Carboxamide compounds and their use as calpain inhibitors

Description

The present invention relates to novel carboxamide compounds and their use for the manufacture of a medicament. The carboxamide compounds are inhibitors of calpain (calcium dependant cysteine proteases). The invention therefore also relates to the use of these carboxamide compounds for treating a disorder associated with an elevated calpain activity.

Calpains are intracellular, proteolytic enzymes from the cysteine protease group and are found in many cells. The enzyme calpain is activated by elevated calcium concentration, with a distinction being made between calpain I or μ-calpain, which is activated by μ-molar concentrations of calcium ions, and calpain II or m-calpain, which is activated by m-molar concentrations of calcium ions. Currently, further calpain isoenzymes are also postulated (M.E. Saez et al.; Drug Discovery Today 2006, 11 (19/20), pp. 917-923; K. Suzuki et al., Biol. Chem. Hoppe-Seyler, 1995, 376 (9), pp.523-9).

Calpains play an important role in various physiological processes. These processes include the cleavage of different regulatory proteins such as protein kinase C, cytoskeletal proteins such as MAP 2 and spectrin, and muscle proteins, protein degradation in rheumatoid arthritis, proteins in the activation of platelets, neuropeptide metabolism, proteins in mitosis, and others which are listed in: M.J.Barrett et al., Life Sci. 1991, 48, pp.1659-69; K. Wang et al., Trends in Pharmacol.Sci. 1994, 15, pp. 412-419.

Elevated calpain levels have been measured in various pathophysiological processes, for example: ischemias of the heart (e.g. myocardial infarction), the kidney or the central nervous system (e.g. stroke), inflammations, muscular dystrophies, cataracts of the eyes, diabetes, HIV disorders, injuries to the central nervous system (e.g. brain trauma), Alzheimer's, Huntington's, Parkinson's diseases, multiple sclerosis etc. (see K.K. Wang, above). It is assumed that there is a connection between these diseases and generally or persistently elevated intracellular calcium levels. This results in calcium-dependent processes becoming hyperactivated and no longer being subject to normal physiological control. A corresponding hyperactivation of calpains can also trigger pathophysiological processes.

For this reason, it was postulated that inhibitors of calpain could be of use for treating these diseases. This postulate was confirmed by a variety of investigations. Thus, Seung-Chyul Hong et al., Stroke 1994, 25 (3), pp. 663-669, and R. T. Bartus et al., Neurological Res. 1995, 17, pp. 249-258, have demonstrated that calpain inhibitors

have a neuroprotective effect in acute neurodegenerative impairments or ischemias such as occur after cerebral stroke. K. E. Saatman et al., Proc. Natl. Acad. Sci. USA, 1996, 93, pp. 3428-3433 describe that following experimental brain traumas, calpain inhibitors also improved recovery from the memory performance deficits and neuromotor impairments. C. L. Edelstein et al., Proc. Natl. Acad. Sci. USA, 1995, 92, pp. 7662-6, found that calpain inhibitors have a protective effect on hypoxia-damaged kidneys. Yoshida, Ken Ischi et al., Jap. Circ. J. 1995, 59 (1), pp. 40-48, pointed out that calpain inhibitors had favorable effects following cardiac damage which was produced by ischemia or reperfusion.

It has been shown in recent years that both the function and the metabolism of a number of important proteins involved in the development of Alzheimer's disease are modulated by calpain. Various external influences such as, for example, excitotoxins, oxidative stress or else the action of amyloid protein lead to hyperactivation of calpain in the nerve cell, causing, as cascade, a dysregulation of the CNS-specific kinase cdk5 and subsequently a hyperphosphorylation of the so-called tau protein. Whereas the actual task of the tau protein consists of stabilizing the microtubules and thus the cytoskeleton, phosphorylated tau is no longer able to fulfil this function; the cytoskeleton collapses, axonal transport of matter is impaired and thus eventually the nerve cell degenerates (G. Patrick et al., Nature 1999, 402, pp. 615-622; E. A. Monaco et al.; Curr. Alzheimer Res. 2004, 1 (1), pp. 33-38). Accumulation of phosphorylated tau additionally leads to the formation of so-called neurofibrillary tangles (NFTs) which, together with the well-known amyloid plaques, represent an important feature of Alzheimer's disease. Similar changes in the tau protein, generally referred to as tauopathies are also observed in other (neuro)degenerative disorders such as, for example, following stroke, inflammations of the brain, Parkinsonism, in normal-pressure hydrocephalus and Creutzfeldt-Jakob disease.

It has been possible to demonstrate the involvement of calpain in neurodegenerative processes in transgenic mice with the aid of appropriate inhibitors (Higuchi et al.; J. Biol. Chem. 2005, 280 (15), pp. 15229-15237). It was possible with the aid of a calpain inhibitor to reduce markedly the clinical signs of acute autoimmune encephalomyelitis in a mouse model of multiple sclerosis (F. Mokhtarian et al.; J. Neuroimmunology 2006, Vol. 180, pp. 135-146). It has further been shown that calpain inhibitors on the one hand block the Aß-induced degeneration of neurons (Park et al.; J. Neurosci. 2005, 25, pp. 5365-5375), and in addition reduce the release of the β-amyloid precursor protein (β APP) (J. Higaki et al., Neuron, 1995, 14, pp. 651-659). With this background, calpain inhibitors having sufficient CNS availability represent a novel therapeutic principle for the treatment of neurodegenerative disorders in general and in particular also of Alzheimer's disease.

The release of interleukin-lα is likewise inhibited by calpain inhibitors (N. Watanabe et

al., Cytokine 1994, 6(6), pp. 597-601). It has additionally been found that calpain inhibitors show cytotoxic effects on tumor cells (E. Shiba et al. 20th Meeting Int. Ass. Breast Cancer Res., Sendai Jp, 1994, 25.-28.Sept., Int. J. Oncol. S(Suppl.), 1994, 381).

The involvement of calpain in HIV disorders has only recently been shown. Thus, it has been demonstrated that the HIV-induced neurotoxicity is mediated by calpain (O´Donnell et al.; J. Neurosci. 2006, 26 (3), pp. 981-990). Calpain involvement in the replication of the HIV virus has also been shown (Teranishi et al.; Biochem. Biophys. Res. Comm. 2003, 303 (3), pp. 940-946).

Recent investigations indicate that calpain plays a part in so-called nociception, the perception of pain. Calpain inhibitors showed a distinctly beneficial effect in various preclinically relevant models of pain, e.g. in the thermally induced hyperalgesia in rats (Kunz et al.; Pain 2004, 110, pp.409-418), in Taxol-induced neuropathy (Wang et al.; Brain 2004, 127, pp.671-679) and in acute and chronic inflammatory processes (Cuzzocrea et al.; American Journal of Pathololgy 2000, 157 (6), pp. 2065-2079).

Further possible applications of calpain inhibitors are detailed in: M.E. Saez et al.; Drug Discovery Today 2006, 11 (19/20), pp. 917-923; N. O. Carragher, Curr. Pharm. Design 2006, 12, pp. 615-638; K. K. Wang et al.; Drugs of the Future 1998, 23 (7), pp. 741-749; and Trends in Pharmacol.Sci., 1994, 15, pp. 412-419.

With the calpain inhibitors described to date a general distinction is made between irreversible and reversible inhibitors, and peptide and non-peptide inhibitors.

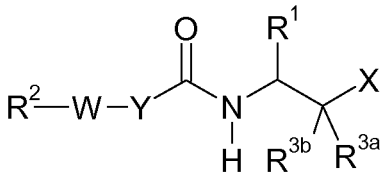
Irreversible inhibitors are usually alkylating substances. They have the disadvantage that they firstly react unselectively and/or are unstable in the body. Thus, corresponding inhibitors often show unwanted side effects such as toxicity, and application thereof is therefore markedly restricted. The irreversible inhibitors include for example epoxides such as E64, α-halo ketones, and disulfides.

A large number of known reversible calpain inhibitors are peptide aldehydes which are derived in particular from di- or tripeptides such as, for example, Z-Val-Phe-H (MDL 28170). Derivatives and prodrugs structurally derived from aldehydes are also described, especially corresponding acetals and hemiacetals (e.g. hydroxytetrahydro-furans, hydroxyoxazolindines, hydroxymorpholines and the like), but also imines or hydrazones. However, under physiological conditions, peptide aldehydes and related compounds usually have the disadvantage that, owing to their reactivity, they are frequently unstable, are rapidly metabolized and are prone to unspecific reactions which may likewise cause toxic effects (J. A. Fehrentz and B.Castro, Synthesis 1983, pp. 676-78).

In recent years, a number of non-peptide carboxamides having a β-keto function in the amine moiety and inhibiting calpain have been described. Thus, WO-98/16512 describes 3-amino-2-oxo carboxylic acid derivatives whose amino group is amidated with a 4-piperidinecarboxylic acid compound. WO-99/17775 describes similar compounds which are amidated with a quinolinecarboxylic acid. WO-98/25883, WO-98/25899 and WO-99/54294 describe 3-amino-2-oxo carboxylic acid derivatives whose amino group is amidated with a substituted benzoic acid. WO-99/61423 describes 3-amino-2-oxo carboxylic acid derivatives whose amino group is amidated with an aromatic carboxylic acid carrying a tetrahydroquinoline/isoquinoline and 2,3-dihydroindole/isoindole residue. Similar compounds in which the aromatic carboxylic acid residue carries a heterocyloalkyl radical or (hetero)aryl radical which is optionally connected via a linker are described in WO-99/54320, WO-99/54310, WO-99/54304 and WO-99/54305. WO-99/54293 describes benzamides of 4-amino-3-oxo carboxylic acid derivatives. WO-03/080182 describes the use of the aforementioned amides for the treatment of pulmonary diseases. The nonpeptide calpain inhibitors mentioned therein also have a number of disadvantages, in particular a low or absent selectivity in respect of related cysteine proteases, such as various cathepsins, likewise possibly leading to unwanted side effects.

The present invention is thus based on the object of providing compounds which inhibit, in particular selectively, calpain even at low serum concentrations. The compounds were intended in particular to display a high selectivity in relation to the inhibition of calpain, i.e. inhibit other cystein proteases, e.g. cathepsin, not at all or only at higher concentrations.

This object and further objects are achieved by the carboxamide compounds of the general formula I described below, the pharmaceutically suitable salts, the prodrugs and the tautomers thereof:



I

in which

R^1 is hydrogen, C_1-C_{10}-alkyl, C_2-C_{10}-alkenyl, C_2-C_{10}-alkynyl, where the last 3 radicals mentioned may be partly or completely halogenated and/or have 1, 2 or 3 substituents R^{1a},
C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, where a CH_2 group in the cycloalkyl moiety of the last two radicals mentioned may be replaced by O, NH,

or S, or two adjacent C atoms may form a double bond, where the cycloalkyl moiety may further have 1, 2, 3 or 4 radicals R^{1b},
aryl, hetaryl, aryl-C_1-C_6-alkyl, aryl-C_2-C_6-alkenyl, hetaryl-C_1-C_4-alkyl or hetaryl-C_2-C_6-alkenyl, where aryl and hetaryl in the last 6 radicals mentioned may be unsubstituted or carry 1, 2, 3 or 4 identical or different radicals R^{1c}; where

R^{1a} is selected independently of one another from OH, SH, COOH, CN, OCH_2COOH, C_1-C_6-alkoxy, C_1-C_6-halolkoxy, C_3-C_7-cycloalkyloxy, C_1-C_6-alkylthio, C_1-C_6-haloalkylthio, $COOR^{a1}$, $CONR^{a2}R^{a3}$, $SO_2NR^{a2}R^{a3}$, $-NR^{a2}$-SO_2-R^{a4}, NR^{a2}-CO-R^{a5}, SO_2-R^{a4}, $NR^{a6}R^{a7}$,

R^{1b} is selected independently of one another from OH, SH, COOH, CN, OCH_2COOH, halogen, phenyl which optionally has 1, 2 or 3 substituents R^{1d}, or C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-alkylthio, where the alkyl moieties in the last 3 substituents mentioned may be partly or completely halogenated and/or have 1, 2 or 3 substituents R^{1a},
$COOR^{b1}$, $CONR^{b2}R^{b3}$, $SO_2NR^{b2}R^{b3}$, NR^{b2}-SO_2-R^{b4}, NR^{b2}-CO-R^{b5}, SO_2-R^{b4}, $NR^{b6}R^{b7}$,
in addition two R^{1b} radicals may together form a C_1-C_4-alkylene group, or 2 R^{1b} radicals bonded to adjacent C atoms of cycloalkyl may form together with the carbon atoms to which they are bonded also a benzene ring,

R^{1c} is selected independently of one another from OH, SH, halogen, NO_2, NH_2, CN, CF_3, CHF_2, CH_2F, O-CF_3, O-CHF_2, O-CH_2F, COOH, OCH_2COOH, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-alkoxy-C_1-C_4-alkyl, C_1-C_6-alkylthio, where the alkyl moieties in the last 4 substituents mentioned may be partly or completely halogenated and/or have 1, 2 or 3 substituents R^{1a},
C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-cycloalkyloxy, where the cycloalkyl moiety of the last three radicals mentioned may have 1, 2, 3 or 4 R^{1b} radicals,
aryl, hetaryl, O-aryl, O-CH_2-aryl, where the last three radicals mentioned are unsubstituted in the aryl moiety or may carry 1, 2, 3 or 4 R^{1d} radicals,
$COOR^{c1}$, $CONR^{c2}R^{c3}$, $SO_2NR^{c2}R^{c3}$, NR^{c2}-SO_2-R^{c4},
NR^{c2}-CO-R^{c5}, SO_2-R^{c4},
$-(CH_2)_p$-$NR^{c6}R^{c7}$ with p = 0, 1, 2, 3, 4, 5 or 6 and
O-$(CH_2)_q$-$NR^{c6}R^{c7}$ with q = 2, 3, 4, 5 or 6; where

R^{a1}, R^{b1} and R^{c1} are independently of one another H, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{1a}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, aryl, aryl-C_1-C_4-alkyl, hetaryl or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{1d},

R^{a2}, R^{b2} and R^{c2} are independently of one another H, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{1a}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, aryl, aryl-C_1-C_4-alkyl, hetaryl or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{1d}, and

R^{a3}, R^{b3} and R^{c3} are independently of one another H, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{1a}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, aryl, aryl-C_1-C_4-alkyl, hetaryl or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{1d}, or
the two radicals R^{a2} and R^{a3}, or R^{b2} and R^{b3} or R^{c2} and R^{c3} form together with the N atom a 3 to 7-membered, optionally substituted nitrogen heterocycle which may optionally have 1, 2 or 3 further different or identical heteroatoms from the group of O, N, S as ring members,

R^{a4}, R^{b4} and R^{c4} are independently of one another C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{1a}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, aryl, aryl-C_1-C_4-alkyl, hetaryl or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{1d}, and

R^{a5}, R^{b5} and R^{c5} have independently of one another one of the meanings mentioned for R^{a1}, R^{b1} and R^{c1};

R^{a6}, R^{b6} and R^{c6} are independently of one another H, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{1a}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, CO-C_1-C_6-alkyl, CO-O-C_1-C_6-alkyl, SO_2-C_1-C_6-alkyl, aryl, hetaryl,

O-aryl, OCH_2-aryl, aryl-C_1-C_4-alkyl, hetaryl-C_1-C_4-alkyl, CO-aryl, CO-hetaryl, CO-(aryl-C_1-C_4-alkyl), CO-(hetaryl-C_1-C_4-alkyl), CO-O-aryl, CO-O-hetaryl, CO-O-(aryl-C_1-C_4-alkyl), CO-O-(hetaryl-C_1-C_4-alkyl), SO_2-aryl, SO_2-hetaryl, SO_2-(aryl-C_1-C_4-alkyl) or SO_2-(hetaryl-C_1-C_4-alkyl), where aryl and hetaryl in the last 18 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{1d}, and

R^{a7}, R^{b7} and R^{c7} are independently of one another H, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{1a}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, aryl, aryl-C_1-C_4-alkyl, hetaryl or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{1d}, or
the two radicals R^{a6} and R^{a7}, or R^{b6} and R^{b7} or R^{c6} and R^{c7} form together with the N atom a 3 to 7-membered, optionally substituted nitrogen heterocycle which may optionally have 1, 2 or 3 further different or identical heteroatoms from the group of O, N and S as ring members,
or two radicals R^{1b} and R^{1c} bonded to adjacent C atoms form together with the C atoms to which they are bonded a 4, 5, 6 or 7-membered, optionally substituted carbocycle or an optionally substituted heterocycle which has 1, 2 or 3 different or identical heteroatoms from the group of O, N and S as ring members;

R^{1d} is selected from halogen, OH, SH, NO_2, COOH, $C(O)NH_2$, CHO, CN, NH_2, OCH_2COOH, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_1-C_6-alkylthio, C_1-C_6-haloalkylthio, CO-C_1-C_6-alkyl, CO-O-C_1-C_6-alkyl, NH-C_1-C_6-alkyl, NHCHO, NH-C(O)C_1-C_6-alkyl, and SO_2-C_1-C_6-alkyl;

R^2 is hydrogen, C_1-C_{10}-alkyl, C_1-C_{10}-alkoxy, C_2-C_{10}-alkenyl, C_2-C_{10}-alkynyl, where the last 4 radicals mentioned may be partly or completely halogenated and/or have 1, 2 or 3 substituents R^{2a},

C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, where a CH_2 group in the cycloalkyl moiety of the last two radicals mentioned may be replaced by O, NH, or S, or two adjacent C atoms may form a double bond, where the cycloalkyl moiety may additionally have 1, 2, 3 or 4 R^{2b} radicals;
aryl, O-aryl, O-CH_2-aryl, hetaryl, aryl-C_1-C_6-alkyl, aryl-C_2-C_6-alkenyl, hetaryl-C_1-C_4-alkyl or hetaryl-C_2-C_6-alkenyl, where aryl and hetaryl in the last 8 radicals mentioned may be unsubstituted or carry 1, 2, 3 or 4 identical or different R^{2c} radicals; where

R^{2a} has one of the meanings indicated for R^{1a},
R^{2b} has one of the meanings indicated for R^{1b}, and
R^{2c} has one of the meanings indicated for R^{1c};

R^{3a} and R^{3b} are independently of one another hydroxy or C_1-C_4-alkoxy, or together with the carbon atom to which they are bonded are C=O;

X is hydrogen or a radical of the formulae C(=O)-O-R^{x1}, C(=O)-$NR^{x2}R^{x3}$, C(=O)-N(R^{x4})-(C_1-C_6-alkylene)-$NR^{x2}R^{x3}$ or C(=O)-N(R^{x4})$NR^{x2}R^{x3}$, in which

R^{x1} is hydrogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{xa}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, where alkyl, alkenyl, alkoxy, alkynyl, cycloalkyl, heterocycloalkyl in the last 6 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xa}, or aryl, aryl-C_1-C_4-alkyl, hetaryl or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xd},

R^{x2} is H, OH, CN, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{xa}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, CO-C_1-C_6-alkyl, CO-O-C_1-C_6-alkyl, SO_2-C_1-C_6-alkyl, O-C_1-C_6-alkyl, where alkyl, alkoxy, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl in the last 10 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xa},
aryl, O-aryl, O-CH_2-aryl, hetaryl, O-CH_2-hetaryl, aryl-C_1-C_4-alkyl, hetaryl-C_1-C_4-alkyl, CO-aryl, CO-hetaryl, CO-(aryl-C_1-C_4-alkyl), CO-(hetaryl-C_1-C_4-alkyl), CO-O-aryl, CO-O-hetaryl, CO-O-(aryl-C_1-C_4-alkyl), CO-O-(hetaryl-C_1-C_4-alkyl), SO_2-aryl, SO_2-hetaryl, SO_2-(aryl-C_1-C_4-alkyl) or SO_2-(hetaryl-C_1-C_4-alkyl), where aryl and hetaryl in the last 19 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xd}, and

R^{x3} is H, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{xa}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, where alkyl, alkenyl, alkoxy, alkynyl, cycloalkyl, heterocycloalkyl in the last 6 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xa},
aryl, aryl-C_1-C_4-alkyl, hetaryl or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xd}, or
the two radicals R^{x2} and R^{x3} form together with the N atom a 3 to 7-membered nitrogen heterocycle which may optionally have 1, 2 or 3 further different or identical heteroatoms from the group of O, N, S as ring members, and which may have 1, 2 or 3 substituents R^{xb},

R^{x4} is H, OH, CN, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{xa}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, CO-C_1-C_6-alkyl, CO-O-C_1-C_6-alkyl, SO_2-C_1-C_6-alkyl, where

alkyl, alkenyl, alkoxy, alkynyl, cycloalkyl, heterocycloalkyl in the last 9 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xa}, aryl, O-aryl, O-CH_2-aryl, hetaryl, aryl-C_1-C_4-alkyl, hetaryl-C_1-C_4-alkyl, CO-aryl, CO-hetaryl, CO-(aryl-C_1-C_4-alkyl), CO-(hetaryl-C_1-C_4-alkyl), CO-O-aryl, CO-O-hetaryl, CO-O-(aryl-C_1-C_4-alkyl), CO-O-(hetaryl-C_1-C_4-alkyl), SO_2-aryl, SO_2-hetaryl, SO_2-(aryl-C_1-C_4-alkyl) or SO_2-(hetaryl-C_1-C_4-alkyl), where aryl and hetaryl in the last 18 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xd}, and

where R^{xa} has one of the meanings indicated for R^{1a}, R^{xb} has one of the meanings indicated for R^{1b}, and R^{xd} has one of the meanings indicated for R^{1d};

Y is a divalent, aromatic or 6-membered heteroaromatic radical which has 1 or 2 nitrogen atoms as ring members and which optionally has 1 or 2 identical or different substituents R^y:

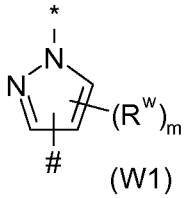
R^y is selected independently of one another from OH, SH, halogen, NO_2, NH_2, CN, CF_3, CHF_2, CH_2F, O-CF_3, O-CHF_2, O-CH_2F, COOH, OCH_2COOH, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-alkoxy-C_1-C_4-alkyl, C_1-C_6-alkylthio, where the last 4 radicals mentioned may be partly or completely halogenated and/or have 1, 2 or 3 substituents R^{ya},
C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-cycloalkyl-O, where the cycloalkyl moiety in the last three radicals mentioned may have 1, 2, 3 or 4 R^{yb} radicals,
aryl, O-aryl, CH_2-aryl, O-CH_2-aryl, where the last 4 radicals mentioned are unsubstituted in the aryl moiety or may carry 1, 2, 3 or 4 radicals R^{yd},
$COOR^{y1}$, $CONR^{y2}R^{y3}$, $SO_2NR^{y2}R^{y3}$, -NH-SO_2-R^{y4},
NH-CO-R^{y5}, SO_2-R^{y4},
-$(CH_2)_p$-$NR^{y6}R^{y7}$ with p = 0, 1, 2, 3, 4, 5 or 6 and
O-$(CH_2)_q$-$NR^{y6}R^{y7}$ with q = 2, 3, 4, 5 or 6;

or two R^y radicals bonded to adjacent C atoms form together with the C atoms to which they are bonded a 4, 5, 6 or 7-membered, optionally substituted carbocycle or an optionally substituted heterocycle which has 1, 2 or 3 different or identical heteroatoms from the group of O, N, S as ring members, where

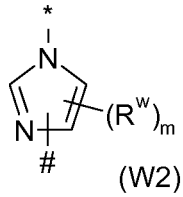
R^{ya} has one of the meanings indicated for R^{1a},
R^{yb} has one of the meanings indicated for R^{1b},
R^{yd} has one of the meanings indicated for R^{1d},
R^{y1} has one of the meanings indicated for R^{c1},

R^{y2} has one of the meanings indicated for R^{c2},
R^{y3} has one of the meanings indicated for R^{c3},
R^{y4} has one of the meanings indicated for R^{c4},
R^{y5} has one of the meanings indicated for R^{c5},
R^{y6} has one of the meanings indicated for R^{c6}, and
R^{y7} has one of the meanings indicated for R^{c7};

W is a radical of the formulae W1 or W2 which is linked via nitrogen:



(W1)



(W2)

in which
* means the linkage to Y, and # means the linkage to R^2,
m is 0, 1 or 2, and

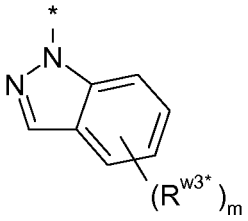
R^w is selected from OH, SH, halogen, NO_2, NH_2, CN, CF_3, CHF_2, CH_2F, O-CF_3, O-CHF_2, O-CH_2F, COOH, OCH_2COOH, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-alkoxy-C_1-C_4-alkyl, C_1-C_6-alkylthio, where the last 4 radicals mentioned may be partly or completely halogenated and/or have 1, 2 or 3 substituents R^{wa}, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-cycloalkyloxy, where the cycloalkyl moiety of the last three radicals mentioned may have 1, 2, 3 or 4 radicals R^{wb},
aryl, O-aryl, O-CH_2-aryl, hetaryl, where the last four radicals mentioned are unsubstituted in the aryl moiety or may carry 1, 2, 3 or 4 radicals R^{wd},
$COOR^{w1}$, $CONR^{w2}R^{w3}$, $SO_2NR^{w2}R^{w3}$, NR^{w2}-SO_2-R^{w4},
NR^{w2}-CO-R^{w5}, SO_2-R^{w4},
-$(CH_2)_p$-$NR^{w6}R^{w7}$ with p = 0, 1, 2, 3, 4, 5 or 6 and
O-$(CH_2)_q$-$NR^{w6}R^{w7}$ with q = 2, 3, 4, 5 or 6;

or two R^w radicals bonded to adjacent C atoms form together with the C atoms to which they are bonded a 4, 5, 6 or 7-membered, optionally substituted carbocycle or an optionally substituted heterocycle which has 1, 2 or 3 different or identical heteroatoms from the group of O, N, S as ring members, where
R^{wa} has one of the meanings indicated for R^{1a},
R^{wb} has one of the meanings indicated for R^{1b},
R^{wd} has one of the meanings indicated for R^{1d},
R^{w1} has one of the meanings indicated for R^{c1},
R^{w2} has one of the meanings indicated for R^{c2},
R^{w3} has one of the meanings indicated for R^{c3},

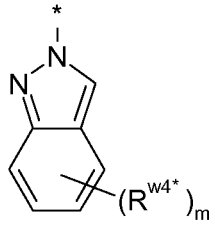
R^{w4} has one of the meanings indicated for R^{c4},
R^{w5} has one of the meanings indicated for R^{c5},
R^{w6} has one of the meanings indicated for R^{c6},
R^{w7} has one of the meanings indicated for R^{c7},

or

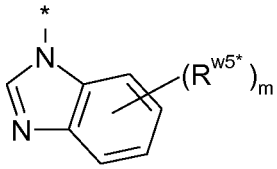
W forms together with R^2 a bi- or tricyclic radical of the formulae W3, W4, W5, W6, W7 or W8 which is linked via nitrogen:



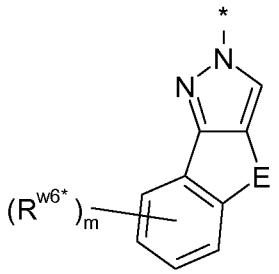
(W3)



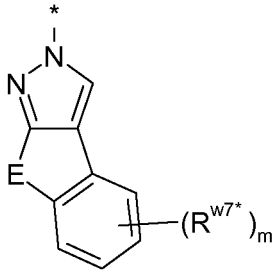
(W4)



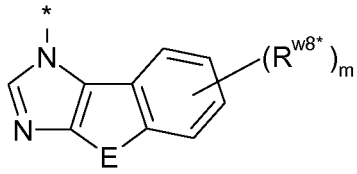
(W5)



(W6)



(W7)



(W8)

in which

* means the linkage to Y,
m is 0, 1 or 2, and
R^{w3*}, R^{w4*}, R^{w5*}, R^{w6*}, R^{w7*} and R^{w8*} have independently of one another one of the meanings indicated for R^w,
E has one of the following meanings: $-CR_E^2R_E^3-$, $-CHR_E^2-CHR_E^3$, $CH_2-CH_2-CH_2-$, -CO-, $-CO-NR_E^1-$, $-NR_E^1-CO-$, -O-, $-CH_2-O-$, $-O-CH_2-$, -S-, $-S-CH_2-$, $-CH_2-S-$, -SO-, CH_2-SO-, $-SO-CH_2-$, $-SO_2-$, $-CH_2-SO_2-$, $-SO_2-CH_2-$, $-NR_E^1-$, $-NR_E^1-CH_2-$, $-CH_2-NR_E^1$, $-SO_2-NR_E^1-$, $-NR_E^1-SO_2-$, -CO-O-, -O-CO-, $-C(=CR_E^2R_E^3)-$, $-CR_E^2=CR_E^3-$,
R_E^1 is H, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R_E^{1a}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, CO-C_1-C_6-alkyl, CO-O-C_1-C_6-alkyl, SO_2-C_1-C_6-alkyl, aryl, hetaryl, aryl-C_1-C_4-alkyl, hetaryl-C_1-C_4-alkyl, CO-aryl, CO-hetaryl, CO-(aryl-

C_1-C_4-alkyl), CO-(hetaryl-C_1-C_4-alkyl), CO-O-aryl, CO-O-hetaryl, CO-O-(aryl-C_1-C_4-alkyl), CO-O-(hetaryl-C_1-C_4-alkyl), SO_2-aryl, SO_2-hetaryl, SO_2-(aryl-C_1-C_4-alkyl) or SO_2-(hetaryl-C_1-C_4-alkyl), where aryl and hetaryl in the last 16 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R_E^{1d}, and

R_E^2, R_E^3 are independently of one another selected from hydrogen, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_2-C_6-alkenyl, C_2-C_6-alkynyl, where the last 4 radicals mentioned may be partly or completely halogenated and/or have 1, 2 or 3 substituents R_E^{1a},

C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-cycloalkyl-O, where a CH_2 group in the cycloalkyl moiety of the last three radicals mentioned may be replaced by O, NH, or S, or two adjacent C atoms may form a double bond, where the cycloalkyl moiety may further have 1, 2, 3 or 4 R_E^{1b} radicals,

aryl, hetaryl, aryl-C_1-C_6-alkyl, or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 4 radicals mentioned may be unsubstituted or carry 1, 2, 3 or 4 identical or different radicals R_E^{1d}; and where

R_E^{1a} has one of the meanings indicated for R^{1a}, R_E^{1b} has one of the meanings indicated for R^{1b}, and R_E^{1d} has one of the meanings indicated for R^{1d}.

The present invention therefore relates to the carboxamide compounds of the general formula I, their tautomers, the pharmaceutically suitable salts of the carboxamide compounds I, the prodrugs of I and the pharmaceutically suitable salts of the prodrugs or tautomers of I.

The carboxamide compounds of the invention of the formula I, their salts, their prodrugs and their tautomers effectively inhibit calpain even at low concentrations. They are additionally distinguished by a high selectivity in relation to the inhibition of the calpain compared with other cysteine proteases such as cathepsin B, cathepsin K, cathepsin L and cathepsin S.

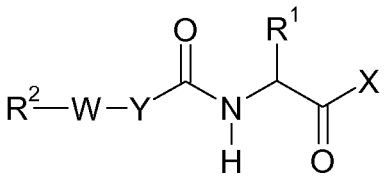
The carboxamide compounds of the invention of the formula I, their salts, their prodrugs and their tautomers are therefore particularly suitable for treating disorders and conditions in creatures, especially human creatures, which are associated with an elevated calpain activity.

The invention therefore also relates to the use of carboxamide compounds of the formula I, their tautomers and their pharmaceutically suitable salts for the manufacture of a medicament, in particular of a medicament which is suitable for the treatment of a disorder or a condition which is associated with an elevated calpain activity.

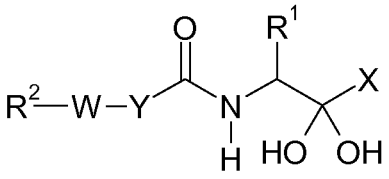
The invention further relates to a medicament, in particular a medicament which is suitable for the treatment of a disorder or a condition which is associated with an elevated calpain activity. The medicament comprises at least one carboxamide compound of the formula I, as described herein, a tautomer or a pharmaceutically suitable salt of the compound I or of the tautomer or a prodrug of I, or a salt or tautomer of said prodrug.

The carboxamide compounds of the formula I may be in the form of ß-keto compounds, i.e. the radicals R^{3a} and R^{3b} in the compounds of the formula I form together with the carbon atom to which they are bonded a carbonyl group as shown in the formula on the left in Scheme A. The compounds of the invention may also be in the form of a hydrate, i.e. the radicals R^{3a} and R^{3b} are each OH, as shown in the formula on the right in Scheme A. R^1, R^2, W, X and Y in Scheme A have the aforementioned meanings.

Scheme A:



I (R^{3a}/R^{3b} = O)

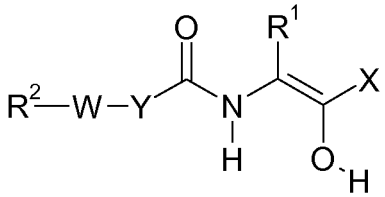


I (R^{3a}= R^{3b} = OH)

In the presence of water, especially under physiological conditions, usually both the ß-keto form and the hydrate form are present in a mixture.

Where only the ß-keto form is indicated in the following formulae and descriptions, this is intended to include also the hydrate and mixtures thereof with the ß-keto form unless indicated otherwise. Hydrates and ß-keto forms are equally suitable as calpain inhibitors.

The carboxamide compounds of the invention of the formula I are also able to form tautomers when R^{3a} and R^{3b} form a carbonyl group together with the carbon atom to which they are bonded. The tautomers are equally suitable as calpain inhibitors. Particular examples of tautomers to be mentioned are the compounds of the formula I-T:



I-T

R^1, R^2, W, X and Y in formula I-T have the aforementioned meanings.

The carboxamide compounds of the invention of the formula I can also form hemiacetals, hemiketals, acetals or ketals with alkanols. These compounds are equally suitable as calpain inhibitors as they are prodrugs of the compounds I, where $CR^{3a}R^{3b}$ is a carbonyl group (i.e. C=O) or $C(OH)_2$. Accordingly, compounds where one or both radicals R^{3a} and R^{3b} are a radical derived from an alkanol, and especially C_1-C_6-alkoxy, can also be used according to the invention.

The term prodrug, as used herein and in the claims refers to a compound which is transformed under metabolic conditions into a compound of the formula I. Apart from the aforementioned hemiacetals, hemiketals, acetals and ketals prodrugs of the compounds I include the compounds of the formula I, wherein R^{3a} and R^{3b} together form a group O-Alk-O, S-Alk-O or S-Alk-S, where Alk is linear C_2-C_5-alkandiyl, which may be unsubstituted or substituted with 1, 2, 3 or 4 radicals selected from C_1-C_4-alkyl or halogen, examples for such groups including $O(CH_2)_2O$, $O(CH_2)_5O$, $O(CH_2)_4O$, $S(CH_2)_2O$, $S(CH_2)_5O$, $S(CH_2)_4O$, etc. Further prodrugs or the compounds I include the compounds of the formula I, wherein R^{3a} and R^{3b} together whith the carbon atom form a group $C=NR^3$, where R^3 is selected from H, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_2-C_6-alkenyl, C_3-C_6-cycloalkyl, C_3-C_6-cycloalkyl-C_1-C_4-alkyl, $C3_2$-C_6-alkenyloxy, C_3-C_6-cycloalkyloxy, C_3-C_6-cycloalkyl-C_1-C_4-alkyloxy. Under metabolic conditions, the aforementioned prodrugs are transformed into the corresponding ß-keto compounds of the formula I ($CR^{3a}R^{3b}$ is C=O) or into the hydrates thereof ($CR^{3a}R^{3b}$ is $C(OH)_2$). Therefore, said prodrugs and their pharmaceutically acceptable salts are also part of the invention.

It is equally possible to use pharmaceutically suitable salts of the carboxamide compounds of the formula I of their tautomers or of their prodrugs, especially acid addition salts with physiologically tolerated organic or inorganic acids. Examples of suitable physiologically tolerated organic and inorganic acids are hydrochloric acid, hydrobromic acid, phosphoric acid, nitric acid, sulfuric acid, organic sulfonic acids having 1 to 12 carbon atoms, e.g. C_1-C_4-alkylsulfonic acids such as methanesulfonic acid, cycloaliphatic sulfonic acids such as S-(+)-10-camphorsulfonic acids, and aromatic sulfonic acids such as benzenesulfonic acid and toluenesulfonic acid, di- and tricarboxylic acids and hydroxy carboxylic acids having 2 to 10 carbon atoms, such as oxalic acid, malonic acid, maleic acid, fumaric acid, mucic acid, lactic acid, tartaric acid, citric acid, glycolic acid and adipic acid, as well as cis- and trans-cinnamic acid, furan-2-carboxylic acid and benzoic acid. Further suitable acids are described in Fortschritte der Arzneimittelforschung, Volume 10, pages 224 et seq., Birkhäuser Verlag, Basel and Stuttgart, 1966. The physiologically tolerated salts of the compounds of the formula I may be in the form of mono-, di-, tri- or tetrasalts, meaning that they may comprise 1, 2, 3 or 4 of the aforementioned acid molecules per molecule of the formula I. The acid molecules may be present in their acidic form or as anion.

