TEMPLATE - FIXED PEPTIDOMIMETICS WITH CXCR7 MODULATING ACTIVITY

The present invention provides novel peptidomimetics incorporating a chain of α-amino acid residues as defined below attached to a template which provides specific structural constrains for a β-hairpin like conformation. These template-fixed β-hairpin mimetics have a selective modulating activity on the CXCR7 receptor and are thus useful in the treatment of a variety of diseases and disorders mediated by or sustained through the activity of CXCR7 or in the support of therapeutic treatments of specific disease conditions of primarily different cause. The present invention relates to methods of using these compounds in the treatment of the various diseases and disorders, 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. As for other ligand/receptor pairs of their super family, the GPCRs, for some receptors the full scope of downstream activity and sometimes organ specific function still remains not fully understood. One of this recently deorphanized GPCRs is the chemokine receptor CXCR7 (RDC1), which binds with high affinity the inflammatory and homing chemokines CXCL11 (ITAC) and CXCL12 (SDF-1) (K. Balabanian, B. Lagane et al., *J. Biol. Chem.* **2005**, *280*, 35760-35766).

CXCL12 also binds to another chemokine receptor, CXCR4, and the CXCL12/CXCR4 axis has been demonstrated to play a crucial role in different inflammatory and cancer diseases. The recent finding that CXCL12 binds to both CXCR4 and CXCR7 indicates that the physiological and pathological functions of CXCL12 might be mediated by two distinct receptors (C. Dambly-Chaudière et al., *BMC Dev. Biol.* **2007**, 7-23).

In contrast to CXCR4, CXCR7 does not induce typical chemokine responses such as calcium mobilization. Instead, recent findings indicate that the receptor has a key function in the generation of a CXCL12 local gradient for CXCR4-dependent migration by scavenging CXCL12. These observations seem to be in favor of a main role of CXCR7 as a decoy receptor ("CXCL12 sink") with the critical function of clearing excess CXCL12 by internalization (B. Boldajipour, H. Mahabaleshwar et al., *Cell* **2008**, *132*, 463-73; Cell Adh. Migr. **2008**, *2*, 69-70). Moreover, it has been shown that CXCR7 can modulate CXCR4 activity by forming heterodimers and that it may activate other intracellular signaling pathways (A. Levoye, K. Balabanian et al., *Blood* **2009**, *113*, 6085-93).

As a consequence of the close functional relation between the two receptors, CXCR7 may be involved in the same disease conditions in which CXCR4 has been shown to play an important role. In particular, CXCR7 is markedly expressed in a variety of tumors and their respective tumor cell lines (e.g. prostate, bladder, breast cancer, multiple myeloma, rhabdomyosarcoma, non-small cell lung cancer); its expression level is often correlated with tumor growth and, moreover, with invasiveness. Two major mechanisms have been suggested for the role of CXCR7 in tumor development and metastasis: 1) increase of cancer cell proliferation and survival, which may be supported by a pro-angiogenic effect; 2) CXCR7 favors adhesion and transendothelial migration of cancer cells together with CXCR4-mediated migration.

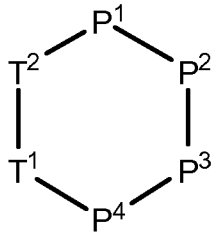
Moreover, recent studies suggest that CXCR7 may also be implicated in rheumatoid arthritis, other chronic and/or autoimmune inflammatory diseases (G. Graham et al., *Curr. Mol. Med.* **2009**, *9* (2), 86-93) or pulmonary arterial hypertension since it is up-regulated in certain specific tissues, such as in lungs under hypoxic conditions (C. M. Costello, P. McLoughlin et al., *Am. J. Physiol. Lung Cell Mol. Physiol.* **2008**, *295* (2), 272-284).

Now the present invention provides new chemical entities for a potential use as potent, selective and drugable ligands for the GPC-receptor CXCR7. In the compounds described below, a special strategy is utilized to stabilize β-hairpin conformations in backbone-cyclic β-hairpin mimetics exhibiting selective activity against the CXCR7 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 β-hairpin geometry.

Template-bound hairpin mimetic peptides have been described in the literature (D. Obrecht, 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 have 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.

There are few studies in the field describing tetrameric peptides linked to a template as agonist and/or antagonists of GPCRs in general (e.g. WO2008092281). The present invention is now providing novel compounds, which differ significantly in structure and exhibit a high biological activity and surprising selectivity for a specific novel receptor in this field, namely, for the CXCR7 receptor.

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

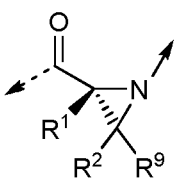


(I)

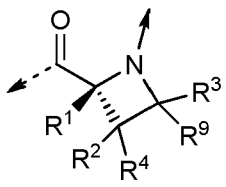
wherein the single elements T or P are connected in either direction from the carbonyl (C=O) point of attachment to the nitrogen (N) of the next element and wherein

– either

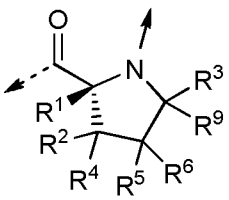
T^1 is an α-amino acid residue of one of the formulae



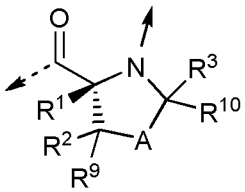
AA1



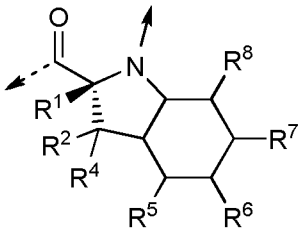
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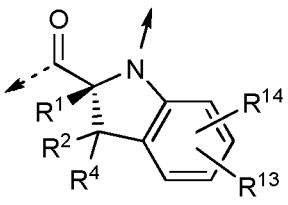
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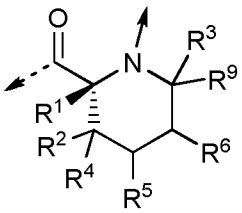
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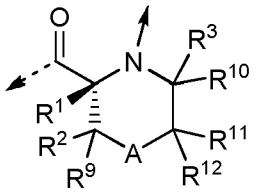
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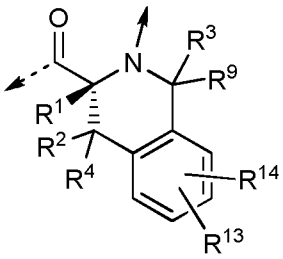
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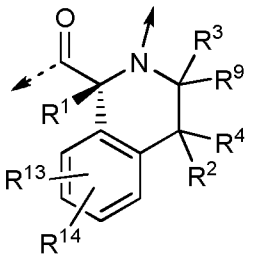
AA7



AA8



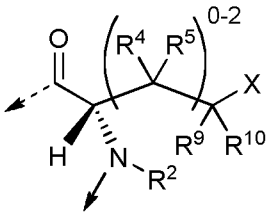
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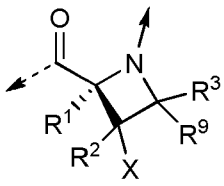
AA10

and

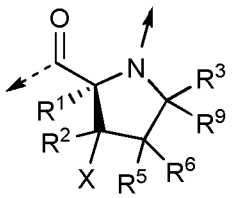
T^2 is an α-amino acid residue of one of the formulae



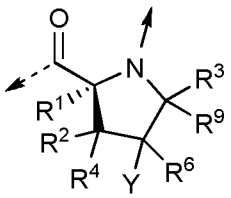
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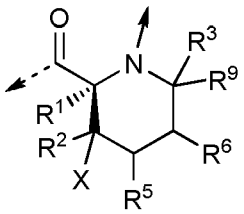
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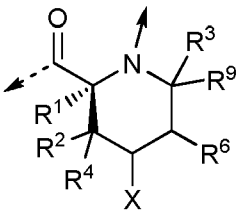
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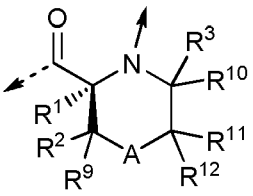
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AA15



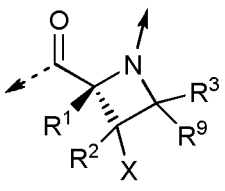
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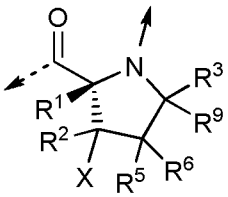
AA17

– or

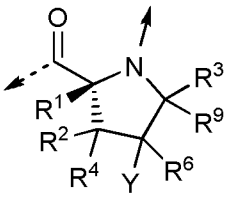
T^1 is an α-amino acid residue of one of the formulae



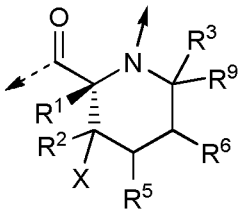
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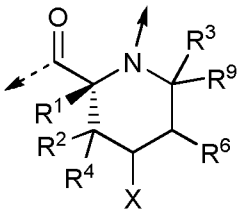
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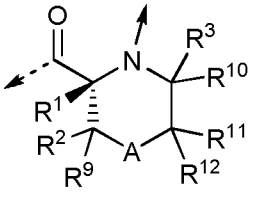
AA20



AA21



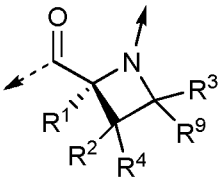
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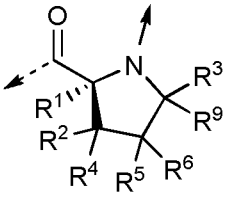
AA23

and

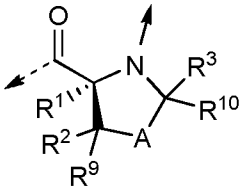
T^2 is an α-amino acid residue of one of the formulae AA11 to AA17, hereinabove, or an α-amino acid residue of one of the formulae



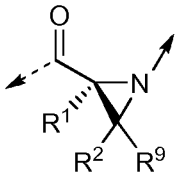
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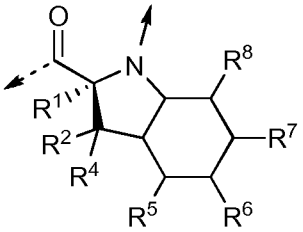
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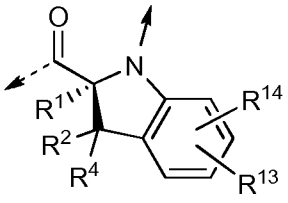
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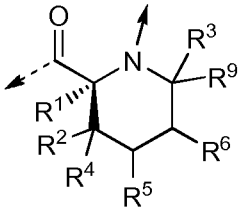
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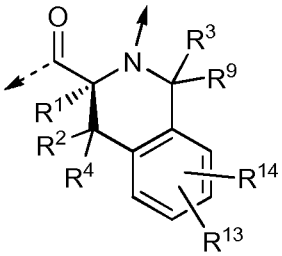
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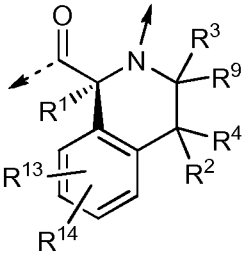
AA29



AA30



AA31

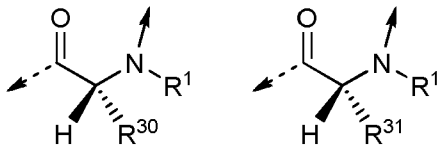


AA32

P^1, P^3 and P^4 are independently

-$NR^1CH(R^{29})CO$-; -$NR^1CH(R^{30})CO$-; or -$NR^1CH(R^{31})CO$-;

P^2 is an α-amino acid residue of one of the formulae



AA33 AA34

A is O; NR^{17}; S; SO; or SO_2;

X is OH; NH_2; OR^{16}; NR^1R^{16}; or $NR^{17}R^{18}$;

Y is NH_2; F; OR^{16}; NR^1R^{16}; or $NR^{17}R^{18}$;

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; $-(CHR^{15})_oOR^{17}$; $-(CHR^{15})_oSR^{17}$; $-(CHR^{15})_oNR^{17}R^{18}$; $-(CHR^{15})_oOCONR^{17}R^{18}$; $-(CHR^{15})_oNR^1CONR^{17}R^{18}$; $-(CHR^{15})_oNR^1COR^{17}$; $-(CHR^{15})_oCOOR^{17}$; $-(CHR^{15})_oCONR^{17}R^{18}$; $-(CHR^{15})_oPO(OR^1)_2$; $-(CHR^{15})_oSO_2R^{17}$; $-(CHR^{15})_oNR^1SO_2R^{17}$; $-(CHR^{15})_oSO_2NR^{17}R^{18}$; $-(CR^1R^{15})_oR^{35}$; or $-(CHR^1)_nO(CHR^2)_mR^{35}$; or

R^4 and R^2 taken together can form

=O; $-(CHR^{15})_p-$; $-(CH_2)_nO(CH_2)_m-$; $-(CH_2)_nS(CH_2)_m-$; 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:

$-(CHR^{15})_p-$; $-(CH_2)_nO(CH_2)_m-$; $-(CH_2)_nS(CH_2)_m-$; or $-(CH_2)_nNR^1(CH_2)_m-$; or

R^4 and R^5 are independently X;

R^9, R^{10}, R^{11} and R^{12} are independently

H; F; CF_3; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl; aryl; heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; $-(CHR^{15})_rOR^{17}$; $-(CHR^{15})_rSR^{17}$; $-(CHR^{15})_rNR^{17}R^{18}$; $-(CHR^{15})_rOCONR^{17}R^{18}$; $-(CHR^{15})_rNR^1CONR^{17}R^{18}$; $-(CHR^{15})_rNR^1COR^{17}$; $-(CHR^{15})_oCOOR^{17}$; $-(CHR^{15})_oCONR^{17}R^{18}$; $-(CHR^{15})_rPO(OR^1)_2$; $-(CHR^{15})_rSO_2R^{17}$; $-(CHR^{15})_rNR^1SO_2R^{17}$; $-(CHR^{15})_rSO_2NR^{17}R^{18}$; $-(CR^1R^{15})_oR^{35}$; or

$-(CHR^1)_rO(CHR^1)_oR^{35}$; or

R^{11} and R^{12} taken together can form

=O; or $=NR^1$;

R^{13} and R^{14} 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; $-(CHR^{15})_oOR^{17}$; $-(CHR^{15})_oSR^{17}$; $-(CHR^{15})_oNR^{17}R^{18}$; $-(CHR^{15})_oOCONR^{17}R^{18}$; $-(CHR^{15})_oNR^1CONR^{17}R^{18}$; $-(CHR^{15})_oNR^1COR^{17}$; $-(CHR^{15})_oCOOR^{17}$; $-(CHR^{15})_oCONR^{17}R^{18}$; $-(CHR^{15})_oPO(OR^1)_2$; $-(CHR^{15})_oSO_2R^{17}$; $-(CHR^{15})_oNR^1SO_2R^{17}$; $-(CHR^{15})_oSO_2NR^{17}R^{18}$; $-(CR^1R^{15})_oR^{35}$; or $-(CHR^1)_rO(CHR^1)_oR^{35}$;

R^{15} 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; $-(CHR^1)_oOR^{17}$; $-(CHR^1)_oSR^{17}$; $-(CHR^1)_oNR^{17}R^{18}$; $-(CHR^1)_oNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CHR^1)_oCOOR^{17}$; $-(CHR^1)_oCONR^{17}R^{18}$; $-(CHR^1)_oSO_2R^{17}$; or $-(CHR^1)_oSO_2NR^{17}R^{18}$;

R^{16} is 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; $-(CHR^1)_sOR^{17}$; $-(CHR^1)_sSR^{17}$; $-(CHR^1)_sNR^{17}R^{18}$; $-(CHR^1)_oCOR^{17}$; $-(CHR^1)_oCOOR^{17}$; $-(CHR^1)_oCONR^{17}R^{18}$; or $-(CHR^1)_oSO_2R^{17}$;

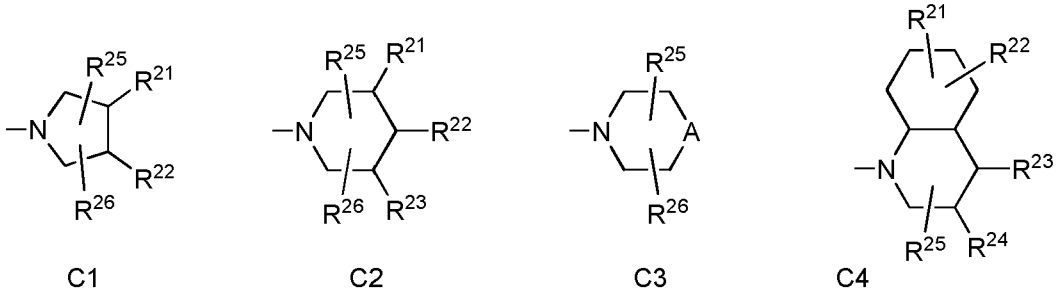
R^{17}, R^{18}, R^{19} and R^{20} are independently

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; aryl-heterocycloalkyl; heteroaryl-cycloalkyl; or heteroaryl-heterocycloalkyl; or

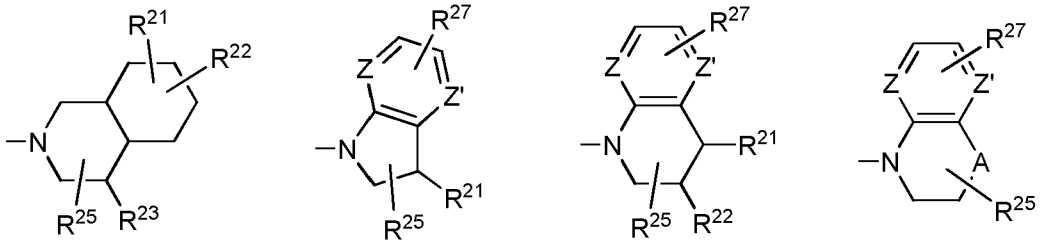
the structural elements $-NR^{17}R^{18}$ and $-NR^{19}R^{20}$ can independently form:

heterocycloalkyl; aryl-heterocycloalkyl; or heteroaryl-heterocycloalkyl;

or a group of one of the formulae



C1 C2 C3 C4



C5 C6 C7 C8

Z, Z' and Z'' are independently

$-CR^{39}$; or N;

R^{21}, R^{22}, R^{23} and R^{24} are independently

H; F; CF_3; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl; aryl; heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; $-(CHR^1)_oOR^{17}$; $-(CHR^1)_oSR^{17}$; $-(CHR^1)_oNR^2R^{17}$; $-(CHR^1)_oOCONR^2R^{17}$; $-(CHR^1)_oNR^2CONR^3R^{17}$; $-(CHR^1)_oNR^2COR^{17}$; $-(CHR^1)_oCOOR^{17}$; $-(CHR^1)_oCONR^2R^{17}$; $-(CHR^1)_oPO(OR^2)_2$; $-(CHR^1)_oSO_2R^{17}$; $-(CHR^1)_oNR^2SO_2R^{17}$; $-(CHR^1)_oSO_2NR^2R^{17}$; $-(CR^1R^2)_oR^{38}$; or $-(CHR^1)_nO(CHR^2)_mR^{38}$;

R^{25} and R^{26} are independently

H; F; CF_3; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl; aryl; heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; $-(CHR^1)_rOR^{17}$; $-(CHR^1)_rSR^{17}$; $-(CHR^1)_rNR^2R^{17}$; $-(CHR^1)_rOCONR^2R^{17}$; $-(CHR^1)_rNR^2CONR^3R^{17}$;$-(CHR^1)_rNR^2COR^{17}$; $-(CHR^1)_oCOOR^{17}$; $-(CHR^1)_oCONR^2R^{17}$; $-(CHR^1)_rPO(OR^2)_2$; $-(CHR^1)_rSO_2R^{17}$; $-(CHR^1)_rNR^2SO_2R^{17}$; $-(CHR^1)_rSO_2NR^2R^{17}$; $-(CR^1R^2)_oR^{38}$; or $-(CHR^1)_rO(CHR^2)_oR^{38}$;

R^{27} is 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; $-(CHR^1)_oOR^{17}$; $-(CHR^1)_oSR^{17}$; $-(CHR^1)_oNR^2R^{17}$; $-(CHR^1)_oOCONR^2R^{17}$; $-(CHR^1)_oNR^2CONR^3R^{17}$; $-(CHR^1)_oNR^2COR^{17}$; $-(CHR^1)_oCOOR^{17}$; $-(CHR^1)_oCONR^2R^{17}$; $-(CHR^1)_oPO(OR^2)_2$; $-(CHR^1)_oSO_2R^{17}$; $-(CHR^1)_oNR^2SO_2R^{17}$; $-(CHR^1)_oSO_2NR^2R^{17}$; $-(CR^1R^2)_oR^{38}$; or $-(CHR^1)_rO(CHR^2)_oR^{38}$;

R^{29} is H; alkyl; alkenyl; cycloalkyl-lower alkyl; heterocycloalkyl-lower alkyl; $-(CHR^4)_oOR^{17}$; $-(CHR^4)_oSR^{17}$; or $-(CHR^4)_rNR^{17}R^{18}$;

R^{30} is $-(CR^1R^4)_nR^{35}$; $-(CH_2)_nO(CH_2)_mR^{35}$; $-(CH_2)_nS(CH_2)_mR^{35}$; or $-(CH_2)_nNR^1(CH_2)_mR^{35}$;

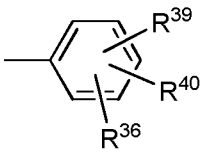
R^{31} is alkyl; alkenyl; $-(CR^1R^{15})_qNR^{17}R^{18}$; $-(CR^1R^{15})_qNR^2R^{16}$; $-(CR^1R^{15})_qNR^{17}R^{32}$; $-(CR^1R^{15})_qNR^{17}COR^{18}$; $-(CH_2)_qC(=NR^{15})NR^{17}R^{18}$; $-(CH_2)_qC(=NOR^{19})NR^{17}R^{18}$; $-(CH_2)_qC(=NNR^{17}R^{18})NR^{19}R^{20}$; $-(CR^1R^{15})_qNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CR^1R^{15})_qN=C(NR^{17}R^{18})NR^{19}R^{20}$; $-(CR^1R^{15})_qOR^{17}$; $-(CR^1R^{15})_qOR^{32}$; $-(CR^1R^{15})_qSR^{17}$; $-(CR^1R^{15})_qSO_2R^{17}$; $-(CR^1R^{15})_qNR^{17}SO_2R^{18}$; $-(CR^1R^{15})_qSO_2NR^2R^{16}$; $-(CR^1R^{15})_qSO_2NR^{17}R^{18}$; $-(CR^1R^{15})_qNR^{19}SO_2NR^{17}R^{18}$; $-(CR^1R^{15})_qPO(OR^2)_2$; $-(CH_2)_nO(CH_2)_mNR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mC(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mC(=NOR^{19})NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mC(=NNR^{17}R^{18})NR^{19}R^{20}$; $-(CH_2)_nO(CH_2)_mNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mN=C(NR^{17}R^{18})NR^{19}R^{20}$; $-(CH_2)_nS(CH_2)_mNR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mC(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mC(=NOR^{19})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mC(=NNR^{17}R^{18})NR^{19}R^{20}$; $-(CH_2)_nS(CH_2)_mNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mN=C(NR^{17}R^{18})NR^{19}R^{20}$; $-(CR^1R^{15})_qCOOR^{17}$; $-(CR^1R^{15})_qCONR^{17}R^{18}$; or $-(CR^1R^{15})_qCOR^{33}$;

