3Pal	^D Pic	Oic	B	99	923.2	2.90	D

a) Abbreviations of amino acid see listing above.

b) %-purity of compounds after prep. HPLC.

c) Double peak.

d) Post peptide sequence modifications.

2. Biological methods

2.1 Preparation of the peptide samples.

Lyophilized peptides were weighed on a Microbalance (Mettler MX5) and dissolved in aqueous 90 % DMSO to a final concentration of 10 mM unless otherwise stated. Stock solutions were kept at +4°C, and protected from light.

2.2 CCR10 antagonism assays

Peptides were assayed for CCR10 antagonism in a calcium flux assay and in a chemotaxis assay using a mouse pre-B cell line 300-19 stably transfected with human CCR10, and with human CCL27 as agonist.

Calcium Flux Assay

The calcium flux release was assessed using CCR10 transfected 300-19 murine pre-B cells. These cells were labeled as a batch with Calcium4 Reagent (Molecular Devices, Sunnyvale, CA) in HBSS buffer for 60 min.

After dispensing 8×10^4 cells in each well of a 384-well black plate, a concentrated solution of the β -hairpin peptidomimetics of this invention in HBSS + 0.1% BSA + 0.1% DMSO (final concentration) was added to the cells. The entire plate was centrifuged and placed in a Flexstation II (Molecular Devices) automated plate reader. After reading a 20 s baseline, the Flexstation dispensed CCL27 (RnD systems) at a final concentration of 30 nM in HBSS + 0.1% BSA onto the cells and calcium flux was measured for an additional 70 s.

Alternatively a FlipR384 (Molecular Devices) was used for read out of the 384-well plates. In this case about 8×10^4 cells were placed in each well, centrifuged, placed in the FlipR and after 5 s of baseline reading, the β -hairpin peptidomimetics in HBSS + 0.1% BSA + 0.1% DMSO (final concentration) were added. After an incubation time of 5 min, the CCL27 solution was added to the mixture and the calcium flux was measured for 200 s.

The maximum signal was determined from control wells without inhibitor. Percentage of inhibition was calculated from a range of compound concentrations, which were subsequently used to calculate IC₅₀ values (Softmax Pro, Molecular Devices). All steps were carried out at room temperature.

5

Chemotaxis Assay

The chemotactic response of CCR10-transfected 300-19 murine pre-B cells to a gradient of CCL27 (CTACK) was measured using disposable Transwell® assay plates from Costar (5 µm pore size) according to the protocol of the manufacturer. Briefly, cells were grown under sterile conditions at 37 °C with 5% CO₂ in flasks containing RPMI + 5% FCS, glutamine, penicillin/streptomycin (all media components were from Life Technologies) and the appropriate selection antibiotics (Puromycin, G418 or Tetracycline). For the assay, cells were pelleted by centrifugation, washed once in Dulbecco's phosphate buffered saline (DPBS), and resuspended to give 1 x 10⁶ cells/ml in RPMI + 0.5% bovine serum albumin (BSA). 100 µl of cell suspension was applied to the top of the assay filter. The β-hairpin peptidomimetics, diluted in the same assay medium, were added to both top and bottom chambers. The cells were allowed to migrate for 4-6 hours at 37°C into the bottom chamber of the assay plate containing 30 nM of CCL27 (RnD systems). Migrated cells were counted using a FACS cytometer (Cytomics FC500, Beckman Coulter). Data normalization was performed using the number of any cells that had migrated in the absence of the β-hairpin peptidomimetic and the number of cells that have randomly migrated in absence of CCL27 [these values were taken as 100% (no inhibitory activity) and 0%, respectively]. From a range of compound concentrations IC₅₀ were determined using Prism5 (GraphPad software).

25

2.3 Results

Table 2: Biological Results

Ex.	Sequence ID	IC ₅₀ (nM) Calcium Flux Assay			IC ₅₀ (nM) Chemotaxis Assay
1	SEQ ID NO:1	225.8	±	186.5	94.0
2	SEQ ID NO:2	199.9	±	56.5	21.6
3	SEQ ID NO:3	78.5	±	38.6	nd
4	SEQ ID NO:4	860.5	±	381.8	42.0
5	SEQ ID NO:5	70.6	±	20.1	nd
6	SEQ ID NO:6	133.7	±	73.3	19.6
7	SEQ ID NO:7	144.5	±	84.1	3.1
8	SEQ ID NO:8	52.5	±	3.5	nd
9	SEQ ID NO:9	9.2	±	3.6	2.0
10	SEQ ID NO:10	43.2	±	44.9	9.7
11	SEQ ID NO:11	548.0	±	82.5	11.6
12	SEQ ID NO:12	246.4	±	79.0	nd
13	SEQ ID NO:13	26.0	±	18.0	17.0
14	SEQ ID NO:14	70.5	±	70.2	nd
15	SEQ ID NO:15	35.3	±	14.3	nd
16	SEQ ID NO:16	40.4	±	24.4	4.2
17	SEQ ID NO:17	44.3	±	11.0	nd
18	SEQ ID NO:18	332.9	±	149.0	3.1
20	SEQ ID NO:20	353.4	±	282.8	1.7
21	SEQ ID NO:21	823.1	±	407.5	21.9
22	SEQ ID NO:22	119.8	±	63.6	nd
23	SEQ ID NO:23	214.3	±	54.0	3.8
24	SEQ ID NO:24	283.3	±	103.5	30.3
25	SEQ ID NO:25	70.4	±	19.2	nd
26	SEQ ID NO:26	57.0	±	26.4	nd
27	SEQ ID NO:27	242.8	±	101.4	nd
28	SEQ ID NO:28	122.8	±	86.3	29.0
29	SEQ ID NO:29	214.0	±	105.9	109.0
30	SEQ ID NO:30	608.2	±	188.5	nd

Table 2: Biological Results (continued)

Ex.	Sequence ID	IC ₅₀ (nM) Calcium Flux Assay			IC ₅₀ (nM) Chemotaxis Assay
31	SEQ ID NO:31	131.9	±	30.8	nd
32	SEQ ID NO:32	8.8	±	5.0	12.0
33	SEQ ID NO:33	6.1	±	0.8	2.7
34	SEQ ID NO:34	58.6	±	5.7	38.7
36	SEQ ID NO:36	602.0	±	96.2	208.5
37	SEQ ID NO:37	14.8	±	12.0	22.0
38	SEQ ID NO:38	26.1	±	8.1	2.3
39	SEQ ID NO:39	15.8	±	10.3	9.0
40	SEQ ID NO:40	27.9	±	10.5	3.8
41	SEQ ID NO:41	54.3	±	22.0	140.0
42	SEQ ID NO:42	82.5	±	30.4	14.2
43	SEQ ID NO:43	39.9	±	34.8	nd
44	SEQ ID NO:44	1.9	±	2.1	13.5
45	SEQ ID NO:45	65.8	±	19.6	14.0
46	SEQ ID NO:46	12.6	±	9.0	35.4
47	SEQ ID NO:47	21.7	±	3.9	nd
48	SEQ ID NO:48	8.5	±	3.5	8.6
49	SEQ ID NO:49	181.0	±	109.6	5.3
50	SEQ ID NO:50	0.5	±	0.2	1.8
51	SEQ ID NO:51	259.9	±	153.7	60.1
52	SEQ ID NO:52	42.0	±	25.1	37.0
53	SEQ ID NO:53	48.9	±	40.0	143.0
54	SEQ ID NO:54	22.6	±	13.6	nd
55	SEQ ID NO:55	5.3	±	3.9	0.6
56	SEQ ID NO:56	11.6	±	9.2	2.5
57	SEQ ID NO:57	149.9	±	109.6	183.5
58	SEQ ID NO:58	11.6	±	15.4	1.2
59	SEQ ID NO:59	25.0	±	11.3	3.7
60	SEQ ID NO:60	54.9	±	35.5	8.7
61	SEQ ID NO:61	25.1	±	17.7	1.0
62	SEQ ID NO:62	12.0	±	7.9	1.8

Table 2: Biological Results (continued)

Ex.	Sequence ID	IC ₅₀ (nM) Calcium Flux Assay			IC ₅₀ (nM) Chemotaxis Assay
63	SEQ ID NO:63	28.0	±	5.7	2.3
64	SEQ ID NO:64	3.0	±	2.0	2.7
65	SEQ ID NO:65	nd			4.4
66	SEQ ID NO:66	333.0	±	7.1	7.0
67	SEQ ID NO:67	49.5	±	19.1	8.8
68	SEQ ID NO:68	4.8	±	0.3	1.2
69	SEQ ID NO:69	1055.7	±	106.8	16.4
70	SEQ ID NO:70	20.0	±	4.2	4.7
71	SEQ ID NO:71	566.8	±	154.8	50.2
72	SEQ ID NO:72	62.8	±	41.6	11.5
73	SEQ ID NO:73	24.2	±	24.5	5.3
74	SEQ ID NO:74	56.8	±	99.8	6.9
75	SEQ ID NO:75	399.2	±	178.4	15.2
76	SEQ ID NO:76	476.0	±	70.7	14.7
77	SEQ ID NO:77	127.4	±	73.0	50.7
78	SEQ ID NO:78	279.6	±	193.4	48.0
79	SEQ ID NO:79	61.6	±	30.9	1.4
80	SEQ ID NO:80	6.9	±	12.3	9.6
81	SEQ ID NO:81	6.3	±	2.0	5.0
82	SEQ ID NO:82	80.3	±	64.6	nd
83	SEQ ID NO:83	106.7	±	9.0	5.9
84	SEQ ID NO:84	46.4	±	30.7	10.1
85	SEQ ID NO:85	20.4	±	1.6	5.4
86	SEQ ID NO:86	8.1	±	3.7	1.8
87	SEQ ID NO:87	516.5	±	246.8	13.0
88	SEQ ID NO:88	220.2	±	129.3	18.9
89	SEQ ID NO:89	nd			16.6
90	SEQ ID NO:90	48.9	±	64.3	6.6
91	SEQ ID NO:91	1.1	±	0.3	1.7
92	SEQ ID NO:92	16.7	±	1.1	2.3
93	SEQ ID NO:93	145.8	±	76.4	76.1

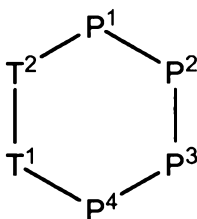
Table 2: Biological Results (continued)