The compounds of the invention may be in the form of a mixture of diastereomers, or of a mixture of diastereomers in which one of the two diastereomers is enriched, or of essentially diastereomerically pure compounds (diastereomeric excess de > 90%). The compounds are preferably in the form of essentially diastereomerically pure compounds (diastereomeric excess de > 90%). The compounds I of the invention may furthermore be in the form of a mixture of enantiomers (for example as racemate), of a mixture of enantiomers in which one of the two enantiomers is enriched, or essentially in enantiomerically pure compounds (enantiomeric excess ee > 90%). However, the compounds of the invention are frequently prone to racemization in relation to the stereochemistry of the carbon atom which carries the radical R^1, so that mixtures are frequently obtained in relation to this carbon atom, or compounds which exhibit a uniform stereochemistry in relation to this C atom form mixtures under physiological conditions. However, in relation to other stereocenters and the occurrence, associatied therewith, of enantiomers and diastereomers, it is preferred to employ the compounds enantiomerically pure or diastereomerically pure.

In the context of the present description, unless stated otherwise, the terms "alkyl", "alkoxy", "alkylthio", "haloalkyl", "haloalkoxy", "haloalkylthio", "alkenyl", "alkynyl", "alkylene" and radicals derived therefrom always include both unbranched and branched "alkyl", "alkoxy", "alkylthio", "haloalkyl", "haloalkoxy", "haloalkylthio", "alkenyl", "alkynyl" and "alkylene", respectively.

The prefix C_n-C_m- indicates the respective number of carbons in the hydrocarbon unit. Unless indicated otherwise, halogenated substituents preferably have one to five identical or different halogen atoms, especially fluorine atoms or chlorine atoms. C_0-Alkylene or $(CH_2)_0$ or similar expressions in the context of the description designate, unless indicated otherwise, a single bond.

The term "halogen" designates in each case, fluorine, bromine, chlorine or iodine, specifically fluorine, chlorine or bromine.

Examples of other meanings are:

Alkyl, and the alkyl moieties for example in alkoxy, alkylthio, arylalkyl, hetarylalkyl, cycloalkylalkyl or alkoxyalkyl: saturated, straight-chain or branched hydrocarbon radicals having one or more C atoms, e.g. 1 to 4, 1 to 6 or 1 to 10 carbon atoms, e.g. C_1-C_6-alkyl such as methyl, ethyl, propyl, 1-methylethyl, butyl, 1-methylpropyl, 2-methylpropyl, 1,1-dimethylethyl, pentyl, 1-methylbutyl, 2-methylbutyl, 3-methylbutyl, 2,2-dimethylpropyl, 1-ethylpropyl, hexyl, 1,1-dimethylpropyl, 1,2-dimethylpropyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 1,1-dimethylbutyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, 2,2-dimethylbutyl, 2,3-dimethylbutyl,

3,3-dimethylbutyl, 1-ethylbutyl, 2-ethylbutyl, 1,1,2-trimethylpropyl, 1,2,2-trimethylpropyl, 1-ethyl-1-methylpropyl, 1-ethyl-2-methylpropyl. In one embodiment of the invention, alkyl stands for small alkyl groups such as C_1-C_4-alkyl. In another embodiment of the invention, alkyl stands for larger alkyl groups such as C_5-C_{10}-alkyl.

Haloalkyl: an alkyl radical having ordinarily 1 to 6 or 1 to 4 C atoms as mentioned above, whose hydrogen atoms are partly or completely replaced by halogen atoms such as fluorine, chlorine, bromine and/or iodine, e.g. chloromethyl, dichloromethyl, trichloromethyl, fluoromethyl, difluoromethyl, trifluoromethyl, chlorofluoromethyl, dichlorofluoromethyl, chlorodifluoromethyl, 2-fluoroethyl, 2-chloroethyl, 2-bromoethyl, 2-iodoethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, 2-chloro-2-fluoroethyl, 2-chloro-2,2-difluoroethyl, 2,2-dichloro-2-fluoroethyl, 2,2,2-trichloroethyl, pentafluoroethyl, 2-fluoropropyl, 3-fluoropropyl, 2,2-difluoropropyl, 2,3-difluoropropyl, 2-chloropropyl, 3-chloropropyl, 2,3-dichloropropyl, 2-bromopropyl, 3-bromopropyl, 3,3,3-trifluoropropyl, 3,3,3-trichloropropyl, 2,2,3,3,3-pentafluoropropyl, heptafluoropropyl, 1-(fluoromethyl)-2-fluoroethyl, 1-(chloromethyl)-2-chloroethyl, 1-(bromomethyl)-2-bromoethyl, 4-fluorobutyl, 4-chlorobutyl, 4-bromobutyl and nonafluorobutyl.

Cycloalkyl, and the cycloalkyl moieties for example in cycloalkoxy or cycloalkyl-C_1-C_6-alkyl: monocyclic, saturated hydrocarbon groups having three or more C atoms, e.g. 3 to 7 carbon ring members, such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl.

Alkenyl, and alkenyl moieties for example in aryl-(C_2-C_6)-alkenyl: monounsaturated, straight-chain or branched hydrocarbon radicals having two or more C atoms, e.g. 2 to 4, 2 to 6 or 2 to 10 carbon atoms and one double bond in any position, e.g. C_2-C_6-alkenyl such as ethenyl, 1-propenyl, 2-propenyl, 1-methylethenyl, 1-butenyl, 2-butenyl, 3-butenyl, 1-methyl-1-propenyl, 2-methyl-1-propenyl, 1-methyl-2-propenyl, 2-methyl-2-propenyl, 1-pentenyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, 1-methyl-1-butenyl, 2-methyl-1-butenyl, 3-methyl-1-butenyl, 1-methyl-2-butenyl, 2-methyl-2-butenyl, 3-methyl-2-butenyl, 1-methyl-3-butenyl, 2-methyl-3-butenyl, 3-methyl-3-butenyl, 1,1-dimethyl-2-propenyl, 1,2-dimethyl-1-propenyl, 1,2-dimethyl-2-propenyl, 1-ethyl-1-propenyl, 1-ethyl-2-propenyl, 1-hexenyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, 5-hexenyl, 1-methyl-1-pentenyl, 2-methyl-1-pentenyl, 3-methyl-1-pentenyl, 4-methyl-1-pentenyl, 1-methyl-2-pentenyl, 2-methyl-2-pentenyl, 3-methyl-2-pentenyl, 4-methyl-2-pentenyl, 1-methyl-3-pentenyl, 2-methyl-3-pentenyl, 3-methyl-3-pentenyl, 4-methyl-3-pentenyl, 1-methyl-4-pentenyl, 2-methyl-4-pentenyl, 3-methyl-4-pentenyl, 4-methyl-4-pentenyl, 1,1-dimethyl-2-butenyl, 1,1-dimethyl-3-butenyl, 1,2-dimethyl-1-butenyl, 1,2-dimethyl-2-butenyl, 1,2-dimethyl-3-butenyl, 1,3-dimethyl-1-butenyl, 1,3-dimethyl-2-butenyl, 1,3-dimethyl-3-butenyl, 2,2-dimethyl-3-butenyl, 2,3-dimethyl-1-butenyl, 2,3-dimethyl-2-butenyl, 2,3-dimethyl-3-butenyl, 3,3-dimethyl-1-butenyl, 3,3-dimethyl-2-butenyl, 1-ethyl-1-butenyl, 1-ethyl-2-butenyl, 1-ethyl-3-butenyl, 2-ethyl-1-butenyl, 2-ethyl-2-butenyl, 2-ethyl-3-butenyl, 1,1,2-trimethyl-2-propenyl, 1-ethyl-1-methyl-2-propenyl, 1-ethyl-2-methyl-1-

propenyl, 1-ethyl-2-methyl-2-propenyl.

Alkynyl: straight-chain or branched hydrocarbon groups having two or more C atoms, e.g. 2 to 4, 2 to 6 or 2 to 10 carbon atoms and one or two triple bonds in any position but nonadjacent, e.g. C_2-C_6-alkynyl such as ethynyl, 1-propynyl, 2-propynyl, 1-butynyl, 2-butynyl, 3-butynyl, 1-methyl-2-propynyl, 1-pentynyl, 2-pentynyl, 3-pentynyl, 4-pentynyl, 1-methyl-2-butynyl, 1-methyl-3-butynyl, 2-methyl-3-butynyl, 3-methyl-1-butynyl, 1,1-dimethyl-2-propynyl, 1-ethyl-2-propynyl, 1-hexynyl, 2-hexynyl, 3-hexynyl, 4-hexynyl, 5-hexynyl, 1-methyl-2-pentynyl, 1-methyl-3-pentynyl, 1-methyl-4-pentynyl, 2-methyl-3-pentynyl, 2-methyl-4-pentynyl, 3-methyl-1-pentynyl, 3-methyl-4-pentynyl, 4-methyl-1-pentynyl, 4-methyl-2-pentynyl, 1,1-dimethyl-2-butynyl, 1,1-dimethyl-3-butynyl, 1,2-dimethyl-3-butynyl, 2,2-dimethyl-3-butynyl, 3,3-dimethyl-1-butynyl, 1-ethyl-2-butynyl, 1-ethyl-3-butynyl, 2-ethyl-3-butynyl, 1-ethyl-1-methyl-2-propynyl.

Alkoxy or alkoxy moieties for example in alkoxyalkyl:
Alkyl as defined above having preferably 1 to 6 or 1 to 4 C atoms, which is linked via an O atom: e.g. methoxy, ethoxy, n-propoxy, 1-methylethoxy, butoxy, 1-methylpropoxy, 2-methylpropoxy or 1,1-dimethylethoxy, pentoxy, 1-methylbutoxy, 2-methylbutoxy, 3-methylbutoxy, 1,1-dimethylpropoxy, 1,2-dimethylpropoxy, 2,2-dimethylpropoxy, 1-ethylpropoxy, hexoxy, 1-methylpentoxy, 2-methylpentoxy, 3-methylpentoxy, 4-methylpentoxy, 1,1-dimethylbutoxy, 1,2-dimethylbutoxy, 1,3-dimethylbutoxy, 2,2-dimethylbutoxy, 2,3-dimethylbutoxy, 3,3-dimethylbutoxy, 1-ethylbutoxy, 2-ethylbutoxy, 1,1,2-trimethylpropoxy, 1,2,2-trimethylpropoxy, 1-ethyl-1-methylpropoxy or 1-ethyl-2-methylpropoxy.

Haloalkoxy: alkoxy as described above, in which the hydrogen atoms of these groups are partly or completely replaced by halogen atoms, i.e. for example C_1-C_6-haloalkoxy, such as chloromethoxy, dichloromethoxy, trichloromethoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, chlorofluoromethoxy, dichlorofluoromethoxy, chlorodifluoromethoxy, 2-fluoroethoxy, 2-chloroethoxy, 2-bromoethoxy, 2-iodoethoxy, 2,2-difluoroethoxy, 2,2,2-trifluoroethoxy, 2-chloro-2-fluoroethoxy, 2-chloro-2,2-difluoroethoxy, 2,2-dichloro-2-fluoroethoxy, 2,2,2-trichloroethoxy, pentafluoroethoxy, 2-fluoropropoxy, 3-fluoropropoxy, 2,2-difluoropropoxy, 2,3-difluoropropoxy, 2-chloropropoxy, 3-chloropropoxy, 2,3-dichloropropoxy, 2-bromopropoxy, 3-bromopropoxy, 3,3,3-trifluoropropoxy, 3,3,3-trichloropropoxy, 2,2,3,3,3-pentafluoropropoxy, heptafluoropropoxy, 1-(fluoromethyl)-2-fluoroethoxy, 1-(chloromethyl)-2-chloroethoxy, 1-(bromomethyl)-2-bromoethoxy, 4-fluorobutoxy, 4-chlorobutoxy, 4-bromobutoxy, nonafluorobutoxy, 5-fluoro-1-pentoxy, 5-chloro-1-pentoxy, 5-bromo-1-pentoxy, 5-iodo-1-pentoxy, 5,5,5-trichloro-1-pentoxy, undecafluoropentoxy, 6-fluoro-1-hexoxy, 6-chloro-1-hexoxy, 6-bromo-1-hexoxy, 6-iodo-1-hexoxy, 6,6,6-trichloro-1-hexoxy or dodecafluorohexoxy, specifically chloromethoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, 2-fluoroethoxy, 2-chloroethoxy or 2,2,2-trifluoroethoxy.

Alkoxyalkyl: an alkyl radical ordinarily having 1 to 4 C atoms, in which one hydrogen atom is replaced by an alkoxy radical ordinarily having 1 to 6 or 1 to 4 C atoms. Examples thereof are CH_2-OCH_3, CH_2-OC_2H_5, n-propoxymethyl, CH_2-$OCH(CH_3)_2$, n-butoxymethyl, (1-methylpropoxy)methyl, (2-methylpropoxy)methyl, CH_2-$OC(CH_3)_3$, 2-(methoxy)ethyl, 2-(ethoxy)ethyl, 2-(n-propoxy)ethyl, 2-(1-methylethoxy)ethyl, 2-(n-butoxy)ethyl, 2-(1-methylpropoxy)ethyl, 2-(2-methylpropoxy)ethyl, 2-(1,1-dimethylethoxy)ethyl, 2-(methoxy)propyl, 2-(ethoxy)propyl, 2-(n-propoxy)propyl, 2-(1-methylethoxy)propyl, 2-(n-butoxy)propyl, 2-(1-methylpropoxy)propyl, 2-(2-methylpropoxy)propyl, 2-(1,1-dimethylethoxy)propyl, 3-(methoxy)propyl, 3-(ethoxy)propyl, 3-(n-propoxy)propyl, 3-(1-methylethoxy)propyl, 3-(n-butoxy)propyl, 3-(1-methylpropoxy)propyl, 3-(2-methylpropoxy)propyl, 3-(1,1-dimethylethoxy)propyl, 2-(methoxy)butyl, 2-(ethoxy)butyl, 2-(n-propoxy)butyl, 2-(1-methylethoxy)butyl, 2-(n-butoxy)butyl, 2-(1-methylpropoxy)butyl, 2-(2-methylpropoxy)butyl, 2-(1,1-dimethylethoxy)butyl, 3-(methoxy)butyl, 3-(ethoxy)butyl, 3-(n-propoxy)butyl, 3-(1-methylethoxy)butyl, 3-(n-butoxy)butyl, 3-(1-methylpropoxy)butyl, 3-(2-methylpropoxy)butyl, 3-(1,1-dimethylethoxy)butyl, 4-(methoxy)butyl, 4-(ethoxy)butyl, 4-(n-propoxy)butyl, 4-(1-methylethoxy)butyl, 4-(n-butoxy)butyl, 4-(1-methylpropoxy)butyl, 4-(2-methylpropoxy)butyl, 4-(1,1-dimethylethoxy)butyl, etc.

Alkylthio: alkyl as defined above preferably having 1 to 6 or 1 to 4 C atoms, which is linked via an S atom, e.g. methylthio, ethylthio, n-propylthio and the like.

Haloalkylthio: haloalkyl as defined above preferably having 1 to 6 or 1 to 4 C atoms, which is linked via an S atom, e.g. fluoromethylthio, difluoromethylthio, trifluoromethylthio, 2-fluoroethylthio, 2,2-difluoroethylthio, 2,2,2-trifluoroethylthio, pentafluoroethylthio, 2-fluoropropylthio, 3-fluoropropylthio, 2,2-difluoropropylthio, 2,3-difluoropropylthio, and heptafluoropropylthio.

Aryl: a mono-, bi- or tricyclic aromatic hydrocarbon radical such as phenyl or naphthyl, especially phenyl.

Heterocyclyl: a heterocyclic radical which may be saturated, partly unsaturated or aromatic and which ordinarily has 3, 4, 5, 6, 7 or 8 ring atoms, where ordinarily 1, 2, 3 or 4, in particular 1, 2 or 3, of the ring atoms are heteroatoms such as N, S or O, besides carbon atoms as ring members.

Examples of saturated heterocycles are in particular:

Heterocycloalkyl: i.e. a saturated heterocyclic radical which ordinarily has 3, 4, 5, 6 or 7 ring atoms, where ordinarily 1, 2 or 3 of the ring atoms are heteroatoms such as N, S or O, besides carbon atoms as ring members. These include for example:

C-bonded, 3-4-membered saturated rings such as
2-oxiranyl, 2-oxetanyl, 3-oxetanyl, 2-aziridinyl, 3-thiethanyl, 1-azetidinyl, 2-azetidinyl.

C-bonded, 5-membered saturated rings such as
tetrahydrofuran-2-yl, tetrahydrofuran-3-yl, tetrahydrothien-2-yl, tetrahydrothien-3-yl, tetrahydropyrrol-2-yl, tetrahydropyrrol-3-yl, tetrahydropyrazol-3-yl, tetrahydropyrazol-4-yl, tetrahydroisoxazol-3-yl, tetrahydroisoxazol-4-yl, tetrahydroisoxazol-5-yl, 1,2-oxathiolan-3-yl, 1,2-oxathiolan-4-yl, 1,2-oxathiolan-5-yl, tetrahydroisothiazol-3-yl, tetrahydroisothiazol-4-yl, tetrahydroisothiazol-5-yl, 1,2-dithiolan-3-yl, 1,2-dithiolan-4-yl, tetrahydroimidazol-2-yl, tetrahydroimidazol-4-yl, tetrahydrooxazol-2-yl, tetrahydrooxazol-4-yl, tetrahydrooxazol-5-yl, tetrahydrothiazol-2-yl, tetrahydrothiazol-4-yl, tetrahydrothiazol-5-yl, 1,3-dioxolan-2-yl, 1,3-dioxolan-4-yl, 1,3-oxathiolan-2-yl, 1,3-oxathiolan-4-yl, 1,3-oxathiolan-5-yl, 1,3-dithiolan-2-yl, 1,3-dithiolan-4-yl, 1,3,2-dioxathiolan-4-yl.

C-bonded, 6-membered saturated rings such as:
tetrahydropyran-2-yl, tetrahydropyran-3-yl, tetrahydropyran-4-yl, piperidin-2-yl, piperidin-3-yl, piperidin-4-yl, tetrahydrothiopyran-2-yl, tetrahydrothiopyran-3-yl, tetrahydrothiopyran-4-yl, 1,3-dioxan-2-yl, 1,3-dioxan-4-yl, 1,3-dioxan-5-yl, 1,4-dioxan-2-yl, 1,3-dithian-2-yl, 1,3-dithian-4-yl, 1,3-dithian-5-yl, 1,4-dithian-2-yl, 1,3-oxathian-2-yl, 1,3-oxathian-4-yl, 1,3-oxathian-5-yl, 1,3-oxathian-6-yl, 1,4-oxathian-2-yl, 1,4-oxathian-3-yl, 1,2-dithian-3-yl, 1,2-dithian-4-yl, hexahydropyrimidin-2-yl, hexahydropyrimidin-4-yl, hexahydropyrimidin-5-yl, hexahydropyrazin-2-yl, hexahydropyridazin-3-yl, hexahydropyridazin-4-yl, tetrahydro-1,3-oxazin-2-yl, tetrahydro-1,3-oxazin-4-yl, tetrahydro-1,3-oxazin-5-yl, tetrahydro-1,3-oxazin-6-yl, tetrahydro-1,3-thiazin-2-yl, tetrahydro-1,3-thiazin-4-yl, tetrahydro-1,3-thiazin-5-yl, tetrahydro-1,3-thiazin-6-yl, tetrahydro-1,4-thiazin-2-yl, tetrahydro-1,4-thiazin-3-yl, tetrahydro-1,4-oxazin-2-yl, tetrahydro-1,4-oxazin-3-yl, tetrahydro-1,2-oxazin-3-yl, tetrahydro-1,2-oxazin-4-yl, tetrahydro-1,2-oxazin-5-yl, tetrahydro-1,2-oxazin-6-yl.

N-bonded, 5-membered saturated rings such as:
tetrahydropyrrol-1-yl, tetrahydropyrazol-1-yl, tetrahydroisoxazol-2-yl, tetrahydroisothiazol-2-yl, tetrahydroimidazol-1-yl, tetrahydrooxazol-3-yl, tetrahydrothiazol-3-yl.

N-bonded, 6-membered saturated rings such as:

piperidin-1-yl, hexahydropyrimidin-1-yl, hexahydropyrazin-1-yl, hexahydropyridazin-1-yl, tetrahydro-1,3-oxazin-3-yl, tetrahydro-1,3-thiazin-3-yl, tetrahydro-1,4-thiazin-4-yl, tetrahydro-1,4-oxazin-4-yl, tetrahydro-1,2-oxazin-2-yl.

Unsaturated heterocyclic radicals which ordinarily have 4, 5, 6 or 7 ring atoms, where ordinarily 1, 2 or 3 of the ring atoms are heteroatoms such as N, S or O, besides carbon atoms as ring members. These include for example:

C-bonded, 5-membered, partially unsaturated rings such as:
2,3-dihydrofuran-2-yl, 2,3-dihydrofuran-3-yl, 2,5-dihydrofuran-2-yl, 2,5-dihydrofuran-3-yl, 4,5-dihydrofuran-2-yl, 4,5-dihydrofuran-3-yl, 2,3-dihydrothien-2-yl, 2,3-dihydrothien-3-yl, 2,5-dihydrothien-2-yl, 2,5-dihydrothien-3-yl, 4,5-dihydrothien-2-yl, 4,5-dihydrothien-3-yl, 2,3-dihydro-1H-pyrrol-2-yl, 2,3-dihydro-1H-pyrrol-3-yl, 2,5-dihydro-1H-pyrrol-2-yl, 2,5-dihydro-1H-pyrrol-3-yl, 4,5-dihydro-1H-pyrrol-2-yl, 4,5-dihydro-1H-pyrrol-3-yl, 3,4-dihydro-2H-pyrrol-2-yl, 3,4-dihydro-2H-pyrrol-3-yl, 3,4-dihydro-5H-pyrrol-2-yl, 3,4-dihydro-5H-pyrrol-3-yl, 4,5-dihydro-1H-pyrazol-3-yl, 4,5-dihydro-1H-pyrazol-4-yl, 4,5-dihydro-1H-pyrazol-5-yl, 2,5-dihydro-1H-pyrazol-3-yl, 2,5-dihydro-1H-pyrazol-4-yl, 2,5-dihydro-1H-pyrazol-5-yl, 4,5-dihydroisoxazol-3-yl, 4,5-dihydroisoxazol-4-yl, 4,5-dihydroisoxazol-5-yl, 2,5-dihydroisoxazol-3-yl, 2,5-dihydroisoxazol-4-yl, 2,5-dihydroisoxazol-5-yl, 2,3-dihydroisoxazol-3-yl, 2,3-dihydroisoxazol-4-yl, 2,3-dihydroisoxazol-5-yl, 4,5-dihydroisothiazol-3-yl, 4,5-dihydroisothiazol-4-yl, 4,5-dihydroisothiazol-5-yl, 2,5-dihydroisothiazol-3-yl, 2,5-dihydroisothiazol-4-yl, 2,5-dihydroisothiazol-5-yl, 2,3-dihydroisothiazol-3-yl, 2,3-dihydroisothiazol-4-yl, 2,3-dihydroisothiazol-5-yl, 4,5-dihydro-1H-imidazol-2-yl, 4,5-dihydro-1H-imidazol-4-yl, 4,5-dihydro-1H-imidazol-5-yl, 2,5-dihydro-1H-imidazol-2-yl, 2,5-dihydro-1H-imidazol-4-yl, 2,5-dihydro-1H-imidazol-5-yl, 2,3-dihydro-1H-imidazol-2-yl, 2,3-dihydro-1H-imidazol-4-yl, 4,5-dihydrooxazol-2-yl, 4,5-dihydrooxazol-4-yl, 4,5-dihydrooxazol-5-yl, 2,5-dihydrooxazol-2-yl, 2,5-dihydrooxazol-4-yl, 2,5-dihydrooxazol-5-yl, 2,3-dihydrooxazol-2-yl, 2,3-dihydrooxazol-4-yl, 2,3-dihydrooxazol-5-yl, 4,5-dihydrothiazol-2-yl, 4,5-dihydrothiazol-4-yl, 4,5-dihydrothiazol-5-yl, 2,5-dihydrothiazol-2-yl, 2,5-dihydrothiazol-4-yl, 2,5-dihydrothiazol-5-yl, 2,3-dihydrothiazol-2-yl, 2,3-dihydrothiazol-4-yl, 2,3-dihydrothiazol-5-yl, 1,3-dioxol-2-yl, 1,3-dioxol-4-yl, 1,3-dithiol-2-yl, 1,3-dithiol-4-yl, 1,3-oxathiol-2-yl, 1,3-oxathiol-4-yl, 1,3-oxathiol-5-yl.

C-bonded, 6-membered, partially unsaturated rings such as:
2H-3,4-dihydropyran-6-yl, 2H-3,4-dihydropyran-5-yl, 2H-3,4-dihydropyran-4-yl, 2H-3,4-dihydropyran-3-yl, 2H-3,4-dihydropyran-2-yl, 2H-3,4-dihydrothiopyran-6-

yl, 2H-3,4-dihydrothiopyran-5-yl, 2H-3,4-dihydrothiopyran-4-yl, 2H-3,4-dihydrothiopyran-3-yl, 2H-3,4-dihydrothiopyran-2-yl, 1,2,3,4-tetrahydropyridin-6-yl, 1,2,3,4-tetrahydropyridin-5-yl, 1,2,3,4-tetrahydropyridin-4-yl, 1,2,3,4-tetrahydropyridin-3-yl, 1,2,3,4-tetrahydropyridin-2-yl, 2H-5,6-dihydropyran-2-yl, 2H-5,6-dihydropyran-3-yl, 2H-5,6-dihydropyran-4-yl, 2H-5,6-dihydropyran-5-yl, 2H-5,6-dihydropyran-6-yl, 2H-5,6-dihydrothiopyran-2-yl, 2H-5,6-dihydrothiopyran-3-yl, 2H-5,6-dihydrothiopyran-4-yl, 2H-5,6-dihydrothiopyran-5-yl, 2H-5,6-dihydrothiopyran-6-yl, 1,2,5,6-tetrahydropyridin-2-yl, 1,2,5,6-tetrahydropyridin-3-yl, 1,2,5,6-tetrahydropyridin-4-yl, 1,2,5,6-tetrahydropyridin-5-yl, 1,2,5,6-tetrahydropyridin-6-yl, 2,3,4,5-tetrahydropyridin-2-yl, 2,3,4,5-tetrahydropyridin-3-yl, 2,3,4,5-tetrahydropyridin-4-yl, 2,3,4,5-tetrahydropyridin-5-yl, 2,3,4,5-tetrahydropyridin-6-yl, 4H-pyran-2-yl, 4H-pyran-3-yl, 4H-pyran-4-yl, 4H-thiopyran-2-yl, 4H-thiopyran-3-yl, 4H-thiopyran-4-yl, 1,4-dihydropyridin-2-yl, 1,4-dihydropyridin-3-yl, 1,4-dihydropyridin-4-yl, 2H-pyran-2-yl, 2H-pyran-3-yl, 2H-pyran-4-yl, 2H-pyran-5-yl, 2H-pyran-6-yl, 2H-thiopyran-2-yl, 2H-thiopyran-3-yl, 2H-thiopyran-4-yl, 2H-thiopyran-5-yl, 2H-thiopyran-6-yl, 1,2-dihydropyridin-2-yl, 1,2-dihydropyridin-3-yl, 1,2-dihydropyridin-4-yl, 1,2-dihydropyridin-5-yl, 1,2-dihydropyridin-6-yl, 3,4-dihydropyridin-2-yl, 3,4-dihydropyridin-3-yl, 3,4-dihydropyridin-4-yl, 3,4-dihydropyridin-5-yl, 3,4-dihydropyridin-6-yl, 2,5-dihydropyridin-2-yl, 2,5-dihydropyridin-3-yl, 2,5-dihydropyridin-4-yl, 2,5-dihydropyridin-5-yl, 2,5-dihydropyridin-6-yl, 2,3-dihydropyridin-2-yl, 2,3-dihydropyridin-3-yl, 2,3-dihydropyridin-4-yl, 2,3-dihydropyridin-5-yl, 2,3-dihydropyridin-6-yl, 2H-5,6-dihydro-1,2-oxazin-3-yl, 2H-5,6-dihydro-1,2-oxazin-4-yl, 2H-5,6-dihydro-1,2-oxazin-5-yl, 2H-5,6-dihydro-1,2-oxazin-6-yl, 2H-5,6-dihydro-1,2-thiazin-3-yl, 2H-5,6-dihydro-1,2-thiazin-4-yl, 2H-5,6-dihydro-1,2-thiazin-5-yl, 2H-5,6-dihydro-1,2-thiazin-6-yl, 4H-5,6-dihydro-1,2-oxazin-3-yl, 4H-5,6-dihydro-1,2-oxazin-4-yl, 4H-5,6-dihydro-1,2-oxazin-5-yl, 4H-5,6-dihydro-1,2-oxazin-6-yl, 4H-5,6-dihydro-1,2-thiazin-3-yl, 4H-5,6-dihydro-1,2-thiazin-4-yl, 4H-5,6-dihydro-1,2-thiazin-5-yl, 4H-5,6-dihydro-1,2-thiazin-6-yl, 2H-3,6-dihydro-1,2-oxazin-3-yl, 2H-3,6-dihydro-1,2-oxazin-4-yl, 2H-3,6-dihydro-1,2-oxazin-5-yl, 2H-3,6-dihydro-1,2-oxazin-6-yl, 2H-3,6-dihydro-1,2-thiazin-3-yl, 2H-3,6-dihydro-1,2-thiazin-4-yl, 2H-3,6-dihydro-1,2-thiazin-5-yl, 2H-3,6-dihydro-1,2-thiazin-6-yl, 2H-3,4-dihydro-1,2-oxazin-3-yl, 2H-3,4-dihydro-1,2-oxazin-4-yl, 2H-3,4-dihydro-1,2-oxazin-5-yl, 2H-3,4-dihydro-1,2-oxazin-6-yl, 2H-3,4-dihydro-1,2-thiazin-3-yl, 2H-3,4-dihydro-1,2-thiazin-4-yl, 2H-3,4-dihydro-1,2-thiazin-5-yl, 2H-3,4-dihydro-1,2-thiazin-6-yl, 2,3,4,5-tetrahydropyridazin-3-yl, 2,3,4,5-tetrahydropyridazin-4-yl, 2,3,4,5-tetrahydropyridazin-5-yl, 2,3,4,5-tetrahydropyridazin-6-yl, 3,4,5,6-tetrahydropyridazin-3-yl, 3,4,5,6-tetrahydropyridazin-4-yl, 1,2,5,6-tetrahydropyridazin-3-yl, 1,2,5,6-tetrahydropyridazin-4-yl, 1,2,5,6-tetrahydropyridazin-5-yl, 1,2,5,6-tetrahydropyridazin-6-yl,

1,2,3,6-tetrahydropyridazin-3-yl, 1,2,3,6-tetrahydropyridazin-4-yl, 4H-5,6-dihydro-1,3-oxazin-2-yl, 4H-5,6-dihydro-1,3-oxazin-4-yl, 4H-5,6-dihydro-1,3-oxazin-5-yl, 4H-5,6-dihydro-1,3-oxazin-6-yl, 4H-5,6-dihydro-1,3-thiazin-2-yl, 4H-5,6-dihydro-1,3-thiazin-4-yl, 4H-5,6-dihydro-1,3-thiazin-5-yl, 4H-5,6-dihydro-1,3-thiazin-6-yl, 3,4,5-6-tetrahydropyrimidin-2-yl, 3,4,5,6-tetrahydropyrimidin-4-yl, 3,4,5,6-tetrahydropyrimidin-5-yl, 3,4,5,6-tetrahydropyrimidin-6-yl, 1,2,3,4-tetrahydropyrazin-2-yl, 1,2,3,4-tetrahydropyrazin-5-yl, 1,2,3,4-tetrahydropyrimidin-2-yl, 1,2,3,4-tetrahydropyrimidin-4-yl, 1,2,3,4-tetrahydropyrimidin-5-yl, 1,2,3,4-tetrahydropyrimidin-6-yl, 2,3-dihydro-1,4-thiazin-2-yl, 2,3-dihydro-1,4-thiazin-3-yl, 2,3-dihydro-1,4-thiazin-5-yl, 2,3-dihydro-1,4-thiazin-6-yl, 2H-1,3-oxazin-2-yl, 2H-1,3-oxazin-4-yl, 2H-1,3-oxazin-5-yl, 2H-1,3-oxazin-6-yl, 2H-1,3-thiazin-2-yl, 2H-1,3-thiazin-4-yl, 2H-1,3-thiazin-5-yl, 2H-1,3-thiazin-6-yl, 4H-1,3-oxazin-2-yl, 4H-1,3-oxazin-4-yl, 4H-1,3-oxazin-5-yl, 4H-1,3-oxazin-6-yl, 4H-1,3-thiazin-2-yl, 4H-1,3-thiazin-4-yl, 4H-1,3-thiazin-5-yl, 4H-1,3-thiazin-6-yl, 6H-1,3-oxazin-2-yl, 6H-1,3-oxazin-4-yl, 6H-1,3-oxazin-5-yl, 6H-1,3-oxazin-6-yl, 6H-1,3-thiazin-2-yl, 6H-1,3-oxazin-4-yl, 6H-1,3-oxazin-5-yl, 6H-1,3-thiazin-6-yl, 2H-1,4-oxazin-2-yl, 2H-1,4-oxazin-3-yl, 2H-1,4-oxazin-5-yl, 2H-1,4-oxazin-6-yl, 2H-1,4-thiazin-2-yl, 2H-1,4-thiazin-3-yl, 2H-1,4-thiazin-5-yl, 2H-1,4-thiazin-6-yl, 4H-1,4-oxazin-2-yl, 4H-1,4-oxazin-3-yl, 4H-1,4-thiazin-2-yl, 4H-1,4-thiazin-3-yl, 1,4-dihydropyridazin-3-yl, 1,4-dihydropyridazin-4-yl, 1,4-dihydropyridazin-5-yl, 1,4-dihydropyridazin-6-yl, 1,4-dihydropyrazin-2-yl, 1,2-dihydropyrazin-2-yl, 1,2-dihydropyrazin-3-yl, 1,2-dihydropyrazin-5-yl, 1,2-dihydropyrazin-6-yl, 1,4-dihydropyrimidin-2-yl, 1,4-dihydropyrimidin-4-yl, 1,4-dihydropyrimidin-5-yl, 1,4-dihydropyrimidin-6-yl, 3,4-dihydropyrimidin-2-yl, 3,4-dihydropyrimidin-4-yl, 3,4-dihydropyrimidin-5-yl or 3,4-dihydropyrimidin-6-yl.

N-bonded, 5-membered, partially unsaturated rings such as:
2,3-dihydro-1H-pyrrol-1-yl, 2,5-dihydro-1H-pyrrol-1-yl, 4,5-dihydro-1H-pyrazol-1-yl, 2,5-dihydro-1H-pyrazol-1-yl, 2,3-dihydro-1H-pyrazol-1-yl, 2,5-dihydroisoxazol-2-yl, 2,3-dihydroisoxazol-2-yl, 2,5-dihydroisothiazol-2-yl, 2,3-dihydroisoxazol-2-yl, 4,5-dihydro-1H-imidazol-1-yl, 2,5-dihydro-1H-imidazol-1-yl, 2,3-dihydro-1H-imidazol-1-yl, 2,3-dihydrooxazol-3-yl, 2,3-dihydrothiazol-3-yl.

N-bonded, 6-membered, partially unsaturated rings such as:
1,2,3,4-tetrahydropyridin-1-yl, 1,2,5,6-tetrahydropyridin-1-yl, 1,4-dihydropyridin-1-yl, 1,2-dihydropyridin-1-yl, 2H-5,6-dihydro-1,2-oxazin-2-yl, 2H-5,6-dihydro-1,2-thiazin-2-yl, 2H-3,6-dihydro-1,2-oxazin-2-yl, 2H-3,6-dihydro-1,2-thiazin-2-yl, 2H-3,4-dihydro-1,2-oxazin-2-yl, 2H-3,4-dihydro-1,2-thiazin-2-yl, 2,3,4,5-tetrahydropyridazin-2-yl, 1,2,5,6-tetrahydropyridazin-1-yl, 1,2,5,6-tetrahydropyridazin-2-yl, 1,2,3,6-tetrahydropyridazin-1-yl, 3,4,5,6-tetrahydropyrimidin-3-yl, 1,2,3,4-

tetrahydropyrazin-1-yl, 1,2,3,4-tetrahydropyrimidin-1-yl, 1,2,3,4-tetrahydro-pyrimidin-3-yl, 2,3-dihydro-1,4-thiazin-4-yl, 2H-1,2-oxazin-2-yl, 2H-1,2-thiazin-2-yl, 4H-1,4-oxazin-4-yl, 4H-1,4-thiazin-4-yl, 1,4-dihydropyridazin-1-yl, 1,4-dihydropyrazin-1-yl, 1,2-dihydropyrazin-1-yl, 1,4-dihydropyrimidin-1-yl or 3,4-dihydropyrimidin-3-yl.