R^{32} is $-COR^{29}$; $-COR^{30}$; $-CO(CR^1R^{15})_oR^{17}$; $-CO(CR^1R^{15})_oOR^{17}$; $-CO(CR^1R^{15})_oNR^{17}R^{18}$; $-CO(CR^1R^{15})_oNR^2R^{16}$; $-CO(CR^1R^{29})NR^{17}R^{18}$; $-CO(CR^1R^{30})NR^{17}R^{18}$; $-CO(CR^1R^{34})NR^{17}R^{18}$; $-CO(CHR^1)_oCONR^{17}R^{18}$; $-CO(CHR^1)_oCONR^{17}SO_2R^{18}$; $-CO(CR^1R^{15})_oNR^{17}SO_2R^{18}$; $-CONR^1(CHR^{17})_nNR^2(CHR^{15})_mR^{16}$; $-CO(CHR^{17})_nO(CHR^{15})_mR^{16}$; $-CONR^1(CHR^{17})_nO(CHR^{15})_mR^{16}$; $-SO_2R^{29}$; $-SO_2R^{30}$; $-SO_2(CR^1R^{15})_oR^{17}$; or $-SO_2(CR^1R^{15})_oNR^{17}R^{18}$;

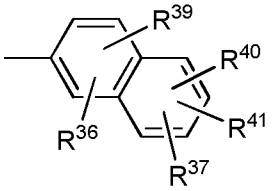
R^{33} is $-NR^1C(R^2)(R^{29})COOR^{17}$; $-NR^1C(R^2)(R^{29})CONR^{17}R^{18}$; $-NR^1C(R^2)(R^{30})COOR^{17}$; $-NR^1C(R^2)(R^{30})CONR^{17}R^{18}$; $-NR^1C(R^2)(R^{34})COOR^{17}$; or $-NR^1C(R^2)(R^{34})CONR^{17}R^{18}$;

R^{34} is $-(CR^1R^{15})_qNR^{17}R^{18}$; $-(CH_2)_qC(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_qC(=NOR^{19})NR^{17}R^{18}$; $-(CH_2)_qC(=NNR^{17}R^{18})NR^{19}R^{20}$; $-(CR^1R^{15})_qNR^2C(=NR^{19})NR^{17}R^{18}$; $-(CR^1R^{15})_qN=C(NR^{17}R^{18})NR^{19}R^{20}$; $-(CR^1R^{15})_qOR^{17}$; $-(CR^1R^{15})_qSR^{17}$; $-(CR^1R^{15})_qSO_2R^{17}$; $-(CR^1R^{15})_qNR^{17}SO_2R^{18}$; $-(CR^1R^{15})_qSO_2NR^1R^{16}$; $-(CR^1R^{15})_qSO_2NR^{17}R^{18}$; $-(CR^1R^{15})_qNR^2SO_2NR^{17}R^{18}$; $-(CR^1R^{15})_qPO(OR^1)_2$; $-(CH_2)_nO(CH_2)_mNR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mC(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mC(=NOR^{19})NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mC(=NNR^{17}R^{18})NR^{19}R^{20}$; $-(CH_2)_nO(CH_2)_mNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mN=C(NR^{17}R^{18})NR^{19}R^{20}$; $-(CH_2)_nS(CH_2)_mNR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mC(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mC(=NOR^{19})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mC(=NNR^{17}R^{18})NR^{19}R^{20}$; $-(CH_2)_nS(CH_2)_mNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mN=C(NR^{17}R^{18})NR^{19}R^{20}$; $-(CR^1R^{15})_qCOOR^{17}$; or $-(CR^1R^{15})_qCONR^{17}R^{18}$;

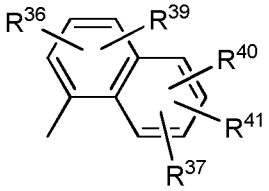
R^{35} is an aryl group of one of the formulae



AR1

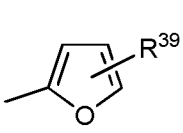


AR2

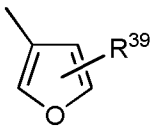


AR3

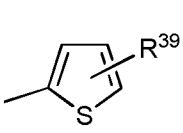
or a heteroaryl group of one of the formulae



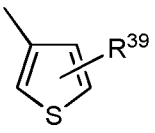
H1



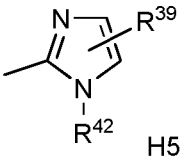
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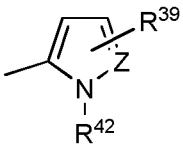
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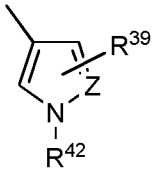
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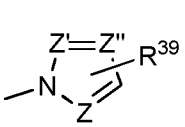
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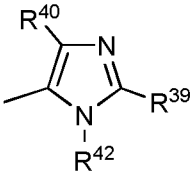
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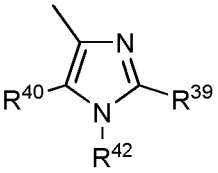
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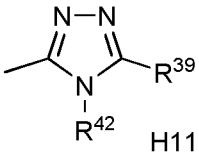
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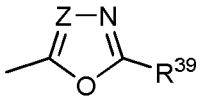
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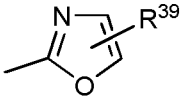
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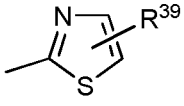
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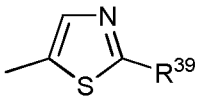
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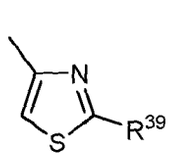
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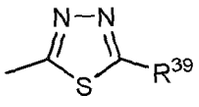
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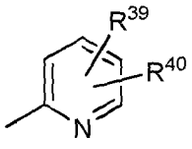
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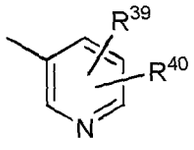
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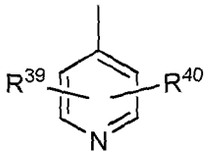
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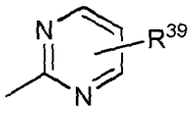
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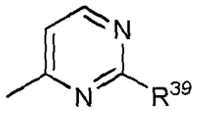
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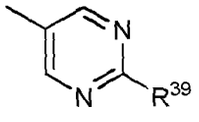
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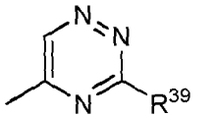
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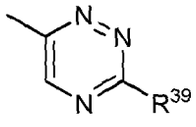
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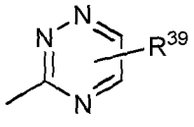
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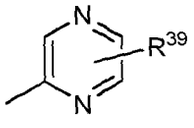
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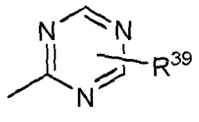
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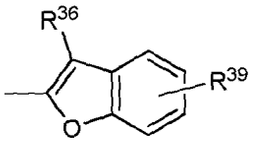
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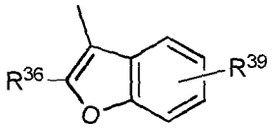
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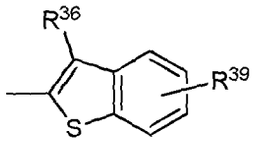
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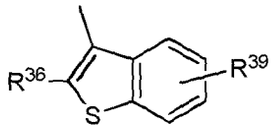
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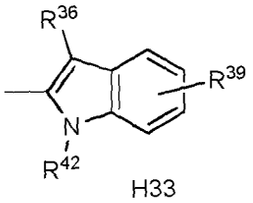
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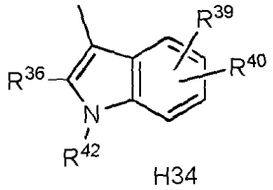
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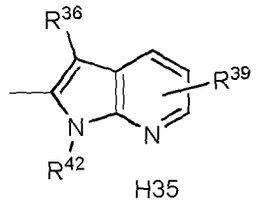
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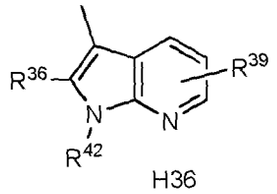
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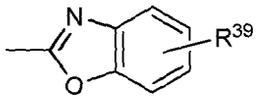
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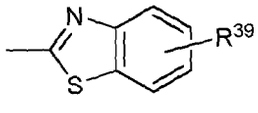
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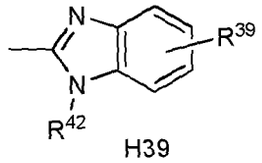
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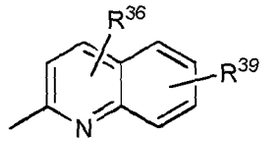
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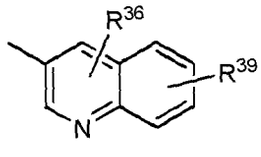
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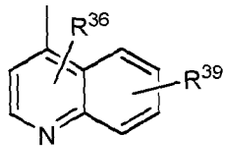
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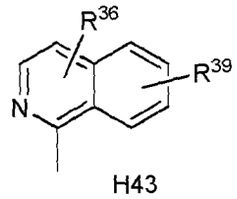
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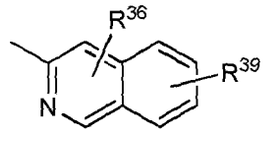
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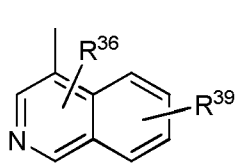
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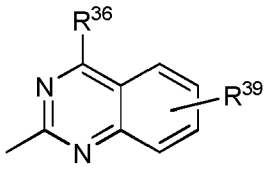
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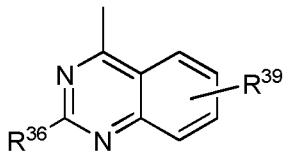
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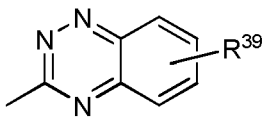
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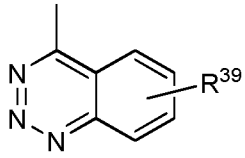
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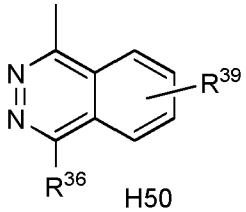
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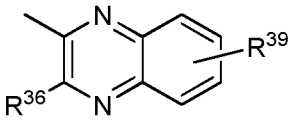
H48



H49



H50

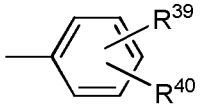


H51

R^{36} and R^{37} 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; $-(CH_2)_oR^{38}$; $-(CH_2)_oOR^{17}$; $-O(CH_2)_oR^{38}$; $-(CH_2)_oSR^{17}$; $-(CH_2)_oNR^{17}R^{18}$; $-(CH_2)_oOCONR^{17}R^{18}$; $-(CH_2)_oNR^1CONR^{17}R^{18}$; $-(CH_2)_oNR^1COR^{17}$; $-(CH_2)_oCOOR^{17}$; $-(CH_2)_oCONR^{17}R^{18}$; $-(CH_2)_oPO(OR^1)_2$; $-(CH_2)_oSO_2R^{16}$; or $-(CH_2)_oCOR^{17}$;

R^{38} is an aryl group of the formula



AR4

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

H; F; Cl; Br; OH; NH_2; NO_2; CN; CF_3; $OCHF_2$; OCF_3; $-NR^1R^{17}$; $-(CH_2)_oCOOR^{17}$; $-(CH_2)_oCONR^1R^{17}$; lower alkyl; lower alkoxy; or lower alkenyl;

R^{42} is H; lower alkyl; or aryl-lower alkyl;

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; s is 0-4

and pharmaceutically acceptable salts thereof.

Each single group "R^x" with the same index-number x for x = 1 - 42 in a specific formula is independently selected and therefore these groups 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 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 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.

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, decalinyl and the like.

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, azetidinyl, pyrrolidinyl, tetrahydrofuranyl, piperidinyl, octahydro-1*H*-indolyl, 1,7-diazaspiro[4.4]nonane and the like. Said heterocycloalkyl ring(s) may be optionally substituted.

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, CF_3, OCF_3, $OCHF_2$, $N(CH_3)_2$, NO_2, lower alkyl, lower alkenyl, phenyl or phenoxy.

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 four heteroatoms selected from the group consisting of O, S and N and whereby the heteroaryl radicals or tautomeric forms thereof may be 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, but are not limited to, benzyl, 1-phenylethyl, 2-phenylethyl, 3-phenylpropyl, 2-phenyl-propyl 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, 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 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-tetrahydro-quinolinyl 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 analogously 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 ($-NH_2$), dimethylamino, nitro ($-NO_2$), halogen (F, Cl, Br, I), CF_3, cyano (-CN), hydroxy, methoxy, oxo (=O), carboxy, phenyl, phenyloxy, benzyl, sulfonic acid, sulfate, phosphonic acid, phosphate, or phosphonate etc.

The term "lower" designates radicals and compounds having up to 6 carbon 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.

The peptidomimetics of the present invention can also be diastereomers (e.g. epimers) of the compounds of formula **(I)** based on chiral centers where the absolute stereo-chemistry is not explicitly defined in the above description. 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 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 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 ^{2}H (D), ^{3}H, ^{11}C, ^{14}C, ^{127}I 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 dosage regimen.

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

R^{16} is CF_3; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl; cycloalkyl-lower alkyl; heterocycloalkyl-lower alkyl; aryl; heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; $-(CHR^1)_sOR^{17}$; $-(CHR^1)_sSR^{17}$; $-(CHR^1)_sNR^{17}R^{18}$; $-(CHR^1)_oCOR^{17}$; $-(CHR^1)_oCOOR^{17}$; $-(CHR^1)_oCONR^{17}R^{18}$; or $-(CHR^1)_oSO_2R^{17}$;

R^{17}, R^{18}, R^{19} and R^{20} 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

the structural elements $-NR^{17}R^{18}$ and $-NR^{19}R^{20}$ can independently form: heterocycloalkyl; aryl-heterocycloalkyl; or heteroaryl-heterocycloalkyl;

or a group of one of the above formulae C1 to C8;

R^{31} is alkyl; alkenyl; $-(CR^1R^{15})_qNR^{17}R^{18}$; $-(CR^1R^{15})_qNR^2R^{16}$; $-(CR^1R^{15})_qNR^{17}COR^{18}$; $-(CH_2)_qC(=NR^{15})NR^{17}R^{18}$; $-(CR^1R^{15})_qNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CR^1R^{15})_qOR^{17}$; $-(CR^1R^{15})_qSR^{17}$; $-(CR^1R^{15})_qSO_2R^{17}$; $-(CR^1R^{15})_qNR^{17}SO_2R^{18}$; $-(CR^1R^{15})_qSO_2NR^2R^{16}$; $-(CR^1R^{15})_qSO_2NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mNR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mC(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mNR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CR^1R^{15})_qCONR^{17}R^{18}$; or $-(CR^1R^{15})_qCOR^{33}$;

s is 2-4

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

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

T^1 is ^{D}Pro; ^{D}Pip; ^{D}Tic; ^{D}Tiq; ^{D}Oic; ^{D}Azt; ^{D}Pro((3*R*)OH); ^{D}Pro((3*S*)OH); ^{D}Pro((3*R*)NH_2); ^{D}Pro((3*S*)NH_2); ^{D}Pro((4*R*)OH); ^{D}Pro((4*S*)OH); ^{D}Pro((4*R*)NH_2); ^{D}Pro((4*S*)NH_2); ^{D}Pro((4*S*)NHBz); or ^{D}Mor;

T^2 is Thr; *allo*Thr; Ser; hSer; Pro((3*R*)OH); Pro((3*S*)OH); Hyp(Bn); (4*S*)-Hyp(Bn); Pro((3*R*)NH_2); Pro((3*S*)NH_2); Pro((4*R*)NH_2); Pro((4*S*)NH_2); Pro((4*S*)F); Pro((4*S*)NHBz); or Mor; or

when T^1 is ^{D}Pro((3*R*)OH); ^{D}Pro((3*S*)OH); ^{D}Pro((3*R*)NH_2); ^{D}Pro((3*S*)NH_2); ^{D}Pro((4*R*)NH_2); ^{D}Pro((4*S*)NH_2); ^{D}Pro((4*S*)NHBz); or ^{D}Mor

then T^2 can in addition be

Pro; Pip; Tic; Tiq; Oic; or Azt;

P^1, P^3 and P^4 are independently

Ala; Arg; Asn; Asp; Cit; Cys; Glu; Gln; Gly; His; Ile; Leu; Lys; Met; Orn; Phe; Pro; Ser; Thr; Trp; Tyr; Val; Abu; Agb; Agp; Ala(*t*Bu); Ala(*c*Pr); Ala(2Furyl); Ala(3Furyl); Ala(Ppz); Ala(1Pyraz); Ala(2Quin); Ala(3Quin); Ala(4Quin); Ala(Tet); Azt; Bbta; Bip; Cha; Chg; Dab; Dab(Ac); Dab(*c*Pr); Dab(*i*Pr); Dab(4Me$_2$NPhSO$_2$); Dab(MeOEtNCO); Dab(MePpzCO); Dab(MeSO$_2$); Dab(morphCO); Dab(1Nal); Dab(2Nal); Dap; Dap(CONH$_2$); Dap(MeOEt); Dap((MeOEt)$_2$); Deg; Gly(*t*Bu); hArg; hCha; hCys; hHis; hLys; hPhe; hSer; hSer(Me); hTrp; hTyr; His(Me); His(Bn);

Hyp(Bn); (4*S*)-Hyp(Bn); Hyp(4BrBn); Hyp(3CNBn); Hyp(4CNBn); Hyp(CONHPh); Hyp(Ph); Lys(Ac); Lys(Bz); Lys(*c*Pr); Lys(*i*Pr); Lys(Me); Lys(Nic); Lys((5*R*)OH); Lys(4Oxa); Met(O_2); 1Nal; 2Nal; Nle; Nle(6OBn); OctG; Oic; Orn(*c*Pr); Orn(*i*Pr); 2Pal; 3Pal; 4Pal; Phe(2Cl); Phe(3Cl); Phe(4Cl); Phe(3,4Cl_2); Phe(2F); Phe(3F); Phe(4F); Phe(4CN); Phe(4CF_3); Phe(4COOMe); Phg; Pip; Pro((4*R*)Bn); Pro((4*S*)F); Pro((4*S*)*c*Hex); Pro(5,5Me_2); Ser(Bn); Ser(Me); Thi; *allo*Thr; Thr(Bn); Thz; Thz(5,5Me_2); Tic; Tic(7OH); Trp(7Aza); Trp(5Br); Trp(6Br); Trp(6CF_3); Trp(5Cl); Trp(6Cl); Trp(5,6Cl); Trp(5OH); Tyr(Bn); Tyr(Me); Tyr(4MeOCOBn); Tyr(Ph); Tyr(4OHPh); Tza; Gln(Alk1); Gln(Alk2); Gln(Alk3); 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); Glu(cN17); Lys(Ar1); Lys(Ar2); Lys(Ar3); Lys(Ar4); Lys(Ar5); Lys(Ar6); Lys(Ar7); Lys(Ar8); Lys(Ar9); Lys(Ar10); Lys(Ar11); Lys(Ar12); Orn(Ar1); Orn(Ar2); Orn(Ar3); Orn(Ar4); Orn(Ar5); Orn(Ar6); Orn(Ar7); Orn(Ar8); Orn(Ar9); Orn(Ar10); Orn(Ar11); Orn(Ar12); Dab(Ar1); Dab(Ar2); Dab(Ar3); Dab(Ar4); Dab(Ar5); Dab(Ar6); Dab(Ar7); Dab(Ar8); Dab(Ar9); Dab(Ar10); Dab(Ar11); Dab(Ar12); Dab(S1); Dab(S2); Dab(S3); 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); 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); Orn(A1); Orn(A2); Orn(A3); Orn(A4); Orn(A5); Orn(A6); Orn(A7); Orn(A8); Orn(A9); Orn(A10); Orn(A11); Orn(A12); Orn(A13); Orn(A14); Orn(A15); Orn(A16); Orn(A17); Orn(A18); Orn(A19); Orn(A20); Orn(A21); Orn(A22); Orn(A23); Orn(A24); Orn(A25); Orn(A26); Orn(A27); Orn(A28); Orn(A29); Orn(A30); Orn(A31); Orn(A32); Orn(A33); Orn(A34); Orn(A35); Orn(A36); Orn(A37); Orn(A38); Orn(A39); Orn(A40); Orn(A41); Orn(A42); Orn(A43); Orn(A44); Orn(A45); Orn(A46); Orn(A47); Orn(A48); Orn(A49); Orn(A50); Orn(A51); Orn(A52); Orn(A53); Orn(A54); Orn(A55); Orn(A56); 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); 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); Dap(Ar1); Dap(Ar2); Dap(Ar3); Dap(Ar4); Dap(Ar5); Dap(Ar6); Dap(Ar7); Dap(Ar8); Dap(Ar9); Dap(Ar10); Dap(Ar11); Dap(Ar12); 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); 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); Dap(A51); Dap(A52); Dap(A53); Dap(A54); or Dap(A55);

P^2 is ^{D}Arg; ^{D}hArg; ^{D}Agb; ^{D}Lys; ^{D}Orn; ^{D}Cit; ^{D}Thr; ^{D}Dab; ^{D}Dab; ^{D}Phe; ^{D}Phe(4CF_3); ^{D}Trp; ^{D}His; ^{D}Tyr; ^{D}2Pal; ^{D}3Pal; ^{D}4Pal; ^{D}Lys(Ar1); ^{D}Lys(Ar2); ^{D}Lys(Ar3); ^{D}Lys(Ar4); ^{D}Lys(Ar5); ^{D}Lys(Ar6); ^{D}Lys(Ar7); ^{D}Lys(Ar8); ^{D}Lys(Ar9); ^{D}Lys(Ar10); ^{D}Lys(Ar11); ^{D}Lys(Ar12); ^{D}Orn(A41); ^{D}Orn(A56); ^{D}Orn(Ar1); ^{D}Orn(Ar2); ^{D}Orn(Ar3); ^{D}Orn(Ar4); ^{D}Orn(Ar5); ^{D}Orn(Ar6); ^{D}Orn(Ar7); ^{D}Orn(Ar8); ^{D}Orn(Ar9); ^{D}Orn(Ar10); ^{D}Orn(Ar11); ^{D}Orn(Ar12); ^{D}Dab(Ar1); ^{D}Dab(Ar2); ^{D}Dab(Ar3); ^{D}Dab(Ar4); ^{D}Dab(Ar5); ^{D}Dab(Ar6); ^{D}Dab(Ar7); ^{D}Dab(Ar8); ^{D}Dab(Ar9); ^{D}Dab(Ar10); ^{D}Dab(Ar11); ^{D}Dab(Ar12); ^{D}Dap(Ar1); ^{D}Dap(Ar2); ^{D}Dap(Ar3); ^{D}Dap(Ar4); ^{D}Dap(Ar5); ^{D}Dap(Ar6); ^{D}Dap(Ar7); ^{D}Dap(Ar8); ^{D}Dap(Ar9); ^{D}Dap(Ar10); ^{D}Dap(Ar11); or ^{D}Dap(Ar12);

and pharmaceutically acceptable salts thereof.