Ex.	Sequence ID	IC ₅₀ (nM) Calcium Flux Assay	IC ₅₀ (nM) Chemotaxis Assay
94	SEQ ID NO:94	392.7 ± 218.2	7.2
95	SEQ ID NO:95	262.0 ± 215.0	17.8
96	SEQ ID NO:96	706.0 ± 73.5	256.8
97	SEQ ID NO:97	8.1 ± 9.1	5.6
98	SEQ ID NO:98	3.0 ± 1.3	11.1
99	SEQ ID NO:99	53.9 ± 33.4	5.3
100	SEQ ID NO:100	0.2 ± 0.1	3.4
101	SEQ ID NO:101	6.4 ± 4.6	nd
102	SEQ ID NO:102	30.3 ± 23.1	4.8
103	SEQ ID NO:103	190.0 ± 89.8	nd
104	SEQ ID NO:104	52.7 ± 38.2	nd
105	SEQ ID NO:105	390.1 ± 228.0	1.2
106	SEQ ID NO:106	12.2 ± 3.8	4.8
107	SEQ ID NO:107	58.1 ± 33.9	13.4
108	SEQ ID NO:108	34.5 ± 17.3	2.5
109	SEQ ID NO:109	41.1 ± 9.7	3.2
110	SEQ ID NO:110	63.2 ± 25.6	2.7

nd = not determined

CLAIMS

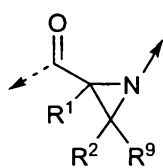
1. Compounds of the general formula (I)



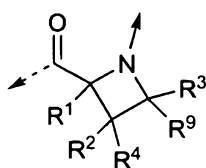
(I)

wherein the single elements T or P are connected in either direction from the carbonyl (C=O) point of attachment to the nitrogen (N) of the next element and wherein

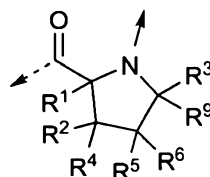
- 10 T^1 and T^2 are independently
an L or D α -amino acid of one of the formulae



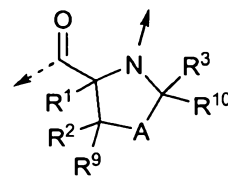
AA1



AA2

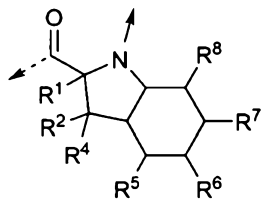


AA3

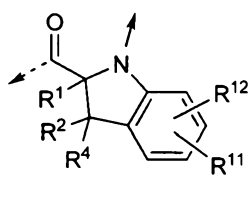


AA4

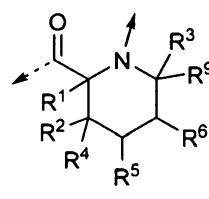
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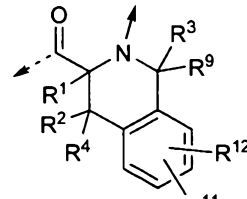
AA5



AA6



AA7



AA8

P¹ and P³ are independently

-NR¹CH(R¹⁹)CO-;

P² is -NR¹C(R²⁰)(R²¹)CO-; or -NR¹C(Z)CO-;

P⁴ is -NR¹CH(R²⁴)CO-;

5

A is O; NR⁹; S; SO; or SO₂

R¹, R² and R³ are independently

H; CF₃; lower alkyl; lower alkenyl; aryl-lower alkyl; or heteroaryl-lower alkyl;

R⁴, R⁵, R⁶, R⁷ and R⁸ are independently

10 H; F; CF₃; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl; aryl;

heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; -(CHR¹³)_oOR¹⁵;

-(CHR¹³)_oSR¹⁵; -(CHR¹³)_oNR¹⁵R¹⁶; -(CHR¹³)_oCONR¹⁵R¹⁶;

-(CHR¹³)_oNR¹CONR¹⁵R¹⁶; -(CHR¹³)_oNR¹COR¹⁵; -(CHR¹³)_oCOOR¹⁵;

-(CHR¹³)_oCONR¹⁵R¹⁶; -(CHR¹³)_oPO(OR¹)₂; -(CHR¹³)_oSO₂R¹⁵;

15 -(CHR¹³)_oNR¹SO₂R¹⁵; -(CHR¹³)_oSO₂NR¹⁵R¹⁶; -(CR¹R¹³)_oR³⁰; or

-(CHR¹)_nO(CHR²)_mR³⁰; or

R⁴ and R² taken together can form:

=O; -(CHR¹⁹)_p-; -(CH₂)_nO(CH₂)_m-; -(CH₂)_nS(CH₂)_m-; or -(CH₂)_nNR¹(CH₂)_m-; or

R⁴ and R⁵; R⁵ and R⁶; R⁶ and R⁷; R⁷ and R⁸; or R⁶ and R⁹ taken together can form:

20 -(CHR¹⁹)_p-; -(CH₂)_nO(CH₂)_m-; -(CH₂)_nS(CH₂)_m-; or -(CH₂)_nNR¹(CH₂)_m-;

R⁹ and R¹⁰ are independently

H; F; CF₃; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl; aryl;

heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; -(CHR¹³)_rOR¹⁵;

-(CHR¹³)_rSR¹⁵; -(CHR¹⁰)_rNR¹⁵R¹⁶; -(CHR¹³)_rCONR¹⁵R¹⁶;

25 -(CHR¹³)_rNR¹CONR¹⁵R¹⁶; -(CHR¹³)_rNR¹COR¹⁵; -(CHR¹³)_oCOOR¹⁵;

-(CHR¹³)_oCONR¹⁵R¹⁶; -(CHR¹³)_rPO(OR¹)₂; -(CHR¹³)_rSO₂R¹⁵;

-(CHR¹³)_rNR¹SO₂R¹⁵; -(CHR¹³)_rSO₂NR¹⁵R¹⁶; -(CR¹R¹³)_oR³⁰; or

-(CHR¹)_rO(CHR¹)_oR³⁰;

R¹¹ and R¹² are independently

30 H; F; Cl; Br; CF₃; OCF₃; OCHF₂; CN; NO₂; lower alkyl; lower alkenyl; aryl;

heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; -(CHR¹³)_oOR¹⁵;

$-(\text{CHR}^{13})_o\text{SR}^{15}$; $-(\text{CHR}^{13})_o\text{NR}^{15}\text{R}^{16}$; $-(\text{CHR}^{13})_o\text{CONR}^{15}\text{R}^{16}$;
 $-(\text{CHR}^{13})_o\text{NR}^1\text{CONR}^{15}\text{R}^{16}$; $-(\text{CHR}^{13})_o\text{NR}^1\text{COR}^{15}$; $-(\text{CHR}^{13})_o\text{COOR}^{15}$;
 $-(\text{CHR}^{13})_o\text{CONR}^{15}\text{R}^{16}$; $-(\text{CHR}^{13})_o\text{PO}(\text{OR}^1)_2$; $-(\text{CHR}^{13})_o\text{SO}_2\text{R}^{15}$;
 $-(\text{CHR}^{13})_o\text{NR}^1\text{SO}_2\text{R}^{15}$; $-(\text{CHR}^{13})_o\text{SO}_2\text{NR}^{15}\text{R}^{16}$; or $-(\text{CR}^1\text{R}^{13})_o\text{R}^{30}$;

5 R^{13} is H; F; CF_3 ; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl;
 cycloalkyl-lower alkyl; heterocycloalkyl-lower alkyl; aryl; heteroaryl;
 aryl-lower alkyl; heteroaryl-lower alkyl; $-(\text{CHR}^1)_o\text{OR}^{15}$; $-(\text{CHR}^1)_o\text{SR}^{15}$;
 $-(\text{CHR}^1)_o\text{NR}^{15}\text{R}^{16}$; $-(\text{CHR}^1)_o\text{NC}(\text{=NR}^{17})\text{NR}^{15}\text{R}^{16}$; $-(\text{CHR}^1)_o\text{COOR}^{15}$;
 $-(\text{CHR}^1)_o\text{CONR}^{15}\text{R}^{16}$; $-(\text{CHR}^1)_o\text{SO}_2\text{R}^{15}$; or $-(\text{CHR}^1)_o\text{SO}_2\text{NR}^{15}\text{R}^{16}$;

10 R^{14} is H; CF_3 ; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl;
 cycloalkyl-lower alkyl; heterocycloalkyl-lower alkyl; aryl; heteroaryl;
 aryl-lower alkyl; heteroaryl-lower alkyl; cycloalkyl-aryl; heterocycloalkyl-aryl;
 cycloalkyl-heteroaryl; heterocycloalkyl-heteroaryl; aryl-cycloalkyl;
 aryl-heterocycloalkyl; heteroaryl-cycloalkyl; heteroaryl-heterocycloalkyl;
 15 $-(\text{CHR}^1)_o\text{OR}^{15}$; $-(\text{CHR}^1)_o\text{SR}^{15}$; $-(\text{CHR}^1)_o\text{NR}^{15}\text{R}^{16}$; $-(\text{CHR}^1)_o\text{COOR}^{15}$;
 $-(\text{CHR}^1)_o\text{CONR}^{15}\text{R}^{16}$; or $-(\text{CHR}^1)_o\text{SO}_2\text{R}^{15}$;

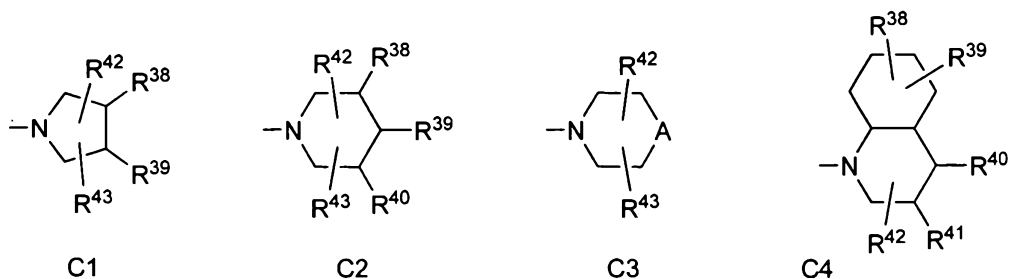
R^{15} , R^{16} , R^{17} and R^{18} are independently

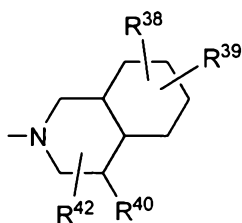
H; lower alkyl; lower alkenyl; lower alkoxy; cycloalkyl; heterocycloalkyl;
 cycloalkyl-lower alkyl; heterocycloalkyl-lower alkyl; aryl; heteroaryl;
 20 aryl-lower alkyl; heteroaryl-lower alkyl; cycloalkyl-aryl; heterocycloalkyl-aryl;
 cycloalkyl-heteroaryl; heterocycloalkyl-heteroaryl; aryl-cycloalkyl;
 aryl-heterocycloalkyl; heteroaryl-cycloalkyl; or heteroaryl-heterocycloalkyl; or

the structural elements $-\text{NR}^{15}\text{R}^{16}$ and $-\text{NR}^{17}\text{R}^{18}$ can independently form:

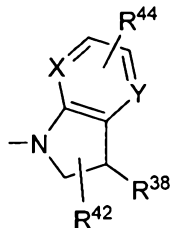
heterocycloalkyl; aryl-heterocycloalkyl; or heteroaryl-heterocycloalkyl;

25 or a group of one of the following formulae

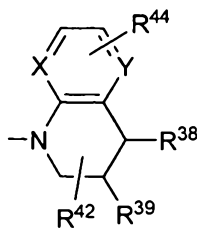




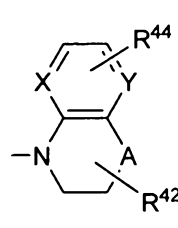
C5



C6



C7



C8

X and Y are independently

5 $-\text{CR}^{45}$; or N;

R^{19} is alkyl; alkenyl; cycloalkyl-lower alkyl; heterocycloalkyl-lower alkyl;

$-(\text{CR}^1\text{R}^4)_n\text{R}^{30}$; $-(\text{CH}_2)_n\text{O}(\text{CH}_2)_m\text{R}^{30}$; $-(\text{CH}_2)_n\text{S}(\text{CH}_2)_m\text{R}^{30}$; or

$-(\text{CH}_2)_n\text{NR}^{14}(\text{CH}_2)_m\text{R}^{30}$;

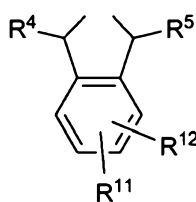
R^{20} and R^{21} are independently

10 alkyl; alkenyl; $-(\text{CHR}^4)_o\text{OR}^{15}$; $-(\text{CHR}^4)_o\text{SR}^{15}$; or $-(\text{CHR}^4)_r\text{NR}^{15}\text{R}^{16}$;

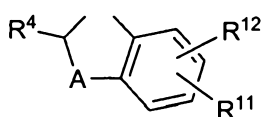
Z is $-(\text{CR}^{22}\text{R}^{23})_{(n+m+1)}-$; $-(\text{CR}^{22}\text{R}^{23})_n\text{NR}^{15}(\text{CR}^{22}\text{R}^{23})_m-$; $-(\text{CR}^{22}\text{R}^{23})_n\text{O}(\text{CR}^{22}\text{R}^{23})_m-$;

$-(\text{CR}^{22}\text{R}^{23})_n\text{S}(\text{CR}^{22}\text{R}^{23})_m-$; $-\text{O}(\text{CR}^{22}\text{R}^{23})_r\text{O}-$;

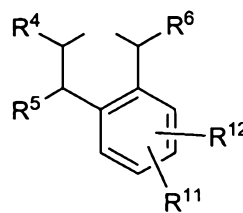
or a group of one of the formulae



Z1



Z2



Z3

15

R^{22} and R^{23} are independently

H; F; CF_3 ; alkyl; alkenyl; cycloalkyl; heterocycloalkyl; aryl; heteroaryl;

aryl-lower alkyl; or heteroaryl-lower alkyl; $-(\text{CR}^1\text{R}^{13})_o\text{OR}^{15}$; $-(\text{CR}^1\text{R}^{13})_o\text{SR}^{15}$;

$-(\text{CR}^1\text{R}^{13})_o\text{NR}^{15}\text{R}^{16}$; $-(\text{CR}^1\text{R}^{13})_o\text{COOR}^{15}$; $-(\text{CR}^1\text{R}^{13})_o\text{CONR}^{15}\text{R}^{16}$; or

20 $-(\text{CR}^1\text{R}^{13})_o\text{SO}_2\text{R}^{15}$; or

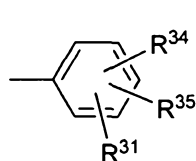
R^{22} and R^{23} taken together can form:

$=\text{O}$; $=\text{NR}^1$; $=\text{NOR}^1$; $=\text{NOCF}_3$; $-(\text{CHR}^1)_p-$; or $-\text{O}(\text{CR}^1\text{R}^2)_r\text{O}-$;

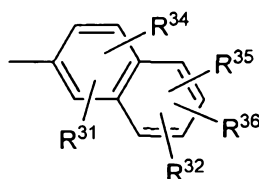
- R^{24} is alkyl; alkenyl; $-(CR^1R^{13})_qNR^{15}R^{16}$; $-(CR^1R^{13})_qNR^{25}R^{26}$; $-(CR^1R^{13})_qNR^{14}R^{27}$;
 $-(CH_2)_qC(=NR^{13})NR^{15}R^{16}$; $-(CH_2)_qC(=NOR^{17})NR^{15}R^{16}$;
 $-(CH_2)_qC(=NNR^{15}R^{16})NR^{17}R^{18}$; $-(CR^1R^{13})_qNR^2C(=NR^{17})NR^{15}R^{16}$;
 $-(CR^1R^{13})_qN=C(NR^{15}R^{16})NR^{17}R^{18}$; $-(CR^1R^{13})_qOR^{14}$; $-(CR^1R^{13})_qOR^{25}$;
5 $-(CR^1R^{13})_qOR^{27}$; $-(CR^1R^{13})_qSR^{15}$; $-(CR^1R^{13})_qSO_2R^{15}$; $-(CR^1R^{13})_qNR^{14}SO_2R^{15}$;
 $-(CR^1R^{13})_qSO_2NR^{14}R^{15}$; $-(CR^1R^{13})_qNR^{14}SO_2NR^{15}R^{16}$; $-(CR^1R^{13})_qSO_2NR^{15}R^{16}$;
 $-(CR^1R^{13})_qPO(OR^1)_2$; $-(CH_2)_nO(CH_2)_mNR^{15}R^{16}$;
 $-(CH_2)_nO(CH_2)_mC(=NR^{17})NR^{15}R^{16}$; $-(CH_2)_nO(CH_2)_mC(=NOR^{17})NR^{15}R^{16}$;
 $-(CH_2)_nO(CH_2)_mC(=NNR^{15}R^{16})NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mNR^1C(=NR^{17})NR^{15}R^{16}$;
10 $-(CH_2)_nO(CH_2)_mN=C(NR^{15}R^{16})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mNR^{15}R^{16}$;
 $-(CH_2)_nS(CH_2)_mC(=NR^{17})NR^{15}R^{16}$; $-(CH_2)_nS(CH_2)_mC(=NOR^{17})NR^{15}R^{16}$;
 $-(CH_2)_nS(CH_2)_mC(=NNR^{15}R^{16})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mNR^1C(=NR^{17})NR^{15}R^{16}$;
 $-(CH_2)_nS(CH_2)_mN=C(NR^{15}R^{16})NR^{17}R^{18}$; $-(CR^1R^{13})_qCOOR^{15}$; $-(CR^1R^{13})_qCOOR^{25}$;
 $-(CR^1R^{13})_qCOOR^{28}$; $-(CR^1R^{13})_qCONR^{15}R^{16}$; or $-(CR^1R^{13})_qCONR^{25}R^{26}$;
15 or alternatively heteroaryl; or heteroarylalkyl;
 R^{25} and R^{26} are independently
H; $-CH_3$; $-[(CH_2)_2O]_rCH_3$; or $-[(CH_2)_2O]_rCF_3$;
 R^{27} is $-COR^{19}$; $-CO(CR^1R^{13})_oR^{15}$; $-CO(CR^1R^{13})_oOR^{14}$; $-CO(CR^1R^{13})_oNR^{15}R^{16}$;
 $-CO(CR^1R^{13})_oNR^2R^{14}$; $-CO(CR^1R^{19})NR^{15}R^{16}$; $-CO(CR^1R^{29})NR^{15}R^{16}$;
20 $-CO(CHR^1)_oCONR^{15}R^{16}$; $-CO(CHR^1)_oCONR^2SO_2R^{15}$; $-CO(CR^1R^{13})_oNR^2SO_2R^{15}$;
 $-CONR^1(CHR^{15})_nNR^2(CHR^{13})_mR^{14}$; $-CO(CHR^{15})_nO(CHR^{13})_mR^{14}$;
 $-CONR^1(CHR^{15})_nO(CHR^{13})_mR^{14}$; $-SO_2R^{19}$; $-SO_2(CR^1R^{13})_oR^{15}$;
 $-SO_2(CR^1R^{13})_oNR^{15}R^{16}$; or $-SO_2(CR^1R^{13})_oNR^1R^{25}$;
 R^{28} is $-NR^1C(R^2)(R^{19})COOR^{15}$; $-NR^1C(R^2)(R^{19})CONR^{15}R^{16}$; $-NR^1C(R^2)(R^{29})COOR^{15}$;
25 $-NR^1C(R^2)(R^{29})CONR^{15}R^{16}$;
 R^{29} is $-(CR^1R^{13})_qNR^{15}R^{16}$; $-(CH_2)_qC(=NR^{17})NR^{15}R^{16}$; $-(CH_2)_qC(=NOR^{17})NR^{15}R^{16}$;
 $-(CH_2)_qC(=NNR^{15}R^{16})NR^{17}R^{18}$; $-(CR^1R^{13})_qNR^2C(=NR^{16})NR^{14}R^{15}$;
 $-(CR^1R^{13})_qN=C(NR^{15}R^{16})NR^{17}R^{18}$; $-(CR^1R^{13})_qOR^{14}$; $-(CR^1R^{13})_qSR^{15}$;
 $-(CR^1R^{13})_qSO_2R^{15}$; $-(CR^1R^{13})_qNR^{14}SO_2R^{15}$; $-(CR^1R^{13})_qSO_2NR^1R^{14}$;
30 $-(CR^1R^{13})_qSO_2NR^{15}R^{16}$; $-(CR^1R^{13})_qNR^2SO_2NR^{15}R^{16}$; $-(CR^1R^{13})_qPO(OR^1)_2$;
 $-(CH_2)_nO(CH_2)_mNR^{15}R^{16}$; $-(CH_2)_nO(CH_2)_mC(=NR^{17})NR^{15}R^{16}$;

- $-(CH_2)_nO(CH_2)_mC(=NOR^{17})NR^{15}R^{16}$; $-(CH_2)_nO(CH_2)_mC(=NNR^{15}R^{16})NR^{17}R^{18}$;
 $-(CH_2)_nO(CH_2)_mNR^{14}C(=NR^{17})NR^{15}R^{16}$; $-(CH_2)_nO(CH_2)_mN=C(NR^{15}R^{16})NR^{17}R^{18}$;
 $-(CH_2)_nS(CH_2)_mNR^{15}R^{16}$; $-(CH_2)_nS(CH_2)_mNR^{15}R^{16}$;
 $-(CH_2)_nS(CH_2)_mC(=NR^{17})NR^{15}R^{16}$; $-(CH_2)_nS(CH_2)_mC(=NOR^{17})NR^{15}R^{16}$;
5 $-(CH_2)_nS(CH_2)_mC(=NNR^{15}R^{16})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mNR^{14}C(=NR^{17})NR^{15}R^{16}$;
 $-(CH_2)_nS(CH_2)_mN=C(NR^{15}R^{16})NR^{17}R^{18}$; $-(CR^1R^{13})_qCOOR^{15}$; or
 $-(CR^1R^{13})_qCONR^{15}R^{16}$;