Hetaryl: a 5- or 6-membered aromatic heterocyclic radical which ordinarily has 1, 2, 3 or 4 nitrogen atoms or a heteroatom selected from oxygen and sulfur and, if appropriate, 1, 2 or 3 nitrogen atoms as ring members besides carbon atoms as ring members: for example

C-bonded, 5-membered heteroaromatic radicals having 1, 2, 3 or 4 nitrogen atoms or a heteroatom selected from oxygen and sulfur and, if appropriate, having 1, 2 or 3 nitrogen atoms as ring members, such as:
2-furyl, 3-furyl, 2-thienyl, 3-thienyl, pyrrol-2-yl, pyrrol-3-yl, pyrazol-3-yl, pyrazol-4-yl, isoxazol-3-yl, isoxazol-4-yl, isoxazol-5-yl, isothiazol-3-yl, isothiazol-4-yl, isothiazol-5-yl, imidazol-2-yl, imidazol-4-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, 1,2,3-oxadiazol-4-yl, 1,2,3-oxadiazol-5-yl, 1,2,4-oxadiazol-3-yl, 1,2,4,-oxadiazol-5-yl, 1,3,4-oxadiazol-2-yl, 1,2,3-thiadiazol-4-yl, 1,2,3-thiadiazol-5-yl, 1,2,4-thiadiazol-3-yl, 1,2,4-thiadiazol-5-yl, 1,3,4-thiadiazolyl-2-yl, 1,2,3-triazol-4-yl, 1,2,4-triazol-3-yl, tetrazol-5-yl.

C-bonded, 6-membered heteroaromatic radicals having 1, 2, 3 or 4 nitrogen atoms as ring members, such as:
pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridazin-3-yl, pyridazin-4-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl, pyrazin-2-yl, 1,3,5-triazin-2-yl, 1,2,4-triazin-3-yl, 1,2,4-triazin-5-yl, 1,2,4-triazin-6-yl, 1,2,4,5-tetrazin-3-yl.

N-bonded, 5-membered heteroaromatic radicals having 1, 2, 3 or 4 nitrogen atoms as ring members, such as:
pyrrol-1-yl, pyrazol-1-yl, imidazol-1-yl, 1,2,3-triazol-1-yl, 1,2,4-triazol-1-yl, tetrazol-1-yl.

Heterocyclyl also includes bicyclic heterocycles which have one of the aforementioned 5- or 6-membered heterocyclic rings and a further saturated, unsaturated or aromatic carbocycle fused thereto, for example a benzene, cyclohexane, cyclohexene or cyclohexadiene ring, or a further 5- or 6-membered heterocyclic ring fused thereto, where the latter may likewise be saturated, unsaturated or aromatic. These include for example quinolinyl, isoquinolinyl, indolyl, indolizynyl, isoindolyl, indazolyl, benzofuryl, benzothienyl, benzo[b]thiazolyl, benzoxazolyl, benzthiazolyl and benzimidazolyl.

Examples of 5- to 6-membered heteroaromatic compounds comprising a fused benzene ring include dihydroindolyl, dihydroindolizynyl, dihydroisoindolyl, dihydroquinolinyl, dihydroisoquinolinyl, chromenyl and chromanyl.

Arylalkyl: an aryl radical as defined above which is linked via an alkylene group, in particular via a methylene, 1,1-ethylene or 1,2-ethylene group, e.g. benzyl, 1-phenylethyl and 2-phenylethyl.

Arylalkenyl: an aryl radical as defined above, which is linked via an alkenylene group, in particular via a 1,1-ethenyl, 1,2-ethenyl or 1,3-propenyl group, e.g. 2-phenylethen-1-yl and 1-phenylethen-1-yl.

Cycloalkoxy: a cycloalkyl radical as defined above which is linked via an oxygen atom, e.g. cyclopropyloxy, cyclobutyloxy, cyclopentyloxy or cyclohexyloxy.

Cycloalkylalkyl: a cycloalkyl radical as defined above which is linked via an alkylene group, in particular via a methylene, 1,1-ethylene or 1,2-ethylene group, e.g. cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl or cyclohexylmethyl.

Heterocyclylalkyl and hetarylalkyl: a heterocyclyl or hetaryl radical as defined above which is linked via an alkylene group, in particular via a methylene, 1,1-ethylene or 1,2-ethylene group.

The expression "optionally substituted" means in the context of the present invention that the respective moiety is substituted or has 1, 2 or 3, in particular 1, substituents which are selected from halogen, C_1-C_4-alkyl, OH, SH, CN, CF_3, O-CF_3, COOH, O-CH_2-COOH, C_1-C_6-alkoxy, C_1-C_6-alkylthio, C_3-C_7-cycloalkyl, COO-C_1-C_6-alkyl, $CONH_2$, CONH-C_1-C_6-alkyl, SO_2NH-C_1-C_6-alkyl, CON-(C_1-C_6-alkyl)$_2$, SO_2N-(C_1-C_6-alkyl)$_2$, NH-SO_2-C_1-C_6-alkyl, NH-CO-C_1-C_6-alkyl, SO_2-C_1-C_6-alkyl, O-phenyl, O-CH_2-phenyl, CONH-phenyl, SO_2NH-phenyl, CONH-hetaryl, SO_2NH-hetaryl, SO_2-phenyl, NH-SO_2-phenyl, NH-CO-phenyl, NH-SO_2-hetaryl and NH-CO-hetaryl, where phenyl and hetaryl in the last 11 radicals mentioned are unsubstituted or may have 1, 2 or 3 substituents which are selected from halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy and C_1-C_4-haloalkoxy.

In relation to their use as calpain inhibitors, the variables R^1, R^2, W, X and Y preferably have the following meanings, where these represent, both considered on their own and in combination with one other, special configurations of the compounds of the formula I:

R^1 C_1-C_{10}-alkyl, preferably C_3-C_8-alkyl, which may be partly or completely halogenated and/or have 1, 2 or 3 substituents R^{1a}, in particular unsubstituted

C_1-C_{10}-alkyl, specifically unsubstituted C_3-C_8-alkyl,

C_3-C_7-cycloalkyl-C_1-C_4-alkyl, specifically C_3-C_7-cycloalkylmethyl, 1-(C_3-C_7-cycloalkyl)ethyl or 2-(C_3-C_7-cycloalkyl)ethyl, where the cycloalkyl moiety may have 1, 2, 3 or 4 radicals R^{1b}, very specifically cyclohexylmethyl,

phenyl-C_1-C_4-alkyl and hetaryl-C_1-C_4-alkyl, in particular benzyl, 1-phenylethyl, 2-phenylethyl, hetarylmethyl, 1-hetarylethyl, 2-hetarylethyl such as thienylmethyl, pyridinylmethyl, where phenyl and hetaryl in the last radicals mentioned may be unsubstituted or carry 1, 2, 3 or 4 identical or different radicals R^{1c}.

In this connection, R^{1a}, R^{1b} and R^{1c} where present have the aforementioned meanings. In particular:

R^{1a} is C_1-C_4-alkoxy or C_1-C_4-haloalkoxy;

R^{1b} is halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy or C_1-C_4-haloalkoxy; and

R^{1c} is halogen, C_1-C_4-alkyl, OH, SH, CN, CF_3, O-CF_3, COOH, O-CH_2-COOH, C_1-C_6-alkoxy, C_1-C_6-alkylthio, C_3-C_7-cycloalkyl, COO-C_1-C_6-alkyl, $CONH_2$, CONH-C_1-C_6-alkyl, SO_2NH-C_1-C_6-alkyl, CON-(C_1-C_6-alkyl)$_2$, SO_2N-(C_1-C_6-alkyl)$_2$, NH-SO_2-C_1-C_6-alkyl, NH-CO-C_1-C_6-alkyl, SO_2-C_1-C_6-alkyl, O-phenyl, O-CH_2-phenyl, CONH-phenyl, SO_2NH-phenyl, CONH-hetaryl, SO_2NH-hetaryl, SO_2-phenyl, NH-SO_2-phenyl, NH-CO-phenyl, NH-SO_2-hetaryl, NH-CO-hetaryl where phenyl and hetaryl in the last 11 radicals mentioned are unsubstituted or may have 1, 2 or 3 substituents which are selected from halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy and C_1-C_4-haloalkoxy,
-$(CH_2)_p$-$NR^{c6}R^{c7}$ with p = 0, 1, 2, 3, 4, 5 or 6, in particular 0, and
-O-$(CH_2)_q$-$NR^{c6}R^{c7}$ with q = 2, 3, 4, 5 or 6, in particular 2, where
R^{c6}, R^{c7} are independently of one another hydrogen or C_1-C_6-alkyl, or together with the nitrogen atom to which they are bonded, are a morpholine, piperidine, pyrrolidine, azetidine or piperazine residue, where the last 5 radicals mentioned are unsubstituted or may carry 1, 2, 3 or 4 radicals selected from C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy or C_1-C_4-haloalkoxy. R^{1c} is in particular halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy or C_1-C_4-haloalkoxy.

R^2 one of the aforementioned radicals different from hydrogen, in particular:

C_1-C_{10}-alkyl which may be partly or completely halogenated and/or carry 1, 2 or 3 substituents R^{2a},

aryl or hetaryl, where aryl and hetaryl in the last 2 radicals mentioned may be

unsubstituted or carry 1, 2, 3 or 4 identical or different radicals R^{2c},

aryl-C_1-C_6-alkyl, aryl-C_2-C_6-alkenyl or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 3 radicals mentioned may be unsubstituted or carry 1, 2, 3 or 4 identical or different radicals R^{2c}.

Preferred among these are those compounds of the general formula I in which R^2 is selected from aryl and hetaryl, specifically from phenyl, thienyl and pyridyl, where aryl and hetaryl (or phenyl, thienyl and pyridyl) may be unsubstituted or carry 1, 2, 3 or 4, in particular 1 or 2, identical or different radicals R^{2c}.

In this connection, R^{2a}, R^{2b} and R^{2c} where present have the aforementioned meanings. In particular:

R^{2a} is OH, CN, CF_3, O-CF_3, COOH, O-CH_2-COOH, C_1-C_6-alkoxy, C_1-C_6-alkylthio, COO-C_1-C_6-alkyl, $CONH_2$, CONH-C_1-C_6-alkyl, SO_2NH-C_1-C_6-alkyl, CONH-phenyl, SO_2NH-phenyl, CONH-hetaryl, SO_2NH-hetaryl, CON-(C_1-C_6-alkyl)$_2$, SO_2N-(C_1-C_6-alkyl)$_2$, NH-SO_2-C_1-C_6-alkyl, NH-CO-C_1-C_6-alkyl, SO_2-C_1-C_6-alkyl, SO_2-phenyl, NH-SO_2-phenyl, NH-CO-phenyl, NH-SO_2-hetaryl, NH-CO-hetaryl, $NR^{a6}R^{a7}$, where
R^{a6}, R^{a7} are independently of one another hydrogen or C_1-C_6-alkyl, or together with the nitrogen atom to which they are bonded are a morpholine, piperidine, pyrrolidine, azetidine or piperazine residue, where the last 5 radicals mentioned are unsubstituted or may carry 1, 2, 3 or 4 radicals selected from C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy or C_1-C_4-haloalkoxy;

R^{2b} is halogen, C_1-C_4-alkyl, OH, CN, CF_3, O-CF_3, COOH, O-CH_2-COOH, C_1-C_6-alkoxy, C_1-C_6-alkylthio, COO-C_1-C_6-alkyl, $CONH_2$, CONH-C_1-C_6-alkyl, SO_2NH-C_1-C_6-alkyl, CONH-phenyl, SO_2NH-phenyl, CONH-hetaryl, SO_2NH-hetaryl, CON-(C_1-C_6-alkyl)$_2$, SO_2N-(C_1-C_6-alkyl)$_2$, NH-SO_2-C_1-C_6-alkyl, NH-CO-C_1-C_6-alkyl, SO_2-C_1-C_6-alkyl, SO_2-phenyl, NH-SO_2-phenyl, NH-CO-phenyl, NH-SO_2-hetaryl, NH-CO-hetaryl or $NR^{b6}R^{b7}$, where R^{b6}, R^{b7} are independently of one another hydrogen or C_1-C_6-alkyl, or together with the nitrogen atom to which they are bonded are a morpholine, piperidine, pyrrolidine, azetidine or piperazine residue, where the last 5 radicals mentioned are unsubstituted or may carry 1, 2, 3 or 4 radicals selected from C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy or C_1-C_4-haloalkoxy; and

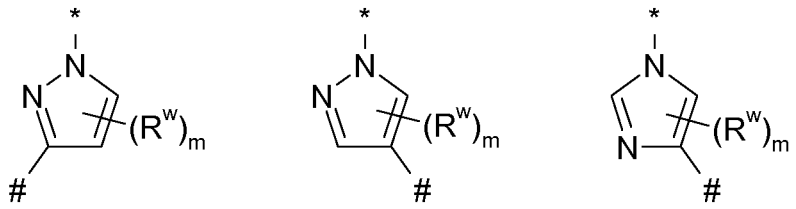
R^{2c} is halogen, C_1-C_4-alkyl, OH, SH, CN, CF_3, O-CF_3, COOH, O-CH_2-COOH, C_1-C_6-alkoxy, C_1-C_6-alkylthio, C_3-C_7-cycloalkyl, COO-C_1-C_6-alkyl, $CONH_2$, CONH-C_1-C_6-alkyl, SO_2NH-C_1-C_6-alkyl, CON-(C_1-C_6-alkyl)$_2$, SO_2N-(C_1-C_6-alkyl)$_2$, NH-SO_2-C_1-C_6-alkyl, NH-CO-C_1-C_6-alkyl, SO_2-C_1-C_6-alkyl, O-phenyl, O-CH_2-phenyl, CONH-phenyl, SO_2NH-phenyl, CONH-hetaryl, SO_2NH-hetaryl, SO_2-phenyl, NH-SO_2-phenyl, NH-CO-phenyl, NH-SO_2-

hetaryl, NH-CO-hetaryl, where phenyl and hetaryl in the last 11 radicals mentioned are unsubstituted or may have 1, 2 or 3 substituents which are selected from halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy and C_1-C_4-haloalkoxy,
$-(CH_2)_p-NR^{c6}R^{c7}$ with p = 0, 1, 2, 3, 4, 5 or 6, in particular 0, and
$-O-(CH_2)_q-NR^{c6}R^{c7}$ with q = 2, 3, 4, 5 or 6, in particular 2, where
R^{c6}, R^{c7} are independently of one another hydrogen or C_1-C_6-alkyl, or together with the nitrogen atom to which they are bonded are a morpholine, piperidine, pyrrolidine, azetidine or piperazine residue, where the last 5 radicals mentioned are unsubstituted or may carry 1, 2, 3 or 4 radicals selected from C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy or C_1-C_4-haloalkoxy.

R^{3a}, R^{3b} in particular OH or the group $CR^{3a}R^{3b}$ is a carbonyl group.

W a radical of the formulae W1 or W2 or the group W-R^2 is a radical of the formula W6.

In the formulae W1 and W2, R^2 is preferably bonded to the carbon in position 3 or 4, as shown in the following formulae W1a, W1b and W2a:



W1a W1b W2a

In the formulae W1a, W1b and W2a, the meanings of *, #, m and R^w are those mentioned above. In particular, m is 0 or 1 and specifically 0. Where m is 1, R^w is preferably selected from halogen, C_1-C_6-alkyl, C_1-C_6-alkyl which is substituted by 1, 2 or 3 substituents R^{wa}, or OH, SH, CN, CF_3, O-CF_3, COOH, O-CH_2-COOH, C_1-C_6-alkoxy, C_1-C_6-alkylthio, C_3-C_7-cycloalkyl, COO-C_1-C_6-alkyl, $CONH_2$, CONH-C_1-C_6-alkyl, SO_2NH-C_1-C_6-alkyl, CON-(C_1-C_6-alkyl)$_2$, SO_2N-(C_1-C_6-alkyl)$_2$, NH-SO_2-C_1-C_6-alkyl, NH-CO-C_1-C_6-alkyl, SO_2-C_1-C_6-alkyl, O-phenyl, O-CH_2-phenyl, CONH-phenyl, SO_2NH-phenyl, CONH-hetaryl, SO_2NH-hetaryl, SO_2-phenyl, NH-SO_2-phenyl, NH-CO-phenyl, NH-SO_2-hetaryl, NH-CO-hetaryl, where phenyl and hetaryl in the last 11 radicals mentioned are unsubstituted or may have 1, 2 or 3 substituents which are selected from halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy and C_1-C_4-haloalkoxy. R^w is in particular selected from OH, F, Cl, CN, CF_3, C_1-C_6-alkyl which is unsubstituted or may have 1, 2 or 3 substituents R^{wa}, or

C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy and C_3-C_7-cycloalkyl. In this connection, R^{wa} has the aforementioned meanings and is in particular C_1-C_4-alkoxy or C_1-C_4-haloalkoxy. R^w is particularly preferably selected from F, Cl, CN, CF_3, CH_3, C_2H_5 and OCH_3.

Where the group W-R^2 is a radical of the formula W6, m is preferably 0 or 1 and specificially 0. Where m is 1, R^{w6*} is preferably selected from halogen, C_1-C_6-alkyl, C_1-C_6-alkyl which is substituted by 1, 2 or 3 substituents R^{wa}, or OH, SH, CN, CF_3, O-CF_3, COOH, O-CH_2-COOH, C_1-C_6-alkoxy, C_1-C_6-alkylthio, C_3-C_7-cycloalkyl, COO-C_1-C_6-alkyl, $CONH_2$, CONH-C_1-C_6-alkyl, SO_2NH-C_1-C_6-alkyl, CON-(C_1-C_6-alkyl)$_2$, SO_2N-(C_1-C_6-alkyl)$_2$, NH-SO_2-C_1-C_6-alkyl, NH-CO-C_1-C_6-alkyl, SO_2-C_1-C_6-alkyl, O-phenyl, O-CH_2-phenyl, CONH-phenyl, SO_2NH-phenyl, CONH-hetaryl, SO_2NH-hetaryl, SO_2-phenyl, NH-SO_2-phenyl, NH-CO-phenyl, NH-SO_2-hetaryl, NH-CO-hetaryl where phenyl and hetaryl in the last 11 radicals mentioned are unsubstituted or may have 1, 2 or 3 substituents which are selected from halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy and C_1-C_4-haloalkoxy. R^{w6*} is in particular selected from OH, F, Cl, CN, CF_3, C_1-C_6-alkyl which is unsubstituted or may have 1, 2 or 3 substituents R^{wa}, or C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy and C_3-C_7-cycloalkyl. In this connection, R^{wa} has the aforementioned meanings and is in particular C_1-C_4-alkoxy or C_1-C_4-haloalkoxy. E in W6 preferably has one of the following meanings: CH_2, CH_2CH_2, CO, CO-NH, O, CH=CH, CH_2O, OCH_2, SO_2, $SO_2NR_E^1$ or $NR_E^1SO_2$, and is in particular CH_2, CH_2CH_2, O, CH=CH, CH_2O, OCH_2, SO_2, $SO_2NR_E^1$ or $NR_E^1SO_2$. In this connection, R_E^1 has one of the aforementioned meanings and is in particular hydrogen or C_1-C_4-alkyl.

Compounds of the formula I which are particularly preferred among the compounds of the invention of the general formula I are those in which W is a radical W1a, and particularly preferred among these are those in which m is 0 or 1 and specifically 0.

Compounds of the formula I which are particularly preferred among the compounds of the invention of the general formula I are those in which W-R^2 is a radical W6, and particularly preferred among these are those in which m is 0 or 1 and specifically 0.

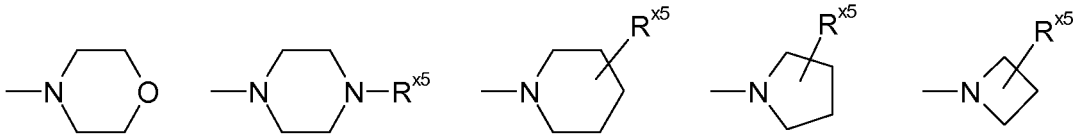
X is a radical C(=O)-$NR^{x2}R^{x3}$ in which R^{x2} and R^{x3} have one of the aforementioned meanings. Compounds preferred among these are those in which:

R^{x2} is H, OH, CN, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{xa}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, aryl, hetaryl, aryl-C_1-C_4-alkyl or hetaryl-C_1-C_4-alkyl, where aryl

and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xd}. In particular, R^{x2} is hydrogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1 or 2 substituents R^{xa}, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, aryl, hetaryl, aryl-C_1-C_4-alkyl or hetaryl-C_1-C_4-alkyl. R^{x2} is very particularly preferably hydrogen.

R^{x3} is H, C_1-C_6-alkyl, C_1-C_6-haloalkyl or C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{xa}. In particular, R^{x3} is hydrogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1 or 2 substituents R^{xa}. R^{x3} is very particularly preferably hydrogen.

Compounds of the formula I which are likewise preferred are those in which the group $NR^{x2}R^{x3}$ is a nitrogen heterocycle of the following formulae:



in which R^{x5} is hydrogen or has the meaning indicated for R^{xb}. In particular, R^{x5} is C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{xa}, or C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, aryl-C_1-C_4-alkyl or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 2 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xd}, or COO-C_1-C_6-alkyl, $CONH_2$, CONH-C_1-C_6-alkyl, SO_2NH-C_1-C_6-alkyl, CON-(C_1-C_6-alkyl)$_2$, SO_2N-(C_1-C_6-alkyl)$_2$, NH-SO_2-C_1-C_6-alkyl, CONH-phenyl, SO_2NH-phenyl, CONH-hetaryl, SO_2NH-hetaryl, where phenyl and hetaryl in the last 4 radicals mentioned are unsubstituted or may have 1, 2 or 3 substituents which are selected from the halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy and C_1-C_4-haloalkoxy. In particular, R^{x5} is hydrogen or C_1-C_4-alkyl.

In a particularly preferred embodiment of the invention, X is C(O)-NH_2.

In another embodiment of the invention, X is hydrogen.

In another embodiment of the invention, X is $C(O)OR^{x1}$ in which R^{x1} has the aforementioned meanings. In particular, R^1 is C_1-C_6-Alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{xa}, or C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, aryl, hetaryl, aryl-C_1-C_4-alkyl or hetaryl-C_1-C_4-alkyl stands, where aryl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xd}.

In this connection, R^{xa} has the aforementioned meanings and is in particular C_1-C_4-alkoxy or C_1-C_4-haloalkoxy. In this connection, R^{xd} has the aforementioned meanings and is preferably F, Cl, OH, COOH, $C(O)NH_2$, CN, NH_2, OCH_2COOH, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_1-C_4-alkylthio, C_1-C_4-haloalkylthio, CO-C_1-C_4-alkyl, CO-O-C_1-C_4-alkyl, NH-C_1-C_4-alkyl, NH-$C(O)C_1$-C_4-alkyl or SO_2-C_1-C_4-alkyl.

Y a divalent, 6-membered heteroaromatic radical which has 1 or 2 nitrogen atoms as ring members and which is preferably selected from pyridinediyl and pyrimidinediyl and which optionally has 1 or 2 identical or different substituents R^y. Y is in particular pyridinediyl which is unsubstituted or has 1 or 2 identical or different substituents R^y. Y is in particular unsubstituted or has one substituent R^y.

W is preferably bonded to a C atom of Y which is located in the position ortho to the C atom of Y which is connected to the carbonyl group. Accordingly, Y is preferably selected from pyridine-2,3-diyl, pyridine-3,4-diyl and pyrimidine-5,6-diyl. A nitrogen atom is preferably present at the other position ortho to the C atom of Y to which W is bonded.

Where R^y is present, R^y is preferably selected from OH, F, Cl, NH_2, CN, CF_3, CHF_2, O-CF_3, O-CHF_2, O-CH_2F, C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_1-C_6-alkylamino, C_1-C_6-dialkylamino, pyrrolidinyl, piperidinyl, morpholinyl, imidazolyl, C_1-C_4-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkyl, $CONR^{y2}R^{y3}$, $SO_2NR^{y2}R^{y3}$, NH-SO_2-R^{y4}, -$(CH_2)_p$-$NR^{y6}R^{y7}$, NH-CO-R^{y5}, in which p is 0, 1, 2, 3, 4, or 5, and in which R^{y2}, R^{y3}, R^{y4}, R^{y5}, R^{y6}, R^{y7} have the aforementioned meanings, preferably the meanings mentioned as preferred below, and are in particular H and C_1-C_6-alkyl,
phenyl, benzyl and O-benzyl, where the phenyl ring in the last 3 groups mentioned may have 1, 2 or 3 substituents selected from halogen, OH, SH, NO_2, COOH, $C(O)NH_2$, CHO, CN, NH_2, OCH_2COOH, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_1-C_6-alkylthio, C_1-C_6-haloalkylthio, CO-C_1-C_6-alkyl, CO-O-C_1-C_6-alkyl, NH-C_1-C_6-alkyl, NHCHO, NH-$C(O)C_1$-C_6-alkyl, and SO_2-C_1-C_6-alkyl.

In particular, R^y is OH, F, Cl, NH_2, CN, CF_3, CHF_2, O-CF_3, O-CHF_2, O-CH_2F, C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_1-C_6-alkylamino, C_1-C_6-dialkylamino, pyrrolidinyl, piperidinyl, morpholinyl, imidazolyl, C_1-C_4-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkyl, CONH-C_1-C_6-alkyl, $SO_2N(C_1$-C_6-alkyl$)_2$, NH-SO_2-C_1-C_6-alkyl, NH-CO-C_1-C_6-alkyl, $(CH_2)_p$-$N(C_1$-C_6-alkyl$)_2$, in which p is 2, 3 or 4.

R^y is particularly preferably F, Cl, CN, CF_3, CHF_2, O-CF_3, O-CHF_2, O-CH_2F or C_1-C_3-alkyl.

Otherwise, the radicals R^{x4}, R^{ya}, R^{wa}, R_E^{1a}, R^{yb}, R^{wb}, R_E^{1b}, R^{yd}, R^{wd}, R_E^{1d}, R^{a1}, R^{b1}, R^{c1}, R^{y1}, R^{w1}, R^{a2}, R^{b2}, R^{c2}, R^{y2}, R^{w2}, R^{a3}, R^{b3}, R^{c3}, R^{y3}, R^{w3}, R^{a4}, R^{b4}, R^{c4}, R^{y4}, R^{w4}, R^{a5}, R^{b5}, R^{c5}, R^{y5}, R^{w5}, R^{a6}, R^{b6}, R^{c6}, R^{y6}, R^{w6}, R^{a7}, R^{b7}, R^{c7}, R^{y7} and R^{w7} have, unless otherwise indicated, independently of one another preferably one of the following meanings:

R^{x4}: hydrogen or C_1-C_6-alkyl.

R^{ya}, R^{wa}, R_E^{1a} independently of one another: C_1-C_4-alkoxy or C_1-C_4-haloalkoxy.

R^{yb}, R^{wb}, R_E^{1b} independently of one another: halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy or C_1-C_4-haloalkoxy.

R^{yd}, R^{wd}, R_E^{1d} independently of one another: F, Cl, OH, COOH, $C(O)NH_2$, CN, NH_2, OCH_2COOH, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_1-C_4-alkylthio, C_1-C_4-haloalkylthio, CO-C_1-C_4-alkyl, CO-O-C_1-C_4-alkyl, NH-C_1-C_4-alkyl, NH-$C(O)C_1$-C_4-alkyl or SO_2-C_1-C_4-alkyl.

R^{a1}, R^{b1}, R^{c1}, R^{y1}, R^{w1} independently of one another: hydrogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, phenyl, benzyl, hetaryl and hetarylmethyl, where phenyl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents which are selected from halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy and C_1-C_4-haloalkoxy.

R^{a2}, R^{b2}, R^{c2}, R^{y2}, R^{w2} independently of one another: hydrogen, C_1-C_6-alkyl, phenyl, benzyl, hetaryl and hetarylmethyl, where phenyl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents which are selected from halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy and C_1-C_4-haloalkoxy.

R^{a3}, R^{b3}, R^{c3}, R^{y3}, R^{w3} independently of one another: hydrogen or C_1-C_6-alkyl,

or R^{a2} with R^{a3} (and likewise R^{b2} with R^{b3}, R^{c2} with R^{c3}, R^{y2} with R^{y3} and R^{w2} with R^{w3}) together with the nitrogen atom to which they are bonded are a morpholine, piperidine, pyrrolidine, azetidine or piperazine residue, where the last 5 radicals mentioned are unsubstituted or may carry 1, 2, 3 or 4 radicals selected from C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy or C_1-C_4-haloalkoxy.

R^{a4}, R^{b4}, R^{c4}, R^{y4}, R^{w4} independently of one another: hydrogen, C_1-C_6-alkyl, phenyl, benzyl, hetaryl and hetarylmethyl, where phenyl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents which are selected from halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy and C_1-C_4-haloalkoxy.

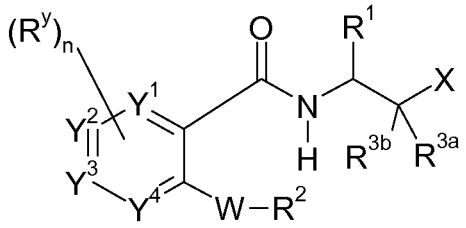
R^{a5}, R^{b5}, R^{c5}, R^{y5}, R^{w5} independently of one another: hydrogen, C_1-C_6-alkyl, phenyl, benzyl, hetaryl and hetarylmethyl, where phenyl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents which are selected from halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy and C_1-C_4-haloalkoxy.

R^{a6}, R^{b6}, R^{c6}, R^{y6}, R^{w6} independently of one another: hydrogen, C_1-C_6-alkyl, phenyl, benzyl, hetaryl and hetarylmethyl, where phenyl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents which are selected from halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy and C_1-C_4-haloalkoxy.

R^{a7}, R^{b7}, R^{c7}, R^{y7}, R^{w7} independently of one another: hydrogen or C_1-C_6-alkyl,

or R^{a6} with R^{a7} (and likewise R^{b6} with R^{b7}, R^{c6} with R^{c7}, R^{y6} with R^{y7} and R^{w6} with R^{w7}) together with the nitrogen atom to which they are bonded are a morpholine, piperidine, pyrrolidine, azetidine or piperazine residue, where the last 5 radicals mentioned are unsubstituted or may carry 1, 2, 3 or 4 radicals selected from C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy or C_1-C_4-haloalkoxy.

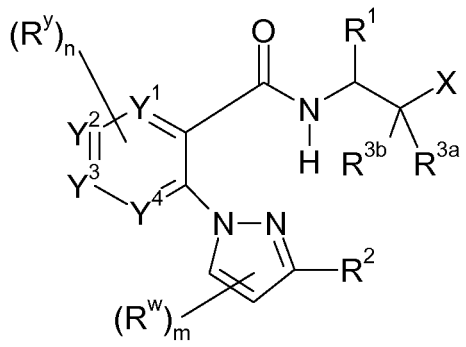
Compounds preferred among the carboxamide compounds of the invention of the formula I are those which correspond to the general formula I-A,



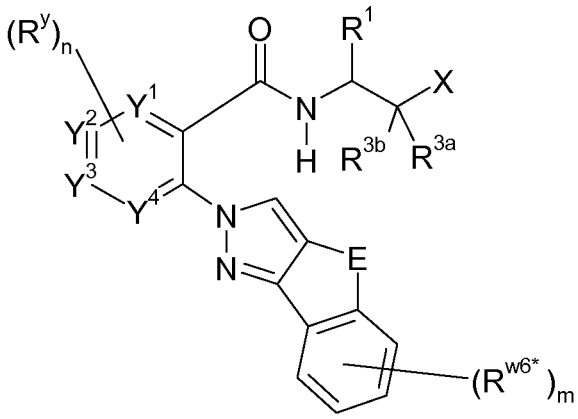
(I-A)

in which X, W, R^1, R^2, R^{3a}, R^{3b}, R^y have the aforementioned meanings, in particular the meanings mentioned as preferred, n is 0, 1 or 2, in particular 0 or 1, one of the variables Y^1, Y^2, Y^3 and Y^4 is a nitrogen atom and the remaining variables Y^1, Y^2, Y^3 or Y^4 are CH (or C-R^y if n is different from 0). Also preferred are the tautomers of I-A, the pharmaceutically suitable salts thereof and the tautomers thereof.

Compounds in turn preferred among the carboxamide compounds of the invention of the formula I-A are those which correspond to the general formulae I-A' or I-A",



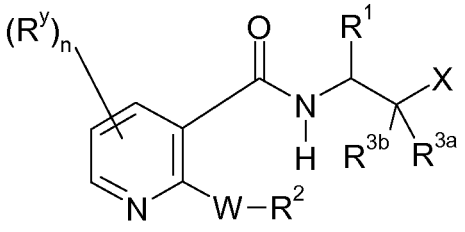
(I-A')



I-A"

in which m, X, E, R^1, R^2, R^{3a}, R^{3b}, R^y, R^w and R^{w6} have the aforementioned meanings, in particular the meanings mentioned as preferred, n is 0, 1 or 2, in particular 0 or 1, one of the variables Y^1, Y^2, Y^3 and Y^4 is a nitrogen atom and the remaining variables Y^1, Y^2, Y^3 or Y^4 are CH (or C-R^y if n is different from 0). Also preferred are the tautomers of I-A' and I-A", the pharmaceutically suitable salts thereof and the tautomers thereof.

Compounds preferred in turn among the carboxamide compounds of the invention of the formula I-A are those which correspond to the general formula I-A.a,

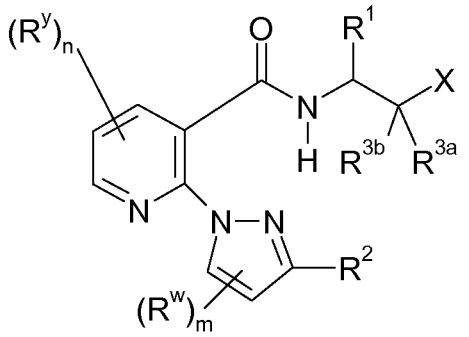


(I-A.a)

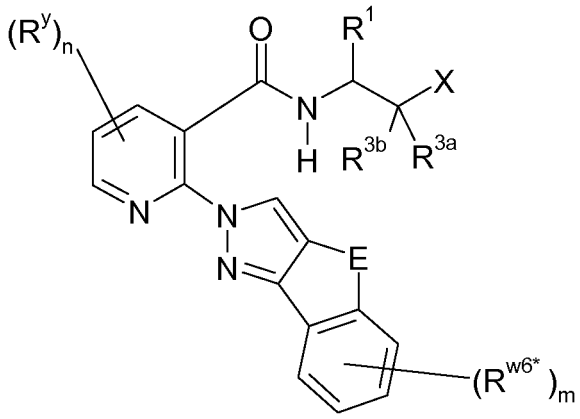
in which X, W, R^1, R^2, R^{3a}, R^{3b}, R^y have the aforementioned meanings, especially those mentioned as preferred, and n is 0, 1 or 2, in particular 0 or 1. Also preferred are the tautomers of I-A.a, the pharmaceutically acceptable salts thereof and the tautomers thereof.

Compounds in turn preferred among the carboxamide compounds of the invention of

the formula I-A.a are those which correspond to the general formulae I-A.a' or I-A.a",



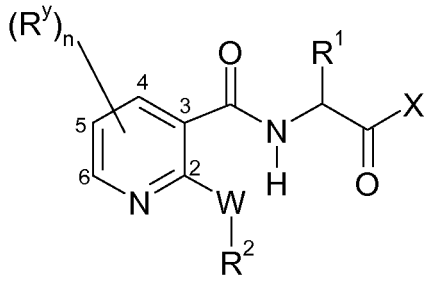
(I-A.a')



I-A.a"

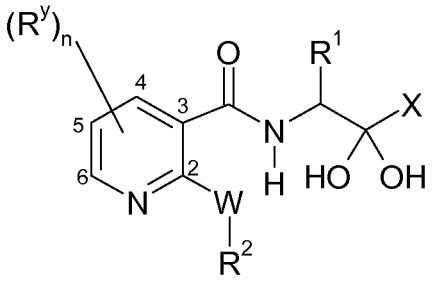
in which m, E, R^1, R^{3a}, R^{3b}, R^2, R^y, R^w and R^{w6} have the aforementioned meanings, especially those mentioned as preferred, and n is 0, 1 or 2, in particular 0 or 1. Also preferred are the tautomers of I-A.a' and I-A.a", the pharmaceutically suitable salts thereof and the tautomers thereof.

The compounds of the general formula I-A.a which are indicated in Tables 1 to 20 below and in which $CR^{3a}R^{3b}$ is a carbonyl function or a $C(OH)_2$ group, and their tautomers, prodrugs and pharmaceutically acceptable salts, represent per se preferred embodiments of the present invention. The meanings for R^1, R^2 and W indicated in Table A below represent embodiments of the invention which are likewise preferred independently of one another and especially in combination.