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

T^1 is ^{D}Pro; ^{D}Pip; ^{D}Tic; ^{D}Tiq; ^{D}Oic; ^{D}Azt; ^{D}Pro((3*R*)OH); ^{D}Pro((3*S*)OH); ^{D}Pro((3*R*)NH_2); ^{D}Pro((3*S*)NH_2); ^{D}Pro((4*R*)OH); ^{D}Pro((4*S*)OH); ^{D}Pro((4*R*)NH_2); ^{D}Pro((4*S*)NH_2); ^{D}Pro((4*S*)NHBz); or ^{D}Mor;

T^2 is Thr; *allo*Thr; Ser; hSer; Pro((3*R*)OH); Pro((3*S*)OH); Hyp(Bn); (4*S*)-Hyp(Bn); Pro((3*R*)NH_2); Pro((3*S*)NH_2); Pro((4*R*)NH_2); Pro((4*S*)NH_2); Pro((4*S*)F); Pro((4*S*)NHBz); or Mor; or

when T^1 is ^{D}Pro((3*R*)OH); ^{D}Pro((3*S*)OH); ^{D}Pro((3*R*)NH_2); ^{D}Pro((3*S*)NH_2); ^{D}Pro((4*R*)NH_2); ^{D}Pro((4*S*)NH_2); ^{D}Pro((4*S*)NHBz); or ^{D}Mor

then T^2 can in addition be

Pro; Pip; Tic; Tiq; Oic; or Azt;

P^1 is Ile; Nle; Leu; Val; Chg; Cha; Abu; Ala; Ala(*c*Pr); Ala(1Pyraz); Ala(Tet); Trp; 1Nal; 2Nal; Phe; Tyr; 2Pal; 3Pal; 4Pal; Thr; His; Arg; hArg; Agb; Pip; Orn(Ar2); or Orn(A56);

P^2 is ^{D}Arg; ^{D}hArg; ^{D}Agb; ^{D}Lys; ^{D}Orn; ^{D}Cit; ^{D}Thr; ^{D}Dab; ^{D}Dap; ^{D}Phe; ^{D}Trp; ^{D}His; ^{D}Tyr; ^{D}2Pal; ^{D}3Pal; or ^{D}4Pal;

P^3 is Arg; hArg; Agb; Agp; Lys; Orn; Orn(A41); Orn(A56); Orn(Ar2); Orn(Ar4); Orn(Ar7); Cit; Thr; Dab; Dap; Phe; Trp; His; Tyr; or Ile

P^4 is Trp; His; Phe; Phe($4CF_3$); 1Nal; 2Nal; Tyr; Leu; Ile; Arg; hArg; Lys; Dab; Dap; Orn; Orn(A56); or Orn(Ar7);

and pharmaceutically acceptable salts thereof.

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

T^1 is ^{D}Pro; ^{D}Pip; ^{D}Tic; ^{D}Pro((4*S*)OH); ^{D}Pro((4*R*)NH_2); or ^{D}Pro((4*S*)NH_2);

T^2 is Thr; *allo*Thr; Ser; hSer; Pro((3*S*)OH); (4*S*)-Hyp(Bn); Pro((4*R*)NH_2); Pro((4*S*)NH_2); Pro((4*S*)F); Pro((4*S*)NHBz); or Mor;

P^1 is Ile; Nle; Leu; Val; Chg; Cha; Abu; Ala; Trp; 1Nal; Tyr; 3Pal; Thr; His; Arg; hArg; Agb; Pip; Ala(1Pyraz); Ala(Tet); Orn(Ar2); or Orn(A56);

P^2 is ^{D}Arg; ^{D}Lys; ^{D}Orn; ^{D}Cit; ^{D}Thr; ^{D}Dab; ^{D}Phe; ^{D}Trp; ^{D}His; or ^{D}3Pal;

P^3 is Arg; hArg; Agb; Agp; Lys; Orn; Orn(A41); Orn(A56); Orn(Ar2); Orn(Ar4); Orn(Ar7); Dab; Trp; or His;

P^4 is Trp; His; Phe; Phe($4CF_3$); 1Nal; 2Nal; Tyr; Ile; Arg; hArg; Lys; Dab; Orn; Orn(A56); or Orn(Ar7);

and pharmaceutically acceptable salts thereof.

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 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
Asn	L-Asparagine
Asp	L-Aspartic acid
Cit	L-Citrulline

Cys	L-Cysteine
Glu	L-Glutamic acid
Gln	L-Glutamine
Gly	Glycine
His	L-Histidine
Ile	L-Isoleucine
Leu	L-Leucine
Lys	L-Lysine
Met	L-Methionine
Orn	L-Ornithine
Phe	L-Phenylalanine
Pro	L-Proline
Ser	L-Serine
Thr	L-Threonine
Trp	L-Tryptophan
Tyr	L-Tyrosine
Val	L-Valine

Abu	(*S*)-2-aminobutanoic acid
Agb	(*S*)-2-amino-4-guanidinobutanoic acid
Agp	(*S*)-2-amino-3-guanidinopropanoic acid
Ala(*t*Bu)	(*S*)-2-amino-4,4-dimethylpentanoic acid
Ala(*c*Pr)	(*S*)-2-amino-3-cyclopropylpropanoic acid
Ala(2Furyl)	(*S*)-2-amino-3-(furan-2-yl)propanoic acid
Ala(3Furyl)	(*S*)-2-amino-3-(furan-3-yl)propanoic acid
Ala(Ppz)	(*S*)-2-amino-3-(piperazin-1-yl)propanoic acid
Ala(1Pyraz)	(*S*)-2-amino-3-(1*H*-pyrazol-1-yl)propanoic acid
Ala(2Quin)	(*S*)-2-amino-3-(quinolin-2-yl)propanoic acid
Ala(3Quin)	(*S*)-2-amino-3-(quinolin-3-yl)propanoic acid
Ala(4Quin)	(*S*)-2-amino-3-(quinolin-4-yl)propanoic acid

Ala(Tet)	(*S*)-2-amino-3-(2*H*-tetrazol-2-yl)propanoic acid
Azt	(*S*)-azetidine-2-carboxylic acid
Bbta	(*S*)-2-amino-3-(1-benzothiophen-3-yl)propanoic acid
Bip	(*S*)-2-amino-3-(4-biphenylyl)propanoic acid
Cha	(*S*)-2-amino-3-cyclohexylpropanoic acid
Dab	(*S*)-2,4-diaminobutanoic acid
Dab(Ac)	(*S*)-4-acetamido-2-aminobutanoic acid
Dab(*c*Pr)	(*S*)-2-amino-4-(cyclopropylamino)butanoic acid
Dab(*i*Pr)	(*S*)-2-amino-4-(isopropylamino)butanoic acid
Dab(4Me_2NPhSO_2)	(*S*)-2-amino-4-(4-(dimethylamino)phenylsulfonamido)butanoic acid
Dab(MeOEtNCO)	(*S*)-2-amino-4-(3-(2-methoxyethyl)ureido)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(1Nal)	(*S*)-2-amino-4-((*S*)-2-amino-3-(naphthalen-1-yl)propanamido)-butanoic acid
Dab(2Nal)	(*S*)-2-amino-4-((*S*)-2-amino-3-(naphthalen-2-yl)-propanamido)-butanoic acid
Dap	(*S*)-2,4-diaminopropanoic acid
Dap($CONH_2$)	(*S*)-2-amino-3-ureidopropanoic acid
Dap(MeOEt)	(*S*)-2-amino-3-(2-methoxyethylamino)propanoic acid
Dap(($MeOEt)_2$)	(*S*)-2-amino-3-(bis(2-methoxyethyl)amino)propanoic acid
Deg	2-amino-2-ethylbutanoic acid
Gly(*t*Bu)	(*S*)-2-amino-3,3-dimethylbutanoic acid
hArg	(*S*)-2-amino-6-guanidinohexanoic acid
hCha	(*S*)-2-amino-4-cyclohexylbutanoic acid
hCys	(*S*)-2-amino-4-mercaptobutanoic acid
hHis	(*S*)-2-amino-4-(1*H*-imidazol-5-yl)butanoic acid
hLys	(*S*)-2,7-diaminoheptanoic acid
hPhe	(*S*)-2-amino-4-phenylbutanoic acid

hSer	(*S*)-2-amino-4-hydroxybutanoic acid
hSer(Me)	(*S*)-2-amino-4-methoxybutanoic acid
hTrp	(*S*)-2-amino-4-(1*H*-indol-3-yl)butanoic acid
hTyr	(*S*)-2-amino-4-(4-hydroxyphenyl)butanoic acid
His(Me)	(*S*)-2-amino-3-(1-methyl-1*H*-imidazol-5-yl)propanoic acid
His(Bn)	(*S*)-2-amino-3-(1-benzyl-1*H*-imidazol-5-yl)propanoic acid
Hyp(Bn)	(2*S*,4*R*)-4-(benzyloxy)pyrrolidine-2-carboxylic acid
(4*S*)-Hyp(Bn)	(2*S*,4*S*)-4-(benzyloxy)pyrrolidine-2-carboxylic acid
Hyp(4BrBn)	(2*S*,4*R*)-4-(4-bromobenzyloxy)pyrrolidine-2-carboxylic acid
Hyp(3CNBn)	(2*S*,4*R*)-4-(3-cyanobenzyloxy)pyrrolidine-2-carboxylic acid
Hyp(4CNBn)	(2*S*,4*R*)-4-(4-cyanobenzyloxy)pyrrolidine-2-carboxylic acid
Hyp(CONHPh)	(2*S*,4*R*)-4-(phenylcarbamoyloxy)pyrrolidine-2-carboxylic acid
Hyp(Ph)	(2*S*,4*R*)-4-phenoxypyrrolidine-2-carboxylic acid
Lys(Ac)	(*S*)-6-acetamido-2-aminohexanoic acid
Lys(Bz)	(*S*)-2-amino-6-benzamidohexanoic acid
Lys(*c*Pr)	(*S*)-2-amino-6-(cyclopropylamino)hexanoic acid
Lys(*i*Pr)	(*S*)-2-amino-6-(isopropylamino)hexanoic acid
Lys(Me)	(*S*)-2-amino-6-(methylamino)hexanoic acid
Lys(Nic)	(*S*)-2-amino-6-(nicotinamido)hexanoic acid
Lys((5*R*)OH)	(2*S*,5*R*)-2,6-diamino-5-hydroxyhexanoic acid
Lys(4Oxa)	(*S*)-2-amino-3-(2-aminoethoxy)propanoic acid
Met(O_2)	(S)-2-amino-4-(methylsulfonyl)butanoic acid
Mor	(*S*)-morpholine-3-carboxylic acid
1Nal	(*S*)-2-amino-3-naphthalen-1-ylpropanoic acid
2Nal	(*S*)-2-amino-3-naphthalen-2-ylpropanoic acid
Nle	(*S*)-2-amino-hexanoic acid
Nle(6OBn)	(*S*)-2-amino-6-(benzyloxy)hexanoic acid
OctG	(*S*)-2-aminodecanoic acid
Oic	(2*S*,3a*S*,7a*S*)-octahydro-1*H*-indole-2-carboxylic acid
Orn(*c*Pr)	(*S*)-2-amino-5-(cyclopropylamino)pentanoic acid

Orn(*i*Pr)	(S)-2-amino-5-(isopropylamino)pentanoic acid
2Pal	(*S*)-2-amino-3-(pyridine-2-yl)-propionic acid
3Pal	(*S*)-2-amino-3-(pyridine-3-yl)-propionic acid
4Pal	(*S*)-2-amino-3-(pyridine-4-yl)-propionic acid
Phe(2Cl)	(*S*)-2-amino-3-(2-chlorophenyl)propanoic acid
Phe(3Cl)	(*S*)-2-amino-3-(3-chlorophenyl)propanoic acid
Phe(4Cl)	(*S*)-2-amino-3-(4-chlorophenyl)propanoic acid
Phe(3,4Cl_2)	(*S*)-2-amino-3-(3,4-dichlorophenyl)propanoic acid
Phe(2F)	(*S*)-2-amino-3-(2-fluorophenyl)propanoic acid
Phe(3F)	(*S*)-2-amino-3-(3-fluorophenyl)propanoic acid
Phe(4F)	(*S*)-2-amino-3-(4-fluorophenyl)propanoic acid
Phe(4CN)	(*S*)-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
Pro((4*R*)Bn)	(2*S*,4*R*)-4-benzylpyrrolidine-2-carboxylic acid
Pro((4*S*)F)	(2*S*,4*S*)-4-fluoropyrrolidine-2-carboxylic acid
Pro((4*S*)*c*Hex)	(2*S*,4*S*)-4-cyclohexylpyrrolidine-2-carboxylic acid
Pro((3*R*)NH_2)	(2*S*,3*R*)-3-aminopyrrolidine-2-carboxylic acid
Pro((3*S*)NH_2)	(2*S*,3*S*)-3-aminopyrrolidine-2-carboxylic acid
Pro((4*R*)NH_2)	(2*S*,4*R*)-4-aminopyrrolidine-2-carboxylic acid
Pro((4*S*)NH_2)	(2*S*,4*S*)-4-aminopyrrolidine-2-carboxylic acid
Pro((4*S*)NHBz)	(2*S*,4*S*)-4-benzamidopyrrolidine-2-carboxylic acid
Pro(5,5Me_2)	(*S*)-3,3-dimethylpyrrolidine-2-carboxylic acid
Pro((3*R*)OH)	(2*S*,3*R*)-3-hydroxypyrrolidine-2-carboxylic acid
Pro((3*S*)OH)	(2*S*,3*S*)-3-hydroxypyrrolidine-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

*allo*Thr	(2*S*,3*S*)-2-amino-3-hydroxybutanoic acid
Thr(Bn)	(2*S*,3*R*)-2-amino-3-(benzyloxy)butanoic acid
Thz	(4*R*)-1,3-thiazolidine-4-carboxylic acid
Thz(5,5Me$_2$)	(4*R*)-5,5-dimethyl-1,3-thiazolidine-4-carboxylic acid
Tic	(3*S*)-1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid
Tic(7OH)	(3*S*)-7-hydroxy-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid
Tiq	(*S*)-1,2,3,4-tetrahydroisoquinoline-1-carboxylic acid
Trp(7Aza)	(*R*)-2-amino-3-(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)propanoic acid
Trp(5Br)	(*S*)-2-amino-3-(5-bromo-1*H*-indol-3-yl)propanoic acid
Trp(6Br)	(*S*)-2-amino-3-(6-bromo-1*H*-indol-3-yl)propanoic acid
Trp(6CF$_3$)	(*S*)-2-amino-3-(6-(trifluoromethyl)-1*H*-indol-3-yl)propanoic acid
Trp(5Cl)	(*S*)-2-amino-3-(5-chloro-1*H*-indol-3-yl)propanoic acid
Trp(6Cl)	(*S*)-2-amino-3-(6-chloro-1*H*-indol-3-yl)propanoic acid
Trp(5,6Cl)	(*S*)-2-amino-3-(5,6-dichloro-1*H*-indol-3-yl)propanoic acid
Trp(5OH)	(*S*)-2-amino-3-(5-hydroxy-1*H*-indol-3-yl)propanoic acid
Tyr(Bn)	(*S*)-2-amino-3-(4-(benzyloxy)phenyl)propanoic acid
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
Tza	(*S*)-2-amino-3-(thiazol-4-yl)propanoic acid

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
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
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
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
Asn(Alk20)	(*S*)-2-amino-4-oxo-4-(piperidin-4-ylmethylamino)butanoic acid
Asn(Alk21)	(*S*)-2-amino-4-(methyl((tetrahydro-2*H*-pyran-4-yl)methyl)amino)-4-oxobutanoic acid
Asn(Alk22)	(2*S*)-2-amino-4-(methyl(2-(1-methylpyrrolidin-2-yl)ethyl)amino)-4-oxobutanoic acid
Asn(Alk23)	(*S*)-2-amino-4-oxo-4-(thiazol-2-ylmethylamino)butanoic acid
Asn(Alk24)	(*S*)-2-amino-4-((1-methyl-1*H*-imidazol-4-yl)methylamino)-4-oxobutanoic acid
Asn(Alk25)	(*S*)-2-amino-4-(benzylamino)-4-oxobutanoic acid
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-1*H*-benzo[*d*]imidazol-2-yl)methylamino)-4-oxobutanoic acid
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
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
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
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
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
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
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
Gln(Alk4)	(*S*)-2-amino-5-oxo-5-(tetrahydro-2*H*-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
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
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
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
Gln(Alk21)	(*S*)-2-amino-5-(methyl((tetrahydro-2*H*-pyran-4-yl)methyl)amino)-5-oxopentanoic acid
Gln(Alk22)	(2*S*)-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-1*H*-imidazol-4-yl)methylamino)-5-oxopentanoic acid
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
Gln(Alk29)	(*S*)-2-amino-5-(2-methoxybenzylamino)-5-oxopentanoic acid
Gln(Alk30)	(*S*)-2-amino-5-((1-methyl-1*H*-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
Gln(Alk32)	(*S*)-5-(2-(1*H*-indol-3-yl)ethylamino)-2-amino-5-oxopentanoic acid
Gln(Alk33)	(2*S*)-2-amino-5-(2,3-dihydro-1*H*-inden-1-ylamino)-5-oxopentanoic acid
Gln(Alk34)	(2*S*)-2-amino-5-oxo-5-(1,2,3,4-tetrahydronaphthalen-1-ylamino)-pentanoic acid
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
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)	(2*S*)-2-amino-5-(7-methyl-1,7-diazaspiro[4.4]nonan-1-yl)-5-oxopentanoic acid
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(8*H*)-yl)-5-oxopentanoic acid
Glu(cN12)	(*S*)-2-amino-5-(3,4-dihydro-1,5-naphthyridin-1(2*H*)-yl)-5-oxopentanoic acid
Glu(cN13)	(*S*)-2-amino-5-(5,6-dihydroimidazo[1,2-a]pyrazin-7(8*H*)-yl)-5-oxopentanoic acid
Glu(cN14)	(*S*)-5-(4-(1*H*-imidazol-1-yl)piperidin-1-yl)-2-amino-5-oxopentanoic acid
Glu(cN15)	(*S*)-5-(4-(1*H*-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
Lys(Ar1)	(*S*)-2-amino-6-(pyridin-2-ylamino)hexanoic acid
Lys(Ar2)	(*S*)-2-amino-6-(pyrimidin-2-ylamino)hexanoic acid
Lys(Ar3)	(*S*)-2-amino-6-(1,2,4-triazin-3-ylamino)hexanoic acid
Lys(Ar4)	(*S*)-2-amino-6-(pyridin-2-ylmethylamino)hexanoic acid
Lys(Ar5)	(*S*)-2-amino-6-(pyrimidin-2-ylmethylamino)hexanoic acid
Lys(Ar6)	(*S*)-2-amino-6-(bis(pyrimidin-2-ylmethyl)amino)hexanoic acid
Lys(Ar7)	(*S*)-2-amino-6-(((1-methyl-1*H*-imidazol-2-yl)methyl)amino)hexanoic acid
Lys(Ar8)	(*S*)-2-amino-6-(((4-methyl-4*H*-1,2,4-triazol-3-yl)methyl)amino)hexanoic acid
Lys(Ar9)	(*S*)-2-amino-6-(((1-methyl-1*H*-1,2,4-triazol-5-yl)methyl)amino)hexanoic acid
Lys(Ar10)	(*S*)-2-amino-6-(1*H*-pyrazol-1-yl)hexanoic acid
Lys(Ar11)	(*S*)-2-amino-6-(bis((1-methyl-1*H*-imidazol-2-yl)methyl)amino)-hexanoic acid
Lys(Ar12)	(*S*)-2-amino-6-(1*H*-1,2,4-triazol-1-yl)hexanoic acid
Orn(Ar1)	(*S*)-2-amino-5-(pyridin-2-ylamino)pentanoic acid
Orn(Ar2)	(*S*)-2-amino-5-(pyrimidin-2-ylamino)pentanoic acid
Orn(Ar3)	(*S*)-2-amino-5-(1,2,4-triazin-3-ylamino)pentanoic acid
Orn(Ar4)	(*S*)-2-amino-5-((pyridin-2-ylmethyl)amino)pentanoic acid
Orn(Ar5)	(*S*)-2-amino-5-(pyrimidin-2-ylmethylamino)pentanoic acid
Orn(Ar6)	(*S*)-2-amino-5-(bis(pyrimidin-2-ylmethyl)amino)pentanoic acid
Orn(Ar7)	(*S*)-2-amino-5-(((1-methyl-1*H*-imidazol-2-yl)methyl)amino)pentanoic acid
Orn(Ar8)	(*S*)-2-amino-5-(((4-methyl-4*H*-1,2,4-triazol-3-yl)methyl)amino)-pentanoic acid
Orn(Ar9)	(*S*)-2-amino-5-(((1-methyl-1*H*-1,2,4-triazol-5-yl)methyl)amino)-pentanoic acid
Orn(Ar10)	(*S*)-2-amino-5-(1*H*-pyrazol-1-yl)pentanoic acid

Orn(Ar11)	(*S*)-2-amino-5-(bis((1-methyl-1*H*-imidazol-2-yl)methyl)amino)-pentanoic acid
Orn(Ar12)	(*S*)-2-amino-5-(1*H*-1,2,4-triazol-1-yl)pentanoic acid
Orn(A1)	(*S*)-5-acetamido-2-aminopentanoic acid
Orn(A2)	(*S*)-2-amino-5-propionamidopentanoic acid
Orn(A3)	(*S*)-2-amino-5-isobutyramidopentanoic acid
Orn(A4)	(*S*)-2-amino-5-(cyclopropanecarboxamido)pentanoic acid
Orn(A5)	(*S*)-2-amino-5-(3,3,3-trifluoropropanamido)pentanoic acid
Orn(A6)	(*S*)-2-amino-5-(4,4,4-trifluorobutanamido)pentanoic acid
Orn(A7)	(*S*)-2-amino-5-(3-aminopropanamido)pentanoic acid
Orn(A8)	(*S*)-2-amino-5-(4-aminobutanamido)pentanoic acid
Orn(A9)	(*S*)-2-amino-5-(5-aminopentanamido)pentanoic acid
Orn(A10)	(*S*)-2-amino-5-(3-methoxypropanamido)pentanoic acid
Orn(A11)	(*S*)-2-amino-5-(3-(methylamino)propanamido)pentanoic acid
Orn(A12)	(*S*)-2-amino-5-(3-(dimethylamino)propanamido)pentanoic acid
Orn(A13)	(*S*)-2-amino-5-(3-(phenylamino)propanamido)pentanoic acid
Orn(A14)	(2*S*)-2-amino-5-(3-aminobutanamido)pentanoic acid
Orn(A15)	(*S*)-2-amino-5-(3-amino-3-methylbutanamido)pentanoic acid
Orn(A16)	(*S*)-2-amino-5-(3-(methylsulfonyl)propanamido)pentanoic acid
Orn(A17)	(*S*)-2-amino-5-(2-cyclopropylacetamido)pentanoic acid
Orn(A18)	(2*S*)-2-amino-5-(2-(pyrrolidin-3-yl)acetamido)pentanoic acid
Orn(A19)	(2*S*)-2-amino-5-(2-(pyrrolidin-2-yl)acetamido)pentanoic acid
Orn(A20)	(*S*)-2-amino-5-(2-(piperidin-4-yl)acetamido)pentanoic acid
Orn(A21)	(2*S*)-2-amino-5-(2-(piperidin-3-yl)acetamido)pentanoic acid
Orn(A22)	(2*S*)-2-amino-5-(2-(piperidin-2-yl)acetamido)pentanoic acid
Orn(A23)	(*S*)-2-amino-5-(3-(piperidin-1-yl)propanamido)pentanoic acid
Orn(A24)	(*S*)-2-amino-5-(3-(piperazin-1-yl)propanamido)pentanoic acid
Orn(A25)	(*S*)-2-amino-5-(3-(4-methylpiperazin-1-yl)propanamido)pentanoic acid
Orn(A26)	(*S*)-2-amino-5-(3-morpholinopropanamido)pentanoic acid