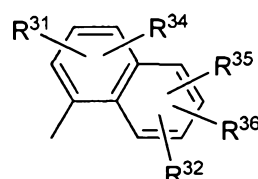
R^{30} is an aryl group of one of the formulae



AR1

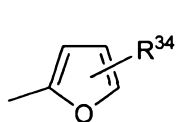


AR2

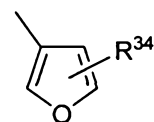


AR3

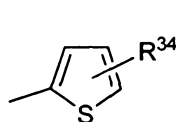
- 10 or a heteroaryl group of one of the formulae



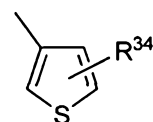
H1



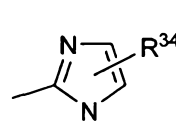
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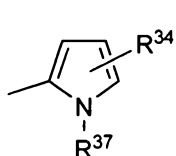
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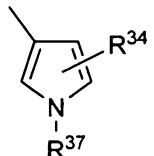
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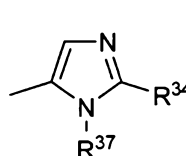
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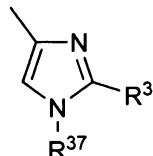
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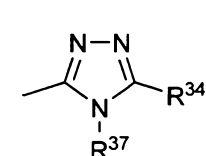
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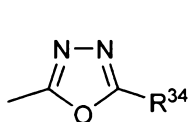
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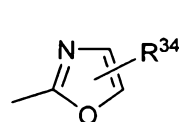
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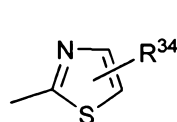
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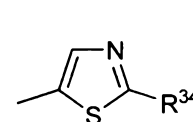
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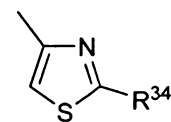
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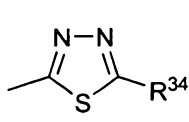
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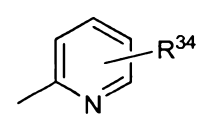
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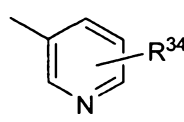
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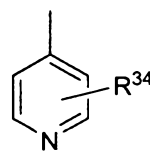
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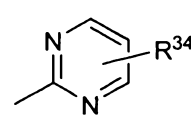
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H18

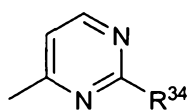


H19

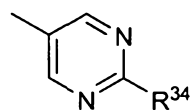


H20

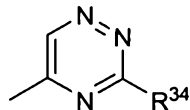
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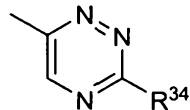
H21



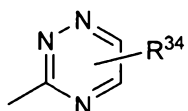
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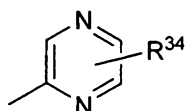
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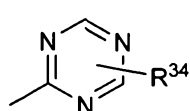
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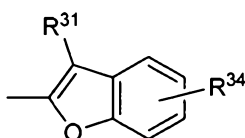
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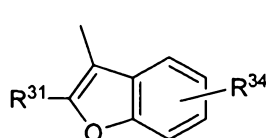
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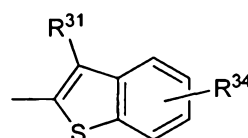
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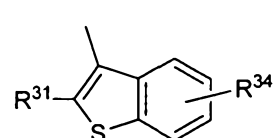
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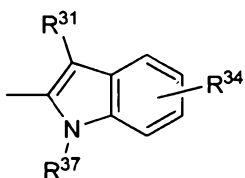
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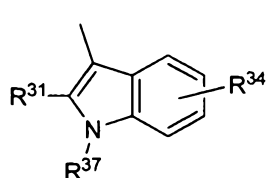
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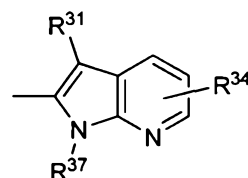
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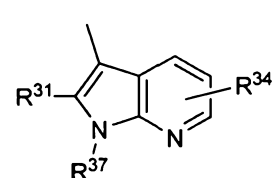
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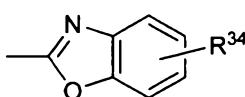
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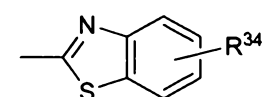
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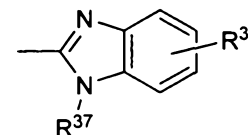
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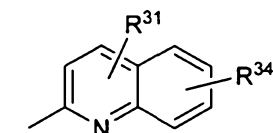
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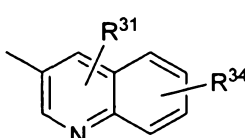
H37



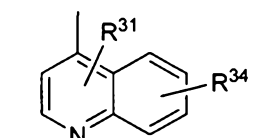
H38



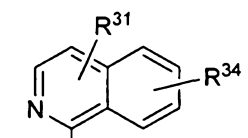
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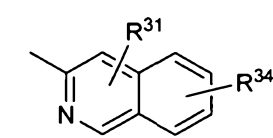
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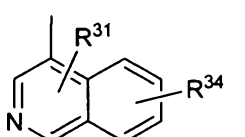
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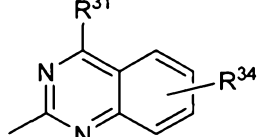
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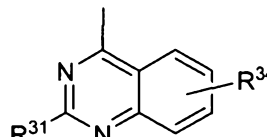
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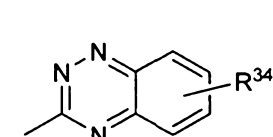
H44



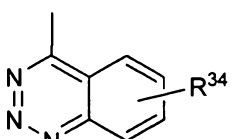
H45



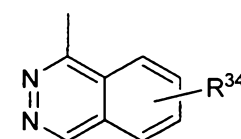
H46



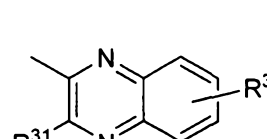
H47



H48



H49



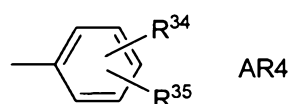
H50

5

R³¹ and R³² are independently

- H; F; Cl; Br; NO₂; CN; CF₃; OCHF₂; OCF₃; lower alkyl; lower alkenyl;
 aryl-lower alkyl; aryl; heteroaryl; -(CH₂)_oR³³; -(CH₂)_oOR¹⁵; -O(CH₂)_oR³³;
 -(CH₂)_oSR¹⁵; -(CH₂)_oNR¹⁵R¹⁶; -(CH₂)_oOCONR¹⁵R¹⁶; -(CH₂)_oNR¹CONR¹⁵R¹⁶;
 5 -(CH₂)_oNR¹COR¹⁵; -(CH₂)_oCOOR¹⁵; -(CH₂)_oCONR¹⁵R¹⁶; -(CH₂)_oPO(OR¹)₂;
 -(CH₂)_oSO₂R¹⁴; or -(CH₂)_oCOR¹⁵;

R³³ is an aryl group of the formula



R³⁴, R³⁵ and R³⁶ are independently

- 10 H; F; Cl; Br; OH; NH₂; NO₂; CN; CF₃; OCHF₂; OCF₃; -NR¹R¹⁵; -(CH₂)_oCOOR¹⁵;
 -(CH₂)_oCONR¹R¹⁵; lower alkyl; lower alkoxy; or lower alkenyl;

R³⁷ is H; lower alkyl; or aryl-lower alkyl;

R³⁸, R³⁹, R⁴⁰ and R⁴¹ are independently

- H; F; CF₃; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl; aryl;
 15 heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; -(CHR¹)_oOR¹⁵;
 -(CHR¹)_oSR¹⁵; -(CHR¹)_oNR²R¹⁵; -(CHR¹)_oOCONR²R¹⁵; -(CHR¹)_oNR²CONR³R¹⁵; -
 (CHR¹)_oNR²COR¹⁵; -(CHR¹)_oCOOR¹⁵; -(CHR¹)_oCONR²R¹⁵;
 -(CHR¹)_oPO(OR²)₂; -(CHR¹)_oSO₂R¹⁵; -(CHR¹)_oNR²SO₂R¹⁵; -(CHR¹)_oSO₂NR²R¹⁵; -
 (CR¹R²)_oR³³; or -(CHR¹)_nO(CHR²)_mR³³;

20 R⁴² and R⁴³ are independently

- H; F; CF₃; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl; aryl; heteroaryl;
 aryl-lower alkyl; heteroaryl-lower alkyl; -(CHR¹)_rOR¹⁵; -(CHR¹)_rSR¹⁵; -
 (CHR¹)_rNR²R¹⁵; -(CHR¹)_rOCONR²R¹⁵; -(CHR¹)_rNR²CONR³R¹⁵;
 -(CHR¹)_rNR²COR¹⁵; -(CHR¹)_oCOOR¹⁵; -(CHR¹)_oCONR²R¹⁵; -(CHR¹)_rPO(OR²)₂; -
 25 (CHR¹)_rSO₂R¹⁵; -(CHR¹)_rNR²SO₂R¹⁵; -(CHR¹)_rSO₂NR²R¹⁵; -(CR¹R²)_oR³³; or
 -(CHR¹)_rO(CHR²)_oR³³;

R⁴⁴ and R⁴⁵ are independently

- H; F; Cl; Br; CF₃; OCF₃; OCHF₂; CN; NO₂; lower alkyl; lower alkenyl; aryl;
 heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; -(CHR¹)_oOR¹⁵;

$-(\text{CHR}^1)_o\text{SR}^{15}$; $-(\text{CHR}^1)_o\text{NR}^2\text{R}^{15}$; $-(\text{CHR}^1)_o\text{OCONR}^2\text{R}^{15}$; $-(\text{CHR}^1)_o\text{NR}^2\text{CONR}^3\text{R}^{15}$;
 $-(\text{CHR}^1)_o\text{NR}^2\text{COR}^{15}$; $-(\text{CHR}^1)_o\text{COOR}^{15}$; $-(\text{CHR}^1)_o\text{CONR}^2\text{R}^{15}$; $-(\text{CHR}^1)_o\text{PO}(\text{OR}^2)_2$;
 $-(\text{CHR}^1)_o\text{SO}_2\text{R}^{15}$; $-(\text{CHR}^1)_o\text{NR}^2\text{SO}_2\text{R}^{15}$; $-(\text{CHR}^1)_o\text{SO}_2\text{NR}^2\text{R}^{15}$; or $-(\text{CR}^1\text{R}^2)_o\text{R}^{33}$;

n and m are independently an integer of 0-5 with the proviso that $n+m \leq 6$;

5 o is 0-4; p is 2-6; q is 1-6; r is 1-3;

or pharmaceutically acceptable salts thereof.