$CR^{3a}R^{3b} = C=O$

(I-A.a)



$CR^{3a}R^{3b} = C(OH)_2$

Table 1
Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is C=O, X is carbamoyl, $n = 0$, i.e. $(R^y)_n$ is absent, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 2
Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is C=O, X is carbamoyl, $(R^y)_n$ is 5-F, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 3
Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is C=O, X is carbamoyl, $(R^y)_n$ is 5-Cl, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 4
Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is C=O, X is carbamoyl, $(R^y)_n$ is 5-CN, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 5
Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is C=O, X is carbamoyl, $(R^y)_n$ is 5-CH_3, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 6
Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is C=O, X is -C(O)$NHCH_3$, $n = 0$, i.e. $(R^y)_n$ is absent, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 7
Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is C=O, X is $-C(O)NHCH_3$, $(R^y)_n$ is 5-F, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 8
Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is C=O, X is $-C(O)NHCH_3$, $(R^y)_n$ is 5-Cl, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 9
Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is C=O, X is $-C(O)NHCH_3$, $(R^y)_n$ is 5-CN, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 10
Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is C=O, X is $-C(O)NHCH_3$, $(R^y)_n$ is 5-CH_3, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 11
Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is $C(OH)_2$, X is carbamoyl, n = 0, i.e. $(R^y)_n$ is absent, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 12
Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is $C(OH)_2$, X is carbamoyl, $(R^y)_n$ is 5-F, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 13
Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is $C(OH)_2$, X is carbamoyl, $(R^y)_n$ is 5-Cl, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 14
Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is $C(OH)_2$, X is carbamoyl, $(R^y)_n$ is 5-CN, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 15
Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is $C(OH)_2$, X is

carbamoyl, $(R^y)_n$ is 5-CH_3, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 16

Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is $C(OH)_2$, X is -C(O)$NHCH_3$, n = 0, i.e. $(R^y)_n$ is absent, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 17

Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is $C(OH)_2$, X is -C(O)$NHCH_3$, $(R^y)_n$ is 5-F, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 18

Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is $C(OH)_2$, X is -C(O)$NHCH_3$, $(R^y)_n$ is 5-Cl, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 19

Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is $C(OH)_2$, X is -C(O)$NHCH_3$, $(R^y)_n$ is 5-CN, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table 20

Compounds of the formula I-A.a in which the group $C(R^{3a}R^{3b})$ is $C(OH)_2$, X is -C(O)$NHCH_3$, $(R^y)_n$ is 5-CH_3, and the combination of R^1, R^2 and W for a compound in each case corresponds to one line of Table A.

Table A

No.	R^1	R^2	W
A-1	n-Butyl	Phenyl	W1a (m= 0)
A-2	n-Butyl	2-Methylphenyl	W1a (m= 0)
A-3	n-Butyl	2-Methoxyphenyl	W1a (m= 0)
A-4	n-Butyl	2-Chlorophenyl	W1a (m= 0)
A-5	n-Butyl	2-Fluorophenyl	W1a (m= 0)
A-6	n-Butyl	2-Trifluoromethylphenyl	W1a (m= 0)
A-7	n-Butyl	3-Methylphenyl	W1a (m= 0)
A-8	n-Butyl	3-Methoxyphenyl	W1a (m= 0)
A-9	n-Butyl	3-Chlorophenyl	W1a (m= 0)
A-10	n-Butyl	3-Fluorophenyl	W1a (m= 0)

No.	R^1	R^2	W
A-11	n-Butyl	3-Trifluoromethyl	W1a (m= 0)
A-12	n-Butyl	3-[(Phenylmethyl)oxy]phenyl	W1a (m= 0)
A-13	n-Butyl	3-Morpholin-4-ylphenyl	W1a (m= 0)
A-14	n-Butyl	3-(Morpholin-4-ylmethyl)phenyl	W1a (m= 0)
A-15	n-Butyl	3-Pyrrolidin-1-ylphenyl	W1a (m= 0)
A-16	n-Butyl	4-Methylphenyl	W1a (m= 0)
A-17	n-Butyl	4-(1-Methylethyl)phenyl	W1a (m= 0)
A-18	n-Butyl	4-Methoxyphenyl	W1a (m= 0)
A-19	n-Butyl	4-Chlorophenyl	W1a (m= 0)
A-20	n-Butyl	4-Fluorophenyl	W1a (m= 0)
A-21	n-Butyl	4-Trifluoromethylphenyl	W1a (m= 0)
A-22	n-Butyl	4-Diethylaminophenyl	W1a (m= 0)
A-23	n-Butyl	4-[(Diethylamino)methyl]phenyl	W1a (m= 0)
A-24	n-Butyl	4-Cyanophenyl	W1a (m= 0)
A-25	n-Butyl	4-(Piperidin-1-yl)phenyl	W1a (m= 0)
A-26	n-Butyl	4-(4-Methylpiperazin-1-yl)phenyl	W1a (m= 0)
A-27	n-Butyl	4-Pyrrolidin-1-ylphenyl	W1a (m= 0)
A-28	n-Butyl	4-(1H-Imidazol-1-yl)phenyl	W1a (m= 0)
A-29	n-Butyl	4-Morpholin-4-ylphenyl	W1a (m= 0)
A-30	n-Butyl	4-(Morpholin-4-ylmethyl)phenyl	W1a (m= 0)
A-31	n-Butyl	2,4-Difluorophenyl	W1a (m= 0)
A-32	n-Butyl	2,6-Difluorophenyl	W1a (m= 0)
A-33	n-Butyl	3,5-Difluorophenyl	W1a (m= 0)
A-34	n-Butyl	2,4-Dichlorophenyl	W1a (m= 0)
A-35	n-Butyl	2,6-Dichlorophenyl	W1a (m= 0)
A-36	n-Butyl	3,5-Dichlorophenyl	W1a (m= 0)
A-37	n-Butyl	2-Chloro-4-fluorophenyl	W1a (m= 0)
A-38	n-Butyl	2-Chloro-4-morpholin-4-ylphenyl	W1a (m= 0)
A-39	n-Butyl	2-Fluoro-4-morpholin-4-ylphenyl	W1a (m= 0)
A-40	n-Butyl	Pyridin-2-yl	W1a (m= 0)
A-41	n-Butyl	Pyridin-4-yl	W1a (m= 0)
A-42	n-Butyl	Thien-2-yl	W1a (m= 0)
A-43	n-Butyl	2,3-Dihydrobenzo[b]furan-5-yl	W1a (m= 0)
A-44	Isobutyl	Phenyl	W1a (m= 0)
A-45	Isobutyl	2-Methylphenyl	W1a (m= 0)
A-46	Isobutyl	2-Methoxyphenyl	W1a (m= 0)
A-47	Isobutyl	2-Chlorophenyl	W1a (m= 0)
A-48	Isobutyl	2-Fluorophenyl	W1a (m= 0)
A-49	Isobutyl	2-Trifluoromethylphenyl	W1a (m= 0)

No.	R^1	R^2	W
A-50	Isobutyl	3-Methylphenyl	W1a (m= 0)
A-51	Isobutyl	3-Methoxyphenyl	W1a (m= 0)
A-52	Isobutyl	3-Chlorophenyl	W1a (m= 0)
A-53	Isobutyl	3-Fluorophenyl	W1a (m= 0)
A-54	Isobutyl	3-Trifluoromethyl	W1a (m= 0)
A-55	Isobutyl	3-[(Phenylmethyl)oxy]phenyl	W1a (m= 0)
A-56	Isobutyl	3-Morpholin-4-ylphenyl	W1a (m= 0)
A-57	Isobutyl	3-(Morpholin-4-ylmethyl)phenyl	W1a (m= 0)
A-58	Isobutyl	3-Pyrrolidin-1-ylphenyl	W1a (m= 0)
A-59	Isobutyl	4-Methylphenyl	W1a (m= 0)
A-60	Isobutyl	4-(1-Methylethyl)phenyl	W1a (m= 0)
A-61	Isobutyl	4-Methoxyphenyl	W1a (m= 0)
A-62	Isobutyl	4-Chlorophenyl	W1a (m= 0)
A-63	Isobutyl	4-Fluorophenyl	W1a (m= 0)
A-64	Isobutyl	4-Trifluoromethylphenyl	W1a (m= 0)
A-65	Isobutyl	4-Diethylaminophenyl	W1a (m= 0)
A-66	Isobutyl	4-[(Diethylamino)methyl]phenyl	W1a (m= 0)
A-67	Isobutyl	4-Cyanophenyl	W1a (m= 0)
A-68	Isobutyl	4-(Piperidin-1-yl)phenyl	W1a (m= 0)
A-69	Isobutyl	4-(4-Methylpiperazin-1-yl)phenyl	W1a (m= 0)
A-70	Isobutyl	4-Pyrrolidin-1-ylphenyl	W1a (m= 0)
A-71	Isobutyl	4-(1H-Imidazol-1-yl)phenyl	W1a (m= 0)
A-72	Isobutyl	4-Morpholin-4-ylphenyl	W1a (m= 0)
A-73	Isobutyl	4-(Morpholin-4-ylmethyl)phenyl	W1a (m= 0)
A-74	Isobutyl	2,4-Difluorophenyl	W1a (m= 0)
A-75	Isobutyl	2,6-Difluorophenyl	W1a (m= 0)
A-76	Isobutyl	3,5-Difluorophenyl	W1a (m= 0)
A-77	Isobutyl	2,4-Dichlorophenyl	W1a (m= 0)
A-78	Isobutyl	2,6-Dichlorophenyl	W1a (m= 0)
A-79	Isobutyl	3,5-Dichlorophenyl	W1a (m= 0)
A-80	Isobutyl	2-Chloro-4-fluorophenyl	W1a (m= 0)
A-81	Isobutyl	2-Chloro-4-morpholin-4-ylphenyl	W1a (m= 0)
A-82	Isobutyl	2-Fluoro-4-morpholin-4-ylphenyl	W1a (m= 0)
A-83	Isobutyl	Pyridin-2-yl	W1a (m= 0)
A-84	Isobutyl	Pyridin-4-yl	W1a (m= 0)
A-85	Isobutyl	Thien-2-yl	W1a (m= 0)
A-86	Isobutyl	2,3-Dihydrobenzo[b]furan-5-yl	W1a (m= 0)
A-87	Benzyl	Phenyl	W1a (m= 0)
A-88	Benzyl	2-Methylphenyl	W1a (m= 0)

No.	R^1	R^2	W
A-89	Benzyl	2-Methoxyphenyl	W1a (m= 0)
A-90	Benzyl	2-Chlorophenyl	W1a (m= 0)
A-91	Benzyl	2-Fluorophenyl	W1a (m= 0)
A-92	Benzyl	2-Trifluoromethylphenyl	W1a (m= 0)
A-93	Benzyl	3-Methylphenyl	W1a (m= 0)
A-94	Benzyl	3-Methoxyphenyl	W1a (m= 0)
A-95	Benzyl	3-Chlorophenyl	W1a (m= 0)
A-96	Benzyl	3-Fluorophenyl	W1a (m= 0)
A-97	Benzyl	3-Trifluoromethyl	W1a (m= 0)
A-98	Benzyl	3-[(Phenylmethyl)oxy]phenyl	W1a (m= 0)
A-99	Benzyl	3-Morpholin-4-ylphenyl	W1a (m= 0)
A-100	Benzyl	3-(Morpholin-4-ylmethyl)phenyl	W1a (m= 0)
A-101	Benzyl	3-Pyrrolidin-1-ylphenyl	W1a (m= 0)
A-102	Benzyl	4-Methylphenyl	W1a (m= 0)
A-103	Benzyl	4-(1-Methylethyl)phenyl	W1a (m= 0)
A-104	Benzyl	4-Methoxyphenyl	W1a (m= 0)
A-105	Benzyl	4-Chlorophenyl	W1a (m= 0)
A-106	Benzyl	4-Fluorophenyl	W1a (m= 0)
A-107	Benzyl	4-Trifluoromethylphenyl	W1a (m= 0)
A-108	Benzyl	4-Diethylaminophenyl	W1a (m= 0)
A-109	Benzyl	4-[(Diethylamino)methyl]phenyl	W1a (m= 0)
A-110	Benzyl	4-Cyanophenyl	W1a (m= 0)
A-111	Benzyl	4-(Piperidin-1-yl)phenyl	W1a (m= 0)
A-112	Benzyl	4-(4-Methylpiperazin-1-yl)phenyl	W1a (m= 0)
A-113	Benzyl	4-Pyrrolidin-1-ylphenyl	W1a (m= 0)
A-114	Benzyl	4-(1H-Imidazol-1-yl)phenyl	W1a (m= 0)
A-115	Benzyl	4-Morpholin-4-ylphenyl	W1a (m= 0)
A-116	Benzyl	4-(Morpholin-4-ylmethyl)phenyl	W1a (m= 0)
A-117	Benzyl	2,4-Difluorophenyl	W1a (m= 0)
A-118	Benzyl	2,6-Difluorophenyl	W1a (m= 0)
A-119	Benzyl	3,5-Difluorophenyl	W1a (m= 0)
A-120	Benzyl	2,4-Dichlorophenyl	W1a (m= 0)
A-121	Benzyl	2,6-Dichlorophenyl	W1a (m= 0)
A-122	Benzyl	3,5-Dichlorophenyl	W1a (m= 0)
A-123	Benzyl	2-Chloro-4-fluorophenyl	W1a (m= 0)
A-124	Benzyl	2-Chloro-4-morpholin-4-ylphenyl	W1a (m= 0)
A-125	Benzyl	2-Fluoro-4-morpholin-4-ylphenyl	W1a (m= 0)
A-126	Benzyl	Pyridin-2-yl	W1a (m= 0)
A-127	Benzyl	Pyridin-4-yl	W1a (m= 0)

No.	R^1	R^2	W
A-128	Benzyl	Thien-2-yl	W1a (m= 0)
A-129	Benzyl	2,3-Dihydrobenzo[b]furan-5-yl	W1a (m= 0)
A-130	4-Chlorobenzyl	Phenyl	W1a (m= 0)
A-131	4-Chlorobenzyl	2-Methylphenyl	W1a (m= 0)
A-132	4-Chlorobenzyl	2-Methoxyphenyl	W1a (m= 0)
A-133	4-Chlorobenzyl	2-Chlorophenyl	W1a (m= 0)
A-134	4-Chlorobenzyl	2-Fluorophenyl	W1a (m= 0)
A-135	4-Chlorobenzyl	2-Trifluoromethylphenyl	W1a (m= 0)
A-136	4-Chlorobenzyl	3-Methylphenyl	W1a (m= 0)
A-137	4-Chlorobenzyl	3-Methoxyphenyl	W1a (m= 0)
A-138	4-Chlorobenzyl	3-Chlorophenyl	W1a (m= 0)
A-139	4-Chlorobenzyl	3-Fluorophenyl	W1a (m= 0)
A-140	4-Chlorobenzyl	3-Trifluoromethyl	W1a (m= 0)
A-141	4-Chlorobenzyl	3-[(Phenylmethyl)oxy]phenyl	W1a (m= 0)
A-142	4-Chlorobenzyl	3-Morpholin-4-ylphenyl	W1a (m= 0)
A-143	4-Chlorobenzyl	3-(Morpholin-4-ylmethyl)phenyl	W1a (m= 0)
A-144	4-Chlorobenzyl	3-Pyrrolidin-1-ylphenyl	W1a (m= 0)
A-145	4-Chlorobenzyl	4-Methylphenyl	W1a (m= 0)
A-146	4-Chlorobenzyl	4-(1-Methylethyl)phenyl	W1a (m= 0)
A-147	4-Chlorobenzyl	4-Methoxyphenyl	W1a (m= 0)
A-148	4-Chlorobenzyl	4-Chlorophenyl	W1a (m= 0)
A-149	4-Chlorobenzyl	4-Fluorophenyl	W1a (m= 0)
A-150	4-Chlorobenzyl	4-Trifluoromethylphenyl	W1a (m= 0)
A-151	4-Chlorobenzyl	4-Diethylaminophenyl	W1a (m= 0)
A-152	4-Chlorobenzyl	4-[(Diethylamino)methyl]phenyl	W1a (m= 0)
A-153	4-Chlorobenzyl	4-Cyanophenyl	W1a (m= 0)
A-154	4-Chlorobenzyl	4-(Piperidin-1-yl)phenyl	W1a (m= 0)
A-155	4-Chlorobenzyl	4-(4-Methylpiperazin-1-yl)phenyl	W1a (m= 0)
A-156	4-Chlorobenzyl	4-Pyrrolidin-1-ylphenyl	W1a (m= 0)
A-157	4-Chlorobenzyl	4-(1H-Imidazol-1-yl)phenyl	W1a (m= 0)
A-158	4-Chlorobenzyl	4-Morpholin-4-ylphenyl	W1a (m= 0)
A-159	4-Chlorobenzyl	4-(Morpholin-4-ylmethyl)phenyl	W1a (m= 0)
A-160	4-Chlorobenzyl	2,4-Difluorophenyl	W1a (m= 0)
A-161	4-Chlorobenzyl	2,6-Difluorophenyl	W1a (m= 0)
A-162	4-Chlorobenzyl	3,5-Difluorophenyl	W1a (m= 0)
A-163	4-Chlorobenzyl	2,4-Dichlorophenyl	W1a (m= 0)
A-164	4-Chlorobenzyl	2,6-Dichlorophenyl	W1a (m= 0)
A-165	4-Chlorobenzyl	3,5-Dichlorophenyl	W1a (m= 0)
A-166	4-Chlorobenzyl	2-Chloro-4-fluorophenyl	W1a (m= 0)

No.	R^1	R^2	W
A-167	4-Chlorobenzyl	2-Chloro-4-morpholin-4-ylphenyl	W1a (m= 0)
A-168	4-Chlorobenzyl	2-Fluoro-4-morpholin-4-ylphenyl	W1a (m= 0)
A-169	4-Chlorobenzyl	Pyridin-2-yl	W1a (m= 0)
A-170	4-Chlorobenzyl	Pyridin-4-yl	W1a (m= 0)
A-171	4-Chlorobenzyl	Thien-2-yl	W1a (m= 0)
A-172	4-Chlorobenzyl	2,3-Dihydrobenzo[b]furan-5-yl	W1a (m= 0)
A-173	4-Methoxybenzyl	Phenyl	W1a (m= 0)
A-174	4-Methoxybenzyl	2-Methylphenyl	W1a (m= 0)
A-175	4-Methoxybenzyl	2-Methoxyphenyl	W1a (m= 0)
A-176	4-Methoxybenzyl	2-Chlorophenyl	W1a (m= 0)
A-177	4-Methoxybenzyl	2-Fluorophenyl	W1a (m= 0)
A-178	4-Methoxybenzyl	2-Trifluoromethylphenyl	W1a (m= 0)
A-179	4-Methoxybenzyl	3-Methylphenyl	W1a (m= 0)
A-180	4-Methoxybenzyl	3-Methoxyphenyl	W1a (m= 0)
A-181	4-Methoxybenzyl	3-Chlorophenyl	W1a (m= 0)
A-182	4-Methoxybenzyl	3-Fluorophenyl	W1a (m= 0)
A-183	4-Methoxybenzyl	3-Trifluoromethyl	W1a (m= 0)
A-184	4-Methoxybenzyl	3-[(Phenylmethyl)oxy]phenyl	W1a (m= 0)
A-185	4-Methoxybenzyl	3-Morpholin-4-ylphenyl	W1a (m= 0)
A-186	4-Methoxybenzyl	3-(Morpholin-4-ylmethyl)phenyl	W1a (m= 0)
A-187	4-Methoxybenzyl	3-Pyrrolidin-1-ylphenyl	W1a (m= 0)
A-188	4-Methoxybenzyl	4-Methylphenyl	W1a (m= 0)
A-189	4-Methoxybenzyl	4-(1-Methylethyl)phenyl	W1a (m= 0)
A-190	4-Methoxybenzyl	4-Methoxyphenyl	W1a (m= 0)
A-191	4-Methoxybenzyl	4-Chlorophenyl	W1a (m= 0)
A-192	4-Methoxybenzyl	4-Fluorophenyl	W1a (m= 0)
A-193	4-Methoxybenzyl	4-Trifluoromethylphenyl	W1a (m= 0)
A-194	4-Methoxybenzyl	4-Diethylaminophenyl	W1a (m= 0)
A-195	4-Methoxybenzyl	4-[(Diethylamino)methyl]phenyl	W1a (m= 0)
A-196	4-Methoxybenzyl	4-Cyanophenyl	W1a (m= 0)
A-197	4-Methoxybenzyl	4-(Piperidin-1-yl)phenyl	W1a (m= 0)
A-198	4-Methoxybenzyl	4-(4-Methylpiperazin-1-yl)phenyl	W1a (m= 0)
A-199	4-Methoxybenzyl	4-Pyrrolidin-1-ylphenyl	W1a (m= 0)
A-200	4-Methoxybenzyl	4-(1H-Imidazol-1-yl)phenyl	W1a (m= 0)
A-201	4-Methoxybenzyl	4-Morpholin-4-ylphenyl	W1a (m= 0)
A-202	4-Methoxybenzyl	4-(Morpholin-4-ylmethyl)phenyl	W1a (m= 0)
A-203	4-Methoxybenzyl	2,4-Difluorophenyl	W1a (m= 0)
A-204	4-Methoxybenzyl	2,6-Difluorophenyl	W1a (m= 0)
A-205	4-Methoxybenzyl	3,5-Difluorophenyl	W1a (m= 0)

No.	R^1	R^2	W
A-206	4-Methoxybenzyl	2,4-Dichlorophenyl	W1a (m= 0)
A-207	4-Methoxybenzyl	2,6-Dichlorophenyl	W1a (m= 0)
A-208	4-Methoxybenzyl	3,5-Dichlorophenyl	W1a (m= 0)
A-209	4-Methoxybenzyl	2-Chloro-4-fluorophenyl	W1a (m= 0)
A-210	4-Methoxybenzyl	2-Chloro-4-morpholin-4-ylphenyl	W1a (m= 0)
A-211	4-Methoxybenzyl	2-Fluoro-4-morpholin-4-ylphenyl	W1a (m= 0)
A-212	4-Methoxybenzyl	Pyridin-2-yl	W1a (m= 0)
A-213	4-Methoxybenzyl	Pyridin-4-yl	W1a (m= 0)
A-214	4-Methoxybenzyl	Thien-2-yl	W1a (m= 0)
A-215	4-Methoxybenzyl	2,3-Dihydrobenzo[b]furan-5-yl	W1a (m= 0)
A-216	Cyclohexylmethyl	Phenyl	W1a (m= 0)
A-217	Cyclohexylmethyl	2-Methylphenyl	W1a (m= 0)
A-218	Cyclohexylmethyl	2-Methoxyphenyl	W1a (m= 0)
A-219	Cyclohexylmethyl	2-Chlorophenyl	W1a (m= 0)
A-220	Cyclohexylmethyl	2-Fluorophenyl	W1a (m= 0)
A-221	Cyclohexylmethyl	2-Trifluoromethylphenyl	W1a (m= 0)
A-222	Cyclohexylmethyl	3-Methylphenyl	W1a (m= 0)
A-223	Cyclohexylmethyl	3-Methoxyphenyl	W1a (m= 0)
A-224	Cyclohexylmethyl	3-Chlorophenyl	W1a (m= 0)
A-225	Cyclohexylmethyl	3-Fluorophenyl	W1a (m= 0)
A-226	Cyclohexylmethyl	3-Trifluoromethyl	W1a (m= 0)
A-227	Cyclohexylmethyl	3-[(Phenylmethyl)oxy]phenyl	W1a (m= 0)
A-228	Cyclohexylmethyl	3-Morpholin-4-ylphenyl	W1a (m= 0)
A-229	Cyclohexylmethyl	3-(Morpholin-4-ylmethyl)phenyl	W1a (m= 0)
A-230	Cyclohexylmethyl	3-Pyrrolidin-1-ylphenyl	W1a (m= 0)
A-231	Cyclohexylmethyl	4-Methylphenyl	W1a (m= 0)
A-232	Cyclohexylmethyl	4-(1-Methylethyl)phenyl	W1a (m= 0)
A-233	Cyclohexylmethyl	4-Methoxyphenyl	W1a (m= 0)
A-234	Cyclohexylmethyl	4-Chlorophenyl	W1a (m= 0)
A-235	Cyclohexylmethyl	4-Fluorophenyl	W1a (m= 0)
A-236	Cyclohexylmethyl	4-Trifluoromethylphenyl	W1a (m= 0)
A-237	Cyclohexylmethyl	4-Diethylaminophenyl	W1a (m= 0)
A-238	Cyclohexylmethyl	4-[(Diethylamino)methyl]phenyl	W1a (m= 0)
A-239	Cyclohexylmethyl	4-Cyanophenyl	W1a (m= 0)
A-240	Cyclohexylmethyl	4-(Piperidin-1-yl)phenyl	W1a (m= 0)
A-241	Cyclohexylmethyl	4-(4-Methylpiperazin-1-yl)phenyl	W1a (m= 0)
A-242	Cyclohexylmethyl	4-Pyrrolidin-1-ylphenyl	W1a (m= 0)
A-243	Cyclohexylmethyl	4-(1H-Imidazol-1-yl)phenyl	W1a (m= 0)
A-244	Cyclohexylmethyl	4-Morpholin-4-ylphenyl	W1a (m= 0)

No.	R^1	R^2	W
A-245	Cyclohexylmethyl	4-(Morpholin-4-ylmethyl)phenyl	W1a (m= 0)
A-246	Cyclohexylmethyl	2,4-Difluorophenyl	W1a (m= 0)
A-247	Cyclohexylmethyl	2,6-Difluorophenyl	W1a (m= 0)
A-248	Cyclohexylmethyl	3,5-Difluorophenyl	W1a (m= 0)
A-249	Cyclohexylmethyl	2,4-Dichlorophenyl	W1a (m= 0)
A-250	Cyclohexylmethyl	2,6-Dichlorophenyl	W1a (m= 0)
A-251	Cyclohexylmethyl	3,5-Dichlorophenyl	W1a (m= 0)
A-252	Cyclohexylmethyl	2-Chloro-4-fluorophenyl	W1a (m= 0)
A-253	Cyclohexylmethyl	2-Chloro-4-morpholin-4-ylphenyl	W1a (m= 0)
A-254	Cyclohexylmethyl	2-Fluoro-4-morpholin-4-ylphenyl	W1a (m= 0)
A-255	Cyclohexylmethyl	Pyridin-2-yl	W1a (m= 0)
A-256	Cyclohexylmethyl	Pyridin-4-yl	W1a (m= 0)
A-257	Cyclohexylmethyl	Thien-2-yl	W1a (m= 0)
A-258	Cyclohexylmethyl	2,3-Dihydrobenzo[b]furan-5-yl	W1a (m= 0)
A-259	2-Thienylmethyl	Phenyl	W1a (m= 0)
A-260	2-Thienylmethyl	2-Methylphenyl	W1a (m= 0)
A-261	2-Thienylmethyl	2-Methoxyphenyl	W1a (m= 0)
A-262	2-Thienylmethyl	2-Chlorophenyl	W1a (m= 0)
A-263	2-Thienylmethyl	2-Fluorophenyl	W1a (m= 0)
A-264	2-Thienylmethyl	2-Trifluoromethylphenyl	W1a (m= 0)
A-265	2-Thienylmethyl	3-Methylphenyl	W1a (m= 0)
A-266	2-Thienylmethyl	3-Methoxyphenyl	W1a (m= 0)
A-267	2-Thienylmethyl	3-Chlorophenyl	W1a (m= 0)
A-268	2-Thienylmethyl	3-Fluorophenyl	W1a (m= 0)
A-269	2-Thienylmethyl	3-Trifluoromethyl	W1a (m= 0)
A-270	2-Thienylmethyl	3-[(Phenylmethyl)oxy]phenyl	W1a (m= 0)
A-271	2-Thienylmethyl	3-Morpholin-4-ylphenyl	W1a (m= 0)
A-272	2-Thienylmethyl	3-(Morpholin-4-ylmethyl)phenyl	W1a (m= 0)
A-273	2-Thienylmethyl	3-Pyrrolidin-1-ylphenyl	W1a (m= 0)
A-274	2-Thienylmethyl	4-Methylphenyl	W1a (m= 0)
A-275	2-Thienylmethyl	4-(1-Methylethyl)phenyl	W1a (m= 0)
A-276	2-Thienylmethyl	4-Methoxyphenyl	W1a (m= 0)
A-277	2-Thienylmethyl	4-Chlorophenyl	W1a (m= 0)
A-278	2-Thienylmethyl	4-Fluorophenyl	W1a (m= 0)
A-279	2-Thienylmethyl	4-Trifluoromethylphenyl	W1a (m= 0)
A-280	2-Thienylmethyl	4-Diethylaminophenyl	W1a (m= 0)
A-281	2-Thienylmethyl	4-[(Diethylamino)methyl]phenyl	W1a (m= 0)
A-282	2-Thienylmethyl	4-Cyanophenyl	W1a (m= 0)
A-283	2-Thienylmethyl	4-(Piperidin-1-yl)phenyl	W1a (m= 0)

No.	R^1	R^2	W
A-284	2-Thienylmethyl	4-(4-Methylpiperazin-1-yl)phenyl	W1a (m= 0)
A-285	2-Thienylmethyl	4-Pyrrolidin-1-ylphenyl	W1a (m= 0)
A-286	2-Thienylmethyl	4-(1H-Imidazol-1-yl)phenyl	W1a (m= 0)
A-287	2-Thienylmethyl	4-Morpholin-4-ylphenyl	W1a (m= 0)
A-288	2-Thienylmethyl	4-(Morpholin-4-ylmethyl)phenyl	W1a (m= 0)
A-289	2-Thienylmethyl	2,4-Difluorophenyl	W1a (m= 0)
A-290	2-Thienylmethyl	2,6-Difluorophenyl	W1a (m= 0)
A-291	2-Thienylmethyl	3,5-Difluorophenyl	W1a (m= 0)
A-292	2-Thienylmethyl	2,4-Dichlorophenyl	W1a (m= 0)
A-293	2-Thienylmethyl	2,6-Dichlorophenyl	W1a (m= 0)
A-294	2-Thienylmethyl	3,5-Dichlorophenyl	W1a (m= 0)
A-295	2-Thienylmethyl	2-Chloro-4-fluorophenyl	W1a (m= 0)
A-296	2-Thienylmethyl	2-Chloro-4-morpholin-4-ylphenyl	W1a (m= 0)
A-297	2-Thienylmethyl	2-Fluoro-4-morpholin-4-ylphenyl	W1a (m= 0)
A-298	2-Thienylmethyl	Pyridin-2-yl	W1a (m= 0)
A-299	2-Thienylmethyl	Pyridin-4-yl	W1a (m= 0)
A-300	2-Thienylmethyl	Thien-2-yl	W1a (m= 0)
A-301	2-Thienylmethyl	2,3-Dihydrobenzo[b]furan-5-yl	W1a (m= 0)
A-302	Pyridin-3-ylmethyl	Phenyl	W1a (m= 0)
A-303	Pyridin-3-ylmethyl	2-Methylphenyl	W1a (m= 0)
A-304	Pyridin-3-ylmethyl	2-Methoxyphenyl	W1a (m= 0)
A-305	Pyridin-3-ylmethyl	2-Chlorophenyl	W1a (m= 0)
A-306	Pyridin-3-ylmethyl	2-Fluorophenyl	W1a (m= 0)
A-307	Pyridin-3-ylmethyl	2-Trifluoromethylphenyl	W1a (m= 0)
A-308	Pyridin-3-ylmethyl	3-Methylphenyl	W1a (m= 0)
A-309	Pyridin-3-ylmethyl	3-Methoxyphenyl	W1a (m= 0)
A-310	Pyridin-3-ylmethyl	3-Chlorophenyl	W1a (m= 0)
A-311	Pyridin-3-ylmethyl	3-Fluorophenyl	W1a (m= 0)
A-312	Pyridin-3-ylmethyl	3-Trifluoromethyl	W1a (m= 0)
A-313	Pyridin-3-ylmethyl	3-[(Phenylmethyl)oxy]phenyl	W1a (m= 0)
A-314	Pyridin-3-ylmethyl	3-Morpholin-4-ylphenyl	W1a (m= 0)
A-315	Pyridin-3-ylmethyl	3-(Morpholin-4-ylmethyl)phenyl	W1a (m= 0)
A-316	Pyridin-3-ylmethyl	3-Pyrrolidin-1-ylphenyl	W1a (m= 0)
A-317	Pyridin-3-ylmethyl	4-Methylphenyl	W1a (m= 0)
A-318	Pyridin-3-ylmethyl	4-(1-Methylethyl)phenyl	W1a (m= 0)
A-319	Pyridin-3-ylmethyl	4-Methoxyphenyl	W1a (m= 0)
A-320	Pyridin-3-ylmethyl	4-Chlorophenyl	W1a (m= 0)
A-321	Pyridin-3-ylmethyl	4-Fluorophenyl	W1a (m= 0)
A-322	Pyridin-3-ylmethyl	4-Trifluoromethylphenyl	W1a (m= 0)

No.	R^1	R^2	W
A-323	Pyridin-3-ylmethyl	4-Diethylaminophenyl	W1a (m= 0)
A-324	Pyridin-3-ylmethyl	4-[(Diethylamino)methyl]phenyl	W1a (m= 0)
A-325	Pyridin-3-ylmethyl	4-Cyanophenyl	W1a (m= 0)
A-326	Pyridin-3-ylmethyl	4-(Piperidin-1-yl)phenyl	W1a (m= 0)
A-327	Pyridin-3-ylmethyl	4-(4-Methylpiperazin-1-yl)phenyl	W1a (m= 0)
A-328	Pyridin-3-ylmethyl	4-Pyrrolidin-1-ylphenyl	W1a (m= 0)
A-329	Pyridin-3-ylmethyl	4-(1H-Imidazol-1-yl)phenyl	W1a (m= 0)
A-330	Pyridin-3-ylmethyl	4-Morpholin-4-ylphenyl	W1a (m= 0)
A-331	Pyridin-3-ylmethyl	4-(Morpholin-4-ylmethyl)phenyl	W1a (m= 0)
A-332	Pyridin-3-ylmethyl	2,4-Difluorophenyl	W1a (m= 0)
A-333	Pyridin-3-ylmethyl	2,6-Difluorophenyl	W1a (m= 0)
A-334	Pyridin-3-ylmethyl	3,5-Difluorophenyl	W1a (m= 0)
A-335	Pyridin-3-ylmethyl	2,4-Dichlorophenyl	W1a (m= 0)
A-336	Pyridin-3-ylmethyl	2,6-Dichlorophenyl	W1a (m= 0)
A-337	Pyridin-3-ylmethyl	3,5-Dichlorophenyl	W1a (m= 0)
A-338	Pyridin-3-ylmethyl	2-Chloro-4-fluorophenyl	W1a (m= 0)
A-339	Pyridin-3-ylmethyl	2-Chloro-4-morpholin-4-ylphenyl	W1a (m= 0)
A-340	Pyridin-3-ylmethyl	2-Fluoro-4-morpholin-4-ylphenyl	W1a (m= 0)
A-341	Pyridin-3-ylmethyl	Pyridin-2-yl	W1a (m= 0)
A-342	Pyridin-3-ylmethyl	Pyridin-4-yl	W1a (m= 0)
A-343	Pyridin-3-ylmethyl	Thien-2-yl	W1a (m= 0)
A-344	Pyridin-3-ylmethyl	2,3-Dihydrobenzo[b]furan-5-yl	W1a (m= 0)
A-345	n-Butyl	Phenyl	W1b (m = 0)
A-346	n-Butyl	2-Methylphenyl	W1b (m = 0)
A-347	n-Butyl	2-Methoxyphenyl	W1b (m = 0)
A-348	n-Butyl	2-Chlorophenyl	W1b (m = 0)
A-349	n-Butyl	2-Fluorophenyl	W1b (m = 0)
A-350	n-Butyl	2-Trifluoromethylphenyl	W1b (m = 0)
A-351	n-Butyl	3-Methylphenyl	W1b (m = 0)
A-352	n-Butyl	3-Methoxyphenyl	W1b (m = 0)
A-353	n-Butyl	3-Chlorophenyl	W1b (m = 0)
A-354	n-Butyl	3-Fluorophenyl	W1b (m = 0)
A-355	n-Butyl	3-Trifluoromethyl	W1b (m = 0)
A-356	n-Butyl	3-[(Phenylmethyl)oxy]phenyl	W1b (m = 0)
A-357	n-Butyl	3-Morpholin-4-ylphenyl	W1b (m = 0)
A-358	n-Butyl	3-(Morpholin-4-ylmethyl)phenyl	W1b (m = 0)
A-359	n-Butyl	3-Pyrrolidin-1-ylphenyl	W1b (m = 0)
A-360	n-Butyl	4-Methylphenyl	W1b (m = 0)
A-361	n-Butyl	4-(1-Methylethyl)phenyl	W1b (m = 0)