Orn(A27)	(*S*)-2-amino-5-(2-(1-aminocyclohexyl)acetamido)pentanoic acid
Orn(A28)	(*S*)-2-amino-5-(2-(4-aminotetrahydro-2*H*-pyran-4-yl)acetamido)-pentanoic acid
Orn(A29)	(2*S*)-2-amino-5-(2,2-dimethyl-1,3-dioxolane-4-carboxamido)pentanoic acid
Orn(A30)	(*S*)-2-amino-5-benzamidopentanoic acid
Orn(A31)	(*S*)-2-amino-5-(isonicotinamido)pentanoic acid
Orn(A32)	(*S*)-2-amino-5-(nicotinamido)pentanoic acid
Orn(A33)	(*S*)-2-amino-5-(picolinamido)pentanoic acid
Orn(A34)	(*S*)-2-amino-5-(6-(trifluoromethyl)nicotinamido)pentanoic acid
Orn(A35)	(*S*)-2-amino-5-(3-methoxybenzamido)pentanoic acid
Orn(A36)	(*S*)-2-amino-5-(3-(difluoromethoxy)benzamido)pentanoic acid
Orn(A37)	(*S*)-2-amino-5-(4-(methylsulfonyl)benzamido)pentanoic acid
Orn(A38)	(*S*)-2-amino-5-(benzo[*d*][1,3]dioxole-5-carboxamido)pentanoic acid
Orn(A39)	(*S*)-2-amino-5-(2-(pyridin-3-yl)acetamido)pentanoic acid
Orn(A40)	(*S*)-2-amino-5-(pyrimidine-4-carboxamido)pentanoic acid
Orn(A41)	(*S*)-2-amino-5-(pyrazine-2-carboxamido)pentanoic acid
Orn(A42)	(*S*)-2-amino-5-(3-cyanobenzamido)pentanoic acid
Orn(A43)	(*S*)-2-amino-5-(thiophene-2-carboxamido)pentanoic acid
Orn(A44)	(*S*)-2-amino-5-(1-methyl-1*H*-pyrrole-2-carboxamido)pentanoic acid
Orn(A45)	(*S*)-2-amino-5-(thiazole-2-carboxamido)pentanoic acid
Orn(A46)	(*S*)-2-amino-5-(thiazole-4-carboxamido)pentanoic acid
Orn(A47)	(*S*)-2-amino-5-(1-methyl-*1H*-imidazole-2-carboxamido)pentanoic acid
Orn(A48)	(*S*)-2-amino-5-(1-methyl-1*H*-imidazole-5-carboxamido)pentanoic acid
Orn(A49)	(*S*)-2-amino-5-(1-methyl-1*H*-indole-2-carboxamido)pentanoic acid
Orn(A50)	(*S*)-2-amino-5-(benzo[*d*]thiazole-2-carboxamido)pentanoic acid
Orn(A51)	(S)-2-amino-5-(quinoxaline-2-carboxamido)pentanoic acid
Orn(A52)	(*S*)-5-(3-(1*H*-indol-3-yl)propanamido)-2-aminopentanoic acid
Orn(A53)	(*S*)-2-amino-5-(2-aminothiazole-4-carboxamido)pentanoic acid
Orn(A54)	(*S*)-2-amino-5-(2-(2-aminothiazol-4-yl)acetamido)pentanoic acid
Orn(A55)	(*S*)-2-amino-5-(4-guanidinobutanamido)pentanoic acid

Orn(A56)	(*S*)-2-amino-5-(1,4,5,6-tetrahydropyrimidin-2-ylamino)pentanoic acid
Dab(Ar1)	(*S*)-2-amino-4-(pyridin-2-ylamino)butanoic acid
Dab(Ar2)	(*S*)-2-amino-4-(pyrimidin-2-ylamino)butanoic acid
Dab(Ar3)	(*S*)-2-amino-4-(1,2,4-triazin-3-ylamino)butanoic acid
Dab(Ar4)	(*S*)-2-amino-4-(pyridin-2-ylmethylamino)butanoic acid
Dab(Ar5)	(*S*)-2-amino-4-(pyrimidin-2-ylmethylamino)butanoic acid
Dab(Ar6)	(*S*)-2-amino-4-(bis(pyrimidin-2-ylmethyl)amino)butanoic acid
Dab(Ar7)	(*S*)-2-amino-4-(((1-methyl-1*H*-imidazol-2-yl)methyl)amino)butanoic acid
Dab(Ar8)	(*S*)-2-amino-4-(((4-methyl-4*H*-1,2,4-triazol-3-yl)methyl)amino)butanoic acid
Dab(Ar9)	(*S*)-2-amino-4-(((1-methyl-1*H*-1,2,4-triazol-5-yl)methyl)amino)butanoic acid
Dab(Ar10)	(*S*)-2-amino-4-(1*H*-pyrazol-1-yl)butanoic acid
Dab(Ar11)	(*S*)-2-amino-4-(bis((1-methyl-1*H*-imidazol-2-yl)methyl)amino)-butanoic acid
Dab(Ar12)	(*S*)-2-amino-4-(1*H*-1,2,4-triazol-1-yl)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
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-2*H*-pyran-4-sulfonamido)butanoic acid
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

Dab(S15) (*S*)-2-amino-4-(5-cyanopyridine-2-sulfonamido)butanoic acid

Dab(S16) (*S*)-2-amino-4-(1*H*-pyrazole-4-sulfonamido)butanoic acid

Dab(S17) (*S*)-2-amino-4-(1*H*-1,2,4-triazole-5-sulfonamido)butanoic acid

Dab(S18) (*S*)-2-amino-4-(1,1-dimethylethylsulfonamido)butanoic acid

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

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

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) (2*S*)-2-amino-4-(3-aminobutanamido)butanoic acid

Dab(A15) (*S*)-2-amino-4-(3-amino-3-methylbutanamido)butanoic acid

Dab(A16) (*S*)-2-amino-4-(3-(methylsulfonyl)propanamido)butanoic acid

Dab(A17) (*S*)-2-amino-4-(2-cyclopropylacetamido)butanoic acid

Dab(A18) (2*S*)-2-amino-4-(2-(pyrrolidin-3-yl)acetamido)butanoic acid

Dab(A19) (2*S*)-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) (2*S*)-2-amino-4-(2-(piperidin-3-yl)acetamido)butanoic acid

Dab(A22) (2*S*)-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
	Dab(A27)	(*S*)-2-amino-4-(2-(1-aminocyclohexyl)acetamido)butanoic acid
	Dab(A28)	(*S*)-2-amino-4-(2-(4-aminotetrahydro-2*H*-pyran-4-yl)acetamido)-butanoic acid
5	Dab(A29)	(2*S*)-2-amino-4-(2,2-dimethyl-1,3-dioxolane-4-carboxamido)butanoic acid
	Dab(A30)	(*S*)-2-amino-4-benzamidobutanoic acid
	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
10	Dab(A34)	(*S*)-2-amino-4-(6-(trifluoromethyl)nicotinamido)butanoic acid
	Dab(A35)	(*S*)-2-amino-4-(3-methoxybenzamido)butanoic acid
	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
15	Dab(A39)	(*S*)-2-amino-4-(2-(pyridin-3-yl)acetamido)butanoic acid
	Dab(A40)	(*S*)-2-amino-4-(pyrimidine-4-carboxamido)butanoic acid
	Dab(A41)	(*S*)-2-amino-4-(pyrazine-2-carboxamido)butanoic acid
	Dab(A42)	(*S*)-2-amino-4-(3-cyanobenzamido)butanoic acid
	Dab(A43)	(*S*)-2-amino-4-(thiophene-2-carboxamido)butanoic acid
20	Dab(A44)	(*S*)-2-amino-4-(1-methyl-1*H*-pyrrole-2-carboxamido)butanoic acid
	Dab(A45)	(*S*)-2-amino-4-(thiazole-2-carboxamido)butanoic acid
	Dab(A46)	(*S*)-2-amino-4-(thiazole-4-carboxamido)butanoic acid
	Dab(A47)	(*S*)-2-amino-4-(1-methyl-*1H*-imidazole-2-carboxamido)butanoic acid
	Dab(A48)	(*S*)-2-amino-4-(1-methyl-1*H*-imidazole-5-carboxamido)butanoic acid
25	Dab(A49)	(*S*)-2-amino-4-(1-methyl-1*H*-indole-2-carboxamido)butanoic acid
	Dab(A50)	(*S*)-2-amino-4-(benzo[*d*]thiazole-2-carboxamido)butanoic acid
	Dab(A51)	(S)-2-amino-4-(quinoxaline-2-carboxamido)butanoic acid
	Dab(A52)	(*S*)-4-(3-(1*H*-indol-3-yl)propanamido)-2-aminobutanoic acid
	Dab(A53)	(*S*)-2-amino-4-(2-aminothiazole-4-carboxamido)butanoic acid
30	Dab(A54)	(*S*)-2-amino-4-(2-(2-aminothiazol-4-yl)acetamido)butanoic acid

Dab(A55)	(*S*)-2-amino-4-(4-guanidinobutanamido)butanoic acid
Dap(Ar1)	(*S*)-2-amino-3-(pyridin-2-ylamino)propanoic acid
Dap(Ar2)	(*S*)-2-amino-3-(pyrimidin-2-ylamino)propanoic acid
Dap(Ar3)	(*S*)-2-amino-3-(1,2,4-triazin-3-ylamino)propanoic acid
Dap(Ar4)	(*S*)-2-amino-3-(pyridin-2-ylmethylamino)propanoic acid
Dap(Ar5)	(*S*)-2-amino-3-(pyrimidin-2-ylmethylamino)propanoic acid
Dap(Ar6)	(*S*)-2-amino-3-(bis(pyrimidin-2-ylmethyl)amino)propanoic acid
Dap(Ar7)	(*S*)-2-amino-3-((1-methyl-1*H*-imidazol-2-yl)methylamino)propanoic acid
Dap(Ar8)	(*S*)-2-amino-3-((4-methyl-4*H*-1,2,4-triazol-3-yl)methylamino)-propanoic acid
Dap(Ar9)	(*S*)-2-amino-3-((1-methyl-1*H*-1,2,4-triazol-5-yl)methylamino)-propanoic acid
Dap(Ar10)	(*S*)-2-amino-3-(1*H*-pyrazol-1-ylamino)propanoic acid
Dap(Ar11)	(*S*)-2-amino-3-(bis((1-methyl-1*H*-imidazol-2-yl)methyl)amino)-propanoic acid
Dap(Ar12)	(*S*)-2-amino-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid
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
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-2*H*-pyran-4-sulfonamido)propanoic acid
Dap(S10)	(*S*)-2-amino-3-(phenylsulfonamido)propanoic acid
Dap(S11)	(*S*)-2-amino-3-(4-aminophenylsulfonamido)propanoic acid
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-(1*H*-pyrazole-4-sulfonamido)propanoic acid
Dap(S17)	(*S*)-2-amino-3-(1*H*-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
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
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
Dap(A13)	(*S*)-2-amino-3-(3-(phenylamino)propanamido)propanoic acid
Dap(A14)	(2*S*)-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
Dap(A18)	(2*S*)-2-amino-3-(2-(pyrrolidin-3-yl)acetamido)propanoic acid
Dap(A19)	(2*S*)-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)	(2*S*)-2-amino-3-(2-(piperidin-3-yl)acetamido)propanoic acid
Dap(A22)	(2*S*)-2-amino-3-(2-(piperidin-2-yl)acetamido)propanoic acid
Dap(A23)	(*S*)-2-amino-3-(3-(piperidin-1-yl)propanamido)propanoic acid

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-2*H*-pyran-4-yl)acetamido)-propanoic acid

Dap(A29) (2*S*)-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

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

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-(pyrazine-2-carboxamido)propanoic acid

Dap(A42) (*S*)-2-amino-3-(3-cyanobenzamido)propanoic acid

Dap(A43) (*S*)-2-amino-3-(thiophene-2-carboxamido)propanoic acid

Dap(A44) (*S*)-2-amino-3-(1-methyl-1*H*-pyrrole-2-carboxamido)propanoic acid

Dap(A45) (*S*)-2-amino-3-(thiazole-2-carboxamido)propanoic acid

Dap(A46) (*S*)-2-amino-3-(thiazole-4-carboxamido)propanoic acid

Dap(A47) (*S*)-2-amino-3-(1-methyl-*1H*-imidazole-2-carboxamido)propanoic acid

Dap(A48) (*S*)-2-amino-3-(1-methyl-1*H*-imidazole-5-carboxamido)propanoic acid

Dap(A49) (*S*)-2-amino-3-(1-methyl-1*H*-indole-2-carboxamido)propanoic acid

Dap(A50) (*S*)-2-amino-3-(benzo[*d*]thiazole-2-carboxamido)propanoic acid

Dap(A51) (S)-2-amino-3-(quinoxaline-2-carboxamido)propanoic acid

Dap(A52) (*S*)-3-(3-(1*H*-indol-3-yl)propanamido)-2-aminopropanoic acid

Dap(A53) (*S*)-2-amino-3-(2-aminothiazole-4-carboxamido)propanoic acid

Dap(A54) (*S*)-2-amino-3-(2-(2-aminothiazol-4-yl)acetamido)propanoic acid

Dap(A55) (*S*)-2-amino-3-(4-guanidinobutanamido)propanoic acid

The abbreviation of D-isomers, e.g. ^{D}Lys(Ar1) corresponds to the epimer at the 2-position of the appropriate amino acid described above.

In a preferred embodiment of the invention the compounds of the general formula **(I)** are selected from the group consisting of:

cyclo(-Ile-^{D}Arg-Arg-Ile-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Tyr-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Lys-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Dab-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Dab-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Phe-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Thr-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro-hSer-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro-*allo*Thr-);

cyclo(-1Nal-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Lys-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}His-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Cit-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pip-Thr-);

cyclo(-Ile-^{D}Arg-Arg-2Nal-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-1Nal-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Trp-Arg-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Thr-^{D}Arg-Trp-Arg-^{D}Pro-Thr-);

cyclo(-Trp-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro-Pro((3*S*)OH)-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro-Ser-);

cyclo(-Ile-^{D}Arg-Agp-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Agb-Trp-^{D}Pro-Thr-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro((4*S*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Ala-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Tyr-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Orn-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Dab-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Lys-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-His-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Arg-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Pip-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-hArg-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Agb-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-3Pal-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}3Pal-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Arg-^{D}Phe-Trp-hArg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Arg-^{D}Phe-Trp-Arg-^{D}Pro((4*S*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Oic-);

cyclo(-Arg-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Oic-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro-Pro((4*S*)F)-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro-Pro((4*S*)NH_2)-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro-Pro((4*R*)NH_2)-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro-Mor-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro-Mor-);

cyclo(-Arg-^{D}Phe-Trp-Arg-^{D}Pro-(4*S*)-Hyp(Bn)-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro((4*S*)OH)-(4*S*)-Hyp(Bn)-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-(4*S*)-Hyp(Bn)-);

cyclo(-His-^{D}Trp-His-Trp-^{D}Pro- Pro((4*S*)NHBz)-);

cyclo(-1Nal-^{D}Arg-Arg-Trp-^{D}Pro-Pro((3*S*)OH)-);

cyclo(-Ile-^{D}Arg-Arg-2Nal-^{D}Pro-Pro((3*S*)OH)-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pip-Pro((3*S*)OH)-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro((4*S*)*OH*)-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro((4*R*)NH_2)-Thr-);

cyclo(-Val-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Abu-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Chg-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Leu-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Nle-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Cha-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Orn-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Orn(A41)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Orn-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-hArg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Tic-Thr-);

cyclo(-Ile-^{D}Arg-Orn(Ar2)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Orn(Ar7)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Orn(Ar4)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Orn(A56)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Phe(4CF_3)-^{D}Pro-Thr-);

cyclo(-Trp-^{D}Phe-Trp-Orn(A56)-^{D}Pip-Pro((3*S*)OH)-);

cyclo(-Ala(1Pyraz)-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Ala(Tet)-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Orn(Ar2)-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Orn(A56)-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Orn(Ar7)-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Orn(A56)-^{D}Pro((4*R*)NH_2)-Tiq-);

cyclo(-Trp-^{D}Phe-Trp-Orn(A56)-^{D}Pro((4*R*)NH_2)-Tic-);

and pharmaceutically acceptable salts thereof.

In a most preferred embodiment of the invention the compounds of the general formula **(I)** are selected from the group consisting of:

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pip-Thr-);

cyclo(-Ile-^{D}Arg-Arg-2Nal-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro-Ser-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Dab-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-3Pal-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Oic-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro((4*S*)OH)-(4*S*)-Hyp(Bn)-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pip-Pro((3*S*)OH)-);

cyclo(-Chg-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-hArg-Trp-^{D}Pro-Thr-);

and pharmaceutically acceptable salts thereof.

In an alternative most preferred embodiment of the invention the compounds of the general formula **(I)** are selected from the group consisting of:

cyclo(-Ile-^{D}Arg-Orn(Ar2)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Orn(Ar7)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Orn(Ar4)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Orn(A56)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Phe(4CF_3)-^{D}Pro-Thr-);

cyclo(-Trp-^{D}Phe-Trp-Orn(A56)-^{D}Pip-Pro((3*S*)OH)-);

cyclo(-Ala(1Pyraz)-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Ala(Tet)-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Orn(Ar2)-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Orn(Ar56)-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Orn(Ar7)-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Orn(A56)-^{D}Pro((4*R*)NH_2)-Tiq-);

cyclo(-Trp-^{D}Phe-Trp-Orn(A56)-^{D}Pro((4*R*)NH_2)-Tic-);

and pharmaceutically acceptable salts thereof.

A further embodiment of the invention relates to the preparation of the present β-hairpin 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 T^1 or T^2 or P^1 to P^4 as defined above; any functional group which may 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 of the next element (T or P), following counterclockwise or clockwise the sequence according general formula **(I)** in –COOH to –NH_2 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;

(f) if desired, selectively deprotecting one or several protected functional group(s) present in the molecule and appropriately substituting 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; and/or

(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.

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 allow one to obtain arrays of numerous (normally 24 to 192, typically 96) compounds of general formula **(I)** in high yields and 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), template and site of cyclization play thereby key roles.

The functionalized solid support is conveniently derived from polystyrene crosslinked 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**).

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 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 structures include 4-[(((2,4-dimethoxyphenyl)Fmoc-aminomethyl)phenoxyacetamido)-aminomethyl] PS resin, 4-[(((2,4-dimethoxyphenyl)Fmoc-aminomethyl)phenoxyacet-

amido)aminomethyl]-4-methylbenzydrylamine 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 functionalized by means of the 4-(((2,4-dimethoxyphenyl)Fmoc-aminomethyl)phenoxy-acetamido) 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 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-meth-oxyphenoxy)butyric acid (HMPB linker), trityl and 2-chlorotrityl. Preferably, the support is derived from polystyrene crosslinked with, most preferably 1-5%, divinylbenzene 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 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 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 (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).

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 cleavable with diluted trifluoroacetic acid (0.5-1% TFA in DCM) and is stable to Fmoc deprotection conditions during the peptide synthesis, Boc/*t*Bu-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 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-chlorotritylchloride 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 example,

- for the amino group (as is present e.g. also in the side-chain of lysine)

Cbz	benzyloxycarbonyl
Boc	*tert*.-butyloxycarbonyl
Fmoc	9-fluorenylmethoxycarbonyl
Alloc	allyloxycarbonyl

Teoc	trimethylsilylethoxycarbonyl
Tcc	trichloroethoxycarbonyl
Nps	*o*-nitrophenylsulfonyl
Trt	triphenymethyl or trityl

- 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
Me	methyl
Ph	phenyl
Pac	phenacyl
	allyl
Tse	trimethylsilylethyl
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)
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)

tBu	*tert*.-butyl
Bn	benzyl
Trt	trityl

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

Acm	acetamidomethyl
tBu	*tert*.-butyl

Bn	benzyl
Trt	trityl
Mtr	4-methoxytrityl.

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.

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 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 cooling it 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.

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 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 tetra-fluoroborate (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).

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.

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.

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 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 Pd° and phenylsilane in CH_2Cl_2, 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 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 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 the fully protected linear peptide derivatives which have been 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 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.

Finally, the fully protected peptide derivative is treated with 95% TFA, 2.5% H_2O, 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 which are suitable therefor. 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 compound of the present invention according general formula **(I)** additional synthetic steps are required. These transformations can be applied either on a partially deprotected cyclic or linear peptide, attached to 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 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

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.