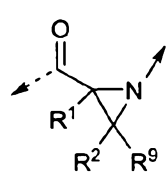
2. Compounds according to claim 1 wherein R^{24} is other than heteroaryl or heteroarylalkyl.

10

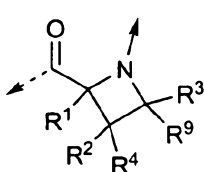
3. Compounds according to claim 1 or 2 wherein

T^1 is $^{\text{D}}\text{Pro}$; $^{\text{D}}\text{Pip}$; or $^{\text{D}}\text{Aze}$;

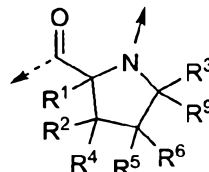
T^2 is an L or D α -amino acid of one of the formulae



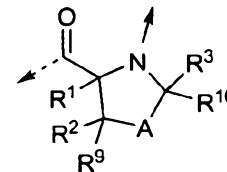
AA1



AA2

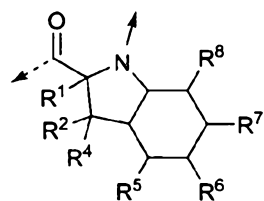


AA3

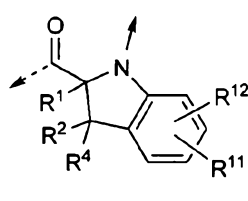


AA4

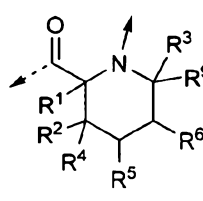
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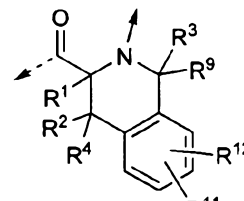
AA5



AA6



AA7



AA8

20

R^{14} is H; CF_3 ; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl;

cycloalkyl-lower alkyl; heterocycloalkyl-lower alkyl; aryl; heteroaryl;

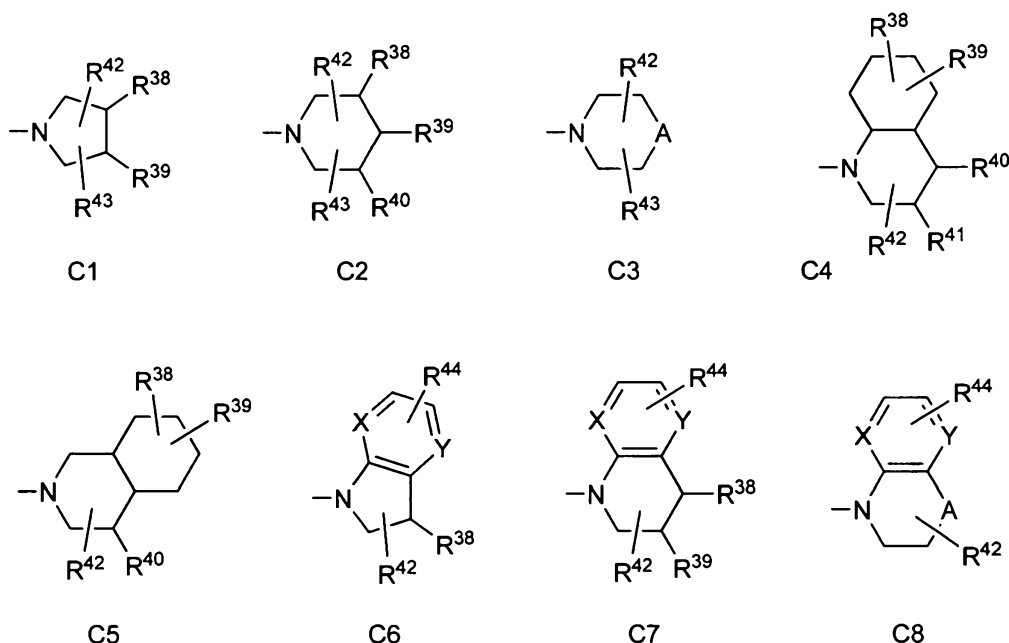
aryl-lower alkyl; heteroaryl-lower alkyl; $-(\text{CHR}^1)_s\text{OR}^{15}$; $-(\text{CHR}^1)_s\text{SR}^{15}$;

$-(\text{CHR}^1)_s\text{NR}^{15}\text{R}^{16}$; $-(\text{CHR}^1)_o\text{COOR}^{15}$; $-(\text{CHR}^1)_o\text{CONR}^{15}\text{R}^{16}$; or $-(\text{CHR}^1)_o\text{SO}_2\text{R}^{15}$;

R^{15} , R^{16} , R^{17} and R^{18} are independently

H; lower alkyl; lower alkenyl; lower alkoxy; cycloalkyl; heterocycloalkyl;
cycloalkyl-lower alkyl; heterocycloalkyl-lower alkyl; aryl; heteroaryl;
aryl-lower alkyl; or heteroaryl-lower alkyl; or

- 5 the structural elements $-NR^{15}R^{16}$ and $-NR^{17}R^{18}$ can independently form a group of one of the formulae



10

R^{24} is alkyl; alkenyl; $-(CR^{13}R^{13})_qNR^{15}R^{16}$; $-(CR^{13}R^{13})_qNR^{25}R^{26}$; $-(CR^{13}R^{13})_qNR^{14}R^{27}$;
 $-(CH_2)_qC(=NR^{17})NR^{15}R^{16}$; $-(CR^{13}R^{13})_qNR^2C(=NR^{17})NR^{15}R^{16}$; $-(CR^{13}R^{13})_qOR^{15}$;
 $-(CR^{13}R^{13})_qOR^{25}$; $-(CR^{13}R^{13})_qOR^{27}$; $-(CR^{13}R^{13})_qSR^{15}$; $-(CR^{13}R^{13})_qSO_2R^{15}$;
 $-(CR^{13}R^{13})_qNR^{15}SO_2R^{16}$; $-(CR^{13}R^{13})_qSO_2NR^{14}R^{14}$; $-(CR^{13}R^{13})_qSO_2NR^{15}R^{16}$;
 15 $-(CH_2)_nO(CH_2)_mNR^{15}R^{16}$; $-(CH_2)_nO(CH_2)_mC(=NR^{17})NR^{15}R^{16}$;
 $-(CH_2)_nO(CH_2)_mNR^1C(=NR^{17})NR^{15}R^{16}$; $-(CH_2)_nO(CH_2)_mN=C(NR^{15}R^{16})NR^{17}R^{18}$;
 $-(CH_2)_nS(CH_2)_mNR^{15}R^{16}$; $-(CR^{13}R^{13})_qCOOR^{15}$; $-(CR^{13}R^{13})_qCOOR^{25}$;
 $-(CR^{13}R^{13})_qCOOR^{28}$; $-(CR^{13}R^{13})_qCONR^{15}R^{16}$; or $-(CR^{13}R^{13})_qCONR^{25}R^{26}$;
 or alternatively heteroaryl; or heteroarylalkyl;

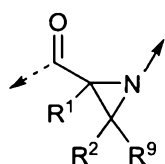
20 s is 2-4

or pharmaceutically acceptable salts thereof.

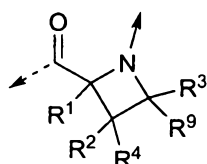
4. Compounds according to claim 3 wherein

T¹ is ^DPro; ^DPip; or ^DAze;

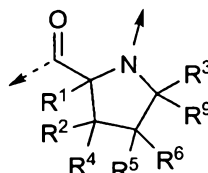
T² is an L or D α-amino acid of one of the formulae



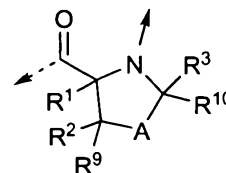
AA1



AA2

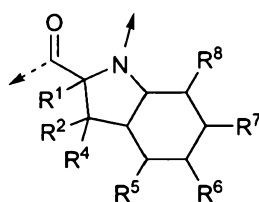


AA3

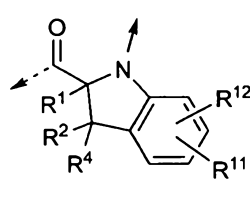


AA4

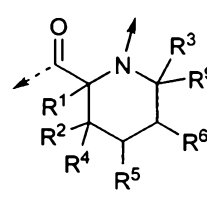
5



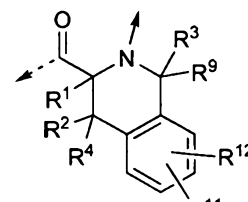
AA5



AA6



AA7



AA8

P¹ and P³ are independently

His; His(Me); His(Bn); hHis; Phe; Phe(2Cl); Phe(3Cl); Phe(4Cl); Phe(3,4Cl₂);

10 Phe(2F); Phe(3F); Phe(4F); Phe(3,4F₂); Phe(3CN); Phe(4CN); Phe(2CF₃);

Phe(3CF₃); Phe(4CF₃); Phe(3,4(CF₃)₂); Phe(4COOMe); hPhe; Thi; Tza; Trp;

Trp(5OH); Trp(5Cl); Trp(6Cl); Trp(5,6Cl₂); Trp(5Br); Trp(6Br); Trp(6CF₃);

Trp(7Aza); hTrp; Tyr; Tyr(Me); Tyr(Ph); Tyr(Bn); Tyr(4OHPh); Tyr(4MeOCOBn);

hTyr; Thr(Bn); Ser(Bn); 2Pal; 3Pal; 4Pal; Phg; Ala(2Furyl); Ala(3Furyl); Ala(2Quin);

15 Ala(3Quin); Ala(4Quin); Ala(tBu); Gly(tBu); 1Nal; 2Nal; Nle(6OBn); Cha; hCha;

Bip; Bbta; or OctG;

P² is Aib; Ac3c; Ac4c; Cyp; Chx; Chx(4oxo); Ac7c; Ac8c; ^DAtc; ^LAtc; ^{DL}Atc; Deg; or 4,4-
AC-ThioTHP;