No.	R^1	R^2	W
A-362	n-Butyl	4-Methoxyphenyl	W1b (m = 0)
A-363	n-Butyl	4-Chlorophenyl	W1b (m = 0)
A-364	n-Butyl	4-Fluorophenyl	W1b (m = 0)
A-365	n-Butyl	4-Trifluoromethylphenyl	W1b (m = 0)
A-366	n-Butyl	4-Diethylaminophenyl	W1b (m = 0)
A-367	n-Butyl	4-[(Diethylamino)methyl]phenyl	W1b (m = 0)
A-368	n-Butyl	4-Cyanophenyl	W1b (m = 0)
A-369	n-Butyl	4-(Piperidin-1-yl)phenyl	W1b (m = 0)
A-370	n-Butyl	4-(4-Methylpiperazin-1-yl)phenyl	W1b (m = 0)
A-371	n-Butyl	4-Pyrrolidin-1-ylphenyl	W1b (m = 0)
A-372	n-Butyl	4-(1H-Imidazol-1-yl)phenyl	W1b (m = 0)
A-373	n-Butyl	4-Morpholin-4-ylphenyl	W1b (m = 0)
A-374	n-Butyl	4-(Morpholin-4-ylmethyl)phenyl	W1b (m = 0)
A-375	n-Butyl	2,4-Difluorophenyl	W1b (m = 0)
A-376	n-Butyl	2,6-Difluorophenyl	W1b (m = 0)
A-377	n-Butyl	3,5-Difluorophenyl	W1b (m = 0)
A-378	n-Butyl	2,4-Dichlorophenyl	W1b (m = 0)
A-379	n-Butyl	2,6-Dichlorophenyl	W1b (m = 0)
A-380	n-Butyl	3,5-Dichlorophenyl	W1b (m = 0)
A-381	n-Butyl	2-Chloro-4-fluorophenyl	W1b (m = 0)
A-382	n-Butyl	2-Chloro-4-morpholin-4-ylphenyl	W1b (m = 0)
A-383	n-Butyl	2-Fluoro-4-morpholin-4-ylphenyl	W1b (m = 0)
A-384	n-Butyl	Pyridin-2-yl	W1b (m = 0)
A-385	n-Butyl	Pyridin-4-yl	W1b (m = 0)
A-386	n-Butyl	Thien-2-yl	W1b (m = 0)
A-387	n-Butyl	2,3-Dihydrobenzo[b]furan-5-yl	W1b (m = 0)
A-388	Isobutyl	Phenyl	W1b (m = 0)
A-389	Isobutyl	2-Methylphenyl	W1b (m = 0)
A-390	Isobutyl	2-Methoxyphenyl	W1b (m = 0)
A-391	Isobutyl	2-Chlorophenyl	W1b (m = 0)
A-392	Isobutyl	2-Fluorophenyl	W1b (m = 0)
A-393	Isobutyl	2-Trifluoromethylphenyl	W1b (m = 0)
A-394	Isobutyl	3-Methylphenyl	W1b (m = 0)
A-395	Isobutyl	3-Methoxyphenyl	W1b (m = 0)
A-396	Isobutyl	3-Chlorophenyl	W1b (m = 0)
A-397	Isobutyl	3-Fluorophenyl	W1b (m = 0)
A-398	Isobutyl	3-Trifluoromethyl	W1b (m = 0)
A-399	Isobutyl	3-[(Phenylmethyl)oxy]phenyl	W1b (m = 0)
A-400	Isobutyl	3-Morpholin-4-ylphenyl	W1b (m = 0)

No.	R^1	R^2	W
A-401	Isobutyl	3-(Morpholin-4-ylmethyl)phenyl	W1b (m = 0)
A-402	Isobutyl	3-Pyrrolidin-1-ylphenyl	W1b (m = 0)
A-403	Isobutyl	4-Methylphenyl	W1b (m = 0)
A-404	Isobutyl	4-(1-Methylethyl)phenyl	W1b (m = 0)
A-405	Isobutyl	4-Methoxyphenyl	W1b (m = 0)
A-406	Isobutyl	4-Chlorophenyl	W1b (m = 0)
A-407	Isobutyl	4-Fluorophenyl	W1b (m = 0)
A-408	Isobutyl	4-Trifluoromethylphenyl	W1b (m = 0)
A-409	Isobutyl	4-Diethylaminophenyl	W1b (m = 0)
A-410	Isobutyl	4-[(Diethylamino)methyl]phenyl	W1b (m = 0)
A-411	Isobutyl	4-Cyanophenyl	W1b (m = 0)
A-412	Isobutyl	4-(Piperidin-1-yl)phenyl	W1b (m = 0)
A-413	Isobutyl	4-(4-Methylpiperazin-1-yl)phenyl	W1b (m = 0)
A-414	Isobutyl	4-Pyrrolidin-1-ylphenyl	W1b (m = 0)
A-415	Isobutyl	4-(1H-Imidazol-1-yl)phenyl	W1b (m = 0)
A-416	Isobutyl	4-Morpholin-4-ylphenyl	W1b (m = 0)
A-417	Isobutyl	4-(Morpholin-4-ylmethyl)phenyl	W1b (m = 0)
A-418	Isobutyl	2,4-Difluorophenyl	W1b (m = 0)
A-419	Isobutyl	2,6-Difluorophenyl	W1b (m = 0)
A-420	Isobutyl	3,5-Difluorophenyl	W1b (m = 0)
A-421	Isobutyl	2,4-Dichlorophenyl	W1b (m = 0)
A-422	Isobutyl	2,6-Dichlorophenyl	W1b (m = 0)
A-423	Isobutyl	3,5-Dichlorophenyl	W1b (m = 0)
A-424	Isobutyl	2-Chloro-4-fluorophenyl	W1b (m = 0)
A-425	Isobutyl	2-Chloro-4-morpholin-4-ylphenyl	W1b (m = 0)
A-426	Isobutyl	2-Fluoro-4-morpholin-4-ylphenyl	W1b (m = 0)
A-427	Isobutyl	Pyridin-2-yl	W1b (m = 0)
A-428	Isobutyl	Pyridin-4-yl	W1b (m = 0)
A-429	Isobutyl	Thien-2-yl	W1b (m = 0)
A-430	Isobutyl	2,3-Dihydrobenzo[b]furan-5-yl	W1b (m = 0)
A-431	Benzyl	Phenyl	W1b (m = 0)
A-432	Benzyl	2-Methylphenyl	W1b (m = 0)
A-433	Benzyl	2-Methoxyphenyl	W1b (m = 0)
A-434	Benzyl	2-Chlorophenyl	W1b (m = 0)
A-435	Benzyl	2-Fluorophenyl	W1b (m = 0)
A-436	Benzyl	2-Trifluoromethylphenyl	W1b (m = 0)
A-437	Benzyl	3-Methylphenyl	W1b (m = 0)
A-438	Benzyl	3-Methoxyphenyl	W1b (m = 0)
A-439	Benzyl	3-Chlorophenyl	W1b (m = 0)

No.	R^1	R^2	W
A-440	Benzyl	3-Fluorophenyl	W1b (m = 0)
A-441	Benzyl	3-Trifluoromethyl	W1b (m = 0)
A-442	Benzyl	3-[(Phenylmethyl)oxy]phenyl	W1b (m = 0)
A-443	Benzyl	3-Morpholin-4-ylphenyl	W1b (m = 0)
A-444	Benzyl	3-(Morpholin-4-ylmethyl)phenyl	W1b (m = 0)
A-445	Benzyl	3-Pyrrolidin-1-ylphenyl	W1b (m = 0)
A-446	Benzyl	4-Methylphenyl	W1b (m = 0)
A-447	Benzyl	4-(1-Methylethyl)phenyl	W1b (m = 0)
A-448	Benzyl	4-Methoxyphenyl	W1b (m = 0)
A-449	Benzyl	4-Chlorophenyl	W1b (m = 0)
A-450	Benzyl	4-Fluorophenyl	W1b (m = 0)
A-451	Benzyl	4-Trifluoromethylphenyl	W1b (m = 0)
A-452	Benzyl	4-Diethylaminophenyl	W1b (m = 0)
A-453	Benzyl	4-[(Diethylamino)methyl]phenyl	W1b (m = 0)
A-454	Benzyl	4-Cyanophenyl	W1b (m = 0)
A-455	Benzyl	4-(Piperidin-1-yl)phenyl	W1b (m = 0)
A-456	Benzyl	4-(4-Methylpiperazin-1-yl)phenyl	W1b (m = 0)
A-457	Benzyl	4-Pyrrolidin-1-ylphenyl	W1b (m = 0)
A-458	Benzyl	4-(1H-Imidazol-1-yl)phenyl	W1b (m = 0)
A-459	Benzyl	4-Morpholin-4-ylphenyl	W1b (m = 0)
A-460	Benzyl	4-(Morpholin-4-ylmethyl)phenyl	W1b (m = 0)
A-461	Benzyl	2,4-Difluorophenyl	W1b (m = 0)
A-462	Benzyl	2,6-Difluorophenyl	W1b (m = 0)
A-463	Benzyl	3,5-Difluorophenyl	W1b (m = 0)
A-464	Benzyl	2,4-Dichlorophenyl	W1b (m = 0)
A-465	Benzyl	2,6-Dichlorophenyl	W1b (m = 0)
A-466	Benzyl	3,5-Dichlorophenyl	W1b (m = 0)
A-467	Benzyl	2-Chloro-4-fluorophenyl	W1b (m = 0)
A-468	Benzyl	2-Chloro-4-morpholin-4-ylphenyl	W1b (m = 0)
A-469	Benzyl	2-Fluoro-4-morpholin-4-ylphenyl	W1b (m = 0)
A-470	Benzyl	Pyridin-2-yl	W1b (m = 0)
A-471	Benzyl	Pyridin-4-yl	W1b (m = 0)
A-472	Benzyl	Thien-2-yl	W1b (m = 0)
A-473	Benzyl	2,3-Dihydrobenzo[b]furan-5-yl	W1b (m = 0)
A-474	4-Chlorobenzyl	Phenyl	W1b (m = 0)
A-475	4-Chlorobenzyl	2-Methylphenyl	W1b (m = 0)
A-476	4-Chlorobenzyl	2-Methoxyphenyl	W1b (m = 0)
A-477	4-Chlorobenzyl	2-Chlorophenyl	W1b (m = 0)
A-478	4-Chlorobenzyl	2-Fluorophenyl	W1b (m = 0)

No.	R^1	R^2	W
A-479	4-Chlorobenzyl	2-Trifluoromethylphenyl	W1b (m = 0)
A-480	4-Chlorobenzyl	3-Methylphenyl	W1b (m = 0)
A-481	4-Chlorobenzyl	3-Methoxyphenyl	W1b (m = 0)
A-482	4-Chlorobenzyl	3-Chlorophenyl	W1b (m = 0)
A-483	4-Chlorobenzyl	3-Fluorophenyl	W1b (m = 0)
A-484	4-Chlorobenzyl	3-Trifluoromethyl	W1b (m = 0)
A-485	4-Chlorobenzyl	3-[(Phenylmethyl)oxy]phenyl	W1b (m = 0)
A-486	4-Chlorobenzyl	3-Morpholin-4-ylphenyl	W1b (m = 0)
A-487	4-Chlorobenzyl	3-(Morpholin-4-ylmethyl)phenyl	W1b (m = 0)
A-488	4-Chlorobenzyl	3-Pyrrolidin-1-ylphenyl	W1b (m = 0)
A-489	4-Chlorobenzyl	4-Methylphenyl	W1b (m = 0)
A-490	4-Chlorobenzyl	4-(1-Methylethyl)phenyl	W1b (m = 0)
A-491	4-Chlorobenzyl	4-Methoxyphenyl	W1b (m = 0)
A-492	4-Chlorobenzyl	4-Chlorophenyl	W1b (m = 0)
A-493	4-Chlorobenzyl	4-Fluorophenyl	W1b (m = 0)
A-494	4-Chlorobenzyl	4-Trifluoromethylphenyl	W1b (m = 0)
A-495	4-Chlorobenzyl	4-Diethylaminophenyl	W1b (m = 0)
A-496	4-Chlorobenzyl	4-[(Diethylamino)methyl]phenyl	W1b (m = 0)
A-497	4-Chlorobenzyl	4-Cyanophenyl	W1b (m = 0)
A-498	4-Chlorobenzyl	4-(Piperidin-1-yl)phenyl	W1b (m = 0)
A-499	4-Chlorobenzyl	4-(4-Methylpiperazin-1-yl)phenyl	W1b (m = 0)
A-500	4-Chlorobenzyl	4-Pyrrolidin-1-ylphenyl	W1b (m = 0)
A-501	4-Chlorobenzyl	4-(1H-Imidazol-1-yl)phenyl	W1b (m = 0)
A-502	4-Chlorobenzyl	4-Morpholin-4-ylphenyl	W1b (m = 0)
A-503	4-Chlorobenzyl	4-(Morpholin-4-ylmethyl)phenyl	W1b (m = 0)
A-504	4-Chlorobenzyl	2,4-Difluorophenyl	W1b (m = 0)
A-505	4-Chlorobenzyl	2,6-Difluorophenyl	W1b (m = 0)
A-506	4-Chlorobenzyl	3,5-Difluorophenyl	W1b (m = 0)
A-507	4-Chlorobenzyl	2,4-Dichlorophenyl	W1b (m = 0)
A-508	4-Chlorobenzyl	2,6-Dichlorophenyl	W1b (m = 0)
A-509	4-Chlorobenzyl	3,5-Dichlorophenyl	W1b (m = 0)
A-510	4-Chlorobenzyl	2-Chloro-4-fluorophenyl	W1b (m = 0)
A-511	4-Chlorobenzyl	2-Chloro-4-morpholin-4-ylphenyl	W1b (m = 0)
A-512	4-Chlorobenzyl	2-Fluoro-4-morpholin-4-ylphenyl	W1b (m = 0)
A-513	4-Chlorobenzyl	Pyridin-2-yl	W1b (m = 0)
A-514	4-Chlorobenzyl	Pyridin-4-yl	W1b (m = 0)
A-515	4-Chlorobenzyl	Thien-2-yl	W1b (m = 0)
A-516	4-Chlorobenzyl	2,3-Dihydrobenzo[b]furan-5-yl	W1b (m = 0)
A-517	4-Methoxybenzyl	Phenyl	W1b (m = 0)

No.	R^1	R^2	W
A-518	4-Methoxybenzyl	2-Methylphenyl	W1b (m = 0)
A-519	4-Methoxybenzyl	2-Methoxyphenyl	W1b (m = 0)
A-520	4-Methoxybenzyl	2-Chlorophenyl	W1b (m = 0)
A-521	4-Methoxybenzyl	2-Fluorophenyl	W1b (m = 0)
A-522	4-Methoxybenzyl	2-Trifluoromethylphenyl	W1b (m = 0)
A-523	4-Methoxybenzyl	3-Methylphenyl	W1b (m = 0)
A-524	4-Methoxybenzyl	3-Methoxyphenyl	W1b (m = 0)
A-525	4-Methoxybenzyl	3-Chlorophenyl	W1b (m = 0)
A-526	4-Methoxybenzyl	3-Fluorophenyl	W1b (m = 0)
A-527	4-Methoxybenzyl	3-Trifluoromethyl	W1b (m = 0)
A-528	4-Methoxybenzyl	3-[(Phenylmethyl)oxy]phenyl	W1b (m = 0)
A-529	4-Methoxybenzyl	3-Morpholin-4-ylphenyl	W1b (m = 0)
A-530	4-Methoxybenzyl	3-(Morpholin-4-ylmethyl)phenyl	W1b (m = 0)
A-531	4-Methoxybenzyl	3-Pyrrolidin-1-ylphenyl	W1b (m = 0)
A-532	4-Methoxybenzyl	4-Methylphenyl	W1b (m = 0)
A-533	4-Methoxybenzyl	4-(1-Methylethyl)phenyl	W1b (m = 0)
A-534	4-Methoxybenzyl	4-Methoxyphenyl	W1b (m = 0)
A-535	4-Methoxybenzyl	4-Chlorophenyl	W1b (m = 0)
A-536	4-Methoxybenzyl	4-Fluorophenyl	W1b (m = 0)
A-537	4-Methoxybenzyl	4-Trifluoromethylphenyl	W1b (m = 0)
A-538	4-Methoxybenzyl	4-Diethylaminophenyl	W1b (m = 0)
A-539	4-Methoxybenzyl	4-[(Diethylamino)methyl]phenyl	W1b (m = 0)
A-540	4-Methoxybenzyl	4-Cyanophenyl	W1b (m = 0)
A-541	4-Methoxybenzyl	4-(Piperidin-1-yl)phenyl	W1b (m = 0)
A-542	4-Methoxybenzyl	4-(4-Methylpiperazin-1-yl)phenyl	W1b (m = 0)
A-543	4-Methoxybenzyl	4-Pyrrolidin-1-ylphenyl	W1b (m = 0)
A-544	4-Methoxybenzyl	4-(1H-Imidazol-1-yl)phenyl	W1b (m = 0)
A-545	4-Methoxybenzyl	4-Morpholin-4-ylphenyl	W1b (m = 0)
A-546	4-Methoxybenzyl	4-(Morpholin-4-ylmethyl)phenyl	W1b (m = 0)
A-547	4-Methoxybenzyl	2,4-Difluorophenyl	W1b (m = 0)
A-548	4-Methoxybenzyl	2,6-Difluorophenyl	W1b (m = 0)
A-549	4-Methoxybenzyl	3,5-Difluorophenyl	W1b (m = 0)
A-550	4-Methoxybenzyl	2,4-Dichlorophenyl	W1b (m = 0)
A-551	4-Methoxybenzyl	2,6-Dichlorophenyl	W1b (m = 0)
A-552	4-Methoxybenzyl	3,5-Dichlorophenyl	W1b (m = 0)
A-553	4-Methoxybenzyl	2-Chloro-4-fluorophenyl	W1b (m = 0)
A-554	4-Methoxybenzyl	2-Chloro-4-morpholin-4-ylphenyl	W1b (m = 0)
A-555	4-Methoxybenzyl	2-Fluoro-4-morpholin-4-ylphenyl	W1b (m = 0)
A-556	4-Methoxybenzyl	Pyridin-2-yl	W1b (m = 0)

No.	R^1	R^2	W
A-557	4-Methoxybenzyl	Pyridin-4-yl	W1b (m = 0)
A-558	4-Methoxybenzyl	Thien-2-yl	W1b (m = 0)
A-559	4-Methoxybenzyl	2,3-Dihydrobenzo[b]furan-5-yl	W1b (m = 0)
A-560	Cyclohexylmethyl	Phenyl	W1b (m = 0)
A-561	Cyclohexylmethyl	2-Methylphenyl	W1b (m = 0)
A-562	Cyclohexylmethyl	2-Methoxyphenyl	W1b (m = 0)
A-563	Cyclohexylmethyl	2-Chlorophenyl	W1b (m = 0)
A-564	Cyclohexylmethyl	2-Fluorophenyl	W1b (m = 0)
A-565	Cyclohexylmethyl	2-Trifluoromethylphenyl	W1b (m = 0)
A-566	Cyclohexylmethyl	3-Methylphenyl	W1b (m = 0)
A-567	Cyclohexylmethyl	3-Methoxyphenyl	W1b (m = 0)
A-568	Cyclohexylmethyl	3-Chlorophenyl	W1b (m = 0)
A-569	Cyclohexylmethyl	3-Fluorophenyl	W1b (m = 0)
A-570	Cyclohexylmethyl	3-Trifluoromethyl	W1b (m = 0)
A-571	Cyclohexylmethyl	3-[(Phenylmethyl)oxy]phenyl	W1b (m = 0)
A-572	Cyclohexylmethyl	3-Morpholin-4-ylphenyl	W1b (m = 0)
A-573	Cyclohexylmethyl	3-(Morpholin-4-ylmethyl)phenyl	W1b (m = 0)
A-574	Cyclohexylmethyl	3-Pyrrolidin-1-ylphenyl	W1b (m = 0)
A-575	Cyclohexylmethyl	4-Methylphenyl	W1b (m = 0)
A-576	Cyclohexylmethyl	4-(1-Methylethyl)phenyl	W1b (m = 0)
A-577	Cyclohexylmethyl	4-Methoxyphenyl	W1b (m = 0)
A-578	Cyclohexylmethyl	4-Chlorophenyl	W1b (m = 0)
A-579	Cyclohexylmethyl	4-Fluorophenyl	W1b (m = 0)
A-580	Cyclohexylmethyl	4-Trifluoromethylphenyl	W1b (m = 0)
A-581	Cyclohexylmethyl	4-Diethylaminophenyl	W1b (m = 0)
A-582	Cyclohexylmethyl	4-[(Diethylamino)methyl]phenyl	W1b (m = 0)
A-583	Cyclohexylmethyl	4-Cyanophenyl	W1b (m = 0)
A-584	Cyclohexylmethyl	4-(Piperidin-1-yl)phenyl	W1b (m = 0)
A-585	Cyclohexylmethyl	4-(4-Methylpiperazin-1-yl)phenyl	W1b (m = 0)
A-586	Cyclohexylmethyl	4-Pyrrolidin-1-ylphenyl	W1b (m = 0)
A-587	Cyclohexylmethyl	4-(1H-Imidazol-1-yl)phenyl	W1b (m = 0)
A-588	Cyclohexylmethyl	4-Morpholin-4-ylphenyl	W1b (m = 0)
A-589	Cyclohexylmethyl	4-(Morpholin-4-ylmethyl)phenyl	W1b (m = 0)
A-590	Cyclohexylmethyl	2,4-Difluorophenyl	W1b (m = 0)
A-591	Cyclohexylmethyl	2,6-Difluorophenyl	W1b (m = 0)
A-592	Cyclohexylmethyl	3,5-Difluorophenyl	W1b (m = 0)
A-593	Cyclohexylmethyl	2,4-Dichlorophenyl	W1b (m = 0)
A-594	Cyclohexylmethyl	2,6-Dichlorophenyl	W1b (m = 0)
A-595	Cyclohexylmethyl	3,5-Dichlorophenyl	W1b (m = 0)

No.	R^1	R^2	W
A-596	Cyclohexylmethyl	2-Chloro-4-fluorophenyl	W1b (m = 0)
A-597	Cyclohexylmethyl	2-Chloro-4-morpholin-4-ylphenyl	W1b (m = 0)
A-598	Cyclohexylmethyl	2-Fluoro-4-morpholin-4-ylphenyl	W1b (m = 0)
A-599	Cyclohexylmethyl	Pyridin-2-yl	W1b (m = 0)
A-600	Cyclohexylmethyl	Pyridin-4-yl	W1b (m = 0)
A-601	Cyclohexylmethyl	Thien-2-yl	W1b (m = 0)
A-602	Cyclohexylmethyl	2,3-Dihydrobenzo[b]furan-5-yl	W1b (m = 0)
A-603	2-Thienylmethyl	Phenyl	W1b (m = 0)
A-604	2-Thienylmethyl	2-Methylphenyl	W1b (m = 0)
A-605	2-Thienylmethyl	2-Methoxyphenyl	W1b (m = 0)
A-606	2-Thienylmethyl	2-Chlorophenyl	W1b (m = 0)
A-607	2-Thienylmethyl	2-Fluorophenyl	W1b (m = 0)
A-608	2-Thienylmethyl	2-Trifluoromethylphenyl	W1b (m = 0)
A-609	2-Thienylmethyl	3-Methylphenyl	W1b (m = 0)
A-610	2-Thienylmethyl	3-Methoxyphenyl	W1b (m = 0)
A-611	2-Thienylmethyl	3-Chlorophenyl	W1b (m = 0)
A-612	2-Thienylmethyl	3-Fluorophenyl	W1b (m = 0)
A-613	2-Thienylmethyl	3-Trifluoromethyl	W1b (m = 0)
A-614	2-Thienylmethyl	3-[(Phenylmethyl)oxy]phenyl	W1b (m = 0)
A-615	2-Thienylmethyl	3-Morpholin-4-ylphenyl	W1b (m = 0)
A-616	2-Thienylmethyl	3-(Morpholin-4-ylmethyl)phenyl	W1b (m = 0)
A-617	2-Thienylmethyl	3-Pyrrolidin-1-ylphenyl	W1b (m = 0)
A-618	2-Thienylmethyl	4-Methylphenyl	W1b (m = 0)
A-619	2-Thienylmethyl	4-(1-Methylethyl)phenyl	W1b (m = 0)
A-620	2-Thienylmethyl	4-Methoxyphenyl	W1b (m = 0)
A-621	2-Thienylmethyl	4-Chlorophenyl	W1b (m = 0)
A-622	2-Thienylmethyl	4-Fluorophenyl	W1b (m = 0)
A-623	2-Thienylmethyl	4-Trifluoromethylphenyl	W1b (m = 0)
A-624	2-Thienylmethyl	4-Diethylaminophenyl	W1b (m = 0)
A-625	2-Thienylmethyl	4-[(Diethylamino)methyl]phenyl	W1b (m = 0)
A-626	2-Thienylmethyl	4-Cyanophenyl	W1b (m = 0)
A-627	2-Thienylmethyl	4-(Piperidin-1-yl)phenyl	W1b (m = 0)
A-628	2-Thienylmethyl	4-(4-Methylpiperazin-1-yl)phenyl	W1b (m = 0)
A-629	2-Thienylmethyl	4-Pyrrolidin-1-ylphenyl	W1b (m = 0)
A-630	2-Thienylmethyl	4-(1H-Imidazol-1-yl)phenyl	W1b (m = 0)
A-631	2-Thienylmethyl	4-Morpholin-4-ylphenyl	W1b (m = 0)
A-632	2-Thienylmethyl	4-(Morpholin-4-ylmethyl)phenyl	W1b (m = 0)
A-633	2-Thienylmethyl	2,4-Difluorophenyl	W1b (m = 0)
A-634	2-Thienylmethyl	2,6-Difluorophenyl	W1b (m = 0)

No.	R^1	R^2	W
A-635	2-Thienylmethyl	3,5-Difluorophenyl	W1b (m = 0)
A-636	2-Thienylmethyl	2,4-Dichlorophenyl	W1b (m = 0)
A-637	2-Thienylmethyl	2,6-Dichlorophenyl	W1b (m = 0)
A-638	2-Thienylmethyl	3,5-Dichlorophenyl	W1b (m = 0)
A-639	2-Thienylmethyl	2-Chloro-4-fluorophenyl	W1b (m = 0)
A-640	2-Thienylmethyl	2-Chloro-4-morpholin-4-ylphenyl	W1b (m = 0)
A-641	2-Thienylmethyl	2-Fluoro-4-morpholin-4-ylphenyl	W1b (m = 0)
A-642	2-Thienylmethyl	Pyridin-2-yl	W1b (m = 0)
A-643	2-Thienylmethyl	Pyridin-4-yl	W1b (m = 0)
A-644	2-Thienylmethyl	Thien-2-yl	W1b (m = 0)
A-645	2-Thienylmethyl	2,3-Dihydrobenzo[b]furan-5-yl	W1b (m = 0)
A-646	Pyridin-3-ylmethyl	Phenyl	W1b (m = 0)
A-647	Pyridin-3-ylmethyl	2-Methylphenyl	W1b (m = 0)
A-648	Pyridin-3-ylmethyl	2-Methoxyphenyl	W1b (m = 0)
A-649	Pyridin-3-ylmethyl	2-Chlorophenyl	W1b (m = 0)
A-650	Pyridin-3-ylmethyl	2-Fluorophenyl	W1b (m = 0)
A-651	Pyridin-3-ylmethyl	2-Trifluoromethylphenyl	W1b (m = 0)
A-652	Pyridin-3-ylmethyl	3-Methylphenyl	W1b (m = 0)
A-653	Pyridin-3-ylmethyl	3-Methoxyphenyl	W1b (m = 0)
A-654	Pyridin-3-ylmethyl	3-Chlorophenyl	W1b (m = 0)
A-655	Pyridin-3-ylmethyl	3-Fluorophenyl	W1b (m = 0)
A-656	Pyridin-3-ylmethyl	3-Trifluoromethyl	W1b (m = 0)
A-657	Pyridin-3-ylmethyl	3-[(Phenylmethyl)oxy]phenyl	W1b (m = 0)
A-658	Pyridin-3-ylmethyl	3-Morpholin-4-ylphenyl	W1b (m = 0)
A-659	Pyridin-3-ylmethyl	3-(Morpholin-4-ylmethyl)phenyl	W1b (m = 0)
A-660	Pyridin-3-ylmethyl	3-Pyrrolidin-1-ylphenyl	W1b (m = 0)
A-661	Pyridin-3-ylmethyl	4-Methylphenyl	W1b (m = 0)
A-662	Pyridin-3-ylmethyl	4-(1-Methylethyl)phenyl	W1b (m = 0)
A-663	Pyridin-3-ylmethyl	4-Methoxyphenyl	W1b (m = 0)
A-664	Pyridin-3-ylmethyl	4-Chlorophenyl	W1b (m = 0)
A-665	Pyridin-3-ylmethyl	4-Fluorophenyl	W1b (m = 0)
A-666	Pyridin-3-ylmethyl	4-Trifluoromethylphenyl	W1b (m = 0)
A-667	Pyridin-3-ylmethyl	4-Diethylaminophenyl	W1b (m = 0)
A-668	Pyridin-3-ylmethyl	4-[(Diethylamino)methyl]phenyl	W1b (m = 0)
A-669	Pyridin-3-ylmethyl	4-Cyanophenyl	W1b (m = 0)
A-670	Pyridin-3-ylmethyl	4-(Piperidin-1-yl)phenyl	W1b (m = 0)
A-671	Pyridin-3-ylmethyl	4-(4-Methylpiperazin-1-yl)phenyl	W1b (m = 0)
A-672	Pyridin-3-ylmethyl	4-Pyrrolidin-1-ylphenyl	W1b (m = 0)
A-673	Pyridin-3-ylmethyl	4-(1H-Imidazol-1-yl)phenyl	W1b (m = 0)

No.	R^1	R^2	W
A-674	Pyridin-3-ylmethyl	4-Morpholin-4-ylphenyl	W1b (m = 0)
A-675	Pyridin-3-ylmethyl	4-(Morpholin-4-ylmethyl)phenyl	W1b (m = 0)
A-676	Pyridin-3-ylmethyl	2,4-Difluorophenyl	W1b (m = 0)
A-677	Pyridin-3-ylmethyl	2,6-Difluorophenyl	W1b (m = 0)
A-678	Pyridin-3-ylmethyl	3,5-Difluorophenyl	W1b (m = 0)
A-679	Pyridin-3-ylmethyl	2,4-Dichlorophenyl	W1b (m = 0)
A-680	Pyridin-3-ylmethyl	2,6-Dichlorophenyl	W1b (m = 0)
A-681	Pyridin-3-ylmethyl	3,5-Dichlorophenyl	W1b (m = 0)
A-682	Pyridin-3-ylmethyl	2-Chloro-4-fluorophenyl	W1b (m = 0)
A-683	Pyridin-3-ylmethyl	2-Chloro-4-morpholin-4-ylphenyl	W1b (m = 0)
A-684	Pyridin-3-ylmethyl	2-Fluoro-4-morpholin-4-ylphenyl	W1b (m = 0)
A-685	Pyridin-3-ylmethyl	Pyridin-2-yl	W1b (m = 0)
A-686	Pyridin-3-ylmethyl	Pyridin-4-yl	W1b (m = 0)
A-687	Pyridin-3-ylmethyl	Thien-2-yl	W1b (m = 0)
A-688	Pyridin-3-ylmethyl	2,3-Dihydrobenzo[b]furan-5-yl	W1b (m = 0)
A-689	n-Butyl	Phenyl	W2a (m = 0)
A-690	n-Butyl	2-Methylphenyl	W2a (m = 0)
A-691	n-Butyl	2-Methoxyphenyl	W2a (m = 0)
A-692	n-Butyl	2-Chlorophenyl	W2a (m = 0)
A-693	n-Butyl	2-Fluorophenyl	W2a (m = 0)
A-694	n-Butyl	2-Trifluoromethylphenyl	W2a (m = 0)
A-695	n-Butyl	3-Methylphenyl	W2a (m = 0)
A-696	n-Butyl	3-Methoxyphenyl	W2a (m = 0)
A-697	n-Butyl	3-Chlorophenyl	W2a (m = 0)
A-698	n-Butyl	3-Fluorophenyl	W2a (m = 0)
A-699	n-Butyl	3-Trifluoromethyl	W2a (m = 0)
A-700	n-Butyl	3-[(Phenylmethyl)oxy]phenyl	W2a (m = 0)
A-701	n-Butyl	3-Morpholin-4-ylphenyl	W2a (m = 0)
A-702	n-Butyl	3-(Morpholin-4-ylmethyl)phenyl	W2a (m = 0)
A-703	n-Butyl	3-Pyrrolidin-1-ylphenyl	W2a (m = 0)
A-704	n-Butyl	4-Methylphenyl	W2a (m = 0)
A-705	n-Butyl	4-(1-Methylethyl)phenyl	W2a (m = 0)
A-706	n-Butyl	4-Methoxyphenyl	W2a (m = 0)
A-707	n-Butyl	4-Chlorophenyl	W2a (m = 0)
A-708	n-Butyl	4-Fluorophenyl	W2a (m = 0)
A-709	n-Butyl	4-Trifluoromethylphenyl	W2a (m = 0)
A-710	n-Butyl	4-Diethylaminophenyl	W2a (m = 0)
A-711	n-Butyl	4-[(Diethylamino)methyl]phenyl	W2a (m = 0)
A-712	n-Butyl	4-Cyanophenyl	W2a (m = 0)

No.	R^1	R^2	W
A-713	n-Butyl	4-(Piperidin-1-yl)phenyl	W2a (m = 0)
A-714	n-Butyl	4-(4-Methylpiperazin-1-yl)phenyl	W2a (m = 0)
A-715	n-Butyl	4-Pyrrolidin-1-ylphenyl	W2a (m = 0)
A-716	n-Butyl	4-(1H-Imidazol-1-yl)phenyl	W2a (m = 0)
A-717	n-Butyl	4-Morpholin-4-ylphenyl	W2a (m = 0)
A-718	n-Butyl	4-(Morpholin-4-ylmethyl)phenyl	W2a (m = 0)
A-719	n-Butyl	2,4-Difluorophenyl	W2a (m = 0)
A-720	n-Butyl	2,6-Difluorophenyl	W2a (m = 0)
A-721	n-Butyl	3,5-Difluorophenyl	W2a (m = 0)
A-722	n-Butyl	2,4-Dichlorophenyl	W2a (m = 0)
A-723	n-Butyl	2,6-Dichlorophenyl	W2a (m = 0)
A-724	n-Butyl	3,5-Dichlorophenyl	W2a (m = 0)
A-725	n-Butyl	2-Chloro-4-fluorophenyl	W2a (m = 0)
A-726	n-Butyl	2-Chloro-4-morpholin-4-ylphenyl	W2a (m = 0)
A-727	n-Butyl	2-Fluoro-4-morpholin-4-ylphenyl	W2a (m = 0)
A-728	n-Butyl	Pyridin-2-yl	W2a (m = 0)
A-729	n-Butyl	Pyridin-4-yl	W2a (m = 0)
A-730	n-Butyl	Thien-2-yl	W2a (m = 0)
A-731	n-Butyl	2,3-Dihydrobenzo[b]furan-5-yl	W2a (m = 0)
A-732	Isobutyl	Phenyl	W2a (m = 0)
A-733	Isobutyl	2-Methylphenyl	W2a (m = 0)
A-734	Isobutyl	2-Methoxyphenyl	W2a (m = 0)
A-735	Isobutyl	2-Chlorophenyl	W2a (m = 0)
A-736	Isobutyl	2-Fluorophenyl	W2a (m = 0)
A-737	Isobutyl	2-Trifluoromethylphenyl	W2a (m = 0)
A-738	Isobutyl	3-Methylphenyl	W2a (m = 0)
A-739	Isobutyl	3-Methoxyphenyl	W2a (m = 0)
A-740	Isobutyl	3-Chlorophenyl	W2a (m = 0)
A-741	Isobutyl	3-Fluorophenyl	W2a (m = 0)
A-742	Isobutyl	3-Trifluoromethyl	W2a (m = 0)
A-743	Isobutyl	3-[(Phenylmethyl)oxy]phenyl	W2a (m = 0)
A-744	Isobutyl	3-Morpholin-4-ylphenyl	W2a (m = 0)
A-745	Isobutyl	3-(Morpholin-4-ylmethyl)phenyl	W2a (m = 0)
A-746	Isobutyl	3-Pyrrolidin-1-ylphenyl	W2a (m = 0)
A-747	Isobutyl	4-Methylphenyl	W2a (m = 0)
A-748	Isobutyl	4-(1-Methylethyl)phenyl	W2a (m = 0)
A-749	Isobutyl	4-Methoxyphenyl	W2a (m = 0)
A-750	Isobutyl	4-Chlorophenyl	W2a (m = 0)
A-751	Isobutyl	4-Fluorophenyl	W2a (m = 0)

No.	R^1	R^2	W
A-752	Isobutyl	4-Trifluoromethylphenyl	W2a (m = 0)
A-753	Isobutyl	4-Diethylaminophenyl	W2a (m = 0)
A-754	Isobutyl	4-[(Diethylamino)methyl]phenyl	W2a (m = 0)
A-755	Isobutyl	4-Cyanophenyl	W2a (m = 0)
A-756	Isobutyl	4-(Piperidin-1-yl)phenyl	W2a (m = 0)
A-757	Isobutyl	4-(4-Methylpiperazin-1-yl)phenyl	W2a (m = 0)
A-758	Isobutyl	4-Pyrrolidin-1-ylphenyl	W2a (m = 0)
A-759	Isobutyl	4-(1H-Imidazol-1-yl)phenyl	W2a (m = 0)
A-760	Isobutyl	4-Morpholin-4-ylphenyl	W2a (m = 0)
A-761	Isobutyl	4-(Morpholin-4-ylmethyl)phenyl	W2a (m = 0)
A-762	Isobutyl	2,4-Difluorophenyl	W2a (m = 0)
A-763	Isobutyl	2,6-Difluorophenyl	W2a (m = 0)
A-764	Isobutyl	3,5-Difluorophenyl	W2a (m = 0)
A-765	Isobutyl	2,4-Dichlorophenyl	W2a (m = 0)
A-766	Isobutyl	2,6-Dichlorophenyl	W2a (m = 0)
A-767	Isobutyl	3,5-Dichlorophenyl	W2a (m = 0)
A-768	Isobutyl	2-Chloro-4-fluorophenyl	W2a (m = 0)
A-769	Isobutyl	2-Chloro-4-morpholin-4-ylphenyl	W2a (m = 0)
A-770	Isobutyl	2-Fluoro-4-morpholin-4-ylphenyl	W2a (m = 0)
A-771	Isobutyl	Pyridin-2-yl	W2a (m = 0)
A-772	Isobutyl	Pyridin-4-yl	W2a (m = 0)
A-773	Isobutyl	Thien-2-yl	W2a (m = 0)
A-774	Isobutyl	2,3-Dihydrobenzo[b]furan-5-yl	W2a (m = 0)
A-775	Benzyl	Phenyl	W2a (m = 0)
A-776	Benzyl	2-Methylphenyl	W2a (m = 0)
A-777	Benzyl	2-Methoxyphenyl	W2a (m = 0)
A-778	Benzyl	2-Chlorophenyl	W2a (m = 0)
A-779	Benzyl	2-Fluorophenyl	W2a (m = 0)
A-780	Benzyl	2-Trifluoromethylphenyl	W2a (m = 0)
A-781	Benzyl	3-Methylphenyl	W2a (m = 0)
A-782	Benzyl	3-Methoxyphenyl	W2a (m = 0)
A-783	Benzyl	3-Chlorophenyl	W2a (m = 0)
A-784	Benzyl	3-Fluorophenyl	W2a (m = 0)
A-785	Benzyl	3-Trifluoromethyl	W2a (m = 0)
A-786	Benzyl	3-[(Phenylmethyl)oxy]phenyl	W2a (m = 0)
A-787	Benzyl	3-Morpholin-4-ylphenyl	W2a (m = 0)
A-788	Benzyl	3-(Morpholin-4-ylmethyl)phenyl	W2a (m = 0)
A-789	Benzyl	3-Pyrrolidin-1-ylphenyl	W2a (m = 0)
A-790	Benzyl	4-Methylphenyl	W2a (m = 0)