In general the building blocks for the peptidomimetics of the present invention can be synthesized according to the literature methods (examples described below) or are known to a person skilled in the art and/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 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)* **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**, *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). Hydrolytic enzymes involve hydrolysis of amides and nitriles by aminopeptidases or nitrilases, cleavage of N-acyl groups by acylases, and ester hydrolysis by lipases or 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 this invention can be used in a wide range of applications in order to selectively modulate the activity of the CXCR7 receptor and are thus useful in the treatment of a variety of diseases and disorders mediated by or sustained through the activity of CXCR7 or in the support of therapeutic treatments of specific disease conditions of primarily different cause, for example but not limited to the areas of dermatological disorders, metabolic diseases, inflammatory diseases, fibrotic diseases, infectious diseases, neurological diseases, cardiovascular diseases, respiratory diseases, gastro-intestinal tract disorders, urological diseases, ophthalmic diseases, stomatological diseases, haematological diseases and cancer, or the mobilisation of stem cells, 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 conditions such as, but not limited to, HIV infections, Epstein-Barr Virus infection; diabetes mellitus (Type I and/or Type II); conjunctivitis, scleritis, uveitis, rhinosinusitis, Whim syndrome, lupus erythematosus, osteoarthritis, rheumatoid arthritis, synovitis, psoriasis, multiple sclerosis, Crohns disease, inflammatory bowel disease, mixed connective tissue disease, chronic lymphocytic thyroiditis, Graves' disease, graft-versus-host disease, Sjögren's syndrome; dry eye syndrome, glaucoma, age-related macular degeneration; pulmonary arterial hypertension, pulmonary hypoxia, atherosclerosis, myocarditis, heart failure, such as myocardial infarction, arterial thrombosis, stroke, angiogenesis; chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, asthma; sarcoma, such as osteosarcoma, rhabdomyosarcoma, Kaposi's sarcoma, synovial sarcoma; lipoma, such as angiolipoma; glioblastoma multiforme, astrocytomas, neuroblastoma; carcinoma, such as adenocarcinoma; malignant epithelial and mucoepidermoid neoplasms, thyroid neoplasm, gonadal neoplasms, prostate cancer, breast cancer, melanoma, lung carcinoma, pancreatic carcinoma, colorectal cancer; solid tumors; lymphoma, such as Birkitt's lymphoma, Hodgkin's lymphoma, non-Hodgkin's lymphoma; multiple myeloma and leukemia; metastasis; for the inhibition of neointima formation; for stem cell mobilisation of peripheral blood stem cells and/or mesenchymal stem cells; for the mobilisation of

endothelial or neuronal progenitor cells; or for different kinds of tissue-repair in human or other mammals.

For use as medicaments the β-hairpin peptidomimetics can be administered singly, as mixtures of several β-hairpin peptidomimetics or in combination with other pharmaceutically active agents. The β-hairpin peptidomimetics 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.

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 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 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.

For injections, the β-hairpin peptidomimetics of the invention may be formulated in adequate solutions, preferably in physiologically compatible buffers such as Hank's solution, Ringer's solution, or physiological saline solution. The solution may contain

formulatory agents such as suspending, stabilizing and/or dispersing agents. 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.

For oral administration, the compounds can be readily formulated by combining the active β-hairpin peptidomimetics of the invention 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 carboxy-methylcellulose, and/or polyvinylpyrrolidone (PVP); granulating agents; and binding agents. If desired, desintegrating 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.

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.

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, trichlorofluromethane, 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.

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 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, 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 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 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 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 or reduced activity of the CXCR7 receptor and its ligands (e.g. CXCL11 and CXCL12), 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.

The effective dosage of the active ingredients employed may vary depending on the particular compound or pharmaceutical preparation employed, the mode of administration 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 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.

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.

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

The following abbreviations are used:

Boc	*tert*-Butyloxycarbonyl
DBV	Divinyl benzene
DIPEA	Diisopropylethylamine
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
HCTU	O-(6-Chlorobenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate
HOAt	7-Aza-1-hydroxy benzotriazole
HOBt	1-Hydroxybenzotriazole
PyBop®	(Benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate
TATU	O-(7-Aza-benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium tetrafluoroborate
TBTU	2-(1*H*-Benzotriazol-1-yl-)1,1,3,3-tetramethyluronium tetrafluoroborate
TIS	Triisopropylsilane
TPP	Triphenylphosphine
rt	Room temperature
RT	Retention time

Examples

1. Peptide synthesis

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 concept in principle and does not limit or restrict the present invention in any way. A 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.

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) (100-200 mesh, polystyrene, 1% DBV crosslinked, 1.4 mmol/g loading, 0.7 mmol) was filled into a dried flask. The resin was suspended in CH_2Cl_2 (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 and 488 µl (4eq) of diisopropyl-ethylamine (DIPEA) in CH_2Cl_2 (2.5 ml), the mixture was shaken at 25°C for 4 hours. The resin was washed with CH_2Cl_2 (1x), DMF (1x), CH_2Cl_2 (1x), DMF(1x), CH_2Cl_2 (2x). The resin was shaken in 30 ml CH_2Cl_2/MeOH/DIPEA (17:2:1) for 30 min; then washed in the following order with CH_2Cl_2 (1x), DMF (1x), CH_2Cl_2 (1x), MeOH (1x), CH_2Cl_2 (1x), MeOH (1x), CH_2Cl_2 (2x), Et_2O (2x) and dried under vacuum for 6 hours.

Method B:

In a dried flask, 2-chlorotritylchloride resin (100-200 mesh, polystyrene, 1% DBV crosslinked, 1.4 mmol/g loading) is swollen in dry CH_2Cl_2 for 30 min (7 ml CH_2Cl_2 per g

resin). A solution of 0.8 eq of suitably side-chain protected Fmoc-AA-OH and 6 eq of DIPEA in dry CH_2Cl_2/DMF (4:1) (10 ml per g resin) is added. After shaking for 2-4 h at rt the resin is filtered and washed successively with CH_2Cl_2, DMF, CH_2Cl_2, DMF and CH_2Cl_2. Then a solution of dry CH_2Cl_2/MeOH/DIPEA (17:2:1) is added (10 ml per g resin). After shaking for 3 x 30 min the resin is filtered in a pre-weighed sinter funnel and washed successively with CH_2Cl_2, DMF, CH_2Cl_2, MeOH, CH_2Cl_2, MeOH, CH_2Cl_2 (2x) and Et_2O (2x). The resin is dried under high vacuum overnight. The final mass of resin is calculated before the qualitative control.

The following preloaded resins were prepared: Fmoc-Ile-2-chlorotrityl resin, Fmoc-Arg-2-chlorotrityl resin, Fmoc-Trp-2-chlorotrityl resin, Fmoc-Thr-2-chlorotrityl resin, Fmoc-^{D}Pro-2-chlorotrityl resin, Fmoc-Ser-2-chlorotrityl resin, Fmoc-Agp-2-chlorotrityl resin, Fmoc-Agb-2-chlorotrityl resin, Fmoc-Tic-2-chlorotrityl resin, Fmoc-Tiq-2-chlorotrityl resin, Fmoc-Oic-2-chlorotrityl resin, Fmoc-(4*S*)-Hyp(Bn)-2-chlorotrityl resin, Fmoc-Pro((4*S*)NHBz)-2-chlorotrityl resin, Fmoc-^{D}Pip-2-chlorotrityl resin, Fmoc-^{D}Pro((3*S*)OH-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:

Method A:

Step	**Reagent**	**Time**
1	CH_2Cl_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
4	DMF, wash	5 x 1 min

5	5 equiv. Fmoc amino acid/DMF	
	+ 5 eq. HCTU	
	+ 10 eq. DIPEA	2 x 60 min
6	DMF, wash	5 x 1 min
7	CH_2Cl_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:

Step	**Reagent**	**Time**
1	CH_2Cl_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
4	DMF, wash	5 x 1 min
5	3.5 equiv. Fmoc amino acid/DMF	
	+ 3.5 eq. HCTU	
	+ 7 eq. DIPEA	2 x 60 min
6	DMF, wash	5 x 1 min
7	CH_2Cl_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 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

After assembly of the linear peptide, the resin was suspended in 1 ml of 1% TFA in CH_2Cl_2 (*v/v*; 0.14 mmol) for 3 minutes and filtered, and the filtrate was neutralized with 1 ml of 20% DIPEA in CH_2Cl_2 (*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 CH_2Cl_2. The CH_2Cl_2 layers containing product were evaporated to dryness.

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 CH_2Cl_2 and extracted three times with 4.5 ml 10% acetonitrile in water (*v/v*). The CH_2Cl_2 layers were evaporated to dryness.

To fully deprotect the peptide, 4-7 ml of cleavage cocktail TFA/TIS/H_2O (95:2.5:2.5) were added, and the mixture was kept for 2.5-4 h at room temperature until the reaction was complete. 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 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)

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*)

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 of the synthesis. As an example a typical run (purification of **Ex. 29**) was executed with a flow rate of 35 ml/min running a gradient from 0-2 min. 25% B, 6.5 min. 45% B to a final of 6.6-10.7 min. 100% B (retention time: 4.99 min in this case).

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:

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

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

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** (H_2O + 0.1% TFA) and **B** (CH_3CN + 0.085% TFA) and the gradient: 0-0.1 min: 97% A, 3% B; 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 at 45°C.

Analytical method B:

Analytical HPLC retention times (RT, in minutes) were determined using a XBridge C18 column, 50 x 2.0 mm, (cod. 186003084 - Waters) with the following solvents **A** (H_2O + 0.1% TFA) and **B** (CH_3CN + 0.085% 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 at 45°C.

Analytical method C:

Analytical HPLC retention times (RT, in minutes) were determined using an Ascentis Express C18 column, 50 x 3.0 mm, (cod. 53811-U - Supelco) with the following solvents **A** (H_2O + 0.1% TFA) and **B** (CH_3CN + 0.085% TFA) and the gradient: 0-0.05 min: 97% A, 3% B; 2.95 min: 3% A 97% B; 2.95-3.15 min: 3% A, 97% B; 3.17-3.2 min: 97% A, 3% B. Flow rate = 1.3 ml/min at 45°C.

Analytical method C':

Analog method C, but running at 55°C.

Analytical method D:

Analytical HPLC retention times (RT, in minutes) were determined using an Ascentis Express C18 column, 50 x 3.0 mm, (cod. 53811-U - Supelco) with the following solvents **A** (H_2O + 0.1% TFA) and **B** (CH_3CN + 0.085% TFA) and the gradient: 0-0.05 min: 97% A, 3% B; 3.4min: 33% A 67% B; 3.45-3.65 min: 3% A, 97% B; 3.67-3.7 min: 97% A, 3% B. Flow rate = 1.3 ml/min at 55°C.

1.3 Synthesis of peptide sequences

Examples 1 – 5 are shown in *Table 1*.

The peptides were synthesized according general Method B starting with the amino acid L-isoleucin, which was grafted to the resin (Fmoc-Ile-2-chlorotrityl resin). The linear peptides were synthesized on the solid support according to the procedure described above in the following sequence: Resin-Ile-Thr-^{D}Pro-P^4-P^3-P^2. 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 to off-white powders and characterised by HPLC-MS, analytical method A as described above. For analytical data, see **Ex. 1, 2, 3, 4, 5** in *Table 1*.

Examples 6, 7 and 67 are shown in *Table 1*.

The peptides were synthesized according general Method B starting with the amino acid L-arginin, 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-P^2-P^1-T^2-T^1-P^4. 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. 6, 7, 67** in *Table 1*.

Example 8 and 9 are shown in *Table 1*.

The peptides were synthesized according general Method B starting with the amino acid L-tryptophan, which was grafted to the resin (Fmoc-Trp-2-chlorotrityl resin). The linear peptides were synthesized on the solid support according to the procedure described above in the following sequence: Resin-Trp-Arg-^{D}Arg-Ile-T^2-T^1. 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. 8, 9** in *Table 1*.

Example 10 – 16 are shown in *Table 1*.

The peptides were synthesized according general Method B starting with the amino acid L-threonin, which was grafted to the resin (Fmoc-Thr-2-chlorotrityl resin). The linear peptides were synthesized on the solid support according to the procedure described above in the following sequence: Resin-Thr-T^1-P^4-P^3-P^2-P^1. 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 to off-white powders and characterised by HPLC-MS, analytical method A as described above. For analytical data, see **Ex. 10, 11, 12, 13, 14, 15, 16** in *Table 1*.

Examples 17 - 20 are shown in *Table 1*.

The peptides were synthesized according general Method A starting with the amino acid D-proline, which was grafted to the resin (Fmoc-^{D}Pro-2-chlorotrityl resin). The linear peptides were synthesized on the solid support according to the procedure described above in the following sequence: Resin-^{D}Pro-P^4-P^3-P^2-P^1-T^1. 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, except **Ex. 20**, for which analytical method B was used. For analytical data, see **Ex. 17, 18, 19, 20** in *Table 1*.

Examples 21, 52 and 53 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-^{D}Pro-2-chlorotrityl resin). The linear peptides were synthesized on the solid support according to the procedure described above in the following sequence: Resin-^{D}Pro-P^4-P^3-P^2-P^1-T^1. 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, except **Ex. 21**, for which analytical method A was used. For analytical data, see **Ex. 21, 52, 53** in *Table 1*.

Example 22 is shown in *Table 1*.

The peptide was synthesized according general Method B starting with the amino acid L-serin, which was grafted to the resin (Fmoc-Ser-2-chlorotrityl resin). The linear peptide was synthesized on the solid support according to the procedure described above in the following sequence: Resin-Ser-^{D}Pro-Trp-Arg-^{D}Arg-Ile. 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. 22** in *Table 1*.

Example 23 is shown in *Table 1*.

The peptide was synthesized according general Method B starting with the amino acid (*S*)-2-amino-3-guanidinopropanoic acid, which was grafted to the resin (Fmoc-Agp-2-chlorotrityl resin). The linear peptide was synthesized on the solid support according to the procedure described above in the following sequence: Resin-Agp-^{D}Arg-Ile-Thr-^{D}Pro-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 A as described above. For analytical data, see **Ex. 23** in *Table 1*.

Example 24 is shown in *Table 1*.

The peptide was synthesized according general Method B starting with the amino acid (*S*)-2-amino-4-guanidinobutanoic acid, which was grafted to the resin (Fmoc-Agb-2-chlorotrityl resin). The linear peptide was synthesized on the solid support according to the procedure described above in the following sequence: Resin-Agb-^{D}Arg-Ile-Thr-^{D}Pro-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 A as described above. For analytical data, see **Ex. 24** in *Table 1*.

Examples 25 – 40, 74, 75 and 78 are shown in *Table 1*.

The peptides were synthesized according general Method B starting with the amino acid (3*S*)-1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid, which was grafted to the resin (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-T^1-P^4-P^3-P^2-P^1. 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 to off-white powders and characterised by HPLC-MS, analytical method C as described above, except **Ex. 25** and **26**, for which analytical method A was used and **Ex. 74, 75** and **78**, for which analytical method D was used. For analytical data, see **Ex. 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 74, 75, 78** in *Table 1*.

Examples 41 and 42 are shown in *Table 1*.

The peptides were synthesized according general Method B starting with the amino acid (2*S*,3a*S*,7a*S*)-octahydro-1*H*-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-^{D}Pro((4*R*)NH_2)-Arg-Trp-^{D}Phe-P^1. 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. 41, 42** in *Table 1*.

Examples 43 - 46 are shown in *Table 1*.

The peptides were synthesized according general Method B starting with the amino acid L-tryptophan, which was grafted to the resin (Fmoc-Trp-2-chlorotrityl resin). The linear peptides were synthesized on the solid support according to the procedure described above in the following sequence: Resin-Trp-^{D}Phe-Trp-T^2-T^1-P^4. 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 to off-white powders and characterised by HPLC-MS, analytical method C as described above. For analytical data, see **Ex. 43, 44, 45, 46** in *Table 1*.

Example 47 is shown in *Table 1*.

The peptide was synthesized according general Method B starting with the amino acid L-tryptophan, which was grafted to the resin (Fmoc-Trp-2-chlorotrityl resin). The linear peptide was synthesized on the solid support according to the procedure described above in the following sequence: Resin-Trp-Arg-^{D}Arg-Ile-Mor-^{D}Pro. 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. 47** in *Table 1*.

Examples 48 - 50 are shown in *Table 1*.

The peptides were synthesized according general Method B starting with the amino acid (2*S*,4*S*)-4-(benzyloxy)pyrrolidine-2-carboxylic acid, which was grafted to the resin (Fmoc-(4*S*)-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-(4*S*)-Hyp(Bn)-T^1-P^4-P^3-P^2-P^1. 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 to off-white powders and characterised by HPLC-MS, analytical method C as described above. For analytical data, see **Ex. 48, 49, 50** in *Table 1*.

Example 51 is shown in *Table 1*.

The peptide was synthesized according general Method A starting with the amino acid (2*S*,4*S*)-4-benzamidopyrrolidine-2-carboxylic acid, which was grafted to the resin (Fmoc-Pro((4*S*)NHBz)-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*S*)NHBz)-^{D}Pro-Trp-His-^{D}Tpr-His. 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. 51** in *Table 1*.

Example 54 is shown in *Table 1*.

The peptide was synthesized according general Method B starting with the amino acid (*R*)-piperidine-2-carboxylic acid, which was grafted to the resin (Fmoc-^{D}Pip-2-

chlorotrityl resin). The linear peptide was synthesized on the solid support according to the procedure described above in the following sequence: Resin-^{D}Pip-Trp-Arg-^{D}Arg-Ile-Pro((3*S*)OH). 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. 54** in *Table 1*.

Example 55 is shown in *Table 1*.

The peptide was synthesized according general Method B starting with the amino acid (2*R*,3*S*)-3-hydroxypyrrolidine-2-carboxylic acid, which was grafted to the resin (Fmoc-^{D}Pro((3*S*)OH-2-chlorotrityl resin). The linear peptide was synthesized on the solid support according to the procedure described above in the following sequence: Resin-^{D}Pro((3*S*)OH-Trp-Arg-^{D}Arg-Ile-Thr). 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. 55** in *Table 1*.

Examples 56 - 66, 69, 70 and 72 are shown in *Table 1*.

The peptides were synthesized according general Method B starting with the amino acid L-threonin, which was grafted to the resin (Fmoc-Thr-2-chlorotrityl resin). The linear peptides were synthesized on the solid support according to the procedure described above in the following sequence: Resin-Thr-T^{1}-P^{4}-P^{3}-P^{2}-P^{1}. 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 to off-white powders and characterised by HPLC-MS, analytical method C as described above, except **Ex. 69** and **70**, for which analytical method C' was used and **Ex. 72**, for which analytical method D

was used. For analytical data, see **Ex. 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 69, 70, 72** in *Table 1*.

Examples 71, 73, 77, 79 and 80 are shown in *Table 1*.

The peptides were synthesized according general Method B starting with the appropriate protected amino acid at the position T^2 or in case of **Ex. 73** at the position T^1 according *Table 1*, which was grafted to the resin (Fmoc-T^2-chlorotrityl resin respectively Fmoc-T^1-chlorotrityl). The linear peptides were synthesized on the solid support according to the procedure described above in the following sequence: Resin-T^2-T^1-P^4-P^3-P^2-P^1 respectively Resin-T^1-P^4-P^3-P^2-P^1-T^2. At positions where the final amino acid Orn(A56) was intended, Fmoc-protected (*S*)-2-amino-5-(pyrimidin-2-yl-amino)pentanoic acid was used as starting material. The products were cleaved from the resin and cyclized. Deprotection according the above standard procedure using TFA/TIS/H_2O resulted in a reduction to the desired molecule containing the Orn(A56) residue. Consequently the compounds were purified by preparative reverse phase LC-MS as described above.

After lyophilisation, the products were obtained as white to off-white powders and characterised by HPLC-MS, analytical method D as described above, except **Ex. 71**, for which analytical method C' was used. For analytical data, see **Ex. 71, 73, 77, 79, 80** in *Table 1*.

Example 68 is shown in *Table 1*.

The peptide was synthesized according general Method B starting with the amino acid L-threonin, which was grafted to the resin (Fmoc-Thr-2-chlorotrityl resin). The linear peptide was synthesized on the solid support according to the procedure described above in the following sequence: Resin-Thr-^{D}Pro-Trp-Orn(Ar2)-^{D}Arg-Ile. The product was cleaved from the resin and cyclized. In deviation from above general procedure, deprotection was done (avoiding TIS) with a mixture of TFA/H_2O (95:5) and monitored for completion. The compound was 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 D as described above. For analytical data, see **Ex. 68** in *Table 1*.

Example 76 is shown in *Table 1*.

The peptide was synthesized according general Method B starting with the amino acid (3*S*)-1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid, which was grafted to the resin (Fmoc-Tic-2-chlorotrityl resin). The linear peptide was synthesized on the solid support according to the procedure described above in the following sequence: Resin-Tic-^{D}Pro((4*R*)NH_2)-Arg-Trp-^{D}Phe-Orn(Ar2). The product was cleaved from the resin and cyclized. In deviation from above general procedure, deprotection was done (avoiding TIS) with a mixture of TFA/H_2O (95:5) and monitored for completion. The compound was 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 D as described above. For analytical data, see **Ex. 76** in *Table 1*.