P⁴ is Arg; hArg; Ala(Ppz); Thr; *allo*Thr; Gln; Gln(Me); Gln(Me₂); Gln(*i*Pr); Gln(*c*Pr);

20 Gln(*i*Bu); Glu(Ala); Glu(^DAla); Glu(Arg); Glu(^DArg); Glu(Glu); Glu(Gly); Glu(His);

Glu(Leu); Glu(^DLeu); Glu(2Nal); Glu(Sar); Glu(Trp); Glu(^DTrp); Cys; hCys; Ser;

hSer; Ser(Me); hSer(Me); Thr; Met; Met(O₂); Lys; hLys; Lys(Ac); Lys(Me); Lys(Bz);

Lys(Nic); Lys(4Oxa); Lys((5*R*)OH); Orn; Dap; Dap(MeO(CH₂)₂); Dap(CONH₂);

Dap((MeO(CH₂)₂)₂); Dab(Sar); Dab; Dab(Ac); Dab(Ala); Dab(^DAla); Dab(Arg);

Dab(^DArg); Dab(Dab); Dab(Glu); Dab(Gly); Dab(His); Dab(Leu); Dab(^DLeu);
Dab(MEMCO); Dab(4Me₂NPhSO₂); Dab(MeO(CH₂)₂NHCO);
Dab((MeO(CH₂)₂)(Me)NCO); Dab(MePpzCO); Dab(MeSO₂); Dab(morphCO);
Dab(2NaI); Dab(Trp); Dab(^DTrp); Dab(Sar); Gln(Alk1); Gln(Alk2); Gln(Alk3);
5 Gln(Alk4); Gln(Alk5); Gln(Alk6); Gln(Alk7); Gln(Alk8); Gln(Alk9); Gln(Alk10);
Gln(Alk11); Gln(Alk12); Gln(Alk13); Gln(Alk14); Gln(Alk15); Gln(Alk16);
Gln(Alk17); Gln(Alk18); Gln(Alk19); Gln(Alk20); Gln(Alk21); Gln(Alk22);
Gln(Alk23); Gln(Alk24); Gln(Alk25); Gln(Alk26); Gln(Alk27); Gln(Alk28);
Gln(Alk29); Gln(Alk30); Gln(Alk31); Gln(Alk32); Gln(Alk33); Gln(Alk34); Glu(cN1);
10 Glu(cN2); Glu(cN3); Glu(cN4); Glu(cN5); Glu(cN6); Glu(cN7); Glu(cN8); Glu(cN9);
Glu(cN10); Glu(cN11); Glu(cN12); Glu(cN13); Glu(cN14); Glu(cN15); Glu(cN16);
Glu(cN17); Sab(N1); Sab(N2); Sab(N3); Sab(N4); Sab(N5); Sab(N6); Sab(N7);
Sab(N8); Sab(N9); Sab(N10); Sab(N11); Sab(N12); Sab(N13); Sab(N14);
Sab(N15); Sab(N16); Sab(N17); Sab(N18); Sab(N19); Sab(N20); Sab(N21);
15 Sab(N22); Sab(N23); Sab(N24); Sab(N25); Sab(N26); Sab(N27); Sab(N28);
Sab(N29); Sab(N30); Sab(N31); Sab(N32); Sab(N33); Sab(N34); Sab(N35);
Sab(N36); Sab(N37); Sab(N38); Sab(N39); Sab(N40); Sab(N41); Sab(N42);
Sab(N43); Sab(N44); Sab(N45); Sab(N46); Sab(N47); Sab(N48); Sab(N49);
Sab(N50); Sab(N51); Sab(N52); Sab(N53); Sab(N54); Sab(N55); Sab(N56);
20 Sab(N57); Sab(N58); Sab(N59); Sab(N60); Sab(N61); Dab(SN1); Dab(SN2);
Dab(SN3); Dab(SN4); Dab(SN5); Dab(SN6); Dab(SN7); Dab(SN8); Dab(SN9);
Dab(SN10); Dab(SN11); Dab(SN12); Dab(SN13); Dab(SN14); Dab(SN15);
Dab(SN16); Dab(SN17); Dab(SN18); Dab(SN19); Dab(SN20); Dab(SN21);
Dab(SN22); Dab(SN23); Dab(SN24); Dab(SN25); Dab(SN26); Dab(SN27);
25 Dab(SN28); Dab(SN29); Dab(SN30); Dab(SN31); Dab(SN32); Dab(SN33);
Dab(SN34); Dab(SN35); Dab(SN36); Dab(SN37); Dab(SN38); Dab(SN39);
Dab(SN40); Dab(SN41); Dab(SN42); Dab(SN43); Dab(SN44); Dab(SN45);
Dab(SN46); Dab(SN47); Dab(SN48); Dab(SN49); Dab(SN50); Dab(SN51);
Dab(SN52); Dab(SN53); Dab(SN54); Dab(SN55); Dab(SN56); Dab(SN57);
30 Dab(SN58); Dab(SN59); Dab(SN60); Dab(SN61); Dab(UN1); Dab(UN2);
Dab(UN3); Dab(UN4); Dab(UN5); Dab(UN6); Dab(UN7); Dab(UN8); Dab(UN9);

Dab(UN10); Dab(UN11); Dab(UN12); Dab(UN13); Dab(UN14); Dab(UN15);
Dab(UN16); Dab(UN17); Dab(UN18); Dab(UN19); Dab(UN20); Dab(UN21);
Dab(UN22); Dab(UN23); Dab(UN24); Dab(UN25); Dab(UN26); Dab(UN27);
Dab(UN28); Dab(UN29); Dab(UN30); Dab(UN31); Dab(UN32); Dab(UN33);
5 Dab(UN34); Dab(UN35); Dab(UN36); Dab(UN37); Dab(UN38); Dab(UN39);
Dab(UN40); Dab(UN41); Dab(UN42); Dab(UN43); Dab(UN44); Dab(UN45);
Dab(UN46); Dab(UN47); Dab(UN48); Dab(UN49); Dab(UN50); Dab(UN51);
Dab(UN52); Dab(UN53); Dab(UN54); Dab(UN55); Dab(UN56); Dab(UN57);
Dab(UN58); Dab(UN59); Dab(UN60); Dab(UN61); Dab(S1); Dab(S2); Dab(S3);
10 Dab(S4); Dab(S5); Dab(S6); Dab(S7); Dab(S8); Dab(S9); Dab(S10); Dab(S11);
Dab(S12); Dab(S13); Dab(S14); Dab(S15); Dab(S16); Dab(S17); Dab(S18);
Dab(A1); Dab(A2); Dab(A3); Dab(A4); Dab(A5); Dab(A6); Dab(A7); Dab(A8);
Dab(A9); Dab(A10); Dab(A11); Dab(A12); Dab(A13); Dab(A14); Dab(A15);
Dab(A16); Dab(A17); Dab(A18); Dab(A19); Dab(A20); Dab(A21); Dab(A22);
15 Dab(A23); Dab(A24); Dab(A25); Dab(A26); Dab(A27); Dab(A28); Dab(A29);
Dab(A30); Dab(A31); Dab(A32); Dab(A33); Dab(A34); Dab(A35); Dab(A36);
Dab(A37); Dab(A38); Dab(A39); Dab(A40); Dab(A41); Dab(A42); Dab(A43);
Dab(A44); Dab(A45); Dab(A46); Dab(A47); Dab(A48); Dab(A49); Dab(A50);
Dab(A51); Dab(A52); Dab(A53); Dab(A54); Dab(A55); Dab(A56); Dab(Suc1);
20 Dab(Suc2); Dab(Suc3); Dab(Suc4); Dab(Suc5); Dab(Suc6); Dab(Suc7); Dab(Suc8);
Dab(Suc9); Dab(Suc10); Asn(Alk1); Asn(Alk2); Asn(Alk3); Asn(Alk4); Asn(Alk5);
Asn(Alk6); Asn(Alk7); Asn(Alk8); Asn(Alk9); Asn(Alk10); Asn(Alk11); Asn(Alk12);
Asn(Alk13); Asn(Alk14); Asn(Alk15); Asn(Alk16); Asn(Alk17); Asn(Alk18);
Asn(Alk19); Asn(Alk20); Asn(Alk21); Asn(Alk22); Asn(Alk23); Asn(Alk24);
25 Asn(Alk25); Asn(Alk26); Asn(Alk27); Asn(Alk28); Asn(Alk29); Asn(Alk30);
Asn(Alk31); Asn(Alk32); Asn(Alk33); Asn(Alk34); Asp(cN1); Asp(cN2); Asp(cN3);
Asp(cN4); Asp(cN5); Asp(cN6); Asp(cN7); Asp(cN8); Asp(cN9); Asp(cN10);
Asp(cN11); Asp(cN12); Asp(cN13); Asp(cN14); Asp(cN15); Asp(cN16);
Asp(cN17); Sap(N1); Sap(N2); Sap(N3); Sap(N4); Sap(N5); Sap(N6); Sap(N7);
30 Sap(N8); Sap(N9); Sap(N10); Sap(N11); Sap(N12); Sap(N13); Sap(N14);
Sap(N15); Sap(N16); Sap(N17); Sap(N18); Sap(N19); Sap(N20); Sap(N21);