No.	R^1	R^2	W
A-791	Benzyl	4-(1-Methylethyl)phenyl	W2a (m = 0)
A-792	Benzyl	4-Methoxyphenyl	W2a (m = 0)
A-793	Benzyl	4-Chlorophenyl	W2a (m = 0)
A-794	Benzyl	4-Fluorophenyl	W2a (m = 0)
A-795	Benzyl	4-Trifluoromethylphenyl	W2a (m = 0)
A-796	Benzyl	4-Diethylaminophenyl	W2a (m = 0)
A-797	Benzyl	4-[(Diethylamino)methyl]phenyl	W2a (m = 0)
A-798	Benzyl	4-Cyanophenyl	W2a (m = 0)
A-799	Benzyl	4-(Piperidin-1-yl)phenyl	W2a (m = 0)
A-800	Benzyl	4-(4-Methylpiperazin-1-yl)phenyl	W2a (m = 0)
A-801	Benzyl	4-Pyrrolidin-1-ylphenyl	W2a (m = 0)
A-802	Benzyl	4-(1H-Imidazol-1-yl)phenyl	W2a (m = 0)
A-803	Benzyl	4-Morpholin-4-ylphenyl	W2a (m = 0)
A-804	Benzyl	4-(Morpholin-4-ylmethyl)phenyl	W2a (m = 0)
A-805	Benzyl	2,4-Difluorophenyl	W2a (m = 0)
A-806	Benzyl	2,6-Difluorophenyl	W2a (m = 0)
A-807	Benzyl	3,5-Difluorophenyl	W2a (m = 0)
A-808	Benzyl	2,4-Dichlorophenyl	W2a (m = 0)
A-809	Benzyl	2,6-Dichlorophenyl	W2a (m = 0)
A-810	Benzyl	3,5-Dichlorophenyl	W2a (m = 0)
A-811	Benzyl	2-Chloro-4-fluorophenyl	W2a (m = 0)
A-812	Benzyl	2-Chloro-4-morpholin-4-ylphenyl	W2a (m = 0)
A-813	Benzyl	2-Fluoro-4-morpholin-4-ylphenyl	W2a (m = 0)
A-814	Benzyl	Pyridin-2-yl	W2a (m = 0)
A-815	Benzyl	Pyridin-4-yl	W2a (m = 0)
A-816	Benzyl	Thien-2-yl	W2a (m = 0)
A-817	Benzyl	2,3-Dihydrobenzo[b]furan-5-yl	W2a (m = 0)
A-818	4-Chlorobenzyl	Phenyl	W2a (m = 0)
A-819	4-Chlorobenzyl	2-Methylphenyl	W2a (m = 0)
A-820	4-Chlorobenzyl	2-Methoxyphenyl	W2a (m = 0)
A-821	4-Chlorobenzyl	2-Chlorophenyl	W2a (m = 0)
A-822	4-Chlorobenzyl	2-Fluorophenyl	W2a (m = 0)
A-823	4-Chlorobenzyl	2-Trifluoromethylphenyl	W2a (m = 0)
A-824	4-Chlorobenzyl	3-Methylphenyl	W2a (m = 0)
A-825	4-Chlorobenzyl	3-Methoxyphenyl	W2a (m = 0)
A-826	4-Chlorobenzyl	3-Chlorophenyl	W2a (m = 0)
A-827	4-Chlorobenzyl	3-Fluorophenyl	W2a (m = 0)
A-828	4-Chlorobenzyl	3-Trifluoromethyl	W2a (m = 0)
A-829	4-Chlorobenzyl	3-[(Phenylmethyl)oxy]phenyl	W2a (m = 0)

No.	R^1	R^2	W
A-830	4-Chlorobenzyl	3-Morpholin-4-ylphenyl	W2a (m = 0)
A-831	4-Chlorobenzyl	3-(Morpholin-4-ylmethyl)phenyl	W2a (m = 0)
A-832	4-Chlorobenzyl	3-Pyrrolidin-1-ylphenyl	W2a (m = 0)
A-833	4-Chlorobenzyl	4-Methylphenyl	W2a (m = 0)
A-834	4-Chlorobenzyl	4-(1-Methylethyl)phenyl	W2a (m = 0)
A-835	4-Chlorobenzyl	4-Methoxyphenyl	W2a (m = 0)
A-836	4-Chlorobenzyl	4-Chlorophenyl	W2a (m = 0)
A-837	4-Chlorobenzyl	4-Fluorophenyl	W2a (m = 0)
A-838	4-Chlorobenzyl	4-Trifluoromethylphenyl	W2a (m = 0)
A-839	4-Chlorobenzyl	4-Diethylaminophenyl	W2a (m = 0)
A-840	4-Chlorobenzyl	4-[(Diethylamino)methyl]phenyl	W2a (m = 0)
A-841	4-Chlorobenzyl	4-Cyanophenyl	W2a (m = 0)
A-842	4-Chlorobenzyl	4-(Piperidin-1-yl)phenyl	W2a (m = 0)
A-843	4-Chlorobenzyl	4-(4-Methylpiperazin-1-yl)phenyl	W2a (m = 0)
A-844	4-Chlorobenzyl	4-Pyrrolidin-1-ylphenyl	W2a (m = 0)
A-845	4-Chlorobenzyl	4-(1H-Imidazol-1-yl)phenyl	W2a (m = 0)
A-846	4-Chlorobenzyl	4-Morpholin-4-ylphenyl	W2a (m = 0)
A-847	4-Chlorobenzyl	4-(Morpholin-4-ylmethyl)phenyl	W2a (m = 0)
A-848	4-Chlorobenzyl	2,4-Difluorophenyl	W2a (m = 0)
A-849	4-Chlorobenzyl	2,6-Difluorophenyl	W2a (m = 0)
A-850	4-Chlorobenzyl	3,5-Difluorophenyl	W2a (m = 0)
A-851	4-Chlorobenzyl	2,4-Dichlorophenyl	W2a (m = 0)
A-852	4-Chlorobenzyl	2,6-Dichlorophenyl	W2a (m = 0)
A-853	4-Chlorobenzyl	3,5-Dichlorophenyl	W2a (m = 0)
A-854	4-Chlorobenzyl	2-Chloro-4-fluorophenyl	W2a (m = 0)
A-855	4-Chlorobenzyl	2-Chloro-4-morpholin-4-ylphenyl	W2a (m = 0)
A-856	4-Chlorobenzyl	2-Fluoro-4-morpholin-4-ylphenyl	W2a (m = 0)
A-857	4-Chlorobenzyl	Pyridin-2-yl	W2a (m = 0)
A-858	4-Chlorobenzyl	Pyridin-4-yl	W2a (m = 0)
A-859	4-Chlorobenzyl	Thien-2-yl	W2a (m = 0)
A-860	4-Chlorobenzyl	2,3-Dihydrobenzo[b]furan-5-yl	W2a (m = 0)
A-861	4-Methoxybenzyl	Phenyl	W2a (m = 0)
A-862	4-Methoxybenzyl	2-Methylphenyl	W2a (m = 0)
A-863	4-Methoxybenzyl	2-Methoxyphenyl	W2a (m = 0)
A-864	4-Methoxybenzyl	2-Chlorophenyl	W2a (m = 0)
A-865	4-Methoxybenzyl	2-Fluorophenyl	W2a (m = 0)
A-866	4-Methoxybenzyl	2-Trifluoromethylphenyl	W2a (m = 0)
A-867	4-Methoxybenzyl	3-Methylphenyl	W2a (m = 0)
A-868	4-Methoxybenzyl	3-Methoxyphenyl	W2a (m = 0)

No.	R^1	R^2	W
A-869	4-Methoxybenzyl	3-Chlorophenyl	W2a (m = 0)
A-870	4-Methoxybenzyl	3-Fluorophenyl	W2a (m = 0)
A-871	4-Methoxybenzyl	3-Trifluoromethyl	W2a (m = 0)
A-872	4-Methoxybenzyl	3-[(Phenylmethyl)oxy]phenyl	W2a (m = 0)
A-873	4-Methoxybenzyl	3-Morpholin-4-ylphenyl	W2a (m = 0)
A-874	4-Methoxybenzyl	3-(Morpholin-4-ylmethyl)phenyl	W2a (m = 0)
A-875	4-Methoxybenzyl	3-Pyrrolidin-1-ylphenyl	W2a (m = 0)
A-876	4-Methoxybenzyl	4-Methylphenyl	W2a (m = 0)
A-877	4-Methoxybenzyl	4-(1-Methylethyl)phenyl	W2a (m = 0)
A-878	4-Methoxybenzyl	4-Methoxyphenyl	W2a (m = 0)
A-879	4-Methoxybenzyl	4-Chlorophenyl	W2a (m = 0)
A-880	4-Methoxybenzyl	4-Fluorophenyl	W2a (m = 0)
A-881	4-Methoxybenzyl	4-Trifluoromethylphenyl	W2a (m = 0)
A-882	4-Methoxybenzyl	4-Diethylaminophenyl	W2a (m = 0)
A-883	4-Methoxybenzyl	4-[(Diethylamino)methyl]phenyl	W2a (m = 0)
A-884	4-Methoxybenzyl	4-Cyanophenyl	W2a (m = 0)
A-885	4-Methoxybenzyl	4-(Piperidin-1-yl)phenyl	W2a (m = 0)
A-886	4-Methoxybenzyl	4-(4-Methylpiperazin-1-yl)phenyl	W2a (m = 0)
A-887	4-Methoxybenzyl	4-Pyrrolidin-1-ylphenyl	W2a (m = 0)
A-888	4-Methoxybenzyl	4-(1H-Imidazol-1-yl)phenyl	W2a (m = 0)
A-889	4-Methoxybenzyl	4-Morpholin-4-ylphenyl	W2a (m = 0)
A-890	4-Methoxybenzyl	4-(Morpholin-4-ylmethyl)phenyl	W2a (m = 0)
A-891	4-Methoxybenzyl	2,4-Difluorophenyl	W2a (m = 0)
A-892	4-Methoxybenzyl	2,6-Difluorophenyl	W2a (m = 0)
A-893	4-Methoxybenzyl	3,5-Difluorophenyl	W2a (m = 0)
A-894	4-Methoxybenzyl	2,4-Dichlorophenyl	W2a (m = 0)
A-895	4-Methoxybenzyl	2,6-Dichlorophenyl	W2a (m = 0)
A-896	4-Methoxybenzyl	3,5-Dichlorophenyl	W2a (m = 0)
A-897	4-Methoxybenzyl	2-Chloro-4-fluorophenyl	W2a (m = 0)
A-898	4-Methoxybenzyl	2-Chloro-4-morpholin-4-ylphenyl	W2a (m = 0)
A-899	4-Methoxybenzyl	2-Fluoro-4-morpholin-4-ylphenyl	W2a (m = 0)
A-900	4-Methoxybenzyl	Pyridin-2-yl	W2a (m = 0)
A-901	4-Methoxybenzyl	Pyridin-4-yl	W2a (m = 0)
A-902	4-Methoxybenzyl	Thien-2-yl	W2a (m = 0)
A-903	4-Methoxybenzyl	2,3-Dihydrobenzo[b]furan-5-yl	W2a (m = 0)
A-904	Cyclohexylmethyl	Phenyl	W2a (m = 0)
A-905	Cyclohexylmethyl	2-Methylphenyl	W2a (m = 0)
A-906	Cyclohexylmethyl	2-Methoxyphenyl	W2a (m = 0)
A-907	Cyclohexylmethyl	2-Chlorophenyl	W2a (m = 0)

No.	R^1	R^2	W
A-908	Cyclohexylmethyl	2-Fluorophenyl	W2a (m = 0)
A-909	Cyclohexylmethyl	2-Trifluoromethylphenyl	W2a (m = 0)
A-910	Cyclohexylmethyl	3-Methylphenyl	W2a (m = 0)
A-911	Cyclohexylmethyl	3-Methoxyphenyl	W2a (m = 0)
A-912	Cyclohexylmethyl	3-Chlorophenyl	W2a (m = 0)
A-913	Cyclohexylmethyl	3-Fluorophenyl	W2a (m = 0)
A-914	Cyclohexylmethyl	3-Trifluoromethyl	W2a (m = 0)
A-915	Cyclohexylmethyl	3-[(Phenylmethyl)oxy]phenyl	W2a (m = 0)
A-916	Cyclohexylmethyl	3-Morpholin-4-ylphenyl	W2a (m = 0)
A-917	Cyclohexylmethyl	3-(Morpholin-4-ylmethyl)phenyl	W2a (m = 0)
A-918	Cyclohexylmethyl	3-Pyrrolidin-1-ylphenyl	W2a (m = 0)
A-919	Cyclohexylmethyl	4-Methylphenyl	W2a (m = 0)
A-920	Cyclohexylmethyl	4-(1-Methylethyl)phenyl	W2a (m = 0)
A-921	Cyclohexylmethyl	4-Methoxyphenyl	W2a (m = 0)
A-922	Cyclohexylmethyl	4-Chlorophenyl	W2a (m = 0)
A-923	Cyclohexylmethyl	4-Fluorophenyl	W2a (m = 0)
A-924	Cyclohexylmethyl	4-Trifluoromethylphenyl	W2a (m = 0)
A-925	Cyclohexylmethyl	4-Diethylaminophenyl	W2a (m = 0)
A-926	Cyclohexylmethyl	4-[(Diethylamino)methyl]phenyl	W2a (m = 0)
A-927	Cyclohexylmethyl	4-Cyanophenyl	W2a (m = 0)
A-928	Cyclohexylmethyl	4-(Piperidin-1-yl)phenyl	W2a (m = 0)
A-929	Cyclohexylmethyl	4-(4-Methylpiperazin-1-yl)phenyl	W2a (m = 0)
A-930	Cyclohexylmethyl	4-Pyrrolidin-1-ylphenyl	W2a (m = 0)
A-931	Cyclohexylmethyl	4-(1H-Imidazol-1-yl)phenyl	W2a (m = 0)
A-932	Cyclohexylmethyl	4-Morpholin-4-ylphenyl	W2a (m = 0)
A-933	Cyclohexylmethyl	4-(Morpholin-4-ylmethyl)phenyl	W2a (m = 0)
A-934	Cyclohexylmethyl	2,4-Difluorophenyl	W2a (m = 0)
A-935	Cyclohexylmethyl	2,6-Difluorophenyl	W2a (m = 0)
A-936	Cyclohexylmethyl	3,5-Difluorophenyl	W2a (m = 0)
A-937	Cyclohexylmethyl	2,4-Dichlorophenyl	W2a (m = 0)
A-938	Cyclohexylmethyl	2,6-Dichlorophenyl	W2a (m = 0)
A-939	Cyclohexylmethyl	3,5-Dichlorophenyl	W2a (m = 0)
A-940	Cyclohexylmethyl	2-Chloro-4-fluorophenyl	W2a (m = 0)
A-941	Cyclohexylmethyl	2-Chloro-4-morpholin-4-ylphenyl	W2a (m = 0)
A-942	Cyclohexylmethyl	2-Fluoro-4-morpholin-4-ylphenyl	W2a (m = 0)
A-943	Cyclohexylmethyl	Pyridin-2-yl	W2a (m = 0)
A-944	Cyclohexylmethyl	Pyridin-4-yl	W2a (m = 0)
A-945	Cyclohexylmethyl	Thien-2-yl	W2a (m = 0)
A-946	Cyclohexylmethyl	2,3-Dihydrobenzo[b]furan-5-yl	W2a (m = 0)

No.	R^1	R^2	W
A-947	2-Thienylmethyl	Phenyl	W2a (m = 0)
A-948	2-Thienylmethyl	2-Methylphenyl	W2a (m = 0)
A-949	2-Thienylmethyl	2-Methoxyphenyl	W2a (m = 0)
A-950	2-Thienylmethyl	2-Chlorophenyl	W2a (m = 0)
A-951	2-Thienylmethyl	2-Fluorophenyl	W2a (m = 0)
A-952	2-Thienylmethyl	2-Trifluoromethylphenyl	W2a (m = 0)
A-953	2-Thienylmethyl	3-Methylphenyl	W2a (m = 0)
A-954	2-Thienylmethyl	3-Methoxyphenyl	W2a (m = 0)
A-955	2-Thienylmethyl	3-Chlorophenyl	W2a (m = 0)
A-956	2-Thienylmethyl	3-Fluorophenyl	W2a (m = 0)
A-957	2-Thienylmethyl	3-Trifluoromethyl	W2a (m = 0)
A-958	2-Thienylmethyl	3-[(Phenylmethyl)oxy]phenyl	W2a (m = 0)
A-959	2-Thienylmethyl	3-Morpholin-4-ylphenyl	W2a (m = 0)
A-960	2-Thienylmethyl	3-(Morpholin-4-ylmethyl)phenyl	W2a (m = 0)
A-961	2-Thienylmethyl	3-Pyrrolidin-1-ylphenyl	W2a (m = 0)
A-962	2-Thienylmethyl	4-Methylphenyl	W2a (m = 0)
A-963	2-Thienylmethyl	4-(1-Methylethyl)phenyl	W2a (m = 0)
A-964	2-Thienylmethyl	4-Methoxyphenyl	W2a (m = 0)
A-965	2-Thienylmethyl	4-Chlorophenyl	W2a (m = 0)
A-966	2-Thienylmethyl	4-Fluorophenyl	W2a (m = 0)
A-967	2-Thienylmethyl	4-Trifluoromethylphenyl	W2a (m = 0)
A-968	2-Thienylmethyl	4-Diethylaminophenyl	W2a (m = 0)
A-969	2-Thienylmethyl	4-[(Diethylamino)methyl]phenyl	W2a (m = 0)
A-970	2-Thienylmethyl	4-Cyanophenyl	W2a (m = 0)
A-971	2-Thienylmethyl	4-(Piperidin-1-yl)phenyl	W2a (m = 0)
A-972	2-Thienylmethyl	4-(4-Methylpiperazin-1-yl)phenyl	W2a (m = 0)
A-973	2-Thienylmethyl	4-Pyrrolidin-1-ylphenyl	W2a (m = 0)
A-974	2-Thienylmethyl	4-(1H-Imidazol-1-yl)phenyl	W2a (m = 0)
A-975	2-Thienylmethyl	4-Morpholin-4-ylphenyl	W2a (m = 0)
A-976	2-Thienylmethyl	4-(Morpholin-4-ylmethyl)phenyl	W2a (m = 0)
A-977	2-Thienylmethyl	2,4-Difluorophenyl	W2a (m = 0)
A-978	2-Thienylmethyl	2,6-Difluorophenyl	W2a (m = 0)
A-979	2-Thienylmethyl	3,5-Difluorophenyl	W2a (m = 0)
A-980	2-Thienylmethyl	2,4-Dichlorophenyl	W2a (m = 0)
A-981	2-Thienylmethyl	2,6-Dichlorophenyl	W2a (m = 0)
A-982	2-Thienylmethyl	3,5-Dichlorophenyl	W2a (m = 0)
A-983	2-Thienylmethyl	2-Chloro-4-fluorophenyl	W2a (m = 0)
A-984	2-Thienylmethyl	2-Chloro-4-morpholin-4-ylphenyl	W2a (m = 0)
A-985	2-Thienylmethyl	2-Fluoro-4-morpholin-4-ylphenyl	W2a (m = 0)

No.	R^1	R^2	W
A-986	2-Thienylmethyl	Pyridin-2-yl	W2a (m = 0)
A-987	2-Thienylmethyl	Pyridin-4-yl	W2a (m = 0)
A-988	2-Thienylmethyl	Thien-2-yl	W2a (m = 0)
A-989	2-Thienylmethyl	2,3-Dihydrobenzo[b]furan-5-yl	W2a (m = 0)
A-990	Pyridin-3-ylmethyl	Phenyl	W2a (m = 0)
A-991	Pyridin-3-ylmethyl	2-Methylphenyl	W2a (m = 0)
A-992	Pyridin-3-ylmethyl	2-Methoxyphenyl	W2a (m = 0)
A-993	Pyridin-3-ylmethyl	2-Chlorophenyl	W2a (m = 0)
A-994	Pyridin-3-ylmethyl	2-Fluorophenyl	W2a (m = 0)
A-995	Pyridin-3-ylmethyl	2-Trifluoromethylphenyl	W2a (m = 0)
A-996	Pyridin-3-ylmethyl	3-Methylphenyl	W2a (m = 0)
A-997	Pyridin-3-ylmethyl	3-Methoxyphenyl	W2a (m = 0)
A-998	Pyridin-3-ylmethyl	3-Chlorophenyl	W2a (m = 0)
A-999	Pyridin-3-ylmethyl	3-Fluorophenyl	W2a (m = 0)
A-1000	Pyridin-3-ylmethyl	3-Trifluoromethyl	W2a (m = 0)
A-1001	Pyridin-3-ylmethyl	3-[(Phenylmethyl)oxy]phenyl	W2a (m = 0)
A-1002	Pyridin-3-ylmethyl	3-Morpholin-4-ylphenyl	W2a (m = 0)
A-1003	Pyridin-3-ylmethyl	3-(Morpholin-4-ylmethyl)phenyl	W2a (m = 0)
A-1004	Pyridin-3-ylmethyl	3-Pyrrolidin-1-ylphenyl	W2a (m = 0)
A-1005	Pyridin-3-ylmethyl	4-Methylphenyl	W2a (m = 0)
A-1006	Pyridin-3-ylmethyl	4-(1-Methylethyl)phenyl	W2a (m = 0)
A-1007	Pyridin-3-ylmethyl	4-Methoxyphenyl	W2a (m = 0)
A-1008	Pyridin-3-ylmethyl	4-Chlorophenyl	W2a (m = 0)
A-1009	Pyridin-3-ylmethyl	4-Fluorophenyl	W2a (m = 0)
A-1010	Pyridin-3-ylmethyl	4-Trifluoromethylphenyl	W2a (m = 0)
A-1011	Pyridin-3-ylmethyl	4-Diethylaminophenyl	W2a (m = 0)
A-1012	Pyridin-3-ylmethyl	4-[(Diethylamino)methyl]phenyl	W2a (m = 0)
A-1013	Pyridin-3-ylmethyl	4-Cyanophenyl	W2a (m = 0)
A-1014	Pyridin-3-ylmethyl	4-(Piperidin-1-yl)phenyl	W2a (m = 0)
A-1015	Pyridin-3-ylmethyl	4-(4-Methylpiperazin-1-yl)phenyl	W2a (m = 0)
A-1016	Pyridin-3-ylmethyl	4-Pyrrolidin-1-ylphenyl	W2a (m = 0)
A-1017	Pyridin-3-ylmethyl	4-(1H-Imidazol-1-yl)phenyl	W2a (m = 0)
A-1018	Pyridin-3-ylmethyl	4-Morpholin-4-ylphenyl	W2a (m = 0)
A-1019	Pyridin-3-ylmethyl	4-(Morpholin-4-ylmethyl)phenyl	W2a (m = 0)
A-1020	Pyridin-3-ylmethyl	2,4-Difluorophenyl	W2a (m = 0)
A-1021	Pyridin-3-ylmethyl	2,6-Difluorophenyl	W2a (m = 0)
A-1022	Pyridin-3-ylmethyl	3,5-Difluorophenyl	W2a (m = 0)
A-1023	Pyridin-3-ylmethyl	2,4-Dichlorophenyl	W2a (m = 0)
A-1024	Pyridin-3-ylmethyl	2,6-Dichlorophenyl	W2a (m = 0)

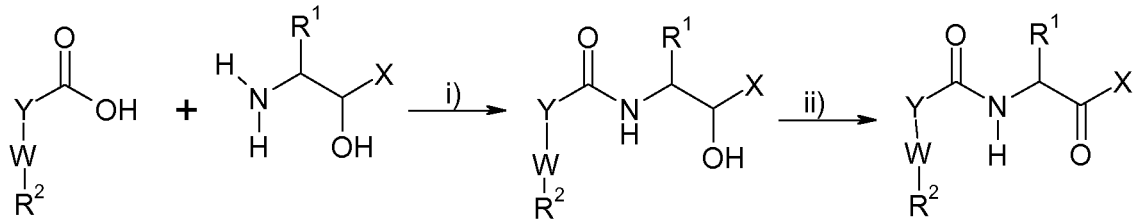
No.	R^1	R^2	W
A-1025	Pyridin-3-ylmethyl	3,5-Dichlorophenyl	W2a (m = 0)
A-1026	Pyridin-3-ylmethyl	2-Chloro-4-fluorophenyl	W2a (m = 0)
A-1027	Pyridin-3-ylmethyl	2-Chloro-4-morpholin-4-ylphenyl	W2a (m = 0)
A-1028	Pyridin-3-ylmethyl	2-Fluoro-4-morpholin-4-ylphenyl	W2a (m = 0)
A-1029	Pyridin-3-ylmethyl	Pyridin-2-yl	W2a (m = 0)
A-1030	Pyridin-3-ylmethyl	Pyridin-4-yl	W2a (m = 0)
A-1031	Pyridin-3-ylmethyl	Thien-2-yl	W2a (m = 0)
A-1032	Pyridin-3-ylmethyl	2,3-Dihydrobenzo[b]furan-5-yl	W2a (m = 0)
A-1033	n-Butyl	4,5-dihydro-2H-benzo[g]indazol-2-yl	
A-1034	n-Butyl	1H-Indazol-1-yl	
A-1035	n-Butyl	2H-Indazol-2-yl	
A-1036	n-Butyl	Chromeno[4,3-c]pyrazol-2(4H)-yl	
A-1037	Isobutyl	4,5-dihydro-2H-benzo[g]indazol-2-yl	
A-1038	Isobutyl	1H-Indazol-1-yl	
A-1039	Isobutyl	2H-Indazol-2-yl	
A-1040	Isobutyl	Chromeno[4,3-c]pyrazol-2(4H)-yl	
A-1041	Benzyl	4,5-dihydro-2H-benzo[g]indazol-2-yl	
A-1042	Benzyl	1H-Indazol-1-yl	
A-1043	Benzyl	2H-Indazol-2-yl	
A-1044	Benzyl	Chromeno[4,3-c]pyrazol-2(4H)-yl	
A-1045	4-Chlorobenzyl	4,5-dihydro-2H-benzo[g]indazol-2-yl	
A-1046	4-Chlorobenzyl	1H-Indazol-1-yl	
A-1047	4-Chlorobenzyl	2H-Indazol-2-yl	
A-1048	4-Chlorobenzyl	Chromeno[4,3-c]pyrazol-2(4H)-yl	
A-1049	4-Methoxybenzyl	4,5-dihydro-2H-benzo[g]indazol-2-yl	
A-1050	4-Methoxybenzyl	1H-Indazol-1-yl	
A-1051	4-Methoxybenzyl	2H-Indazol-2-yl	
A-1052	4-Methoxybenzyl	Chromeno[4,3-c]pyrazol-2(4H)-yl	
A-1053	Cyclohexylmethyl	4,5-dihydro-2H-benzo[g]indazol-2-yl	
A-1054	Cyclohexylmethyl	1H-Indazol-1-yl	
A-1055	Cyclohexylmethyl	2H-Indazol-2-yl	
A-1056	Cyclohexylmethyl	Chromeno[4,3-c]pyrazol-2(4H)-yl	
A-1057	2-Thienylmethyl	4,5-dihydro-2H-benzo[g]indazol-2-yl	
A-1058	2-Thienylmethyl	1H-Indazol-1-yl	
A-1059	2-Thienylmethyl	2H-Indazol-2-yl	
A-1060	2-Thienylmethyl	Chromeno[4,3-c]pyrazol-2(4H)-yl	
A-1061	Pyridin-3-ylmethyl	4,5-dihydro-2H-benzo[g]indazol-2-yl	
A-1062	Pyridin-3-ylmethyl	1H-Indazol-1-yl	
A-1063	Pyridin-3-ylmethyl	2H-Indazol-2-yl	

No.	R^1	R^2	W
A-1064	Pyridin-3-ylmethyl	Chromeno[4,3-c]pyrazol-2(4H)-yl	

The compounds of the invention of the general formula I and the starting materials used to prepare them can be prepared in analogy to known processes of organic chemistry as are described in standard works of organic chemistry, e.g. Houben-Weyl, "Methoden der Organischen Chemie", Thieme-Verlag, Stuttgart, Jerry March "Advanced Organic Chemistry", 5th edition, Wiley & Sons and the literature cited therein, and R. Larock, "Comprehensive Organic Transformations", 2nd edition, Weinheim, 1999 and the literature cited therein. The carboxamide compounds of the invention of the general formula I are advantageously prepared by the methods described below and/or in the experimental section.

The compounds of the formula I can be prepared in analogy to the schemes and methods described in WO 99/54305, pp. 6-10. An important access to compounds of the formula I is depicted in Scheme 1.

Scheme 1:



(II) (III) (IV) (I)

In Scheme 1, R^1, R^2, W, Y and X exhibit the aforementioned meanings.

In a first step i), a carboxylic acid II is converted by reaction with an amino alcohol III into a corresponding hydroxy amide IV. In this connection, conventional peptide coupling methods are ordinarily used, as are described for example in R. C. Larock, Comprehensive Organic Transformations, VCH Publisher, 1989, pages 972-976, or in Houben-Weyl, Methoden der organischen Chemie, 4th edition, E5, Chap. V. It may be advantageous firstly to activate the carboxylic acid II. For this purpose, for example, the carboxylic acid II is reacted with a carbodiimide such as dicyclohexylcarbodiimide (DCC) or 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) in the presence of hydroxybenzotriazole (HOBt), nitrophenol, pentafluorophenol, 2,4,5-trichlorophenol or N-hydroxysuccinimide, to obtain an activated ester IIa. It may further be advantageous to prepare the activated ester IIa in the presence of a base, for example a tertiary amine. The activated ester IIa is subsequently reacted with the amino alcohol of the formula III or its hydrohalide salt to give the hydroxy amide IV. The reaction normally takes place in anhydrous inert solvents such as chlorinated hydrocarbons, e.g. dichloromethane or dichloroethane, ethers, e.g. tetrahydrofuran or 1,4-dioxane or

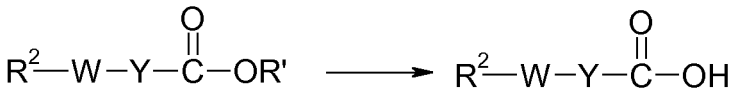
carboxamides, e.g. N,N-dimethylformamide, N,N-dimethylacetamide or N-methylpyrrolidone. Step i) is ordinarily carried out at temperatures in the range from -20°C to +25°C.

Subsequently, in a second step ii), the hydroxy amide compound IV is oxidized to the carboxamide compound I of the invention. Various conventional oxidation reactions are suitable for this (see R. C. Larock, Comprehensive Organic Transformations, VCH Publisher, 1989, page 604 et seq.) such as, for example, swern oxidation and swern analogous oxidations (T.T. Tidwell, Synthesis 1990, pp. 857-870) or Pfitzner-Moffatt oxidation. Suitable oxidizing agents are dimethyl sulfoxide (DMSO) in combination with dicyclohexylcarbodiimide or 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide, dimethyl sulfoxide in combination with the pyridine-SO_3 complex or dimethyl sulfoxide in combination with oxalyl chloride, sodium hypochloride/TEMPO (S. L. Harbenson et al., J. MED: Chem. 1994, 37, 2918-2929) or the Dess-Martin reagent (J. Org. Chem. 1983, 48, 4155). Depending on the oxidizing agent used, the oxidation of the hydroxy amide compound IV takes place at temperatures of from -50 to +25°C.

Compounds of the formula I in which X is -C(O)N(R^{x4})-(C_1-C_6-alkylene)-$NR^{x2}R^{x3}$ or is -C(O)N(R^{x4})$NR^{x2}R^{x3}$ in which R^{x2}, R^{x3} and R^{x4} have the aforementioned meanings can additionally be prepared by reacting compounds of the formula I in which X is COOH with hydrazine compounds of the formula NH(R^{x4})$NR^{x2}R^{x3}$ or diamines of the formula NH(R^{x4})-(C_1-C_6-alkylene)-$NR^{x2}R^{x3}$. The reaction can be carried out in analogy to step i) in Scheme 1.

The amino alcohols III can be obtained by purchase or can be prepared by processes disclosed in the literature (for amino hydroxy carboxylic acid derivatives, see, for example, S. L. Harbenson et al., J. Med. Chem. 1994, 37, 2918-2929 or J. P. Burkhardt et al., Tetrahedron Lett. 1988, 29, 3433-3436) or in analogy to the processes described in the preparation examples.

The carboxylic acid II can be prepared by hydrolyzing the carboxylic ester V with acids or bases under generally customary conditions. The hydrolysis preferably takes place with bases such as alkali metal or alkaline earth metal hydroxides, for example lithium hydroxide, sodium hydroxide or potassium hydroxide in aqueous medium or in a mixture of water and organic solvents, e.g. alcohols such as methanol or ethanol, ethers such as tetrahydrofuran or dioxane, at room temperature or elevated temperature such as 25-100°C.

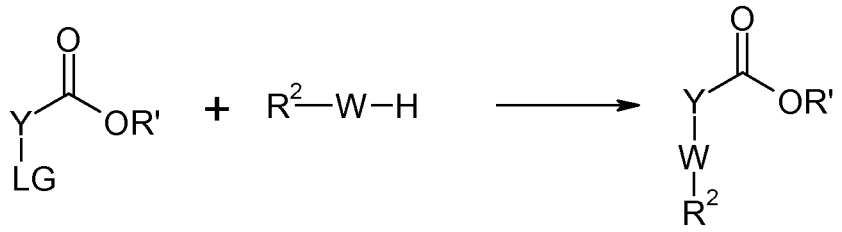


(V) (II)

In formulae II and V, R^2, W and Y have the aforementioned meanings. In formula V, R' is alkyl, preferably C_1-C_6-alkyl.

The carboxylic ester of the formula V can advantageously be obtained by reacting the carboxylic ester of the general formula VI with an imidazole or pyrazole compound VII, see Scheme 2.

Scheme 2:



(VI) (VII) (V)

In scheme 2, LG represents a nucleophilically displaceable leaving group. Examples of suitable nucleophilically displaceable leaving groups are halogen, e.g. chlorine or bromine, or tosylate. R' is alkyl, preferably C_1-C_6-alkyl. R^2, Y and W have the aforementioned meanings.

As shown in Scheme 2, an ester VI is reacted with an appropriate imidazole or pyrazole compound of the formula VII. The reaction is ordinarily carried out under conventional conditions in the presence of a base in an inert solvent at elevated temperature. It may be advantageous where appropriate to carry out the reaction in the presence of catalytically active amounts of a transition metal, in particular of a metal of group 10 or 11 in the periodic table.

In the case where Y is a divalent heteroaromatic radical, in particular a divalent nitrogen-containing heteroaromatic radical, the reaction is preferably carried out at elevated temperature without diluent or in an inert solvent such as an ether, e.g. tetrahydrofuran or dioxane, carboxamides such as N,N-dimethylformamide, N,N-dimethylacetamide or N-methylpyrrolidone, or an aromatic hydrocarbon such as benzene, toluene or o-, m- or p-xylene. The reaction takes place in the presence of inorganic or organic bases and of a crown ether. Suitable inorganic bases are alkali metal or alkaline earth metal amides such as sodium amide, alkali metal or alkaline earth metal carbonates such as potassium carbonate or cesium carbonate or alkali metal hydrides such as sodium hydride. Suitable organic bases are tertiary amines, such as, for example, trimethylamine or triethylamine. A suitable crown ether is 18-crown-6. A Cu(I) salt such as, for example, CuI, CuCN, Cu_2O is added where

appropriate as catalyst (see, for example, US 4,826,835 and WO 88/00468).