1.4 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 [c)]	Anal. Method
1	SEQ ID NO:1	Ile	^{D}Arg	Arg	Ile	^{D}Pro	Thr	B	97	737.4	1.40	A
2	SEQ ID NO:2	Ile	^{D}Arg	Arg	Tyr	^{D}Pro	Thr	B	98	787.3	1.30	A
3	SEQ ID NO:3	Ile	^{D}Arg	Lys	Trp	^{D}Pro	Thr	B	> 98	782.4	1.43	A
4	SEQ ID NO:4	Ile	^{D}Arg	Dab	Trp	^{D}Pro	Thr	B	> 98	754.3	1.42	A
5	SEQ ID NO:5	Ile	^{D}Dab	Arg	Trp	^{D}Pro	Thr	B	94	754.3	1.42	A
6	SEQ ID NO:6	Ile	^{D}Arg	Arg	Phe	^{D}Pro	Thr	B	> 98	771.3	1.44	A
7	SEQ ID NO:7	Ile	^{D}Thr	Arg	Trp	^{D}Pro	Thr	B	95	755.3	1.51	A
8	SEQ ID NO:8	Ile	^{D}Arg	Arg	Trp	^{D}Pro	hSer	B	92	810.4	1.42	A
9	SEQ ID NO:9	Ile	^{D}Arg	Arg	Trp	^{D}Pro	*allo*Thr	B	97	810.4	1.44	A
10	SEQ ID NO:10	1Nal	^{D}Arg	Arg	Trp	^{D}Pro	Thr	B	97	894.4	1.60	A
11	SEQ ID NO:11	Ile	^{D}Lys	Arg	Trp	^{D}Pro	Thr	B	92	782.4	1.42	A
12	SEQ ID NO:12	Ile	^{D}His	Arg	Trp	^{D}Pro	Thr	B	95	791.4	1.42	A
13	SEQ ID NO:13	Ile	^{D}Cit	Arg	Trp	^{D}Pro	Thr	B	88	811.4	1.50	A
14	SEQ ID NO:14	Ile	^{D}Arg	Arg	Trp	^{D}Pip	Thr	B	98	824.4	1.47	A
15	SEQ ID NO:15	Ile	^{D}Arg	Arg	2Nal	^{D}Pro	Thr	B	92	821.4	1.56	A
16	SEQ ID NO:16	Ile	^{D}Arg	Arg	1Nal	^{D}Pro	Thr	B	91	821.4	1.56	A
17	SEQ ID NO:17	Ile	^{D}Arg	Trp	Arg	^{D}Pro	Thr	A	98	810.5	1.28	A
18	SEQ ID NO:18	Ile	^{D}Arg	Arg	Trp	^{D}Pro	Thr	A	97	924.4 [d)]	1.45	A
19	SEQ ID NO:19	Thr	^{D}Arg	Trp	Arg	^{D}Pro	Thr	A	95	912.4 [d)]	1.24	A
20	SEQ ID NO:20	Trp	^{D}Arg	Arg	Trp	^{D}Pro	Thr	A	95	997.5 [d)]	1.83	B
21	SEQ ID NO:21	Ile	^{D}Arg	Arg	Trp	^{D}Pro	Pro((3*S*)OH)	B	98	822.3	1.51	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 [c)]	Anal. Method
22	SEQ ID NO:22	Ile	^{D}Arg	Arg	Trp	^{D}Pro	Ser	B	90	796.4	1.40	A
23	SEQ ID NO:23	Ile	^{D}Arg	Agp	Trp	^{D}Pro	Thr	B	87	782.3	1.46	A
24	SEQ ID NO:24	Ile	^{D}Arg	Agb	Trp	^{D}Pro	Thr	B	98	796.3	1.47	A
25	SEQ ID NO:25	Trp	^{D}Phe	Trp	Arg	^{D}Pro((4*S*)NH_2)	Tic	B	95	947.4	1.75	A
26	SEQ ID NO:26	Trp	^{D}Phe	Trp	Arg	^{D}Pro((4*R*)NH_2)	Tic	B	90	947.3	1.74	A
27	SEQ ID NO:27	Ala	^{D}Phe	Trp	Arg	^{D}Pro((4*R*)NH_2)	Tic	B	94	832.5	1.44	C
28	SEQ ID NO:28	Tyr	^{D}Phe	Trp	Arg	^{D}Pro((4*R*)NH_2)	Tic	B	92	924.5	1.45	C
29	SEQ ID NO:29	Trp	^{D}Phe	Trp	Orn	^{D}Pro((4*R*)NH_2)	Tic	B	92	905.5	1.56	C
30	SEQ ID NO:30	Trp	^{D}Phe	Trp	Dab	^{D}Pro((4*R*)NH_2)	Tic	B	89	891.5	1.57	C
31	SEQ ID NO:31	Trp	^{D}Phe	Trp	Lys	^{D}Pro((4*R*)NH_2)	Tic	B	93	919.5	1.57	C
32	SEQ ID NO:32	Trp	^{D}Phe	Trp	His	^{D}Pro((4*R*)NH_2)	Tic	B	92	928.5	1.58	C
33	SEQ ID NO:33	Arg	^{D}Phe	Trp	Arg	^{D}Pro((4*R*)NH_2)	Tic	B	92	917.5	1.25	C
34	SEQ ID NO:34	Pip	^{D}Phe	Trp	Arg	^{D}Pro((4*R*)NH_2)	Tic	B	92	887.5	1.23	C
35	SEQ ID NO:35	hArg	^{D}Phe	Trp	Arg	^{D}Pro((4*R*)NH_2)	Tic	B	96	931.7	1.26	C
36	SEQ ID NO:36	Agb	^{D}Phe	Trp	Arg	^{D}Pro((4*R*)NH_2)	Tic	B	96	903.5	1.23	C
37	SEQ ID NO:37	3Pal	^{D}Phe	Trp	Arg	^{D}Pro((4*R*)NH_2)	Tic	B	95	909.5	1.25	C
38	SEQ ID NO:38	Trp	^{D}3Pal	Trp	Arg	^{D}Pro((4*R*)NH_2)	Tic	B	80	948.5	1.24	C
39	SEQ ID NO:39	Arg	^{D}Phe	Trp	hArg	^{D}Pro((4*R*)NH_2)	Tic	B	88	1045.6 [d)]	1.25	C
40	SEQ ID NO:40	Arg	^{D}Phe	Trp	Arg	^{D}Pro((4*S*)NH_2)	Tic	B	93	917.5	1.26	C
41	SEQ ID NO:41	Trp	^{D}Phe	Trp	Arg	^{D}Pro((4*R*)NH_2)	Oic	B	94	939.7	1.55	C
42	SEQ ID NO:42	Arg	^{D}Phe	Trp	Arg	^{D}Pro((4*R*)NH_2)	Oic	B	91	909.7	1.23	C
43	SEQ ID NO:43	Trp	^{D}Phe	Trp	Arg	^{D}Pro	Pro((4*S*)F)	B	96	888.5	1.62	C
44	SEQ ID NO:44	Trp	^{D}Phe	Trp	Arg	^{D}Pro	Pro((4*S*)NH_2)	B	> 98	885.5	1.51	C
45	SEQ ID NO:45	Trp	^{D}Phe	Trp	Arg	^{D}Pro	Pro((4*R*)NH_2)	B	95	885.5	1.46	C

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 [c)]	Anal. Method
46	SEQ ID NO:46	Trp	^{D}Phe	Trp	Arg	^{D}Pro	Mor	B	93	886.5	1.61	C
47	SEQ ID NO:47	Ile	^{D}Arg	Arg	Trp	^{D}Pro	Mor	B	74	822.5	1.39	C
48	SEQ ID NO:48	Arg	^{D}Phe	Trp	Arg	^{D}Pro	(4*S*)-Hyp(Bn)	B	91	946.7	1.52	C
49	SEQ ID NO:49	Trp	^{D}Phe	Trp	Arg	^{D}Pro((4*S*)OH)	(4*S*)-Hyp(Bn)	B	89	992.5	1.78	C
50	SEQ ID NO:50	Trp	^{D}Phe	Trp	Arg	^{D}Pro((4*R*)NH_2)	(4*S*)-Hyp(Bn)	B	86	991.7	1.63	C
51	SEQ ID NO:51	His	^{D}Trp	His	Trp	^{D}Pro	Pro((4*S*)NHBz)	A	95	960.4	1.50	A
52	SEQ ID NO:52	1Nal	^{D}Arg	Arg	Trp	^{D}Pro	Pro((3*S*)OH)	B	86	906.5	1.50	C
53	SEQ ID NO:53	Ile	^{D}Arg	Arg	2Nal	^{D}Pro	Pro((3*S*)OH)	B	91	833.5	1.48	C
54	SEQ ID NO:54	Ile	^{D}Arg	Arg	Trp	^{D}Pip	Pro((3*S*)OH)	B	92	836.5	1.37	C
55	SEQ ID NO:55	Ile	^{D}Arg	Arg	Trp	^{D}Pro((4*S*)OH)	Thr	B	85	826.5	1.15	C
56	SEQ ID NO:56	Ile	^{D}Arg	Arg	Trp	^{D}Pro((4*R*)NH_2)	Thr	B	72	825.5	1.19	C
57	SEQ ID NO:57	Val	^{D}Arg	Arg	Trp	^{D}Pro	Thr	B	88	796.5	1.20	C
58	SEQ ID NO:58	Abu	^{D}Arg	Arg	Trp	^{D}Pro	Thr	B	81	782.5	1.16	C
59	SEQ ID NO:59	Chg	^{D}Arg	Arg	Trp	^{D}Pro	Thr	B	96	836.5	1.34	C
60	SEQ ID NO:60	Leu	^{D}Arg	Arg	Trp	^{D}Pro	Thr	B	96	810.5	1.30	C
61	SEQ ID NO:61	Nle	^{D}Arg	Arg	Trp	^{D}Pro	Thr	B	96	810.5	1.31	C
62	SEQ ID NO:62	Cha	^{D}Arg	Arg	Trp	^{D}Pro	Thr	B	94	850.5	1.46	C
63	SEQ ID NO:63	Ile	^{D}Orn	Arg	Trp	^{D}Pro	Thr	B	91	768.5	1.24	C
64	SEQ ID NO:64	Ile	^{D}Arg	Orn(A41)	Trp	^{D}Pro	Thr	B	93	874.5	1.41	C
65	SEQ ID NO:65	Ile	^{D}Arg	Orn	Trp	^{D}Pro	Thr	B	94	768.5	1.24	C
66	SEQ ID NO:66	Ile	^{D}Arg	hArg	Trp	^{D}Pro	Thr	B	91	824.5	1.28	C
67	SEQ ID NO:67	Ile	^{D}Arg	Arg	Trp	^{D}Tic	Thr	B	94	872.5	1.43	C
68	SEQ ID NO:68	Ile	^{D}Arg	Orn(Ar2)	Trp	^{D}Pro	Thr	B	93	846.3	1.74	D
69	SEQ ID NO:69	Ile	^{D}Arg	Orn(Ar7)	Trp	^{D}Pro	Thr	B	97	862.5	1.17	C'

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 [c)]	Anal. Method
70	SEQ ID NO:70	Ile	^{D}Arg	Orn(Ar4)	Trp	^{D}Pro	Thr	B	84	859.1	1.27	C'
71	SEQ ID NO:71	Ile	^{D}Arg	Orn(A56)	Trp	^{D}Pro	Thr	B	95	850.4	1.28	C'
72	SEQ ID NO:72	Ile	^{D}Arg	Arg	Phe($4CF_3$)	^{D}Pro	Thr	B	97	839.3	1.96	D
73	SEQ ID NO:73	Trp	^{D}Phe	Trp	Orn(A56)	^{D}Pip	Pro((3*S*)OH)	B	93	940.7	2.22	D
74	SEQ ID NO:74	Ala(1Pyraz)	^{D}Phe	Trp	Arg	^{D}Pro((4*R*)NH_2)	Tic	B	97	898.7	1.85	D
75	SEQ ID NO:75	Ala(Tet)	^{D}Phe	Trp	Arg	^{D}Pro((4*R*)NH_2)	Tic	B	94	900.7	1.80	D
76	SEQ ID NO:76	Orn(Ar2)	^{D}Phe	Trp	Arg	^{D}Pro((4*R*)NH_2)	Tic	B	90	953.7	1.73	D
77	SEQ ID NO:77	Orn(A56)	^{D}Phe	Trp	Arg	^{D}Pro((4*R*)NH_2)	Tic	B	96	1071.7 [d)]	1.55	D
78	SEQ ID NO78	Trp	^{D}Phe	Trp	Orn(Ar7)	^{D}Pro((4*R*)NH_2)	Tic	B	92	999.7	2.08	D
79	SEQ ID NO:79	Trp	^{D}Phe	Trp	Orn(A56)	^{D}Pro((4*R*)NH_2)	Tiq	B	95	987.7	2.18	D
80	SEQ ID NO:80	Trp	^{D}Phe	Trp	Orn(A56)	^{D}Pro((4*R*)NH_2)	Tic	B	93	987.7	2.16	D

a) Abbreviation of amino acid see listing above.
b) %-purity of compounds after prep. HPLC.
c) Retention Time with applied method.
d) $[M+TFA+H]^+$

2. Biological methods

2.1 Preparation of the peptide samples.

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

2.2 CXCR7 β-arrestin recruitment assay

The PathHunter CHO-CXCR7 (DiscoverX) assay was performed according to the manufacturer's protocol. In brief, CHO CXCR7 β-arrestin cells were seeded at a density of 5000 cells per well in 40µl of F12 medium in black 96-half volume well culture plates and incubated overnight at 37°C in a humidified atmosphere with 5% CO_2. The next day, serial dilutions of PEM compounds have been prepared in DMSO and subsequently diluted in HBSS buffer containing 0.1% BSA.

For agonistic assay, 10 µl of compound solution or a solution of stromal cell-derived factor-1 (SDF-1) as positive control was added to the cells with a final DMSO concentration of 1% (v/v). The plate was incubated for 90 min at 37 °C in 5% CO_2 incubator with gentle shaking (300 rpm) before addition of 40ul of detection reagent per well. Reaction was developed for 90 min at room temperature in the dark with shaking, and chemiluminescence was measured with a Topcount (Perkin Elmer) luminescence counter.

2.3 Results

***Table 2*: Biological Results**

Ex.	Sequence ID	β-Arrestin EC_{50} [nM]
1	SEQ ID NO:1	79.7 ± 99.7
2	SEQ ID NO:2	83.7 ± 77.4
3	SEQ ID NO:3	78.7 ± 114.7
4	SEQ ID NO:4	87.0 ± 84.1
5	SEQ ID NO:5	48.4 ± 67.5
6	SEQ ID NO:6	46.4 ± 57.9
7	SEQ ID NO:7	53.2 ± 35.8
8	SEQ ID NO:8	346.6 ± 10.3
9	SEQ ID NO:9	291.7 ± 101.3
10	SEQ ID NO:10	28.5 ± 12.6
11	SEQ ID NO:11	86.7 ± 9.7
12	SEQ ID NO:12	545.7 ± 241.3
13	SEQ ID NO:13	472.5 ± 68.9
14	SEQ ID NO:14	0.1 ± 0.0
15	SEQ ID NO:15	0.4 ± 0.1
16	SEQ ID NO:16	17.9 ± 2.6
17	SEQ ID NO:17	62.5 ± 1.8
18	SEQ ID NO:18	6.7 ± 5.1
19	SEQ ID NO:19	17.2 ± 18.9
20	SEQ ID NO:20	538.2 ± 105.3
21	SEQ ID NO:21	122.8 ± 85.2
22	SEQ ID NO:22	12.8 ± 3.5
23	SEQ ID NO:23	90.5 ± 60.7
24	SEQ ID NO:24	22.3 ± 29.3
25	SEQ ID NO:25	17.5 ± 12.2
26	SEQ ID NO:26	6.1 ± 3.3

Table 2: Biological Results *(continued)*

Ex.	Sequence ID	β-Arrestin EC_{50} [nM]
27	SEQ ID NO:27	322.0 ± 48.2
28	SEQ ID NO:28	20.9 ± 27.3
29	SEQ ID NO:29	26.1 ± 16.7
30	SEQ ID NO:30	13.6 ± 5.0
31	SEQ ID NO:31	137.6 ± 114.9
32	SEQ ID NO:32	20.4 ± 6.6
33	SEQ ID NO:33	248.0 ± 16.5
34	SEQ ID NO:34	882.0 ± 42.3
35	SEQ ID NO:35	12.2 ± 5.4
36	SEQ ID NO:36	452.5 ± 15.8
37	SEQ ID NO:37	5.1 ± 0.9
38	SEQ ID NO:38	6.1 ± 1.5
39	SEQ ID NO:39	352.0 ± 79.3
40	SEQ ID NO:40	13.1 ± 4.4
41	SEQ ID NO:41	20.9 ± 33.7
42	SEQ ID NO:42	20.5 ± 10.9
43	SEQ ID NO:43	119.1 ± 42.3
44	SEQ ID NO:44	36.9 ± 14.0
45	SEQ ID NO:45	26.9 ± 12.6
46	SEQ ID NO:46	132.5 ± 53.1
47	SEQ ID NO:47	nd
48	SEQ ID NO:48	76.9 ± 24.7
49	SEQ ID NO:49	7.6 ± 10.1
50	SEQ ID NO:50	6.6 ± 1.6
51	SEQ ID NO:51	413.5 ± 225.5
52	SEQ ID NO:52	13.7 ± 5.1
53	SEQ ID NO:53	76.8 ± 47.9
54	SEQ ID NO:54	8.2 ± 3.4

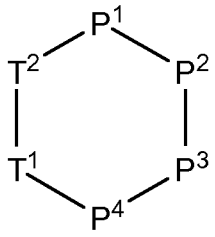
Table 2*: Biological Results *(continued)

Ex.	Sequence ID	β-Arrestin EC_{50} [nM]
55	SEQ ID NO:55	632.5 ± 23.3
56	SEQ ID NO:56	948.5 ± 75.3
57	SEQ ID NO:57	271.0 ± 0.2
58	SEQ ID NO:58	329.8 ± 93.2
59	SEQ ID NO:59	6.7 ± 2.2
60	SEQ ID NO:60	5.3 ± 3.6
61	SEQ ID NO:61	2.8 ± 1.0
62	SEQ ID NO:62	37.7 ± 18.5
63	SEQ ID NO:63	23.3 ± 7.3
64	SEQ ID NO:64	518.0 ± 20.9
65	SEQ ID NO:65	816.5 ± 58.8
66	SEQ ID NO:66	11.0 ± 4.5
67	SEQ ID NO:67	14.2 ± 5.2
68	SEQ ID NO:68	453.3 ± 185.5
69	SEQ ID NO:69	336.50 ± 92.6
70	SEQ ID NO:70	4.6 ± 0.8
71	SEQ ID NO:71	3.2 ± 2.7
72	SEQ ID NO:72	4.5 ± 1.1
73	SEQ ID NO:73	14.0 ± 0.1
74	SEQ ID NO:74	29.9 ± 8.9
75	SEQ ID NO:75	28.1 ± 5.1
76	SEQ ID NO:76	209.0 ± 6.6
77	SEQ ID NO:77	181.0 ± 62.9
78	SEQ ID NO:78	145.0 ± 10.9
79	SEQ ID NO:79	46.9 ± 12.5
80	SEQ ID NO:80	33.4 ± 0.8

nd = not determined

CLAIMS

1. Compounds of the general formula **(I)**

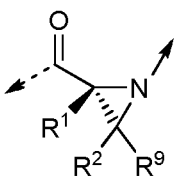


(I)

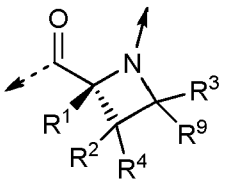
wherein the single elements T or P are connected in either direction from the carbonyl (C=O) point of attachment to the nitrogen (N) of the next element and wherein

– either

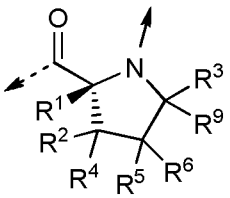
T^1 is an α-amino acid residue of one of the formulae



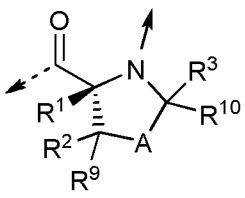
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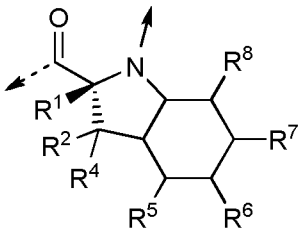
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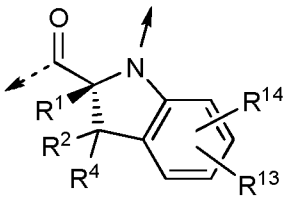
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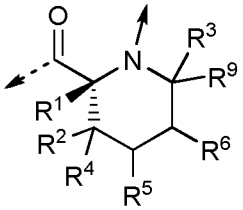
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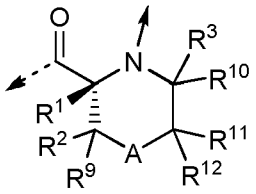
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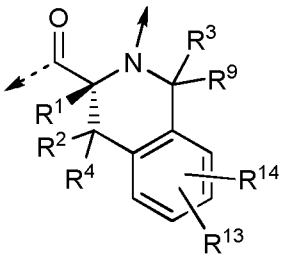
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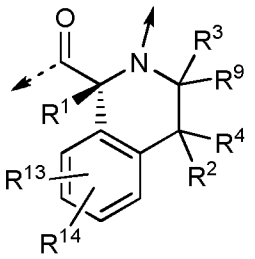
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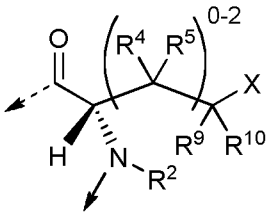
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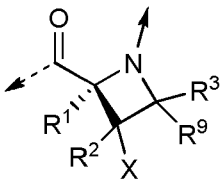
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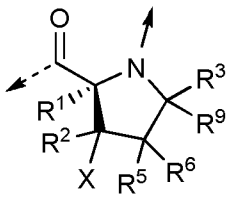
T^2 is an α-amino acid residue of one of the formulae



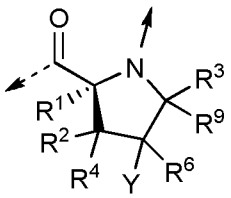
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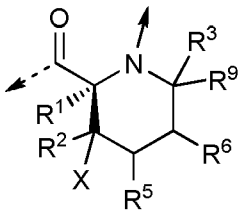
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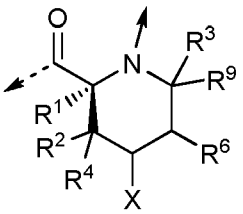
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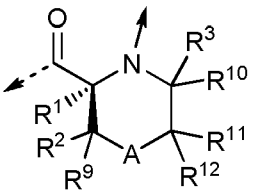
AA14



AA15



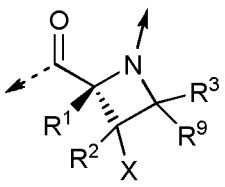
AA16



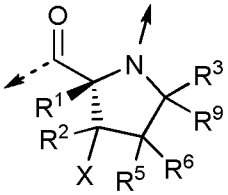
AA17

– or

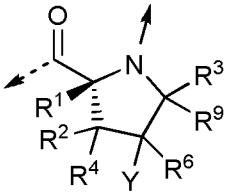
T^1 is an α-amino acid residue of one of the formulae



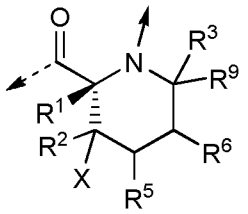
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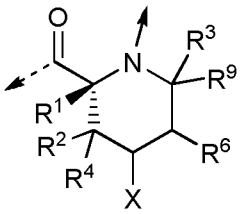
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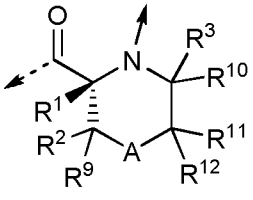
AA20



AA21



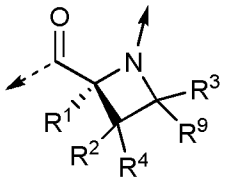
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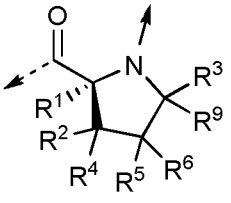
AA23

and

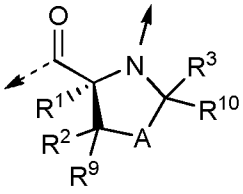
T^2 is an α-amino acid residue of one of the formulae AA11 to AA17, hereinabove, or an α-amino acid residue of one of the formulae



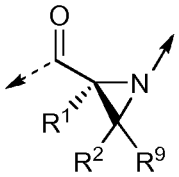
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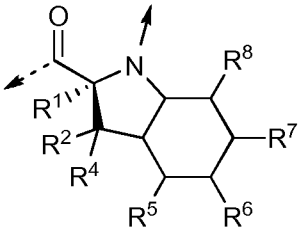
AA25



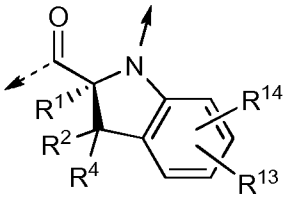
AA26



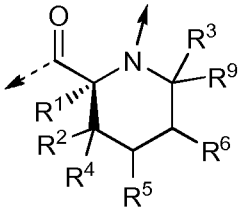
AA27



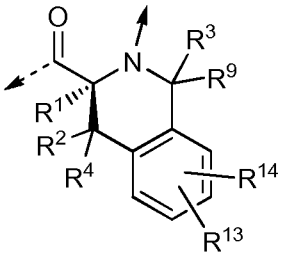
AA28



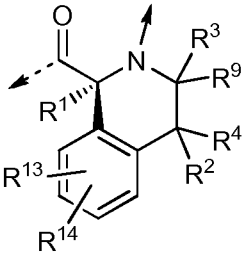
AA29



AA30



AA31

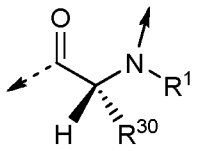


AA32

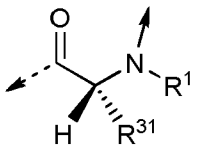
P^1, P^3 and P^4 are independently

-$NR^1CH(R^{29})CO$-; -$NR^1CH(R^{30})CO$-; or -$NR^1CH(R^{31})CO$-;