Sap(N22); Sap(N23); Sap(N24); Sap(N25); Sap(N26); Sap(N27); Sap(N28);
Sap(N29); Sap(N30); Sap(N31); Sap(N32); Sap(N33); Sap(N34); Sap(N35);
Sap(N36); Sap(N37); Sap(N38); Sap(N39); Sap(N40); Sap(N41); Sap(N42);
Sap(N43); Sap(N44); Sap(N45); Sap(N46); Sap(N47); Sap(N48); Sap(N49);
5 Sap(N50); Sap(N51); Sap(N52); Sap(N53); Sap(N54); Sap(N55); Sap(N56);
Sap(N57); Sap(N58); Sap(N59); Sap(N60); Sap(N61); Dap(SN1); Dap(SN2);
Dap(SN3); Dap(SN4); Dap(SN5); Dap(SN6); Dap(SN7); Dap(SN8); Dap(SN9);
Dap(SN10); Dap(SN11); Dap(SN12); Dap(SN13); Dap(SN14); Dap(SN15);
Dap(SN16); Dap(SN17); Dap(SN18); Dap(SN19); Dap(SN20); Dap(SN21);
10 Dap(SN22); Dap(SN23); Dap(SN24); Dap(SN25); Dap(SN26); Dap(SN27);
Dap(SN28); Dap(SN29); Dap(SN30); Dap(SN31); Dap(SN32); Dap(SN33);
Dap(SN34); Dap(SN35); Dap(SN36); Dap(SN37); Dap(SN38); Dap(SN39);
Dap(SN40); Dap(SN41); Dap(SN42); Dap(SN43); Dap(SN44); Dap(SN45);
Dap(SN46); Dap(SN47); Dap(SN48); Dap(SN49); Dap(SN50); Dap(SN51);
15 Dap(SN52); Dap(SN53); Dap(SN54); Dap(SN55); Dap(SN56); Dap(SN57);
Dap(SN58); Dap(SN59); Dap(SN60); Dap(SN61); Dap(UN1); Dap(UN2);
Dap(UN3); Dap(UN4); Dap(UN5); Dap(UN6); Dap(UN7); Dap(UN8); Dap(UN9);
Dap(UN10); Dap(UN11); Dap(UN12); Dap(UN13); Dap(UN14); Dap(UN15);
Dap(UN16); Dap(UN17); Dap(UN18); Dap(UN19); Dap(UN20); Dap(UN21);
20 Dap(UN22); Dap(UN23); Dap(UN24); Dap(UN25); Dap(UN26); Dap(UN27);
Dap(UN28); Dap(UN29); Dap(UN30); Dap(UN31); Dap(UN32); Dap(UN33);
Dap(UN34); Dap(UN35); Dap(UN36); Dap(UN37); Dap(UN38); Dap(UN39);
Dap(UN40); Dap(UN41); Dap(UN42); Dap(UN43); Dap(UN44); Dap(UN45);
Dap(UN46); Dap(UN47); Dap(UN48); Dap(UN49); Dap(UN50); Dap(UN51);
25 Dap(UN52); Dap(UN53); Dap(UN54); Dap(UN55); Dap(UN56); Dap(UN57);
Dap(UN58); Dap(UN59); Dap(UN60); Dap(UN61); Dap(S1); Dap(S2); Dap(S3);
Dap(S4); Dap(S5); Dap(S6); Dap(S7); Dap(S8); Dap(S9); Dap(S10); Dap(S11);
Dap(S12); Dap(S13); Dap(S14); Dap(S15); Dap(S16); Dap(S17); Dap(S18);
Dap(A1); Dap(A2); Dap(A3); Dap(A4); Dap(A5); Dap(A6); Dap(A7); Dap(A8);
30 Dap(A9); Dap(A10); Dap(A11); Dap(A12); Dap(A13); Dap(A14); Dap(A15);
Dap(A16); Dap(A17); Dap(A18); Dap(A19); Dap(A20); Dap(A21); Dap(A22);

Dap(A23); Dap(A24); Dap(A25); Dap(A26); Dap(A27); Dap(A28); Dap(A29);
 Dap(A30); Dap(A31); Dap(A32); Dap(A33); Dap(A34); Dap(A35); Dap(A36);
 Dap(A37); Dap(A38); Dap(A39); Dap(A40); Dap(A41); Dap(A42); Dap(A43);
 Dap(A44); Dap(A45); Dap(A46); Dap(A47); Dap(A48); Dap(A49); Dap(A50);
 5 Dap(A51); Dap(A52); Dap(A53); Dap(A54); Dap(Suc1); Dap(Suc2); Dap(Suc3);
 Dap(Suc4); Dap(Suc5); Dap(Suc6); Dap(Suc7); Dap(Suc8); Dap(Suc9); or
 Dap(Suc10);
 or alternatively His; His(Me); His(Bn); hHis; Lat; Trp; Trp(5OH); Trp(5Cl); Trp(6Cl);
 Trp(5,6Cl₂); Trp(5Br); Trp(6Br); Trp(6CF₃); Trp(7Aza); hTrp; Tza; 2Pal; 3Pal; 4Pal;
 10 h2Pal; h3Pal; h4Pal; Ala(1Im); Ala(2Im); hAla(1Im); hAla(2Im); Ala(Pyrazinyl);
 Ala(1Pyrazolyl); Ala(3Pyrazolyl); Ala(2Pyrimidin); Ala(4Pyrimidin); Ala(5Pyrimidin);
 Ala(2Quin); Ala(3Quin); or Ala(4Quin);
 or pharmaceutically acceptable salts thereof.

15 5. Compounds according to claim 4 wherein

P¹ and P³ are independently

His; His(Me); His(Bn); hHis; Phe; Phe(2Cl); Phe(3Cl); Phe(4Cl); Phe(3,4Cl₂);
 Phe(2F); Phe(3F); Phe(4F); Phe(3,4F₂); Phe(3CN); Phe(4CN); Phe(2CF₃);
 Phe(3CF₃); Phe(4CF₃); Phe(3,4(CF₃)₂); Phe(4COOMe); hPhe; Thi; Tza; Trp;
 20 Trp(5OH); Trp(5Cl); Trp(6Cl); Trp(5,6Cl₂); Trp(5Br); Trp(6Br); Trp(6CF₃);
 Trp(7Aza); hTrp; Tyr; Tyr(Me); Tyr(Ph); Tyr(Bn); Tyr(4OHPh); Tyr(4MeOCOBn);
 hTyr; Thr(Bn); Ser(Bn); 2Pal; 3Pal; 4Pal; Phg; Ala(2Furyl); Ala(3Furyl); Ala(2Quin);
 Ala(3Quin); Ala(4Quin); Ala(tBu); Gly(tBu); 1Nal; 2Nal; Nle(6OBn); Cha; hCha;
 Bip; Bbta; or OctG;

25 P² is Aib; Ac3c; Ac4c; Cyp; Chx; Chx(4oxo); Ac7c; Ac8c; ^DAtc; ^LAtc; ^{DL}Atc; Deg; or 4,4-
 AC-ThioTHP;

P⁴ is Arg; hArg; Ala(Ppz); Thr; *allo*Thr; Gln; Gln(Me); Gln(Me₂); Gln(*i*Pr); Gln(*c*Pr);
 Gln(*i*Bu); Glu(Ala); Glu(^DAla); Glu(Arg); Glu(^DArg); Glu(Glu); Glu(Gly); Glu(His);
 Glu(Leu); Glu(^DLeu); Glu(2Nal); Glu(Sar); Glu(Trp); Glu(^DTrp); Cys; hCys; Ser; hSer;
 30 Ser(Me); hSer(Me); Thr; Met; Met(O₂); Lys; hLys; Lys(Ac); Lys(Me); Lys(Bz);
 Lys(Nic); Lys(4Oxa); Lys((5*R*)OH); Orn; Dap; Dap(MeO(CH₂)₂); Dap(CONH₂);

- Dap((MeO(CH₂)₂)₂); Dab(Sar); Dab; Dab(Ac); Dab(Ala); Dab(^DAla); Dab(Arg);
 Dab(^DArg); Dab(Dab); Dab(Glu); Dab(Gly); Dab(His); Dab(Leu); Dab(^DLeu);
 Dab(MEMCO); Dab(4Me₂NPhSO₂); Dab(MeO(CH₂)₂NHCO);
 Dab((MeO(CH₂)₂)(Me)NCO); Dab(MePpzCO); Dab(MeSO₂); Dab(morphCO);
 5 Dab(2Nal); Dab(Trp); Dab(^DTrp); Dab(Sar); or Dab(SN13);
 or alternatively His; His(Me); hHis; 2Pal; 3Pal; 4Pal; h2Pal; h3Pal; h4Pal; Trp;
 Ala(1Im); Ala(2Im); hAla(1Im); hAla(2Im); or Ala(2Pyrimidin);
 or pharmaceutically acceptable salts thereof.
- 10 6. Compounds according to claim 5 wherein
 T¹ is ^DPro; ^DPip; or ^DAze;
 T² is Pro; ^DPro; Oic; Pip; Tic; Tic(7OH); Thz; Thz(5,5Me₂); Pro((4S)F); Pro(5,5Me₂);
 Pro((4S)cHex); Pro((4R)Ph); Pro((4R)Bn); Pro((4R)4BrBn); Pro((4R)3CNBn);
 Hyp(Ph); Hyp(Bn); Hyp(4BrBn); Hyp(3CNBn); Hyp(4CNBn); Hyp(CONHPh); or
 15 (4S)-Hyp(Bn);
 P¹ and P³ are independently
 Phe; Phe(4Cl); Phe(4F); Phe(4CN); Phe(3CF₃); Phe(4CF₃); Phe(4COOMe); Trp;
 Trp(5OH); Trp(6Cl); Tyr; Tyr(Me) Tyr(Ph); Tyr(4OHPh); Tyr(4MeOCOBn); hTyr;
 Ala(2Furyl); Ala(2Quin); 2Nal; Nle(6OBn); ^{DL}Trp(7Aza); Cha; Bip; Bbta; or OctG;
 20 P² is Aib; Ac3c; Ac4c; Cyp; Chx; Chx(4oxo); Ac7c; Ac8c; ^{DL}Atc; Deg;
 or 4,4-AC-ThioTHP;
 P⁴ is Arg; hArg; Ala(Ppz); Thr; *allo*Thr; Gln; Gln(*i*Pr); Gln(*c*Pr); Glu(Ala); Glu(^DAla);
 Glu(Arg); Glu(^DArg); Glu(Glu); Glu(Gly); Glu(His); Glu(Leu); Glu(^DLeu); Glu(2Nal);
 Glu(Sar); Glu(Trp); Glu(^DTrp); Cys; hCys; Ser; hSer; Ser(Me); hSer(Me); Thr; Met;
 25 Met(O₂); Lys; hLys; Lys(Ac); Lys(Me); Lys(Bz); Lys(Nic); Lys(4Oxa); Lys((5R)OH);
 Dap; Dap(MeO(CH₂)₂); Dap(CONH₂); Dap((MeO(CH₂)₂)₂); Dab; Dab(Ac);
 Dab(morphCO); Dab(MePpzCO); Dab(MEMCO); Dab(MeO(CH₂)₂NHCO);
 Dab((MeO(CH₂)₂)(Me)NCO); Dab(MeSO₂); Dab(4Me₂NPhSO₂); Dab(Dab); or
 Dab(SN13);
 30 or alternatively His; hHis; 2Pal; 3Pal; or 4Pal;
 or pharmaceutically acceptable salts thereof.