In the case where Y is a divalent aromatic radical, the reaction of the carboxylic ester VI with the pyrazole or imidazole compound VII preferably takes place by transition metal-catalyzed N-arylation as described for example by H.J. Cristeau et al., Eur. J. Org. Chem. 2004, pp. 695-709, and S.L. Buchwald et al.; J. Org. Chem. 2004, 69, pages 5578-5587. The reaction frequently takes place in the presence of catalytically active amounts of a metal of group 10 in the periodic table, especially in the presence of a nickel(II) compound, Ni(0) compound, Pd(II) compound or Pd(0) compound. An example of a suitable method is the Buchwald cross-coupling.

The Buchwald cross-coupling normally takes place in the presence of a phosphorus-containing ligand, especially of a monodentate or bidentate phosphine ligand. Preferred ligands on the palladium are bulky, monodentate or bidentate phosphines such as triphenylphosphine, tri(o-tolyl)phosphine, tri(cyclohexyl)phosphine, BINAP (2,2'-bis-(diphenylphosphino)-1,1'-binaphthyl) or the Buchwald phosphines. The ligand may be present in the palladium compound or be added separately. Suitable palladium compounds include tris(dibenzylideneacetone)dipalladium(0), palladium(II) bis(o-tolyl)phosphine chloride and palladium(II) acetate. The Buchwald cross-coupling normally takes place in an organic solvent. Suitable organic solvents are aromatic hydrocarbons such as benzene or toluene, halogenated aromatic hydrocarbons such as chlorobenzene, halogenated hydrocarbons such as dichloromethane, trichloromethane, dichloroethane, ethers such as tetrahydrofuran, dioxane, ethylene glycol dimethyl ether, methyl tert-butyl ether, or amides such as dimethylformamide or N-methylpyrrolidone, and mixtures thereof. The Buchwald coupling reaction can be carried out under normal conditions or with use of microwaves.

The imidazole or pyrazole compounds VII can be purchased or can be prepared by conventional methods, which are briefly outlined below, from precursors which can be obtained by purchase.

A general overview of the preparation of imidazoles is to be found in W. M. Menge, Pharmacochemistry Library 1998, 30, pages 145-158. The imidazole compounds VII used are particularly advantageously prepared by the method described by Bredereck et al. (Chem. Ber. 1953, 86, pages 88-96) in which alpha-halo or alpha-hydroxy ketones are reacted with formamide - ordinarily with heating - to give the imidazoles VII.

General methods for preparing pyrazoles of the general formula VII are described for example in R. Fusco in "The Chemistry of Heterocyclic Compounds: Pyrazoles, Pyrazolines, Pyrazolidines, Indazoles and Condensed Rings", Wiley, R. H., editor; Wiley: New York, 1967; Vol. 22, pages 1-174; or J. Elguero, in "Comprehensive

Heterocyclic Chemistry"; Potts, K. T., Ed.; Pergamon: Oxford 1984; Vol. 5, pages 291-298. One of the most commonly used methods is cyclocondensation of 1,3-dicarbonyl compounds or correspondingly reactive analogs with hydrazine or substituted hydrazine derivatives.

3-Aryl- or 3-hetaryl-substituted pyrazoles VII are particularly advantageously prepared by reacting 1-aryl- or 1-hetaryl-3-dimethylamino-2-propene compounds with hydrazine in analogy to the processes described for example in M.A. Halcrow et al.; J. Chem. Soc. Dalton Trans. 1997, pages 4025-4035. The 1-aryl- or 1-hetaryl-3-dimethylamino-2-propenes required as starting material can easily be prepared by condensing the analogous aromatic acetyl compounds with N,N-dimethylformamide dimethyl acetal (or analogously using the corresponding diethyl acetal). The reaction is normally carried out without diluent or in an inert solvent such as, for example, dimethylformamide or toluene, at elevated temperature. It is particularly advantageous to introduce the activation energy necessary for the reaction into the reaction mixture also by means of microwaves and to carry out the reaction under elevated pressure as described in A.K. Pleier, Synthesis 2001, 1, pages 55-62.

Analogous 4-substituted pyrazoles of the general formula VII are prepared for example starting from aryl- or hetarylacetic acids which are converted by means of the Vilsmeier reagent into the corresponding gamma-dimethylamino-2-propenals, with subsequent cyclization with hydrazine, see, for example, US 4,888,352.

A further general possibility for preparing substituted pyrazoles of the formula VII is the Suzuki coupling of appropriate pyrazoleboronic acids or pyrazoleboronic esters as described for example in: N. Zhe et al.; J. Med. Chem. 2005, 48 (5), pages 1569-1609; Young et al.; J. Med. Chem. 2004, 47 (6), pp. 1547-1552; C. Slee et al.; Bioorg. Med. Chem. Lett. 2001, 9, pages 3243-3253. An appropriate alternative is also Stille coupling of halogenated pyrazole derivatives with appropriate tin organyls as described for example by J. Eluguero et al.; Synthesis 1997, 5, pp. 563-566.

The preparation of 1,4-dihydrobenzopyranopyrazoles can be performed according to the methods described by Chandrasekhar, S. et al.; Tetrahedron Letters 2001, 42(37), 6599-6601.

The reaction mixtures are worked up in a conventional way, e.g. by mixing with water, separating the phases and, where appropriate, purifying the crude products by chromatography. The intermediates and final products in some cases result in the form of colorless or pale brownish, viscous oils which are freed of volatiles or purified under reduced pressure and at moderately elevated temperature. If the intermediates and final products are obtained as solids, the purification can also take place by recrystallization or digestion.

If individual compounds I are not obtainable by the routes described above, they can be prepared by derivatization of other compounds I.

The compounds of the invention exhibit extremely low Ki values in relation to the inhibition of calpain and thus permit efficient inhibition of calpain, especially calpain I, at low serum levels. The compounds of the invention ordinarily exhibit Ki values in relation to the inhibition of calpain in vitro of < 500 nM, in particular < 100 nM and specifically ≤ 40 nM. The compounds of the invention are therefore particularly suitable for the treatment of disorders associated with an elevated calpain activity.

In addition, the compounds of the invention are selective calpain inhibitors, i.e. the inhibition of other cysteine proteases such as cathepsin B, cathepsin K, cathepsin L or cathepsin S takes place only at concentrations which are distinctly higher than the concentrations necessary for inhibition of calpain. Accordingly, the compounds of the invention ought to show distinctly fewer side effects than the prior art compounds which are comparatively unselective in relation to inhibition of calpain and likewise inhibit other cysteine proteases.

Compounds preferred according to the invention accordingly have a selectivity in relation to inhibition of cathepsin B, expressed in the form of the ratio of the Ki for inhibition of cathepsin B to the Ki for inhibition of calpain of ≥ 10, in particular ≥ 30.

Compounds preferred according to the invention accordingly have a selectivity in relation to inhibition of cathepsin K, expressed in the form of the ratio of the Ki for inhibition of cathepsin K to the Ki for inhibition of calpain of ≥ 10, in particular ≥ 30.

Compounds preferred according to the invention accordingly have a selectivity in relation to inhibition of cathepsin L, expressed in the form of the ratio of the Ki for inhibition of cathepsin L to the Ki for inhibition of calpain of ≥ 30, in particular ≥ 50.

Compounds preferred according to the invention accordingly have a selectivity in relation to inhibition of cathepsin S, expressed in the form of the ratio of the Ki for inhibition of cathepsin S to the Ki for inhibition of calpain of ≥ 50, in particular ≥ 100.

Owing to their inhibitory effect on calpain and their selectivity for calpain by comparison with other cysteine proteases, the compounds of the invention of the formula I, their tautomers and their pharmaceutically suitable salts are particularly suitable for the treatment of a disorder or of a condition which is associated with an elevated calpain activity as are described for example in the prior art cited at the outset.

Disorders associated with an elevated calpain activity are in particular

neurodegenerative disorders, especially those neurodegenerative disorders occuring as a result of a chronic brain supply deficit, of an ischemia (stroke) or of a trauma such as brain trauma, and the neurodegenerative disorders Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis and Huntington's disease, also multiple sclerosis and the damage to the nervous system associated therewith, especially damage to the optic nerve (optic neuritis) and the nerves which control the movement of the eye. Accordingly, preferred embodiments of the invention relate to the treatment of neurodegenerative disorders, especially of the aforementioned neurodegenerative disorders in humans, and to the use of the compounds of the invention of the formula I, their tautomers and their pharmaceutically suitable salts for the manufacture of a medicament for the treatment of these disorders.

Disorders associated with an elevated calpain activity also include epilepsy. Accordingly, preferred embodiments of the invention relate to the treatment of epilepsy in humans, and to the use of the compounds of the invention of the formula I, their tautomers and their pharmaceutically suitable salts for the manufacture of a medicament for the treatment of epilepsy.

The disorders or conditions associated with an elevated calpain activity also include pain and painful conditions. Accordingly, preferred embodiments of the invention relate to the treatment of pain and painful conditions in mammals, especially in humans, and to the use of the compounds of the invention of the formula I, their tautomers and their pharmaceutically suitable salts for the manufacture of a medicament for the treatment of pain and painful conditions.

The disorders or conditions associated with an elevated calpain activity also include damage to the heart following cardiac ischemias, damage to the kidneys following renal ischemias, skeletal muscle damage, muscular dystrophies, damage arising through proliferation of smooth muscle cells, coronary vasospasms, cerebral vasospasms, macular degeneration, cataracts of the eyes, or restenosis of blood vessels following angioplasty. Accordingly, preferred embodiments of the invention relate to the treatment of diseases or conditions associated with damage to the heart following cardiac ischemias, damage to the kidneys following renal ischemias, skeletal muscle damage, muscular dystrophies, damage arising through proliferation of smooth muscle cells, coronary vasospasms, cerebral vasospasms, macular degeneration, cataracts of the eyes, or restenosis of blood vessels following angioplasty in mammals, especially in humans, and to the use of the compounds of the invention of the formula I, their tautomers, prodrugs and their pharmaceutically suitable salts for the manufacture of a medicament for the treatment of these disorders.

It has further emerged that inhibition of calpain brings about cytotoxic effects on tumor cells. Accordingly, the compounds of the invention are suitable for the chemotherapy of

tumors and metastasis thereof. Preferred embodiments of the invention therefore relate to the use of the compounds of the invention of the formula I, their tautomers and their pharmaceutically suitable salts in the therapy of tumors and metastases, and to their use for the manufacture of a medicament for the therapy of tumors and metastases.

It has further been found that various impairments associated with an HIV disorder, especially nerve damage (HIV-induced neurotoxicity), are mediated by calpain and therefore inhibition of calpain allows such impairments to be treated or alleviated. Accordingly, the compounds of the invention of the formula I, their tautomers, their prodrugs and their pharmaceutically suitable salts are suitable for the treatment of HIV patients. Preferred embodiments of the invention therefore relate to the use of the compounds of the invention of the formula I, their tautomers and their pharmaceutically suitable salts for the treatment of HIV-infected patients, especially the treatment of those impairments caused by an HIV-induced neurotoxicity, and to their use for the manufacture of a medicament for the treatment of HIV patients.

It has further been found that the release of interleukin-I, TNF or beta-amyloid peptides (Aß or Aß-peptides) can be reduced or completely inhibited by calpain inhibitors. Accordingly, impairments or disorders associated with an elevated interleukin-I, TNF or Aß level can be treated by using the compounds of the invention of the formula I, their tautomers and their pharmaceutically suitable salts. Preferred embodiments of the invention therefore relate to the use of the compounds of the invention of the formula I, their tautomers, their produgs and their pharmaceutically acceptable salts for the treatment of impairments or disorders associated with an elevated interleukin-I, TNF or Aß level such as rheumatism, rheumatoid arthritis and to their use for the manufacture of a medicament for the treatment of such impairments or disorders.

The compounds of the general formula (I) are distinguished in particular also by a good metabolic stability. The metabolic stability of a compound can be measured for example by incubating a solution of this compound with liver microsomes from particular species (for example rat, dog or human) and determining the half-life of the compound under these conditions (RS Obach, Curr Opin Drug Discov Devel. 2001, 4, 36-44). It is possible to conclude from larger half-lives that the metabolic stability of the compound is improved. The stability in the presence of human liver microsomes is of particular interest because it makes it possible to predict the metabolic degradation of the compound in the human liver. Compounds with increased metabolic stability are therefore probably also degraded more slowly in the liver (measured in the liver microsome test). Slower metabolic degradation in the liver can lead to higher and/or longer-lasting concentrations (effective levels) of the compound in the body, so that the elimination half-life of the compounds of the invention is increased. Increased and/or longer-lasting effective levels may lead to a better efficacy of the compound in the treatment or prophylaxis of various calpain-dependent diseases. An improved

metabolic stability may additionally lead to an increased bioavailability after oral administration, because the compound is subjected, after being absorbed in the intestine, to less metabolic degradation in the liver (termed the first pass effect). An increased oral bioavailability may, because the concentration (effective level) of the compound is increased, lead to a better efficacy of the compound after oral administration.

The compounds of the invention of the formula I are further distinguished by exhibiting an improved pharmacological activity, compared with the carboxamide compounds of the formula I disclosed in the prior art, in patients or relevant animal models allowing prognostic statements for use in treatment.

The present invention also relates to pharmaceutical compositions (i.e. medicaments) which comprise at least one compound of the invention of the formula I or a tautomer or a pharmaceutically suitable salt thereof and, where appropriate, one or more suitable drug carriers.

Thes drug carriers are chosen according to the pharmaceutical form and the desired mode of administration.

The compounds of the invention of the general formula I, their tautomers and the pharmaceutically suitable salts of these compounds can be used to manufacture pharmaceutical compositions for oral, sublingual, subcutaneous, intramuscular, intravenous, topical, intratracheal, intranasal, transdermal or rectal administration, and be administered to animals or humans in unit dose forms, mixed with conventional pharmaceutical carriers, for the prophylaxis or treatment of the above impairments or diseases.

Suitable unit dose forms include forms for oral administration, such as tablets, gelatin capsules, powders, granules and solutions or suspensions for oral intake, forms for sublingual, buccal, intratracheal or intranasal administration, aerosols, implants, forms of subcutaneous, intramuscular or intravenous administration and forms of rectal administration.

The compounds of the invention can be used in creams, ointments or lotions for topical administration.

In order to achieve the desired prophylactic or therapeutic effect, the dose of the active basic ingredient may vary between 0.01 and 50 mg per kg of body weight and per day.

Each unit dose may comprise from 0.05 to 5000 mg, preferably 1 to 1000 mg, of the active ingredient in combination with a pharmaceutical carrier. This unit dose can be

administered 1 to 5 times a day, so that a daily dose of from 0.5 to 25 000 mg, preferably 1 to 5000 mg, is administered.

If a solid composition is prepared in the form of tablets, the main ingredient is mixed with a pharmaceutical carrier such as gelatin, starch, lactose, magnesium stearate, talc, silicon dioxide or the like.

The tablets may be coated with sucrose, a cellulose derivative or another suitable substance or be treated otherwise in order to display a prolonged or delayed activity and in order to release a predetermined amount of the active basic ingredient continuously.

A preparation in the form of gelatin capsules is obtained by mixing the active ingredient with an extender and taking up the resulting mixture in soft or hard gelatin capsules.

A preparation in the form of a syrup or elixir or for administration in the form of drops may comprise active ingredients together with a sweetener, which is preferably calorie-free, methylparaben or propylparaben as antiseptics, a flavoring and a suitable coloring.

The water-dispersible powders or granules may comprise the active ingredients mixed with dispersants, wetting agents or suspending agents such as polyvinylpyrrolidones, and sweeteners or taste improvers.

Rectal administration is achieved by the use of suppositories which are prepared with binders which melt at the rectal temperature, for example cocobutter or polyethylene glycols. Parenteral administration is effected by using aqueous suspensions, isotonic salt solutions or sterile and injectable solutions which comprise pharmacologically suitable dispersants and/or wetting agents, for example propylene glycol or polyethylene glycol.

The active basic ingredient may also be formulated as microcapsules or liposomes/centrosomes, if suitable with one or more carriers or additives.

In addition to the compounds of the general formula I, their tautomers or their pharmaceutically suitable salts, the compositions of the invention may comprise further active basic ingredients which may be beneficial for the treatment of the impairments or diseases indicated above.

The present invention thus further relates to pharmaceutical compositions in which a plurality of active basic ingredients are present together, where at least one thereof is a compound of the invention.

The following examples illustrate the invention without restricting it. Depending on the management of the reaction and working up, the compounds of the general formula I result as mixtures of carbonyl form and the corresponding hydrates. Conversion into the pure carbonyl compounds generally takes place by treating the substances with HCl in an inert solvent.

Preparation examples

Example 1:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-(4-phenyl-1H-imidazol-1-yl)nicotinamide

1.1 Ethyl 2-(4-phenyl-1H-imidazol-1-yl)pyridine-3-carboxylate
A mixture of 5.0 g of ethyl 2-chloronicotinate (26.94 mmol), 3.4 g of 4-phenylimidazole (23.58 mmol), 7.6 g of K_2CO_3 and 80 mg of 18-crown-6 in 18 ml of N,N-dimethylformamide was heated in a microwave at 160°C for about 1 hour. This was followed by concentrating, taking up the residue in dichloromethane, washing with water and sat. NaCl solution, drying over $MgSO_4$, filtering and evaporating. Chromatography on silica gel (eluent: CH_2Cl_2/methanol 2%-5%) resulted in 2 g of a dark oil, which was immediately reacted further; ESI-MS $[M+H]^+$ = 294.15.

1.2 2-(4-Phenyl-1H-imidazol-1-yl)pyridin-3-carboxylic acid
15 m of a 2N NaOH solution were added to a solution of 2.0 g of ethyl 2-(4-phenyl-1H-imidazol-1-yl)pyridine-3-carboxylate (6.82 mmol) in 30 ml of methanol, and the mixture was then stirred at room temperature for 2 hours. The reaction mixture was subsequently evaporated to dryness, mixed with 10 ml of H_2O and neutralized by adding 2N HCl. Filtration with suction and drying the precipitate formed resulted in 1.3 g of the acid as brown amorphous solid.
ESI-MS $[M+H]^+$ = 266.05.
^{1}H-NMR (500 MHz DMSO) δ ppm: 13.99-13.45 (s broad, 1H), 8.74 (m, 1H), 8.37 (m, 1H), 8.08 (s, 1H), 8.03 (s, 1H), 7.86 (m, 1H), 7.84 (m, 1H), 7.62 (m, 1H), 7.39 (m, 2H), 7.25 (m, 1H).

1.3 N-[3-Amino-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-2-(4-phenyl-1H-imidazol-1-yl)pyridine-3-carboxamide
0.75 g of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC), 0.51 g of hydroxylbenzotriazole (HOBt) and 0.55 ml of triethylamine (Et_3N) were successively added to a solution of 1.0 g of 2-(4-phenyl-1H-imidazol-1-yl)pyridine-3-carboxylic acid (3.77 mmol) in 50 ml of dichloromethane at 0-4°C, and the mixture was stirred at 0-4°C for 1 hour. 0.9 g of 3-amino-2-hydroxy-4-phenylbutanamide hydrochloride (3.9 mmol) and 0.55 ml of Et_3N were then added and, after about 5 minutes, a pH of 8-9 was adjusted by adding 0.5 ml of Et_3N. The mixture was stirred at 0-4°C for 1 hour and then at room

temperature overnight. 50 ml of saturated $NaHCO_3$ solution were then added to the mixture, and the organic phase was separated off. Drying and evaporating the solvent resulted in 620 mg of a reddish oil, which was reacted further immediately without further purification.

ESI-MS $[M+H]^+$ = 442.15.

1.4 N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-(4-phenyl-1H-imidazol-1-yl)nicotinamide

2.7 g of EDC and 0.5 ml of dichloroacetic acid were added to 620 mg of N-[3-amino-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-2-(4-phenyl-1H-imidazol-1-yl)pyridine-3-carboxamide (1.45 mmol) in 15 ml of dry dimethyl sulfoxide, and the mixture was stirred at room temperature for about 1 hour. To work up the reaction mixture it was mixed with 40 ml of NaCl solution and sat. $NaHCO_3$ solution (1:1), and the resulting solid was filtered off with suction, dried and stirred with methyl tert-butyl ether. The residue obtained in this way was further purified by stirring with 2N HCl and then with 10 ml of 1:1 acetonitrile/water. The remaining residue was filtered off with suction and dried. 50 mg of the target compound were obtained as a pale amorphous solid in this way.

ESI-MS $[M+H_2O+H]^+$= 458.15.

^{1}H-NMR (500 MHz DMSO) δ ppm: 9.51 (d, 1H), 8.72 (dd, 2H), 8.16 (s, 1H), 8.12 (s, 1H), 7.93 (m, 2H), 7.88 (m, 2H), 7.70 (dd, 1H), 7.85 (m, 2H), 7.38 (m, 1H), 7.27 (m, 4H), 7.19 (m, 1H), 6.54 (m, 1H), 3.24 (dd, 1H), 2.87 (dd, 1H).

Example 2:

N-{1-[Amino(oxo)acetyl]pentyl}-2-(4-phenyl-1H-imidazol-1-yl)nicotinamide

2.1 N-[1-(2-Amino-1-hydroxy-2-oxoethyl)pentyl]-2-(4-phenyl-1H-imidazol-1-yl)pyridine-3-carboxamide

Preparation took place in analogy to 1.3 using 0.23 g of 3-amino-2-hydroxyheptanamide hydrochloride (1.17 mmol). During the usual workup, the target product precipitated as a white solid from the aqueous phase. The solid was filtered off with suction and dried at 40°C in a vacuum drying oven. 219 mg of the title compound were obtained.

ESI-MS $[M+H]^+$= 408.15.

2.2 N-{1-[Amino(oxo)acetyl]pentyl}-2-(4-phenyl-1H-imidazol-1-yl)nicotinamide

200 mg of N-[1-(2-amino-1-hydroxy-2-oxoethyl)pentyl]-2-(4-phenyl-1H-imidazol-1-yl)pyridine-3-carboxamide (0.49 mmol) were oxidized in a manner analogous to Example 1.4. The crude product obtained after workup was purified by chromatography on silica gel (eluent: CH_2Cl_2/methanol 0%-7%). Evaporation of the solvent resulted in 37 mg of the title compound.

ESI-MS $[M+H]^+$= 406.15.

^{1}H-NMR (500 MHz DMSO) δ ppm: 9.15(d, 1H), 8.65 (d, 1H), 8.12 (s, 1H), 8.09 (s, 1H),

8.01 (dd, 1H), 7.95 (s, 1H), 7.84 (m, 3H), 7.56 (m, 1H), 7.39 (m, 2H), 7.24 (m, 1H), 5.16 (m, 1H), 1.77 and 1.50 (each m, H), 1.26 (m, 4H), 0.77 (m, 3H).

Example 3:
N-{1-[Amino(oxo)acetyl]pentyl}-2-(4-phenyl-1H-pyrazol-1-yl)nicotinamide

3.1 Ethyl 2-(4-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxylate
A mixture of 3.6 g of ethyl 2-chloronicotinate (19.4 mmol), 1.3 g of 4-phenylpyrazole (8.12 mmol), 4.4 g of K_2CO_3, 40 mg of 18-crown-6 and 30 mg of KI in 30 ml of N,N-dimethylformamide was stirred at 130°C for 6 hours. For workup, H_2O was added and, after extraction with ethyl acetate, the organic phase was washed with H_2O and sat. NaCl solution. The crude product obtained after drying and concentration of the solution was purified by chromatography on silica gel (eluent: CH_2Cl_2/methanol 1-10%). In total, 1.9 g of an oil were obtained, which crystallized completely on standing in a refrigerator.
ESI-MS $[M+H]^+$ = 294.15.

3.2 2-(4-Phenyl-1H-pyrazol-1-yl)pyridine-3-carboxylic acid
Hydrolysis of 1.0 g of ethyl 2-(4-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxylate (6.48 mmol) took place in analogy to 1.2. 0.8 g of the carboxylic acid was obtained as a white amorphous solid.
ESI-MS $[M+H]^+$ = 266.1
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.64 (s, 1H), 8.32 (m, 1H), 8.06 (s, 1H), 7.77 (m, 1H), 7.67 (m, 2H), 7.40 (m, 1H), 7.32 (m, 1H), 7.24 (m, 1H).

3.3 N-[1-(2-Amino-1-hydroxy-2-oxoethyl)pentyl]-2-(4-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide
Preparation took place in analogy to 1.3 using 0.19 g of 3-amino-2-hydroxyheptanamide hydrochloride (1.0 mmol). Completion of the reaction was followed by concentration, addition of H_2O and filtration of the resulting precipitate with suction and drying. Crystallization of the crude product from ethanol afforded 290 mg of the title compound as a white amorphous solid.
ESI-MS $[M+H]^+$= 408.3.

3.4 N-{1-[Amino(oxo)acetyl]pentyl}-2-(4-phenyl-1H-pyrazol-1-yl)nicotinamide
0.47 g of EDC and 0.08 ml of dichloroacetic acid were added to 100 mg of N-[1-(2-amino-1-hydroxy-2-oxoethyl)pentyl]-2-(4-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide (0.25 mmol) in 4 ml of dimethyl sulfoxide, and the mixture was stirred at room temperature overnight. For workup, the reaction mixture was poured into H_2O, and the resulting precipitate was filtered off with suction and dried in a vacuum drying oven at 40°C. 77 mg of the title compound were obtained as an amorphous white solid.
ESI-MS $[M+H]^+$= 406.2

^{1}H-NMR (500 MHz DMSO) δ ppm: 8.87 (d, 1H), 8.68 (d, 1H), 8.60 (dd, 1H), 8.16 (s, 1H), 8.02 (s, 1H), 7.87 (dd, 1H), 7.76 (m, 3H), 7.55 (dd, 1H), 7.41 (m, 2H), 7.27 (m, 1H), 5.11 (m, 1H), 1.76 (m, 1H), 1.51 (m, 1H), 1.35-1.25 (m, 4H), 0.85-0.82 (m, 3H).

Example 4:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-(4-phenyl-1H-pyrazol-1-yl)nicotinamide

4.1 N-[3-Amino-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-2-(4-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide
0.23 g of 3-amino-2-hydroxy-4-phenylbutanamide hydrochloride (1.0 mmol) was reacted with 2-(4-phenyl-1H-imidazol-1-yl)pyridine-3-carboxylic acid in analogy to Example 3.3, resulting in 280 mg of the title compound of a white amorphous solid.
ESI-MS $[M+H]^+$= 442.4.

4.2 N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-(4-phenyl-1H-pyrazol-1-yl)nicotinamide
250 mg of N-[3-amino-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-2-(4-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide (0.57 mmol) were oxidized in analogy to Example 3.4, resulting in 228 mg of the title compound as a white solid.
ESI-MS $[M+H]^+$= 440.1.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.92 (d, 1H), 8.86 (s, 1H), 8.58 (dd, 1H), 8.05 (s, 2H), 7.82 (s, 1H), 7.75 (m, 3H), 7.49 (dd, 1H), 7.43 (m, 2H), 7.30 (m, 5H), 7.20 (m, 1H), 5.39 (m, 1H), 3.18 (dd, 1H), 2.91 (dd, 1H).

Example 5:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-(3-phenyl-1H-pyrazol-1-yl)nicotinamide

5.1 Ethyl 2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxylate
Reaction of 4.3 g of 3-phenyl-1H-pyrazole (29.82 mmol) in a manner analogous to Example 3.1 and chromatography of the resulting crude product on silica gel (eluent: CH_2Cl_2) afforded 9.7 g of the title compound as a pale oil.
ESI-MS $[M+H]^+$= 294.0.

5.2 2-(3-Phenyl-1H-pyrazol-1-yl)pyridine-3-carboxylic acid
Hydrolysis took place in analogy to Example 1.2. After the reaction was complete, the reaction mixture was extracted with ethyl acetate, and the aqueous phase was acidified with 2N HCl and extracted with dichloromethane. Washing with H_2O and sat. NaCl solution, drying and evaporation afforded 5.1 g of the acid as a pale solid.
ESI-MS $[M+H]^+$= 266.0.
^{1}H-NMR (500 MHz DMSO) δ ppm: 13.2 (s broad, 1H), 8.61 (m, 1H), 8.56 (m, 1H), 8.11 (m, 1H), 7.92 (m, 2H), 7.52-7.39 (m, 2H), 7.39 (m, 1H), 7.08 (m, 1H).

5.3 N-[1-(2-Amino-1-hydroxy-2-oxoethyl)pentyl]-2-(3-phenyl-1H-pyrazol-1-yl)pyridine-

3-carboxamide
Coupling and working up in a manner analgous to Example 3.3 afforded 5.1 g of the title compound as a white solid.
ESI-MS $[M+H]^+$= 442.1.

5.4 N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-(3-phenyl-1H-pyrazol-1-yl)nicotinamide
Oxidation of 5.1 g of N-[1-(2-amino-1-hydroxy-2-oxoethyl)pentyl]-2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide (11.55 mmol) in a manner analogous to Example 3.4, and purification of the crude product by recrystallization from ethyl acetate afforded 3.5 g of the title compound as a white solid with a melting point of 190°C.
ESI-MS $[M+H]^+$= 440.0.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.93 (d, 1H), 8.56 (dd, 1H), 8.49 (dd, 1H), 8.48 (m, 1H), 8.06 (s, 1H), 7.84 (s, 1H), 7.78 (m, 2H), 7.7.73 (dd, 1H), 7.48 (dd, 1H), 7.42-7.35 (m, 3H), 7.19 (m, 5H), 7.02 (d,1H), 5.58 (m, 1H), 3.15 (dd, 1H), 2.81 (dd, 1H).

Example 6:
N-{1-[Amino(oxo)acetyl]pentyl}-2-(3-phenyl-1H-pyrazol-1-yl)nicotinamide
Preparation in analogy to Example 5 by coupling 2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxylic acid and 3-amino-2-hydroxyheptanamide hydrochloride and subsequent oxidation afforded 40 mg of the title compound as a white solid.
ESI-MS $[M+H]^+$= 406.1
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.73 (d, 1H), 8.58 (d, 1H), 8.52 (d, 1H), 8.02 (s, 1H), 7.90-7.85 (m, 3H), 7.79 (s, 1H), 7.51 (dd, 1H), 7.45 (m, 2H), 7.37 (m, 1H), 7.05 (m, 1H), 5.17 (m, 1H), 1.73 (m, 1H), 1.46 (m, 1H), 1.15 (m, 4H), 0.70 (m, 3H).

Example 7:
N-{1-[Amino(oxo)acetyl]-3-methylbutyl}-2-(4-phenyl-1H-imidazol-1-yl)nicotinamide
7.1 N-[1-(2-Amino-1-hydroxy-2-oxoethyl)-3-methylbutyl]-2-(4-phenyl-1H-imidazol-1-yl)pyridine-3-carboxamide
Coupling of 0.39 g of 3-amino-2-hydroxy-5-methylhexanamide hydrochloride (1.0 mmol) with 2-(4-phenyl-1H-imidazol-1-yl)pyridine-3-carboxylic acid in a manner analogous to Example 3.3 afforded 280 mg of the title compound as a white amorphous solid.
ESI-MS $[M+H]^+$= 442.4.

7.2 N-{1-[Amino(oxo)acetyl]-3-methylbutyl}-2-(4-phenyl-1H-imidazol-1-yl)nicotinamide
Oxidation of 200 mg of N-[3-amino-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-2-(4-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide (0.49 mmol) afforded 102 mg of the title compound as a pale solid.
ESI-MS $[M+H]^+$= 406.24.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.18 (d, 1H), 8.69 (d, 1H), 8.13 (m, 2H), 8.01 (dd,

1H), 7.95 (s, 1H), 7.85 (m, 3H), 7.61 (m, 1H), 7.41 (m, 2H), 7.27 (m, 1H), 5.25 (m, 1H), 1.65 (m, 1H), 1.53 (dd, 1H), 1.44 (dd, 1H).

The compounds of Examples 8 to 13 can be prepared in a manner analogous to the above examples.

Example 8:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[4-(4-fluorophenyl)-1H-imidazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 458.15.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.34 (m, 1H), 8.63 (m, 1H), 8.16 (s, 1H), 8.03 (s, 1H), 7.91-7.75 (m, 5H), 7.56 (m, 1H), 7.31-7.20 (m, 7H), 5.50 (m, 1H), 3.22 (m overlapped by H_2O), 2.83 (dd, 1H).

Example 9:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[4-(4-chlorophenyl)-1H-imidazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 474.15.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.38 (m, 1H), 8.64 (m, 1H), 8.16 (s, 1H), 8.05 (s, 1H), 7.94-7.91 (m, 2H), 7.83-7.81 (m, 2H), 7.76 (m, 1H), 7.56 (m, 1H), 7.45 (m, 2H), 7.31-7.21 (m, 5H), 5.45 (m, 1H), 3.23 (m overlapped by H_2O), 2.82 (dd, 1H).

Example 10:
N-{1-[Amino(oxo)acetyl]pentyl}-2-[4-(4-chlorophenyl)-1H-imidazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 440.2.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.20 (m, 1H), 8.69 (dd, 1H), 8.17 (s, 1H), 8.14 (m, 1H), 8.03 (m, 2H), 7.89 (m, 3H), 7.61 (dd, 1H), 7.48 (m, 1H), 7.46 (m, 1H), 5.18 (m, 1H), 1.78 and 1.52 (each dd, 1H), 1.26 (m, 4H), 0.79 (m, 3H).

Example 11:
N-{1-[Amino(oxo)acetyl]pentyl}-2-[4-(4-fluorophenyl)-1H-imidazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 424.2.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.17 (m, 1H), 8.68 (m, 1H), 8.13 (m, 1H), 8.11 (m, 1H), 8.03 (m, 1H), 7.97 (s, 1H), 7.91-7.86 (m, 3H), 7.60 (m, 1H), 7.24 (m 3H), 5.17 (m, 1H), 1.78 (m, 1H), 1.52 (m, 1H), 1.27 (m, 4H), 0.79 (m, 3H).

Example 12:
N-{1-[Amino(oxo)acetyl]pentyl}-2-[4-(4-methoxyphenyl)-1H-imidazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 436.25.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.19 (m, 1H), 8.66 (m, 1H), 8.11 (m, 2H), 8.01 (m, 1H), 7.85 (m, 2H), 7.71 (m, 2H), 7.58 (m, 1H), 6.99 (m, 2H), 5.19 (m, 1H), 3.79 (s, 3H), 1.79 (m, 1H), 1.52 (m, 1H), 1.29 (m, 4H), 0.80 (m, 3H).

Example 13:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[4-(4-methoxyphenyl)-1H-imidazol-1-yl]nicotinamide
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.45 (d, 1H), 8.66 (dd, 1H), 8.28 (s, 1H), 8.19 (s, 1H), 7.94 (s, 1H), 7.87 (s, 1H), 7.81 (m, 2H), 7.75 (m, 2H), 7.61 (m, 1H), 7.30-7.24 (m, 5H), 7.01 (d, 1H), 5.46 (m, 1H), 3.82 (s, 3H), 3.26 (dd, 1H), 2.85 (dd, 1H).

Example 14:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[4-(4-morpholin-4-ylphenyl)-1H-imidazol-1-yl]nicotinamide

14.1 4-[4-(1H-Imidazol-4-yl)phenyl]morpholine
3.0 g of 2-bromo-1-(4-morpholin-4-ylphenyl)ethanone and 8 ml of formamide were heated in a microwave at 180°C for about 30 minutes. The mixture was then poured into 150 ml of H_2O, the pH was adjusted to 10-12 by adding 2N NaOH solution, and the resulting solid was filtered off with suction and dried, resulting in 2.2 g of the title compound.
ESI-MS $[M+H]^+$= 230.1.

14.2 Ethyl 2-[4-(4-morpholin-4-ylphenyl)-1H-imidazol-1-yl]pyridine-3-carboxylate
Starting from 0.9 g of 4-[4-(1H-imidazol-4-yl)phenyl]morpholine (3.93 mmol) and reaction in analogy to Example 3.2 resulted in 0.6 g of the title compound as a dark oil.
ESI-MS $[M+H]^+$= 379.15.

Further reactions took place in a manner analogous to the above examples, resulting in 78 mg of N-(3-amino-1-benzyl-2,3-dioxopropyl)-2-[4-(4-morpholin-4-ylphenyl)-1H-imidazol-1-yl]nicotinamide.
ESI-MS $[M+H_2O+H+]$= 543.2.

Example 15:
N-{1-[Amino(oxo)acetyl]pentyl}-2-[4-(4-morpholin-4-ylphenyl)-1H-imidazol-1-yl]nicotinamide hydrochloride
The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H]^+$= 491.29.

Example 16:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-{4-[4-(diethylamino)phenyl]-1H-imidazol-1-yl}nicotinamide hydrochloride
16.1 N,N-Diethyl-4-(1H-imidazol-4-yl)aniline
Preparation took place in a manner analogous to Example 14.1. Chromatography on silica gel (eluent: CH_2Cl_2/methanol 2-7%) resulted in 1.1 g of the title compound as a

dark solid.
ESI-MS $[M+H]^+$= 216.15.

The title compound was prepared in a manner analogous to the above examples, resulting in 32 mg of N-(3-amino-1-benzyl-2,3-dioxopropyl)-2-{4-[4-(diethylamino)phenyl]-1H-imidazol-1-yl}nicotinamide hydrochloride.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.43 (s, 1H), 8.64 (s, 1H), 8.21 (s, 1H), 8.04 (s, 1H), 7.95 (s, 1H), 7.75 (d, 1H), 7.68-7.52 (m, 5H), 7.35-7.17 (m, 7H), 6.72 (s broad, 2H), 5.47 (m, 1H), 3.38 and 3.28 (overlapped by H_2O), 2.86 (dd, 1H), 1.14 (m, 6H).