P^2 is an α-amino acid residue of one of the formulae



AA33



AA34

A is O; NR^{17}; S; SO; or SO_2;

X is OH; NH_2; OR^{16}; NR^1R^{16}; or $NR^{17}R^{18}$;

Y is NH_2; F; OR^{16}; NR^1R^{16}; or $NR^{17}R^{18}$;

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; $-(CHR^{15})_oOR^{17}$; $-(CHR^{15})_oSR^{17}$; $-(CHR^{15})_oNR^{17}R^{18}$; $-(CHR^{15})_oOCONR^{17}R^{18}$; $-(CHR^{15})_oNR^1CONR^{17}R^{18}$; $-(CHR^{15})_oNR^1COR^{17}$; $-(CHR^{15})_oCOOR^{17}$; $-(CHR^{15})_oCONR^{17}R^{18}$; $-(CHR^{15})_oPO(OR^1)_2$; $-(CHR^{15})_oSO_2R^{17}$; $-(CHR^{15})_oNR^1SO_2R^{17}$; $-(CHR^{15})_oSO_2NR^{17}R^{18}$; $-(CR^1R^{15})_oR^{35}$; or $-(CHR^1)_nO(CHR^2)_mR^{35}$; or

R^4 and R^2 taken together can form

=O; $-(CHR^{15})_p-$; $-(CH_2)_nO(CH_2)_m-$; $-(CH_2)_nS(CH_2)_m-$; 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:

$-(CHR^{15})_p-$; $-(CH_2)_nO(CH_2)_m-$; $-(CH_2)_nS(CH_2)_m-$; or $-(CH_2)_nNR^1(CH_2)_m-$; or

R^4 and R^5 are independently X;

R^9, R^{10}, R^{11} and R^{12} are independently

H; F; CF_3; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl; aryl; heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; $-(CHR^{15})_rOR^{17}$; $-(CHR^{15})_rSR^{17}$; $-(CHR^{15})_rNR^{17}R^{18}$; $-(CHR^{15})_rOCONR^{17}R^{18}$; $-(CHR^{15})_rNR^1CONR^{17}R^{18}$; $-(CHR^{15})_rNR^1COR^{17}$; $-(CHR^{15})_oCOOR^{17}$; $-(CHR^{15})_oCONR^{17}R^{18}$; $-(CHR^{15})_rPO(OR^1)_2$; $-(CHR^{15})_rSO_2R^{17}$; $-(CHR^{15})_rNR^1SO_2R^{17}$; $-(CHR^{15})_rSO_2NR^{17}R^{18}$; $-(CR^1R^{15})_oR^{35}$; or

$-(CHR^1)_rO(CHR^1)_oR^{35}$; or

R^{11} and R^{12} taken together can form

=O; or $=NR^1$;

R^{13} and R^{14} 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; $-(CHR^{15})_oOR^{17}$; $-(CHR^{15})_oSR^{17}$; $-(CHR^{15})_oNR^{17}R^{18}$; $-(CHR^{15})_oOCONR^{17}R^{18}$; $-(CHR^{15})_oNR^1CONR^{17}R^{18}$; $-(CHR^{15})_oNR^1COR^{17}$; $-(CHR^{15})_oCOOR^{17}$; $-(CHR^{15})_oCONR^{17}R^{18}$; $-(CHR^{15})_oPO(OR^1)_2$; $-(CHR^{15})_oSO_2R^{17}$; $-(CHR^{15})_oNR^1SO_2R^{17}$; $-(CHR^{15})_oSO_2NR^{17}R^{18}$; $-(CR^1R^{15})_oR^{35}$; or $-(CHR^1)_rO(CHR^1)_oR^{35}$;

R^{15} 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; $-(CHR^1)_oOR^{17}$; $-(CHR^1)_oSR^{17}$; $-(CHR^1)_oNR^{17}R^{18}$; $-(CHR^1)_oNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CHR^1)_oCOOR^{17}$; $-(CHR^1)_oCONR^{17}R^{18}$; $-(CHR^1)_oSO_2R^{17}$; or $-(CHR^1)_oSO_2NR^{17}R^{18}$;

R^{16} is 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; $-(CHR^1)_sOR^{17}$; $-(CHR^1)_sSR^{17}$; $-(CHR^1)_sNR^{17}R^{18}$; $-(CHR^1)_oCOR^{17}$; $-(CHR^1)_oCOOR^{17}$; $-(CHR^1)_oCONR^{17}R^{18}$; or $-(CHR^1)_oSO_2R^{17}$;

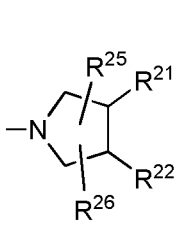
R^{17}, R^{18}, R^{19} and R^{20} are independently

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; aryl-heterocycloalkyl; heteroaryl-cycloalkyl; or heteroaryl-heterocycloalkyl; or

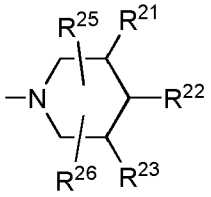
the structural elements $-NR^{17}R^{18}$ and $-NR^{19}R^{20}$ can independently form:

heterocycloalkyl; aryl-heterocycloalkyl; or heteroaryl-heterocycloalkyl;

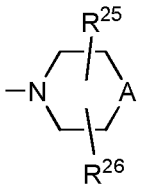
or a group of one of the formulae



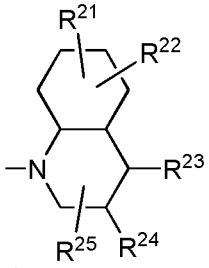
C1



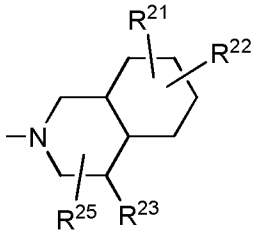
C2



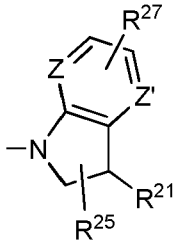
C3



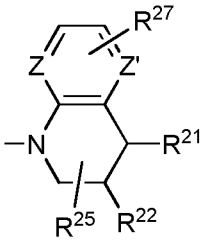
C4



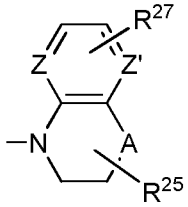
C5



C6



C7



C8

Z, Z' and Z'' are independently

-CR^{39}; or N;

R^{21}, R^{22}, R^{23} and R^{24} are independently

H; F; CF_3; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl; aryl; heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; -$(CHR^1)_oOR^{17}$; -$(CHR^1)_oSR^{17}$; -$(CHR^1)_oNR^2R^{17}$; -$(CHR^1)_oOCONR^2R^{17}$; -$(CHR^1)_oNR^2CONR^3R^{17}$; -$(CHR^1)_oNR^2COR^{17}$; -$(CHR^1)_oCOOR^{17}$; -$(CHR^1)_oCONR^2R^{17}$; -$(CHR^1)_oPO(OR^2)_2$; -$(CHR^1)_oSO_2R^{17}$; -$(CHR^1)_oNR^2SO_2R^{17}$; -$(CHR^1)_oSO_2NR^2R^{17}$; -$(CR^1R^2)_oR^{38}$; or -$(CHR^1)_nO(CHR^2)_mR^{38}$;

R^{25} and R^{26} are independently

H; F; CF_3; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl; aryl; heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; -$(CHR^1)_rOR^{17}$; -$(CHR^1)_rSR^{17}$; -$(CHR^1)_rNR^2R^{17}$; -$(CHR^1)_rOCONR^2R^{17}$; -$(CHR^1)_rNR^2CONR^3R^{17}$;-$(CHR^1)_rNR^2COR^{17}$; -$(CHR^1)_oCOOR^{17}$; -$(CHR^1)_oCONR^2R^{17}$; -$(CHR^1)_rPO(OR^2)_2$; -$(CHR^1)_rSO_2R^{17}$; -$(CHR^1)_rNR^2SO_2R^{17}$; -$(CHR^1)_rSO_2NR^2R^{17}$; -$(CR^1R^2)_oR^{38}$; or -$(CHR^1)_rO(CHR^2)_oR^{38}$;

R^{27} is 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; $-(CHR^1)_oOR^{17}$; $-(CHR^1)_oSR^{17}$; $-(CHR^1)_oNR^2R^{17}$; $-(CHR^1)_oOCONR^2R^{17}$; $-(CHR^1)_oNR^2CONR^3R^{17}$; $-(CHR^1)_oNR^2COR^{17}$; $-(CHR^1)_oCOOR^{17}$; $-(CHR^1)_oCONR^2R^{17}$; $-(CHR^1)_oPO(OR^2)_2$; $-(CHR^1)_oSO_2R^{17}$; $-(CHR^1)_oNR^2SO_2R^{17}$; $-(CHR^1)_oSO_2NR^2R^{17}$; $-(CR^1R^2)_oR^{38}$; or $-(CHR^1)_rO(CHR^2)_oR^{38}$;

R^{29} is H; alkyl; alkenyl; cycloalkyl-lower alkyl; heterocycloalkyl-lower alkyl; $-(CHR^4)_oOR^{17}$; $-(CHR^4)_oSR^{17}$; or $-(CHR^4)_rNR^{17}R^{18}$;

R^{30} is $-(CR^1R^4)_nR^{35}$; $-(CH_2)_nO(CH_2)_mR^{35}$; $-(CH_2)_nS(CH_2)_mR^{35}$; or $-(CH_2)_nNR^1(CH_2)_mR^{35}$;

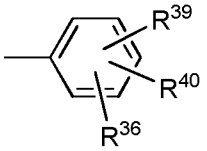
R^{31} is alkyl; alkenyl; $-(CR^1R^{15})_qNR^{17}R^{18}$; $-(CR^1R^{15})_qNR^2R^{16}$; $-(CR^1R^{15})_qNR^{17}R^{32}$; $-(CR^1R^{15})_qNR^{17}COR^{18}$; $-(CH_2)_qC(=NR^{15})NR^{17}R^{18}$; $-(CH_2)_qC(=NOR^{19})NR^{17}R^{18}$; $-(CH_2)_qC(=NNR^{17}R^{18})NR^{19}R^{20}$; $-(CR^1R^{15})_qNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CR^1R^{15})_qN=C(NR^{17}R^{18})NR^{19}R^{20}$; $-(CR^1R^{15})_qOR^{17}$; $-(CR^1R^{15})_qOR^{32}$; $-(CR^1R^{15})_qSR^{17}$; $-(CR^1R^{15})_qSO_2R^{17}$; $-(CR^1R^{15})_qNR^{17}SO_2R^{18}$; $-(CR^1R^{15})_qSO_2NR^2R^{16}$; $-(CR^1R^{15})_qSO_2NR^{17}R^{18}$; $-(CR^1R^{15})_qNR^{19}SO_2NR^{17}R^{18}$; $-(CR^1R^{15})_qPO(OR^2)_2$; $-(CH_2)_nO(CH_2)_mNR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mC(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mC(=NOR^{19})NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mC(=NNR^{17}R^{18})NR^{19}R^{20}$; $-(CH_2)_nO(CH_2)_mNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mN=C(NR^{17}R^{18})NR^{19}R^{20}$; $-(CH_2)_nS(CH_2)_mNR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mC(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mC(=NOR^{19})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mC(=NNR^{17}R^{18})NR^{19}R^{20}$; $-(CH_2)_nS(CH_2)_mNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mN=C(NR^{17}R^{18})NR^{19}R^{20}$; $-(CR^1R^{15})_qCOOR^{17}$; $-(CR^1R^{15})_qCONR^{17}R^{18}$; or $-(CR^1R^{15})_qCOR^{33}$;

R^{32} is $-COR^{29}$; $-COR^{30}$; $-CO(CR^1R^{15})_oR^{17}$; $-CO(CR^1R^{15})_oOR^{17}$; $-CO(CR^1R^{15})_oNR^{17}R^{18}$; $-CO(CR^1R^{15})_oNR^2R^{16}$; $-CO(CR^1R^{29})NR^{17}R^{18}$; $-CO(CR^1R^{30})NR^{17}R^{18}$; $-CO(CR^1R^{34})NR^{17}R^{18}$; $-CO(CHR^1)_oCONR^{17}R^{18}$; $-CO(CHR^1)_oCONR^{17}SO_2R^{18}$; $-CO(CR^1R^{15})_oNR^{17}SO_2R^{18}$; $-CONR^1(CHR^{17})_nNR^2(CHR^{15})_mR^{16}$; $-CO(CHR^{17})_nO(CHR^{15})_mR^{16}$; $-CONR^1(CHR^{17})_nO(CHR^{15})_mR^{16}$; $-SO_2R^{29}$; $-SO_2R^{30}$; $-SO_2(CR^1R^{15})_oR^{17}$; or $-SO_2(CR^1R^{15})_oNR^{17}R^{18}$;

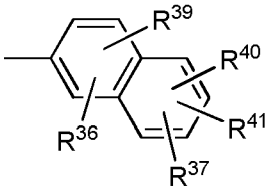
R^{33} is $-NR^1C(R^2)(R^{29})COOR^{17}$; $-NR^1C(R^2)(R^{29})CONR^{17}R^{18}$; $-NR^1C(R^2)(R^{30})COOR^{17}$; $-NR^1C(R^2)(R^{30})CONR^{17}R^{18}$; $-NR^1C(R^2)(R^{34})COOR^{17}$; or $-NR^1C(R^2)(R^{34})CONR^{17}R^{18}$;

R^{34} is $-(CR^1R^{15})_qNR^{17}R^{18}$; $-(CH_2)_qC(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_qC(=NOR^{19})NR^{17}R^{18}$; $-(CH_2)_qC(=NNR^{17}R^{18})NR^{19}R^{20}$; $-(CR^1R^{15})_qNR^2C(=NR^{19})NR^{17}R^{18}$; $-(CR^1R^{15})_qN=C(NR^{17}R^{18})NR^{19}R^{20}$; $-(CR^1R^{15})_qOR^{17}$; $-(CR^1R^{15})_qSR^{17}$; $-(CR^1R^{15})_qSO_2R^{17}$; $-(CR^1R^{15})_qNR^{17}SO_2R^{18}$; $-(CR^1R^{15})_qSO_2NR^1R^{16}$; $-(CR^1R^{15})_qSO_2NR^{17}R^{18}$; $-(CR^1R^{15})_qNR^2SO_2NR^{17}R^{18}$; $-(CR^1R^{15})_qPO(OR^1)_2$; $-(CH_2)_nO(CH_2)_mNR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mC(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mC(=NOR^{19})NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mC(=NNR^{17}R^{18})NR^{19}R^{20}$; $-(CH_2)_nO(CH_2)_mNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mN=C(NR^{17}R^{18})NR^{19}R^{20}$; $-(CH_2)_nS(CH_2)_mNR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mC(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mC(=NOR^{19})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mC(=NNR^{17}R^{18})NR^{19}R^{20}$; $-(CH_2)_nS(CH_2)_mNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mN=C(NR^{17}R^{18})NR^{19}R^{20}$; $-(CR^1R^{15})_qCOOR^{17}$; or $-(CR^1R^{15})_qCONR^{17}R^{18}$;

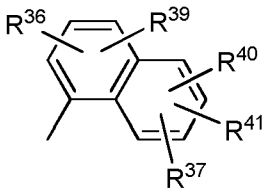
R^{35} is an aryl group of one of the formulae



AR1

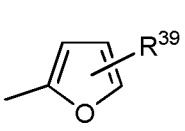


AR2

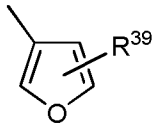


AR3

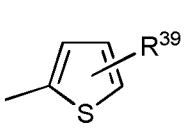
or a heteroaryl group of one of the formulae



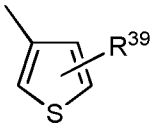
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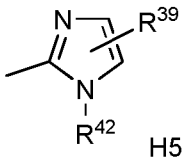
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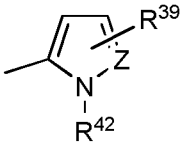
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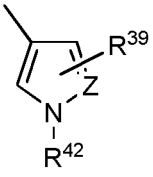
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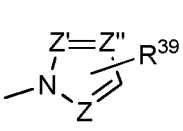
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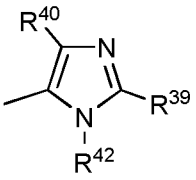
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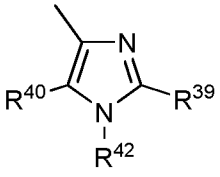
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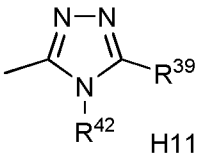
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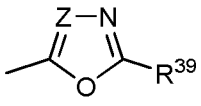
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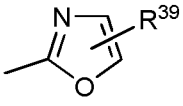
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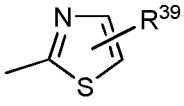
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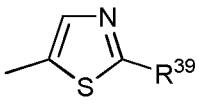
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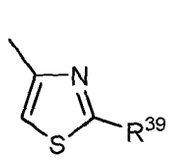
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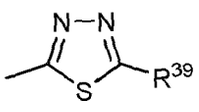
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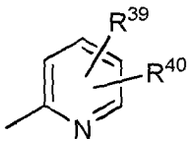
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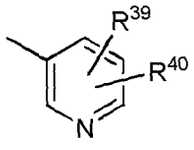
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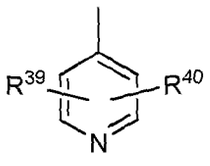
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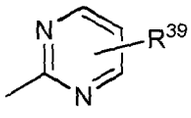
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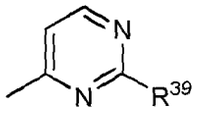
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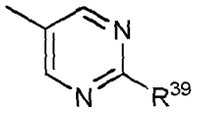
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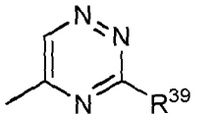
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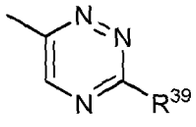
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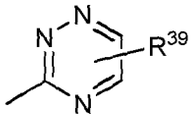
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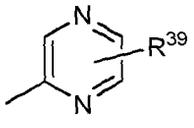
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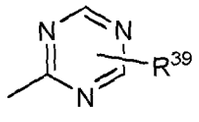
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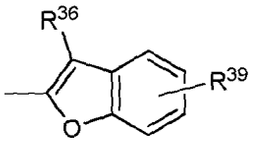
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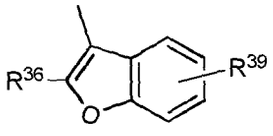
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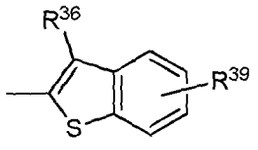
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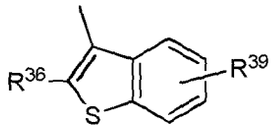
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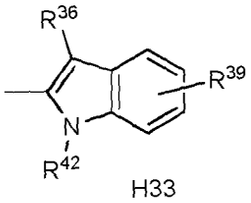
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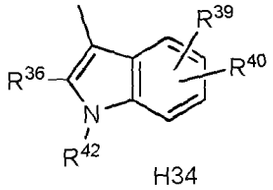
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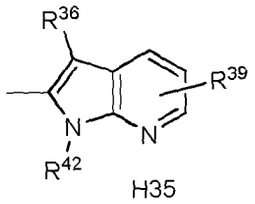
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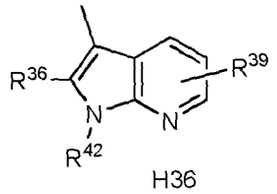
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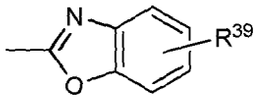
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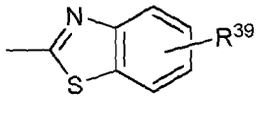
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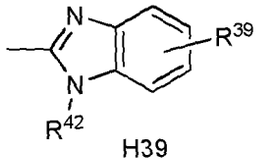
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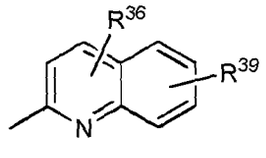
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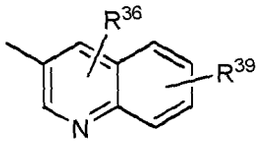
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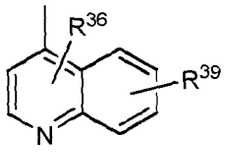
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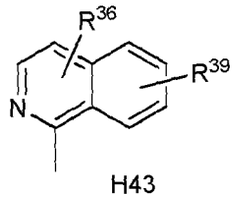
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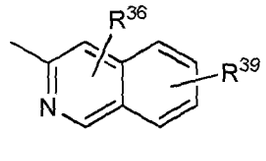
H41



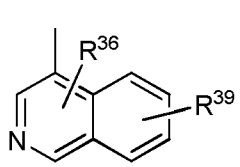
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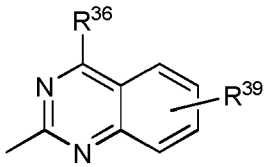


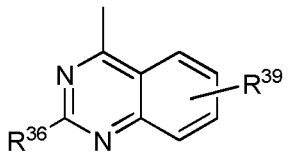
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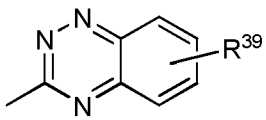


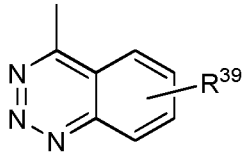
H44

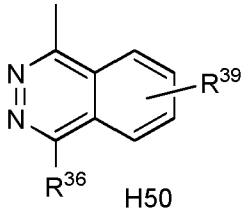

H45

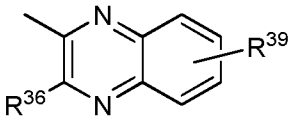

H46


H47


H48


H49

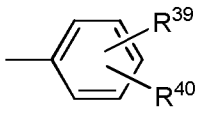

H50


H51

R^{36} and R^{37} 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; $-(CH_2)_oR^{38}$; $-(CH_2)_oOR^{17}$; $-O(CH_2)_oR^{38}$; $-(CH_2)_oSR^{17}$; $-(CH_2)_oNR^{17}R^{18}$; $-(CH_2)_oOCONR^{17}R^{18}$; $-(CH_2)_oNR^1CONR^{17}R^{18}$; $-(CH_2)_oNR^1COR^{17}$; $-(CH_2)_oCOOR^{17}$; $-(CH_2)_oCONR^{17}R^{18}$; $-(CH_2)_oPO(OR^1)_2$; $-(CH_2)_oSO_2R^{16}$; or $-(CH_2)_oCOR^{17}$;

R^{38} is an aryl group of the formula


AR4

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

H; F; Cl; Br; OH; NH_2; NO_2; CN; CF_3; $OCHF_2$; OCF_3; $-NR^1R^{17}$; $-(CH_2)_oCOOR^{17}$; $-(CH_2)_oCONR^1R^{17}$; lower alkyl; lower alkoxy; or lower alkenyl;

R^{42} is H; lower alkyl; or aryl-lower alkyl;

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; s is 0-4

and pharmaceutically acceptable salts thereof.