7. Compounds according to claim 2 which are selected from
 cyclo(-Trp-Aib-Trp-Arg-^DPro-Tic-);
 cyclo(-Trp-Aib-Trp-Dab-^DPro-Tic-);
 cyclo(-Trp-Cyp-Trp-Arg-^DPro-Tic(7OH)-);
 5 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Pro((4S)F)-);
 cyclo(-Trp-Cyp-Trp-Arg-^DPro-Thz-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Thz-);
 cyclo(-Trp(5OH)-Cyp-Trp-Gln-^DPro-Thz-);
 cyclo(-Trp(5OH)-Cyp-Trp-Arg-^DPro-Tic-);
 10 cyclo(-2Nal-Cyp-Trp-Gln-^DPro-Tic-);
 cyclo(-2Nal-Cyp-Trp-Dab-^DPip-Pip-);
 cyclo(-Trp(5OH)-Chx-Trp(5OH)-Arg-^DPro-Oic-);
 cyclo(-Trp(5OH)-Cyp-Trp(5OH)-Dap-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPip-Oic-);
 15 cyclo(-Trp-Cyp-2Nal-Dab-^DPip-Oic-);
 cyclo(-Trp-Cyp-2Nal-Gln-^DPro-Oic-);
 cyclo(-OctG-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Gln-^DPro-Oic-);
 cyclo(-Trp-Chx-Trp-Dab-^DPro-Oic-);
 20 cyclo(-Trp-Ac3c-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Ac4c-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-4,4-AC-ThioTHP-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Phe(4F)-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Tyr(Me)-Dab-^DPro-Oic-);
 25 cyclo(-Trp-Cyp-Ala(2Quin)-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Arg-^DAze-Tic-);
 cyclo(-Trp-Cyp-Trp-Dab-^DAze-Tic-);
 cyclo(-Cha-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Oic-);
 30 cyclo(-Trp(5OH)-Cyp-Trp-Arg-^DPro-Thz(5,5Me₂)-);
 cyclo(-Trp-Atc-Trp-Dab-^DPro-Oic-);

- cyclo(-Trp-Cyp-Ala(2Furyl)-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Phe(4F)-Ser-^DPro-Oic-);
 cyclo(-Trp-Cyp-Phe(4Cl)-Ser-^DPro-Oic-);
 cyclo(-Trp-Cyp-Phe(4CF₃)-Dab-^DPro-Oic-);
 5 cyclo(-Trp-Cyp-DLTrp(7Aza)-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Tyr(Ph)-Dab-^DPro-Oic-);
 cyclo(-Phe(4CF₃)-Cyp-Trp-Dab-^DPip-Pro((4*R*)Ph)-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Pro((4*R*)Bn)-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Pro((4*R*)4BrBn)-);
 10 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Pro((4*R*)3CNBn)-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Pro((4*S*)cHex)-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Pro(5,5Me₂)-);
 cyclo(-Trp-Cyp-Phe(4Cl)-Dab-^DPro-Hyp(Bn)-);
 cyclo(-Phe(4CN)-Cyp-Phe(4F)-Ser-^DPro-Hyp(Bn)-);
 15 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Hyp(Bn)-);
 cyclo(-Trp-Cyp-Trp-Ser-^DPro-Hyp(Bn)-);
 cyclo(-Phe(4CN)-Cyp-Trp-Gln-^DPro-Hyp(Bn)-);
 cyclo(-Trp(6Cl)-Cyp-Trp-Dab-^DPro-Hyp(Bn)-);
 cyclo(-Phe(4CN)-Cyp-Trp-Dab-^DPro-Hyp(Bn)-);
 20 cyclo(-Phe(4CN)-Cyp-Trp-Ser-^DPip-Hyp(Bn)-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPro-(4*S*)-Hyp(Bn)-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Hyp(Ph)-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Hyp(4CNBn)-);
 cyclo(-Phe(4CF₃)-Cyp-Trp-Dab-^DPro-Hyp(4BrBn)-);
 25 cyclo(-Phe(4CN)-Cyp-Trp-Ser-^DPro-Hyp(4BrBn)-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Hyp(4BrBn)-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Hyp(CONHPh)-);
 cyclo(-Trp-Cyp-Trp-alloThr-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-hArg-^DPro-Oic-);
 30 cyclo(-Trp-Cyp-Trp-hCys-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Gln(*i*Pr)-^DPro-Oic-);

- cyclo(-Trp-Cyp-Trp-hSer(Me)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Lys(Ac)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Lys(Bz)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Lys(Me)-^DPro-Oic-);
 5 cyclo(-Trp-Cyp-Trp-Lys((5R)OH)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Lys(Nic)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Met(O₂)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Ala(Ppz)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dap(CONH₂)-^DPro-Oic-);
 10 cyclo(-Trp-Cyp-Trp-Dab(Dab)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab(MEMCO)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab(MeO(CH₂)₂NHCO)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dap(MeO(CH₂)₂)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dap((MeO(CH₂)₂)₂)-^DPro-Oic-);
 15 cyclo(-Ph(4COOMe)-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Hyp(3CNBn)-);
 cyclo(-Phe(4CN)-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Ser-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Ser-^DPip-Oic-);
 20 cyclo(-Trp(6Cl)-Cyp-Trp-Ser-^DPro-Oic-);
 cyclo(-Phe(4CN)-Cyp-Trp-Ser-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Lys(4Oxa)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Ser(Me)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Thr-^DPro-Oic-);
 25 cyclo(-Bip-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-hTyr-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Bbta-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Nle(6OBn)-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Tyr(4OHPh)-Cyp-Trp-Dab-^DPro-Oic-);
 30 cyclo(-Tyr(Ph)-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Tyr(4MeOCOBn)-Cyp-Trp-Dab-^DPro-Oic-);

- cyclo(-Trp-Deg-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Ac7c-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Chx(4oxo)-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Ac8c-Trp-Dab-^DPro-Oic-);
 5 cyclo(-Trp-Cyp-Trp-Dab((MeO(CH₂)₂)(Me)NCO)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab(morphCO)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab(MePpzCO)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab(MeSO₂)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab(4Me₂NPhSO₂)-^DPro-Oic-);
 10 cyclo(-Trp-Cyp-Trp-Dab(Ac)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Hyp-);
 cyclo(-Trp-Cyp-Trp-Dap-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab(SN13)-^DPro-Oic-);

or pharmaceutically acceptable salts thereof.

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8. Compounds according to claim 7 which are selected from
 cyclo(-Cha-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Oic-);
 cyclo(-Phe(4CF₃)-Cyp-Trp-Dab-^DPip-Pro((4*R*)Ph)-);
 20 cyclo(-Trp-Cyp-Trp-Dab-^DPro-Pro(5,5Me₂)-);
 cyclo(-Phe(4CN)-Cyp-Trp-Dab-^DPro-Hyp(Bn)-);
 cyclo(-Trp-Cyp-Trp-Met(O₂)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dap(CONH₂)-^DPro-Oic-);
 cyclo(-Phe(4CN)-Cyp-Trp-Dab-^DPro-Oic-);
 25 cyclo(-Trp-Cyp-Trp-Lys(4Oxa)-^DPro-Oic-);
 cyclo(-Trp-Cyp-Trp-Dab(MePpzCO)-^DPro-Oic-);

or pharmaceutically acceptable salts thereof.

9. Compounds according to claim 1 which are selected from
 30 cyclo(-Trp-Cyp-Trp-Dab(A55)-^DPro-Oic-);
 cyclo(-Phe(4CF₃)-Cyp-Trp-Dab-^DPro-Oic-);

cyclo(-Phe(4CF₃)-Cyp-Trp-Dab(A56)-^DPro-Oic-);

cyclo(-Phe(3CF₃)-Cyp-Trp-Dab-^DPro-Oic-);

cyclo(-Phe(4CF₃)-Cyp-Trp-3Pal-^DPic-Oic-);

or pharmaceutically acceptable salts thereof.

5

10. Diastereomers, epimers and enantiomers of the compounds of formula (I) as defined in claim 1.

11. Compounds according to any one of claims 1 to 10 for use as therapeutically
10 active substances.

12. Compounds according to any one of claims 1 to 10 having antagonizing activity against the CCR10 receptor.

15 13. Compounds according to any one of claims 1 to 10 selectively interfering with the natural activity of the CCR10 receptor and its natural ligands CCL27 and/or CCL28.

14. A pharmaceutical composition containing a compound or a mixture of compounds according to any one of claims 1 to 10 and a pharmaceutically inert carrier.

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15. Compositions according to claim 14 in a form suitable for oral, topical, transdermal, injection, buccal, transmucosal, rectal, pulmonary or inhalation administration, especially in the form of tablets, dragees, capsules, solutions, liquids, gels, plaster, creams, ointments, syrup, slurries, suspensions, spray, nebuliser or

25 suppositories.

16. The use of compounds according to any one of claims 1 to 10 for the manufacture of a medicament for treating or preventing dermatological disorders, metabolic diseases, inflammatory diseases, neurological diseases, respiratory diseases,
30 gastro-intestinal tract disorders, ophthalmic diseases, haematological diseases and cancer, especially for the manufacture of a medicament for treating or preventing

diseases or conditions associated with the immune response in the area of inflammation, cutaneous disorders or cancer, such as psoriasis, atypical dermatitis, contact sensitivity and allergic dermatitis, Stevens-Johnson syndrome, bullous cutaneous diseases, systemic lupus erythematosus, systemic and multiple sclerosis, 5 allergic asthma, arthritis, graft versus host disease, certain melanoma and cutaneous lymphoma, inflammatory processes of the gastro-intestinal tract and the eye.

17. A process for the preparation of compounds according to any one of claims 1 to 10 which comprises

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(a) coupling an appropriately functionalized solid support with an appropriately N-protected derivative of that amino acid which in the desired end-product is in position T¹ or T² or P¹ to P⁴ as defined above; any functional group which may be present in said N-protected amino acid derivative being likewise 15 appropriately protected;

(b) removing the N-protecting group from the product obtained in step (a);
(c) coupling the product thus obtained with an appropriately N-protected derivative of that amino acid which in the desired end-product is in the position of the next element (T or P), following counterclockwise or clockwise the 20 sequence according to general formula (I) in -COOH to -NH₂ orientation; any functional group which may be present in said N-protected amino acid derivative being likewise appropriately protected;

(d) removing the N-protecting group from the product thus obtained;

(e) repeating steps (c) and (d) until all amino acid residues have been introduced;

25 (f) if desired, selectively deprotecting one or several protected functional group(s) present in the molecule and chemically transforming the reactive group(s) thus liberated;

(g) detaching the product thus obtained from the solid support;

(h) cyclizing the product cleaved from the solid support;

- (i) removing any protecting groups present on functional groups of any members of the chain of amino acid residues and, if desired, any protecting group(s) which may in addition be present in the molecule; and
- (j) if desired, implementing additional chemical transformations of one or more reactive group(s) present in the molecule;
- (k) if desired, converting the product thus obtained into a pharmaceutically acceptable salt or converting a pharmaceutically acceptable, or unacceptable, salt thus obtained into the corresponding free compound of formula (I) or into a different, pharmaceutically acceptable salt.

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18. A modification of the process of claim 17 for the manufacture of stereoisomeric compounds according to claim 10 wherein stereoisomers of chiral starting materials are used.