2. Compounds according to claim 1 wherein

R^{16} is CF_3; lower alkyl; lower alkenyl; cycloalkyl; heterocycloalkyl; cycloalkyl-lower alkyl; heterocycloalkyl-lower alkyl; aryl; heteroaryl; aryl-lower alkyl; heteroaryl-lower alkyl; $-(CHR^1)_sOR^{17}$; $-(CHR^1)_sSR^{17}$; $-(CHR^1)_sNR^{17}R^{18}$; $-(CHR^1)_oCOR^{17}$; $-(CHR^1)_oCOOR^{17}$; $-(CHR^1)_oCONR^{17}R^{18}$; or $-(CHR^1)_oSO_2R^{17}$;

R^{17}, R^{18}, R^{19} and R^{20} 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

the structural elements $-NR^{17}R^{18}$ and $-NR^{19}R^{20}$ can independently form: heterocycloalkyl; aryl-heterocycloalkyl; or heteroaryl-heterocycloalkyl; or a group of one of the above formulae C1 to C8;

R^{31} is alkyl; alkenyl; $-(CR^1R^{15})_qNR^{17}R^{18}$; $-(CR^1R^{15})_qNR^2R^{16}$; $-(CR^1R^{15})_qNR^{17}COR^{18}$; $-(CH_2)_qC(=NR^{15})NR^{17}R^{18}$; $-(CR^1R^{15})_qNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CR^1R^{15})_qOR^{17}$; $-(CR^1R^{15})_qSR^{17}$; $-(CR^1R^{15})_qSO_2R^{17}$; $-(CR^1R^{15})_qNR^{17}SO_2R^{18}$; $-(CR^1R^{15})_qSO_2NR^2R^{16}$; $-(CR^1R^{15})_qSO_2NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mNR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mC(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nO(CH_2)_mNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mNR^{17}R^{18}$; $-(CH_2)_nS(CH_2)_mNR^{20}C(=NR^{19})NR^{17}R^{18}$; $-(CR^1R^{15})_qCONR^{17}R^{18}$; or $-(CR^1R^{15})_qCOR^{33}$;

s is 2-4

and pharmaceutically acceptable salts thereof.

3. Compounds according to claim 1 wherein

T^1 is ^{D}Pro; ^{D}Pip; ^{D}Tic; ^{D}Tiq; ^{D}Oic; ^{D}Azt; ^{D}Pro((3*R*)OH); ^{D}Pro((3*S*)OH); ^{D}Pro((3*R*)NH_2); ^{D}Pro((3*S*)NH_2); ^{D}Pro((4*R*)OH); ^{D}Pro((4*S*)OH); ^{D}Pro((4*R*)NH_2); ^{D}Pro((4*S*)NH_2); ^{D}Pro((4*S*)NHBz); or ^{D}Mor;

T^2 is Thr; *allo*Thr; Ser; hSer; Pro((3*R*)OH); Pro((3*S*)OH); Hyp(Bn); (4*S*)-Hyp(Bn); Pro((3*R*)NH_2); Pro((3*S*)NH_2); Pro((4*R*)NH_2); Pro((4*S*)NH_2); Pro((4*S*)F); Pro((4*S*)NHBz); or Mor; or

when T^1 is ^{D}Pro((3*R*)OH); ^{D}Pro((3*S*)OH); ^{D}Pro((3*R*)NH_2); ^{D}Pro((3*S*)NH_2); ^{D}Pro((4*R*)NH_2); ^{D}Pro((4*S*)NH_2); ^{D}Pro((4*S*)NHBz); or ^{D}Mor

then T^2 can in addition be

Pro; Pip; Tic; Tiq; Oic; or Azt;

P^1, P^3 and P^4 are independently

Ala; Arg; Asn; Asp; Cit; Cys; Glu; Gln; Gly; His; Ile; Leu; Lys; Met; Orn; Phe; Pro; Ser; Thr; Trp; Tyr; Val; Abu; Agb; Agp; Ala(*t*Bu); Ala(*c*Pr); Ala(2Furyl); Ala(3Furyl); Ala(Ppz); Ala(1Pyraz); Ala(2Quin); Ala(3Quin); Ala(4Quin); Ala(Tet); Azt; Bbta; Bip; Cha; Chg; Dab; Dab(Ac); Dab(*c*Pr); Dab(*i*Pr); Dab(4Me_2NPhSO_2); Dab(MeOEtNCO); Dab(MePpzCO); Dab(MeSO_2); Dab(morphCO); Dab(1Nal); Dab(2Nal); Dap; Dap($CONH_2$); Dap(MeOEt); Dap((MeOEt)$_2$); Deg; Gly(*t*Bu); hArg; hCha; hCys; hHis; hLys; hPhe; hSer; hSer(Me); hTrp; hTyr; His(Me); His(Bn); Hyp(Bn); (4*S*)-Hyp(Bn); Hyp(4BrBn); Hyp(3CNBn); Hyp(4CNBn); Hyp(CONHPh); Hyp(Ph); Lys(Ac); Lys(Bz); Lys(*c*Pr); Lys(*i*Pr); Lys(Me); Lys(Nic); Lys((5*R*)OH); Lys(4Oxa); Met(O_2); 1Nal; 2Nal; Nle; Nle(6OBn); OctG; Oic; Orn(*c*Pr); Orn(*i*Pr); 2Pal; 3Pal; 4Pal; Phe(2Cl); Phe(3Cl); Phe(4Cl); Phe(3,4Cl_2); Phe(2F); Phe(3F); Phe(4F); Phe(4CN); Phe(4CF_3); Phe(4COOMe); Phg; Pip; Pro((4*R*)Bn); Pro((4*S*)F); Pro((4*S*)*c*Hex); Pro(5,5Me_2); Ser(Bn); Ser(Me); Thi; *allo*Thr; Thr(Bn); Thz; Thz(5,5Me_2); Tic; Tic(7OH); Trp(7Aza); Trp(5Br); Trp(6Br); Trp(6CF_3); Trp(5Cl); Trp(6Cl); Trp(5,6Cl); Trp(5OH); Tyr(Bn); Tyr(Me); Tyr(4MeOCOBn); Tyr(Ph); Tyr(4OHPh); Tza; Gln(Alk1); Gln(Alk2); Gln(Alk3); 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); Glu(cN17); Lys(Ar1); Lys(Ar2); Lys(Ar3); Lys(Ar4); Lys(Ar5); Lys(Ar6); Lys(Ar7); Lys(Ar8); Lys(Ar9);

Lys(Ar10); Lys(Ar11); Lys(Ar12); Orn(Ar1); Orn(Ar2); Orn(Ar3); Orn(Ar4); Orn(Ar5); Orn(Ar6); Orn(Ar7); Orn(Ar8); Orn(Ar9); Orn(Ar10); Orn(Ar11); Orn(Ar12); Dab(Ar1); Dab(Ar2); Dab(Ar3); Dab(Ar4); Dab(Ar5); Dab(Ar6); Dab(Ar7); Dab(Ar8); Dab(Ar9); Dab(Ar10); Dab(Ar11); Dab(Ar12); Dab(S1); Dab(S2); Dab(S3); 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); 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); Orn(A1); Orn(A2); Orn(A3); Orn(A4); Orn(A5); Orn(A6); Orn(A7); Orn(A8); Orn(A9); Orn(A10); Orn(A11); Orn(A12); Orn(A13); Orn(A14); Orn(A15); Orn(A16); Orn(A17); Orn(A18); Orn(A19); Orn(A20); Orn(A21); Orn(A22); Orn(A23); Orn(A24); Orn(A25); Orn(A26); Orn(A27); Orn(A28); Orn(A29); Orn(A30); Orn(A31); Orn(A32); Orn(A33); Orn(A34); Orn(A35); Orn(A36); Orn(A37); Orn(A38); Orn(A39); Orn(A40); Orn(A41); Orn(A42); Orn(A43); Orn(A44); Orn(A45); Orn(A46); Orn(A47); Orn(A48); Orn(A49); Orn(A50); Orn(A51); Orn(A52); Orn(A53); Orn(A54); Orn(A55); Orn(A56); 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); 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); Dap(Ar1); Dap(Ar2);

Dap(Ar3); Dap(Ar4); Dap(Ar5); Dap(Ar6); Dap(Ar7); Dap(Ar8); Dap(Ar9); Dap(Ar10); Dap(Ar11); Dap(Ar12); 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); 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); Dap(A51); Dap(A52); Dap(A53); Dap(A54); or Dap(A55);

P^2 is ^{D}Arg; ^{D}hArg; ^{D}Agb; ^{D}Lys; ^{D}Orn; ^{D}Cit; ^{D}Thr; ^{D}Dab; ^{D}Dab; ^{D}Phe; ^{D}Phe($4CF_3$); ^{D}Trp; ^{D}His; ^{D}Tyr; ^{D}2Pal; ^{D}3Pal; ^{D}4Pal; ^{D}Lys(Ar1); ^{D}Lys(Ar2); ^{D}Lys(Ar3); ^{D}Lys(Ar4); ^{D}Lys(Ar5); ^{D}Lys(Ar6); ^{D}Lys(Ar7); ^{D}Lys(Ar8); ^{D}Lys(Ar9); ^{D}Lys(Ar10); ^{D}Lys(Ar11); ^{D}Lys(Ar12); ^{D}Orn(A41); ^{D}Orn(A56); ^{D}Orn(Ar1); ^{D}Orn(Ar2); ^{D}Orn(Ar3); ^{D}Orn(Ar4); ^{D}Orn(Ar5); ^{D}Orn(Ar6); ^{D}Orn(Ar7); ^{D}Orn(Ar8); ^{D}Orn(Ar9); ^{D}Orn(Ar10); ^{D}Orn(Ar11); ^{D}Orn(Ar12); ^{D}Dab(Ar1); ^{D}Dab(Ar2); ^{D}Dab(Ar3); ^{D}Dab(Ar4); ^{D}Dab(Ar5); ^{D}Dab(Ar6); ^{D}Dab(Ar7); ^{D}Dab(Ar8); ^{D}Dab(Ar9); ^{D}Dab(Ar10); ^{D}Dab(Ar11); ^{D}Dab(Ar12); ^{D}Dap(Ar1); ^{D}Dap(Ar2); ^{D}Dap(Ar3); ^{D}Dap(Ar4); ^{D}Dap(Ar5); ^{D}Dap(Ar6); ^{D}Dap(Ar7); ^{D}Dap(Ar8); ^{D}Dap(Ar9); ^{D}Dap(Ar10); ^{D}Dap(Ar11); or ^{D}Dap(Ar12);

and pharmaceutically acceptable salts thereof.

4. Compounds according to claim 1 wherein

T^1 is ^{D}Pro; ^{D}Pip; ^{D}Tic; ^{D}Tiq; ^{D}Oic; ^{D}Azt; ^{D}Pro((3*R*)OH); ^{D}Pro((3*S*)OH); ^{D}Pro((3*R*)NH_2); ^{D}Pro((3*S*)NH_2); ^{D}Pro((4*R*)OH); ^{D}Pro((4*S*)OH); ^{D}Pro((4*R*)NH_2); ^{D}Pro((4*S*)NH_2); ^{D}Pro((4*S*)NHBz); or ^{D}Mor;

T^2 is Thr; *allo*Thr; Ser; hSer; Pro((3*R*)OH); Pro((3*S*)OH); Hyp(Bn); (4*S*)-Hyp(Bn); Pro((3*R*)NH_2); Pro((3*S*)NH_2); Pro((4*R*)NH_2); Pro((4*S*)NH_2); Pro((4*S*)F); Pro((4*S*)NHBz); or Mor; or

when T^1 is ^{D}Pro((3*R*)OH); ^{D}Pro((3*S*)OH); ^{D}Pro((3*R*)NH_2); ^{D}Pro((3*S*)NH_2); ^{D}Pro((4*R*)NH_2); ^{D}Pro((4*S*)NH_2); ^{D}Pro((4*S*)NHBz); or ^{D}Mor

then T^2 can in addition be

Pro; Pip; Tic; Tiq; Oic; or Azt;

P^1 is Ile; Nle; Leu; Val; Chg; Cha; Abu; Ala; Ala(*c*Pr); Ala(1Pyraz); Ala(Tet); Trp; 1Nal; 2Nal; Phe; Tyr; 2Pal; 3Pal; 4Pal; Thr; His; Arg; hArg; Agb; Pip; Orn(Ar2); or Orn(A56);

P^2 is ^{D}Arg; ^{D}hArg; ^{D}Agb; ^{D}Lys; ^{D}Orn; ^{D}Cit; ^{D}Thr; ^{D}Dab; ^{D}Dap; ^{D}Phe; ^{D}Trp; ^{D}His; ^{D}Tyr; ^{D}2Pal; ^{D}3Pal; or ^{D}4Pal;

P^3 is Arg; hArg; Agb; Agp; Lys; Orn; Orn(A41); Orn(A56); Orn(Ar2); Orn(Ar4); Orn(Ar7); Cit; Thr; Dab; Dap; Phe; Trp; His; Tyr; or Ile

P^4 is Trp; His; Phe; Phe(4CF_3); 1Nal; 2Nal; Tyr; Leu; Ile; Arg; hArg; Lys; Dab; Dap; Orn; Orn(A56); or Orn(Ar7);

and pharmaceutically acceptable salts thereof.

5. Compounds according to claim 1 wherein

T^1 is ^{D}Pro; ^{D}Pip; ^{D}Tic; ^{D}Pro((4*S*)OH); ^{D}Pro((4*R*)NH_2); or ^{D}Pro((4*S*)NH_2);

T^2 is Thr; *allo*Thr; Ser; hSer; Pro((3*S*)OH); (4*S*)-Hyp(Bn); Pro((4*R*)NH_2); Pro((4*S*)NH_2); Pro((4*S*)F); Pro((4*S*)NHBz); or Mor;

P^1 is Ile; Nle; Leu; Val; Chg; Cha; Abu; Ala; Trp; 1Nal; Tyr; 3Pal; Thr; His; Arg; hArg; Agb; Pip; Ala(1Pyraz); Ala(Tet); Orn(Ar2); or Orn(A56);

P^2 is ^{D}Arg; ^{D}Lys; ^{D}Orn; ^{D}Cit; ^{D}Thr; ^{D}Dab; ^{D}Phe; ^{D}Trp; ^{D}His; or ^{D}3Pal;

P^3 is Arg; hArg; Agb; Agp; Lys; Orn; Orn(A41); Orn(A56); Orn(Ar2); Orn(Ar4); Orn(Ar7); Dab; Trp; or His;

P^4 is Trp; His; Phe; Phe($4CF_3$); 1Nal; 2Nal; Tyr; Ile; Arg; hArg; Lys; Dab; Orn; Orn(A56); or Orn(Ar7);

and pharmaceutically acceptable salts thereof.

6. Compounds according claim 1 selected from

cyclo(-Ile-^{D}Arg-Arg-Ile-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Tyr-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Lys-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Dab-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Dab-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Phe-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Thr-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro-hSer-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro-*allo*Thr-);

cyclo(-1Nal-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Lys-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}His-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Cit-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pip-Thr-);

cyclo(-Ile-^{D}Arg-Arg-2Nal-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-1Nal-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Trp-Arg-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Thr-^{D}Arg-Trp-Arg-^{D}Pro-Thr-);

cyclo(-Trp-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro-Pro((3*S*)OH)-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro-Ser-);

cyclo(-Ile-^{D}Arg-Agp-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Agb-Trp-^{D}Pro-Thr-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro((4*S*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Ala-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Tyr-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Orn-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Dab-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Lys-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-His-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Arg-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Pip-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-hArg-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Agb-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-3Pal-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}3Pal-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Arg-^{D}Phe-Trp-hArg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Arg-^{D}Phe-Trp-Arg-^{D}Pro((4*S*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Oic-);

cyclo(-Arg-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Oic-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro-Pro((4*S*)F)-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro-Pro((4*S*)NH_2)-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro-Pro((4*R*)NH_2)-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro-Mor-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro-Mor-);

cyclo(-Arg-^{D}Phe-Trp-Arg-^{D}Pro-(4*S*)-Hyp(Bn)-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro((4*S*)OH)-(4*S*)-Hyp(Bn)-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-(4*S*)-Hyp(Bn)-);

cyclo(-His-^{D}Trp-His-Trp-^{D}Pro- Pro((4*S*)NHBz)-);

cyclo(-1Nal-^{D}Arg-Arg-Trp-^{D}Pro-Pro((3*S*)OH)-);

cyclo(-Ile-^{D}Arg-Arg-2Nal-^{D}Pro-Pro((3*S*)OH)-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pip-Pro((3*S*)OH)-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro((4*S*)OH)-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro((4*R*)NH_2)-Thr-);

cyclo(-Val-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Abu-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Chg-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Leu-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Nle-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Cha-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Orn-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Orn(A41)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Orn-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-hArg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Tic-Thr-);

cyclo(-Ile-^{D}Arg-Orn(Ar2)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Orn(Ar7)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Orn(Ar4)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Orn(A56)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Phe(4CF_3)-^{D}Pro-Thr-);

cyclo(-Trp-^{D}Phe-Trp-Orn(A56)-^{D}Pip-Pro((3*S*)OH)-);

cyclo(-Ala(1Pyraz)-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Ala(Tet)-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Orn(Ar2)-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Orn(A56)-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Orn(Ar7)-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Orn(A56)-^{D}Pro((4*R*)NH_2)-Tiq-);

cyclo(-Trp-^{D}Phe-Trp-Orn(A56)-^{D}Pro((4*R*)NH_2)-Tic-);

and pharmaceutically acceptable salts thereof.

7. Compounds according claim 6 selected from

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pip-Thr-);

cyclo(-Ile-^{D}Arg-Arg-2Nal-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pro-Ser-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Dab-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-3Pal-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Oic-);

cyclo(-Trp-^{D}Phe-Trp-Arg-^{D}Pro((4*S*)OH)-(4*S*)-Hyp(Bn)-);

cyclo(-Ile-^{D}Arg-Arg-Trp-^{D}Pip-Pro((3*S*)OH)-);

cyclo(-Chg-^{D}Arg-Arg-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-hArg-Trp-^{D}Pro-Thr-);

and pharmaceutically acceptable salts thereof.

8. Compounds according claim 6 selected from

cyclo(-Ile-^{D}Arg-Orn(Ar2)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Orn(Ar7)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Orn(Ar4)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Orn(A56)-Trp-^{D}Pro-Thr-);

cyclo(-Ile-^{D}Arg-Arg-Phe(4CF_3)-^{D}Pro-Thr-);

cyclo(-Trp-^{D}Phe-Trp-Orn(A56)-^{D}Pip-Pro((3*S*)OH)-);

cyclo(-Ala(1Pyraz)-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Ala(Tet)-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Orn(Ar2)-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Orn(Ar56)-^{D}Phe-Trp-Arg-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Orn(Ar7)-^{D}Pro((4*R*)NH_2)-Tic-);

cyclo(-Trp-^{D}Phe-Trp-Orn(A56)-^{D}Pro((4*R*)NH_2)-Tiq-);

cyclo(-Trp-^{D}Phe-Trp-Orn(A56)-^{D}Pro((4*R*)NH_2)-Tic-);

and pharmaceutically acceptable salts thereof.

9. Epimers and diastereomers of the compounds of formula **(I)** as defined in claim 1 based on one or more chiral center not explicitly specified in formula **(I)**.

10. Compounds according to any one of claims 1 to 9 for use as therapeutically active substances, especially for use as therapeutically active substances against diseases or conditions mediated or sustained through the activity of CXCR7.

11. Compounds according any one of claims 1 to 9 having modulating activity against the CXCR7 receptor, especially interfering selectively with the natural activity of the CXCR7 receptor and its natural ligands CXCL11 and/or CXCL12.

12. A pharmaceutical composition containing a compound or a mixture of compounds according to any one of claims 1 to 9 and a pharmaceutically inert carrier.

13. Compositions according to claim 12 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 suppositories.

14. The use of compounds according to any one of claims 1 to 9 for the manufacture of a medicament as the sole active pharmaceutical ingredient or in combination with other active pharmaceutical ingredients.

15. The use of compounds according to any one of claims 1 to 9 for the manufacture of a medicament for the treatment, prevention or the supportive treatment of diseases or conditions related to the activity of CXCR7 in the area of dermatological disorders, metabolic diseases, inflammatory diseases, fibrotic diseases, infectious diseases, neurological diseases, cardiovascular diseases, respiratory diseases, gastro-intestinal tract disorders, urological diseases, ophthalmic diseases,

stomatological diseases, haematological diseases and oncology, or the mobilisation of stem cells,

especially for the manufacture of a medicament for the treatment, prevention or the supportive treatment of diseases or conditions such as HIV infections, Epstein-Barr Virus infection; diabetes mellitus (Type I and/or Type II); conjunctivitis, scleritis, uveitis, rhinosinusitis, Whim syndrome, lupus erythematosus, osteoarthritis, rheumatoid arthritis, synovitis, psoriasis, multiple sclerosis, Crohns disease, inflammatory bowel disease, mixed connective tissue disease, chronic lymphocytic thyroiditis, Graves' disease, graft-versus-host disease, Sjögren's syndrome; dry eye syndrome, glaucoma, age-related macular degeneration; pulmonary arterial hypertension, pulmonary hypoxia, atherosclerosis, myocarditis, heart failure, such as myocardial infarction, arterial thrombosis, stroke, angiogenesis; chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, asthma; sarcoma, such as osteosarcoma, rhabdomyosarcoma, Kaposi's sarcoma, synovial sarcoma; lipoma, such as angiolipoma; glioblastoma multiforme, astrocytomas, neuroblastoma; carcinoma, such as adenocarcinoma; malignant epithelial and mucoepidermoid neoplasms, thyroid neoplasm, gonadal neoplasms, prostate cancer, breast cancer, melanoma, lung carcinoma, pancreatic carcinoma, colorectal cancer; solid tumors; lymphoma, such as Birkitt's lymphoma, Hodgkin's lymphoma, non-Hodgkin's lymphoma; multiple myeloma and leukemia; metastasis; for the inhibition of neointima formation; for stem cell mobilisation of peripheral blood stem cells and/or mesenchymal stem cells; for the mobilisation of endothelial or neuronal progenitor cells; or for different kinds of tissue-repair in human or other mammals.

16. A process for the preparation of compounds according to any one of claims 1 to 9, which comprises

(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 T^1 or T^2 or P^1 to P^4 as defined above; any functional group which may

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 of the next element (T or P), following counterclockwise or clockwise the sequence according general formula **(I)** in –COOH to $–NH_2$ 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;

(f) if desired, selectively deprotecting one or several protected functional group(s) present in the molecule and appropriately substituting 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; and/or

(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.