Example 17:
N-{1-[Amino(oxo)acetyl]pentyl}-2-{4-[4-(trifluoromethyl)phenyl]-1H-imidazol-1-yl}nicotinamide hydrochloride
The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H]^+$= 474.21.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.24 (m, 1H), 8.74 (m, 1H), 8.63 (s, 1H), 8.31 (s, 1H), 8.15-8.12 (m, 4H), 7.88 (s, 1H), 7.90 (m, 2H), 7.71 (m, 1H), 6.13 (s broad), 5.17 (m, 1H), 1.78 (m, 1H), 1.52 (m, 1H), 1.25 (m, 4H), 0.77 (m, 3H).

Example 18:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-{4-[4-(trifluoromethyl)phenyl]-1H-imidazol-1-yl}nicotinamide hydrochloride
The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H]^+$= 508.26.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.46 (m, 1H), 8.69 (m, 1H), 8.37 (s, 1H), 8.20 (m, 2H), 8.07 (m, 2H), 7.95 (s, 1H), 7.86 (m, 3H), 7.65 (m, 1H), 7.28 (m, 4H), 7.21 (m, 1H), 5.47 (m, 1H), 5.27 (s broad), 3.26 and 2.86 (each dd, 1H).

Example 19:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[4-(2-chlorophenyl)-1H-imidazol-1-yl]nicotinamide hydrochloride
The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H_2O+H+]$= 492.17.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.46 (m, 1H), 8.71 (m, 2H), 8.14 (s, 2H), 8.04 (d, 1H), 7.93 (dd, 1H), 7.69 (m, 1H), 7.58 (d, 1H), 7.49 (m, 1H), 7.42 (m, 1H), 7.24 (m, 5H), 7.14 (m, 1H), 5.45 (m, 1H), 3.23 and 2.84 (each dd, 1H).

Example 20:
N-{1-[Amino(oxo)acetyl]pentyl}-2-[4-(2-chlorophenyl)-1H-imidazol-1-yl]nicotinamide hydrochloride
The title compound was prepared in a manner analogous to the above examples. The crude product was purified by chromatography on silica gel (eluent: CH_2Cl_2/methanol

1-10%) and lyophilized after addition of 1 equivalent of HCl to afford 50 mg of the title compound as a white solid.
ESI-MS $[M+H]^+$= 440.21.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.17 (d, 1H), 8.72 (m, 1H), 8.49 (s, 1H), 8.21 (s, 1H), 8.15 (m, 1H), 8.08 (m, 1H), 8.06 (m, 1H), 7.85 (s, 1H), 7.67 (dd, 1H), 7.56 (d, 1H), 7.46 (m, 1H), 7.36 (m, 1H), 5.16 (m, 1H), 4.09 (s broad), 1.75 and 1.49 (each m, 1H), 1.21 (m, 4H), 0.74 (m, 3H).

Example 21:
N-{1-[Amino(oxo)acetyl]pentyl}-2-[4-(3-chlorophenyl)-1H-imidazol-1-yl]nicotinamide
The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H]^+$= 440.21.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.16 (m, 1H), 8.69 (m, 1H), 8.14-8.03 (m, 4H), 7.91-7.82 (m, 3H), 7.62 (m 1H), 7.44 (m, 1H), 7.32 (m, 1H), 5.16 (m, 1H), 1.78 (m, 1H), 1.51 (m, 1H), 1.25 (m, 4H), 0.79 (m, 3H).

Example 22:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[4-(3-chlorophenyl)-1H-imidazol-1-yl]nicotinamide
The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H_3O]^+$= 492.14.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.40 (dd, 1H), 8.66 (m, 1H), 8.16 (s, 1H), 8.04 (m, 2H), 7.95 (s, 1H), 7.89 (s, 1H), 7.78 (m, 2H), 7.59 (m, 1H), 7.45 (m, 1H), 7.33-7.25 (m, 5H), 7.22 (m, 1H), 5.46 (m, 1H), 3.26 (dd, overlapped by H_2O), 2.84 (dd, 1H).

Example 23:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-5-chloro-2-(4-phenyl-1H-imidazol-1-yl)nicotinamide hydrochloride
5.4 g of methyl 2,5-dichloronicotinate (26.2 mmol) and 2.8 g of 4-phenylimidazole were reacted in a manner analogous to Example 3.1. Purification by chromatography resulted in 1.7 g of methyl 5-chloro-2-(4-phenyl-1H-imidazol-1-yl)pyridine-3-carboxylate as a dark oil.
ESI-MS $[M+H]^+$= 314.05.

The title compound was prepared in a manner analogous to the above examples starting from methyl 5-chloro-2-(4-phenyl-1H-imidazol-1-yl)pyridine-3-carboxylate.
110 mg of the title compound were obtained as a pale solid.
ESI-MS $[M+H_2O+H+]$= 492.11.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.54 (dd, 1H), 8.83 (s, 1H), 8.59 (s, 1H), 8.18 (s, 1H), 8.07 (s, 1H), 7.95 (m, 2H), 7.85 (m, 2H), 7.48 (m, 2H), 7.37 (m, 1H), 7.27 (m, 4H), 7.21 (m, 1H), 5.45 (m, 1H), 4.97 (s broad), 3.26 and 2.89 (each dd, 1H).

Example 24:
N-{1-[Amino(oxo)acetyl]pentyl}-5-chloro-2-(4-phenyl-1H-imidazol-1-yl)nicotinamide hydrochloride
The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H]^+$= 440.19.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.26 (m, 1H), 8.77 (m, 1H), 8.16 (m, 1H), 8.13 (m, 2H), 7.96 (s, 1H), 7.89-7.84 (m, 3H), 7.41 (m, 2H), 7.27 (m, 1H), 5.19 (m, 1H), 1.79 and 1.54 (each m, 1H), 1.28 (m, 4H), 0.80 (m, 3H).

Example 25:
N-{1-[Amino(oxo)acetyl]-3-methylbutyl}-5-chloro-2-(4-phenyl-1H-imidazol-1-yl)nicotinamide
The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H]^+$= 440.2.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.26 (m, 1H), 8.78 (m, 1H), 8.13 (m, 3H), 7.94 (s, 1H), 7.85 (m, 3H), 7.41 (m, 2H), 7.28 (m, 1H), 5.26 (m, 1H), 1.68 (m, 1H), 1.54 (m, 1H), 1.44 (m, 1H), 0.87 (m, 6H).

Example 26:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-{4-[4-(morpholin-4-ylmethyl)phenyl]-1H-imidazol-1-yl}nicotinamide hydrochloride
26.1 1-[4-(Morpholin-4-ylmethyl)phenyl]ethanone
4.7 g of 1,4-dihydro-2,6-dimethyl-3,5-pyridinecarboxylate and 1.3 g of scandium triflate were added to 2.75 g of 4-acetylbenzaldehyde (18.56 mmol), 1.7 ml of morpholine and 3 g of 4Å molecular sieves in 100 ml of tetrahydrofuran under argon, and the mixture was heated to reflux for 3 hours. The mixture was concentrated. The residue was mixed with ethyl acetate and washed with sat. $NaHCO_3$ solution and sat. NaCl solution. Drying and evaporation of the mixture resulted in a crude product which was purified by chromatography on silica gel (eluent: cyclohexane/ethyl acetate 40-80%). 1.85 g of a yellowish oil were obtained.
ESI-MS $[M+H]^+$= 220.1.

26.2 4-{[4-(1H-Imidazol-4-yl)phenyl]methyl}morpholine
0.55 ml of bromine (dissolved in 5 ml of 47% HBr) was added dropwise to 1.76 g of 1-[4-(morpholin-4-ylmethyl)phenyl]ethanone (8.03 mmol) in 15 ml of 47% HBr at 5°C, and the mixture was stirred at room temperature for about 2 hours. Water was then added to the reaction mixture, and it was neutralized by adding $NaHCO_3$ and extracted with dichloromethane. The combined organic phases were washed with saturated NaCl solution, dried and evaporated. The resulting yellowish oil (2.7 g) was mixed with 8 ml of formamide and heated in a microwave at 185°C for 30 minutes. The reaction mixture was worked up by diluting with H_2O, adjusting the pH to 11-12 by adding 2N NaOH, extracting with dichloromethane and washing the combined organic phases anew with

saturated NaCl solution. Drying of the organic phase and evaporation of the solvent was followed by treating the remaining residue with methyl tert-butyl ether, resulting in 1.3 g of the title compound as a brown oil.
ESI-MS $[M+H]^+$= 244.15.

The title compound was prepared in a manner analogous to the above examples.
115 mg of N-(3-amino-1-benzyl-2,3-dioxopropyl)-2-{4-[4-(morpholin-4-ylmethyl)phenyl]-1H-imidazol-1-yl}nicotinamide were obtained as hydrochloride.
ESI-MS $[M+H]^+$= 541.1.

Example 27:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-5-chloro-2-(3-phenyl-1H-pyrazol-1-yl)nicotinamide
The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H]^+$= 474.2.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.02 (d, 1H), 8.64 (d, 1H), 8.48 (s, 1H), 8.10 (s, 1H), 7.88 (s, 1H), 7.75 (m, 2H), 7.66 (d, 1H), 7.38 (m, 3H), 7.21 (m, 6H), 5.59 (m, 1H), 3.20 (dd, 1H), 2.83 (dd, 1H).

Example 28:
N-{1-[Amino(oxo)acetyl]pentyl}-5-chloro-2-(3-phenyl-1H-pyrazol-1-yl)nicotinamide
The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H]^+$= 440.2.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.84 (dd, 1H), 8.67 (s, 1H), 8.52 (s, 1H), 8.05 (s, 1h), 7.94 (s, 1H), 7.84 (m, 3H), 7.45 (m, 2H), 7.39 (m, 1H), 7.08 (s, 1H), 5.19 (m, 1H), 1.75 (m, 1H), 1.49 (m, 1H), 1.17 (m, 4H), 0.71 (m, 3H).

Example 29:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[3-(4-morpholin-4-ylphenyl)-1H-pyrazol-1-yl]nicotinamide hydrochloride
29.1 4-[4-(1H-Pyrazol-3-yl)phenyl]morpholine
A mixture of 2.05 g of 4-morpholinoacetophenone (10 mmol) and N,N-dimethylformamide dimethyl acetal was heated under reflux for 7 hours. The mixture was then mixed with 30 ml of methanol and, after addition of 0.57 ml of hydrazine hydrate, again heated under reflux for about 6 hours. The solid formed on cooling the mixture was filtered off with suction and thoroughly washed with methanol, resulting in 3.8 g of the title compound.
ESI-MS $[M+H]^+$= 230.1.

The title compound was prepared in a manner analogous to the above examples.
82 mg of N-(3-amino-1-benzyl-2,3-dioxopropyl)-2-[3-(4-morpholin-4-ylphenyl)-1H-pyrazol-1-yl]nicotinamide hydrochloride were obtained.

ESI-MS $[M+H]^+$= 525.3.

^{1}H-NMR (500 MHz DMSO) δ ppm: 8.93 (d, 1H), 8.54 (d, 1H), 8.45 (d, 1H), 8.08 (s, 1H), 7.86 (s, 1H), 7.70 (m, 3H), 7.46 (dd, 1H), 7.30 (m, 8H), 6.94 (d, 1H), 5.58 (m, 1H), 4.86 (s broad), 3.87 (m, 4H), 3.29 (m, 4H), 3.16 (dd, 1H), 2.81 (dd, 1H).

Example 30:

N-{1-[Amino(oxo)acetyl]-3-methylbutyl}-2-(3-phenyl-1H-pyrazol-1-yl)nicotinamide

The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H]^+$= 406.02.

^{1}H-NMR (500 MHz DMSO) δ ppm: 8.73 (d, 1H), 8.58 (dd, 1H), 8.49 (d, 1H), 8.01 (s, 1H), 7.89 (dd, 1H), 7.85 (m, 2H), 7.78 (s broad, 1H), 7.51 (dd, 1H), 7.44 (m, 2H), 7.37 (m, 1H), 7.03 (d, 1H), 5.25 (m, 1H), 1.60 (m, 1H), 1.47 (m, 1H), 1.35 (m, 1H), 0.79 and 0.76 (each d, 3H).

Example 31:

N-(3-Amino-1-benzyl-2,3-dioxopropyl)-5-chloro-2-[3-(4-morpholin-4-ylphenyl)-1H-pyrazol-1-yl]nicotinamide

The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H]^+$= 559.2.

^{1}H-NMR (500 MHz DMSO) δ ppm: 8.96 (d, 1H), 8.57 (d, 1H), 8.38 (d, 1H), 8.08 (s, 1H), 7.87 (s, 1H), 7.59 (dd, 1H), 7.18 (m, 5H), .89 (m, 3H), 5.57 (m, 1H), 3.74 (m, 4H), 3.14 (m, 5H), 2.81 (dd, 1H).

Example 32:

N-{1-[Amino(oxo)acetyl]-3-methylbutyl}-5-chloro-2-(3-phenyl-1H-pyrazol-1-yl)nicotinamide

The title compound was prepared in a manner analogous to the above examples.ESI-MS [M + H+]= 440.04.

^{1}H-NMR (500 MHz DMSO) δ ppm: 8.34 (d, 1H), 8.67 (s, 1H), 8.50 (s, 1H), 8.03 (s, 1H), 7.95 (s,1H), 7.83 (m, 3H), 7.40-7.37 (3H), 7.07 (d, 1H), 5.25 (m, 1H), 1.62 (m, 1H), 1.51 (m, 1H), 1.41 (m, 1H), 0.80 (m, 6H).

Example 33:

N-{1-[Amino(oxo)acetyl]pentyl}-2-[3-(4-morpholin-4-ylphenyl)-1H-pyrazol-1-yl]nicotinamide

The title compound was prepared in a manner analogous to the above examples.ESI-MS [M + H+]= 491.1.

^{1}H-NMR (500 MHz DMSO) δ ppm: 8.70 (d, 1H), 8.55 (d, 1H), 8.46 (d, 1H), 8.03 (s, 1H), 7.85 (d, 1H), 7.80 (s, 1H), 7.72 (m, 2H), 7.47 (dd, 1H), 7.01 (m, 2H), 6.93 (m, 1H), 5.18 (m, 1H), 3.85 (s broad, overlapped by H_2O), 3.19 (m, 4H), 1.72 (m, 1H), 1.47 (m, 1H), 1.25-1.15 (m, 4H), 0.82 (m, 3H).

Example 34:
N-{1-[Amino(oxo)acetyl]-3-methylbutyl}-2-[3-(4-morpholin-4-ylphenyl)-1H-pyrazol-1-yl]nicotinamide
The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H]^+$= 491.2.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.71 (d, 1H), 8.56 (d, 1H), 8.45 (d, 1H), 8.02 (s, 1H), 7.87 (d, 1H), 7.79 (s, 1H), 7.71 (m, 2H), 7.48 (dd, 1H), 7.02 (d, 1H), 6.92 (m, 1H), 5.28 (m, 1H), 3.78 (m broad, 4H), 3.20 (m, 4H), 1.63 (m, 1H), 1.48 (m, 1H), 1.39 (m, 1H), 0.81 (m, 6H).

Example 35:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-(3-pyridin-2-yl-1H-pyrazol-1-yl)nicotinamide
The title compound was prepared in a manner analogous to the above examples.^{1}H-NMR (500 MHz DMSO) δ ppm: 8.97 (d, 1H), 8.60 (m, 2H), 8.49 (m, 2H), 8.08 (s, 1H), 7.85 (s, 1H), 7.80-7.69 (m, 3H), 7.51 (m, 1H), 7.35 (m, 1H), 7.19-7.13 (m, 5H), 7.04 (m, 1H), 5.55 (m, 1H), 3.15 (m, 1H), 2.79 (m, 1H).

Example 36:
N-{1-[Amino(oxo)acetyl]pentyl}-2-(3-pyridin-2-yl-1H-pyrazol-1-yl)nicotinamide
The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H]^+$= 407.2.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.73 (d, 1H), 8.62 (m, 2H), 8.53 (d, 1H), 8.03 (s, 1H), 7.90 (m, 3H), 7.79 (s, 1H), 7.54 (dd, 1H), 7.38 (m, 1H), 7.08 (d, 1H), 5.18 (m, 1H), 1.71 (m, 1H), 1.44 (m, 1H), 1.11 (m, 4H), 0.67 (m, 3H).

Example 37:
N-{1-[Amino(oxo)acetyl]pentyl}-2-[3-(4-chlorophenyl)-1H-pyrazol-1-yl]nicotinamide
The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H]^+$= 440.05.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.71 (d, 1H), 8.59 (d, 1H), 8.52 (s broad, 1H), 8.04 (s, 1H), 7.98-7.88 (m, 3H), 7.81 (s, 1H), 7.51 (m, 3H), 7.08 (m, 1H), 5.17 (m, 1H), 1.70 (m, 1H), 1.44 (m, 1H), 1.12 (m, 4H), 0.69 (m, 3H).

Example 38:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[3-(4-fluorophenyl)-1H-pyrazol-1-yl]nicotinamide
The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H]^+$= 458.1.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.93 (d, 1H), 8.55 (dd, 1H), 8.47 (d, 1H), 8.09 (s, 1H), 7.87 (s, 1H), 7.78 (m, 2H), 7.71 (m, 1H), 7.48 (dd, 1H), 7.20-7.16 (m, 7H), 7.0 (m, 1H), 5.58 (m, 1H), 3.15 (m, 1H), 2.79 (m, 1H).

Example 39:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[3-(4-chlorophenyl)-1H-pyrazol-1-yl]nicotinamide
The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H]^+$= 474.05.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.94 (dd, 1H), 8.57 (dd, 1H), 8.48 (d, 1H), 8.10 (s, 1H), 7.88 (s, 1H), 7.77 (m, 2H), 7.72 (dd, 1H), 7.48 (dd, 1H), 7.44 (m, 2H), 7.19 (m, 5H), 7.04 (m, 1H), 5.56 (m, 1H), 3.15 and 2.78 (each dd, 1H).

Example 40:
N-[3-Amino-2,3-dioxo-1-(2-thienylmethyl)propyl]-2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide
40.1 Phenylmethyl [2-hydroxy-1-(2-thienylmethyl)ethyl]carbamate
24.8 g of 3-(2-thienyl)alanine (144.8 mmol) were added in portions to 11.0 g of $LiAlH_4$ in 550 ml of tetrahydrofuran, heated to reflux. The mixture was then heated under reflux for 8 hours and subsequently stirred at room temperature overnight. 17.6 ml of 10% NaOH solution were added and then 22 ml of H_2O were slowly added dropwise, and the mixture was stirred for 5 minutes. Then, first 391 ml of 10% NaOH solution and subsequently, at -5°C, 22.2 g of benzyl chloroformate (130.32 mmol) were added, and the mixture was stirred at room temperature for 3 hours. For workup, the mixture was extracted with dichloromethane, the organic phase was dried, the solvent was evaporated and the remaining residue was filtered through silica gel (eluent: CH_2Cl_2/methanol 2.5%). 36.8 g of the title compound were obtained as a yellowish oil. ESI-MS $[M+H]^+$= 292.

40.2 Phenylmethyl [3-amino-2-hydroxy-3-oxo-1-(2-thienylmethyl)propyl]carbamate
40.2 g of pyridine-SO_3 complex were added in portions to a mixture of 36.8 g of phenylmethyl [2-hydroxy-1-(2-thienylmethyl)ethyl]carbamate (126.3 mmol) and 51.2 g of triethylamine in 220 ml of dimethyl sulfoxide at about 16°C, and the mixture was stirred at room temperature for 3 hours. It was then poured into ice-water (1.5 l) and extracted with ethyl acetate, and the organic phase was washed with 1N HCl and sat. NaCl solution, dried and evaporated. The resulting oil (38 g) was dissolved in 150 ml of tetrahydrofuran, and a solution of 44.4 g of NaCN in 225 ml of saturated $NaHCO_3$ solution was added dropwise. After 2 hours, the phases were separated, the aqueous phase was extracted with ethyl acetate, and the combined organic phases were washed with H_2O and saturated NaCl solution, dried and concentrated. The residue obtained in this way was again dissolved in 400 ml of tetrahydrofuran and, over the course of 30 minutes, 65 ml of conc. HCl and 150 ml of conc. H_2SO_4 were added dropwise in parallel while cooling in ice, and the mixture was stirred at room temperature. After the reaction was complete, the reaction mixture was poured into ice-water and extracted with ethyl acetate, and the organic phase was washed with 1N NaOH and sat. NaCl solution, dried and concentrated. The remaining oily residue was

stirred with diethyl ether, and the resulting solid was filtered off with suction and dried, resulting in 16.3 g of the title compound as a whitish gray amorphous solid.
ESI-MS $[M+H]^+$= 335.

40.3 3-Amino-2-hydroxy-4-(2-thienyl)butanamide
70 ml of 30% HBr in glacial acetic acid were added to 11 g of phenylmethyl [3-amino-2-hydroxy-3-oxo-1-(2-thienylmethyl)propyl]carbamate (29.66 mmol) in 30 ml of glacial acetic acid. After about 2 hours, the mixture was concentrated and the resulting residue was stirred firstly with cyclohexane and then with dichloromethane. 7.8 g of the title compound were obtained as hydrobromide.
ESI-MS $[M+H]^+$= 201.

The title compound was prepared in a manner analogous to the above examples, resulting in 25 mg of N-[3-amino-2,3-dioxo-1-(2-thienylmethyl)propyl]-2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide as a white solid.
ESI-MS $[M+H]^+$= 446.05.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.01 (d, 1H), 8.59 (m, 1H), 8.50 (m, 1H), 8.05 (s, 1H), 7.84-7.78 (m, 4H), 7.50 (m, 1H), 7.41 (m, 2H), 7.36-7.31 (m, 2H), 7.02 (m, 1H), 6.84 (m, 2H), 5.52 (m, 1H), 3.38 and 3.12 (each dd, 1H).

Example 41:
N-{1-[Amino(oxo)acetyl]pentyl}-2-[3-(4-fluorophenyl)-1H-pyrazol-1-yl]nicotinamide
The title compound was prepared in a manner analogous to the above examples.
ESI-MS $[M+H]^+$= 424.05.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.71 (d, 1H), 8.57 (d, 1H), 8.51 (m, 1H), 8.03 (s, 1H), 7.89 (m, 2H), 7.80 (s, 1H), 7.51 (m, 1H), 7.28 (m, 1H), 7.04 (s, 1H), 5.17 (m, 1H), 1.70 (m, 1H), 1.44 (m, 1H), 1.13 (m, 4H), 0.70 (m, 3H).

Example 42:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-{3-[4-(diethylamino)phenyl]-1H-pyrazol-1-yl}nicotinamide
The title compound was prepared in a manner analogous to the above examples.ESI-MS $[M+H]^+$= 511.3.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.91 (d, 1H), 8.52 (d, 1H), 8.41 (d, 1H), 8.07 (s, 1H), 7.82 (s, 1H), 7.71 (d, 1H), 7.56 (m, 2H), 7.42 (dd, 1H), 7.21 (m, 5H), 6.82 (d, 1H), 6.66 and 6.63 (each s, 1H), 5.57 (m, 1H), 3.39 (m, 4H), 3.17 and 2.84 (each dd, 1H), 1.15 (m, 6H).

Example 43:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-(3-{4-[(diethylamino)methyl]phenyl}-1H-pyrazol-1-yl)nicotinamide hydrochloride

43.1 1-{4-[(Diethylamino)methyl]phenyl}ethanone
5.3 g of diethylamine were added to 10 g of 4-[chloromethyl]benzonitrile (65.96 mmol), 18.24 g of K_2CO_3 and 1.1 g of KI in 150 ml of N,N-dimethylformamide at room temperature, and the mixture was stirred at room temperature until the reaction was complete. The mixture was then poured into ice-water and extracted with diethyl ether, and the organic phase was washed with saturated NaCl solution, dried and evaporated, resulting in 12.1 g of 4-[diethylaminomethyl]benzonitrile as an oil.
ESI-MS $[M+H]^+$= 189.05.

A solution of 12.1 g of 4-[diethylaminomethyl]benzonitrile in 40 ml of toluene was added to a solution of methylmagnesium bromide (43 ml of a 3 M solution in diethyl ether) in 40 ml of toluene, and the mixture was heated to reflux. Completion of the reaction was followed by pouring into ice-water, extracting with methyl tert-butyl ether, adjusting the aqueous phase to pH 11-12 by adding NaOH, and renewed extracting with methyl tert-butyl ether. The organic phase was dried and the solvent was evaporated. 12.1 g of the title compound were obtained.
ESI-MS $[M+H]^+$= 206.15.

It was possible in a manner analogous to the above examples to prepare N-(3-amino-1-benzyl-2,3-dioxopropyl)-2-(3-{4-[(diethylamino)methyl]phenyl}-1H-pyrazol-1-yl)nicotinamide hydrochloride.
ESI-MS $[M+H]^+$= 525.35.
^{1}H-NMR (500 MHz DMSO) δ ppm: 10.02 (s broad, 1H), 8.95 (d, 1H), 8.51 (d, 1H), 8.05 (s, 1H), 7.86-7.81 (m, 3H), 7.76 (m, 1H), 7.61 (m, 2H), 7.52 (m, 1H), 7.19-7.12 (m, 5H), 7.07 8m, 1H), 5.53 (m, 1H), 4.35 (d, 2H), 3.10 (m, 5H), 2.80 (dd, 1H), 1.29 (m, 6H).

It was possible to prepare the compounds of Examples 44 to 105 in a manner analogous to the above examples.

Example 44:
N-{1-[Amino(oxo)acetyl]pentyl}-2-(3-{4-[(diethylamino)methyl]phenyl}-1H-pyrazol-1-yl)nicotinamide
ESI-MS $[M+H]^+$= 491.35.

Example 45:
N-{1-[Amino(oxo)acetyl]pentyl}-2-{3-[4-(morpholin-4-ylmethyl)phenyl]-1H-pyrazol-1-yl}nicotinamide
ESI-MS $[M+H]^+$= 505.15.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.72 (d, 1H), 8.58 (d, 1H), 8.51 (m, 1H), 8.02 (s, 1H), 7.88 (d, 1H), 7.82-7.78 (m, 3H), 7.50 (dd, 1H), 7.38-7.36 (m, 2H), 7.02 (m, 1H), 5.16 (m, 1H), 3.61 (m, 4H), 3.52 (m, 2H), 2.40 (m, 4H), 1.71 and 1.43 (each m, 1H), 1.26-1.11 (m, 4H), 0.69 (m, 1H).

Example 46:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-{3-[4-(morpholin-4-ylmethyl)phenyl]-1H-pyrazol-1-yl}nicotinamide
ESI-MS $[M+H]^+$= 539.35
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.92 (d, 1H), 8.56 (dd, 1H), 8.47 (d, 1H), 8.05 (s, 1H), 7.83 (s, 1H), 7.73 (m, 3H), 7.47 (dd, 1H), 7.33 (s, 1H), 7.31 (s, 1H), 7.17 (m, 5H), 6.98 (d, 1H), 5.56 (m, 1H), 3.61 (m, 4H), 3.51 (s, 2H), 3.12 (m, 1H), 2.82 (m, 1H), 2.39 (m, 4H).

Example 47:
N-{1-[Amino(oxo)acetyl]pentyl}-2-{3-[4-(diethylamino)phenyl]-1H-pyrazol-1-yl}nicotinamide
ESI-MS $[M+H]^+$= 477.15
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.71 (d, 1H), 8.54 (d, 1H), 8.44 (m, 1H), 8.03 (s, 1H), 7.84 (d, 1H), 7.78 (s, 1H), 7.63 (m, 1H), 7.44 (m, 1H), 6.84 (s, 1H), 6.69 (m, 2H), 5.18 (m, 1H), 3.40 (m, 4H), 1.74 and 1.50 (each m, 1H), 1.30-1.12 (m, 10H), 0.75 (m, 3H).

Example 48:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[3-(4-methoxyphenyl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 470.45.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.92 (d, 1H), 8.54 (dd, 1H), 8.44 (d, 1H), 8.08 (s, 1H), 7.86 (s, 1H), 7.72-7.68 (m, 3H), 7.45 (dd, 1H), 7.21 (m, 5H), 6.96 (s, 1H), 6.93 (m, 2H), 5.59 (m, 1H), 3.82 (s, 3H), 3.16 and 2.81 (each dd, 1H).

Example 49:
N-{1-[Amino(oxo)acetyl]pentyl}-2-[3-(4-methoxyphenyl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 436.45.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.72 (d, 1H), 8.56 (d, 1H), 8.47 (d, 1H), 8.03 (s, 1H), 7.87 (dd, 1H), 7.79-7.70 (m, 3H), 7.49 (m, 1H), 7.01 (s, 1H), 6.99 (s, 1H), 6.96 (dd, 1H), 5.18 (m, 1H), 3.83 (s, 3H), 1.73 and 1.47 (each m, 1H), 1.17 (m, 4H), 0.72 (m, 3H).

Example 50:
N-[3-Amino-1-(4-chlorobenzyl)-2,3-dioxopropyl]-2-(3-phenyl-1H-pyrazol-1-yl)nicotinamide
ESI-MS $[M+H]^+$= 474.13.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.57 (dd, 1H), 8.48 (d, 1H), 8.07 (s, 1H), 7.86 (s, 1H), 7.78 (dd, 1H), 7.74 (m, 2H), 7.49 (dd, 1H), 7.41-7.30 (m, 3H), 7.18 (m, 4H), 7.0 (m, 1H), 5.50 (m, 1H), 3.12 and 2.77 (each m, 1H).

3-Amino-4-(4-chlorophenyl)-2-hydroxybutanamide was prepared in a manner analogous to the preparation of 3-amino-2-hydroxy-4-(2-thienyl)butanamide in Example 40.

Example 51:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-5-fluoro-2-(3-phenyl-1H-pyrazol-1-yl)nicotinamide
ESI-MS $[M+H]^+$= 458.6.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.01 (d, 1H), 8.62 (d, 1H), 8.42 (d, 1H), 8.08 (s, 1H), 7.87 (s, 1H), 7.77 (s, 1H), 7.75 (s, 1H), 7.58 (dd, 1H), 7.42-7.32 (m, 3H), 7.23-7.17 (m, 5H), 7.02 (d, 1H), 5.58 (m, 1H), 3.17 and 2.83 (each dd, 1H).

Example 52:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-{3-[3-(morpholin-4-ylmethyl)phenyl]-1H-pyrazol-1-yl}nicotinamide hydrochloride
ESI-MS $[M+H]^+$= 539.35.
^{1}H-NMR (500 MHz DMSO) δ ppm: 10.89 (s, broad, 1H), 8.96 (d, 1H), 8.58 (m, 1H), 8.49 (d, 1H), 8.08 (s, 2H), 7.84 (m, 2H), 7.76 (dd, 1H), 7.58 (m, 1H), 7.52-7.48 (m, 2H), 7.15 (5H), 7.03 (d, 1H), 5.52 (m, 1H), 4.38 (s broad, 2H), 3.95 and 3.77 (each m, 2H), 3.26 (dd, 1H), 3.10 (m, 4H), 2.80 (dd, 1H).

Example 53:
N-{1-[Amino(oxo)acetyl]pentyl}-2-{3-[3-(morpholin-4-ylmethyl)phenyl]-1H-pyrazol-1-yl}nicotinamide hydrochloride
ESI-MS $[M+H]^+$= 505.35.
^{1}H-NMR (500 MHz DMSO) δ ppm: 11.03 (s broad, 1H), 8.72 (d, 1H), 8.60 (dd, 1H), 8.54 (d, 1H), 8.13 (s, 1H), 8.05 (s, 1H), 7.95-7.89 (m, 2H), 7.81 (m, 1H), 7.62 (m, 1H), 7.54 (m, 2H), 7.06 (d, 1H), 5.16 (m, 1H), 4.43 (s, 2H), 3.96 and 3.81 (each m, 2H), 3.3 (m, overlapped by H_2O), 3.15 (m, 2H), 1.67 and 1.43 (each m, 1H), 1.14 (m, 4H), 0.68 (m, 3H).

Example 54:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[3-(2-chlorophenyl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 474.06.
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.94 (d, 1H), 8.57 (d, 1H), 8.50 (d, 1H), 7.98 (s, 1H), 7.80 (s, 1H), 7.70 (dd, 2H), 7.47-7.54 (m, 2H), 7.30-7.37 (m, 2H), 7.13 (s, 5H), 7.02 (s, 1H), 5.48-5.53 (m, 1H), 3.11 (dd, 1H), 2.77 (dd, 1H).

Example 55:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[3-(2-thienyl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 446.0.

^{1}H-NMR (400 MHz DMSO) δ ppm: 8.94 (d, 0.5H), 8.58 (s, 1H), 8.43 (s, 1H), 8.04 (s, 0.5H), 7.75-7.86 (m, 2H), 7.46-7.52 (m, 3H), 7.22-7.264 (m, 5H), 7.12 (s, 1H), 6.89 (s, 0.5H), 6.70 (s, 0.5H), 6.39 (s, 0.5H), 6.11 (s, 0.5H) 5.50-5.56 (m, 0.5H), 4.46-4.52 (m, 0.5H), 3.18 (dd, 0.5H), 3.06 (dd, 0.5H), 2.85-2.92 (m, 0.5H), 2.71-2.77 (m, 0.5H).
The compound is in the form of a mixture of carbonyl and hydrate forms.

Example 56:
N-{1-[Amino(oxo)acetyl]pentyl}-2-(3-pyridin-4-yl-1H-pyrazol-1-yl)nicotinamide
ESI-MS $[M+H]^+$ = 407.15.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.75 (d, 1H), 8.65-8.58 (m, 3H), 8.03 (s, 1H), 7.93 (m, 1H), 7.80 (m, 3H), 7.56 (dd, 1H), 7.22 (d, 1H), 5.17 (m, 1H), 1.71 and 1.43 (each m, 1H), 1.12 (m, 4H), 0.69 (m, 3H).

Example 57:
N-[3-Amino-2,3-dioxo-1-(2-thienylmethyl)propyl]-2-[3-(4-fluorophenyl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 464.45.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.75 (d, 1H), 8.65-8.58 (m, 3H), 8.03 (s, 1H), 7.93 (m, 1H), 7.80 (m, 3H), 7.56 (dd, 1H), 7.22 (d, 1H), 5.17 (m, 1H), 1.71 and 1.43 (each m, 1H), 1.12 (m, 4H), 0.69 (m, 3H).

Example 58:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[3-(3-morpholin-4-ylphenyl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 525.25.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.90 (d, 1H), 8.56 (dd, 1H), 8.47 (d, 1H), 8.02 (s, 1H), 7.81 (s, 1H), 7.75 (dd, 1H), 7.48 (m, 2H), 7.29 (m, 2H), 7.12 (m, 5H), 7.03 (d, 1H), 6.99 (m, 1H), 5.50 (m, 1H), 3.80 (m, 4H), 3.21 (m, 4H), 3.13 and 2.80 (each dd, 1H).

Example 59:
N-{1-[Amino(oxo)acetyl]pentyl}-2-[3-(3-morpholin-4-ylphenyl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 491.25.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.68 (d, 1H), 5.57 (d, 1H), 8.51 (m, 1H), 8.00 (s, 1H), 7.86 (m, 1H), 7.78 (d, 1H), 7.50 (m, 1H), 7.44 (s, 1H), 7.31 (m, 2H), 7.04 (m, 1H), 6.95 (d, 1H), 5.14 (m, 1H), 3.81 (m, 4H), 3.20 (m, 4H), 1.67 (m, 1H), 1.45 (m, 1H), 1.14 (m, 4H), 0.67 (m, 3H).

Example 60:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-{3-[4-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl}nicotinamide
ESI-MS $[M+H]^+$= 508.0.

^{1}H-NMR (400 MHz DMSO) δ ppm: 8.95 (d, 1H), 8.57 (d, 1H), 8.51 (d,1H), 8.10 (s, 1H), 7.94 (d, 2H), 7.86 (s, 1H), 7.74 (d, 1H), 7.71 (d, 2H), 7.50 (dd, 1H), 7.14-7.16 (m, 4H), 7.11-7.13 (m, 2H), 5.51-5.56 (m, 1H), 3.11 (dd, 1H), 2.75 (dd, 1H).

Example 61:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-(5-methyl-3-phenyl-1H-pyrazol-1-yl)nicotinamide
ESI-MS $[M+H]^+$= 454.1
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.83 (d, 1H), 8.58 (d, 1H), 7.96 (s, 1H), 7.85 (d, 1H), 7.74 (s, 1H), 7.66 (d, 2H), 7.50-7.54 (m, 1H), 7.34 (dd, 2H), 7.27 (dd, 1H), 7.10-7.17 (m, 3H), 7.06 (d, 2H), 6.64 (s, 1H), 5.26-5.31 (m, 1H), 3.02 (dd, 1H), 2.67 (dd, 1H), 2.49 (s, 3H).

Example 62:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[3-(4-cyanophenyl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 465.1.
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.96 (d, 1H), 8.57 (s, 1H), 8.51 (s,1H), 8.09 (s, 1H), 7.82-7.92 (m, 5H), 7.72 (d, 1H), 7.50 (dd, 1H), 7.17 (s, 5H), 7.14 (s, 1H), 5.51-5.56 (m, 1H), 3.12 (dd, 1H), 2.74 (dd, 1H)

Example 63:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-(4,5-dihydro-2H-benzo[g]indazol-2-yl)nicotinamide
ESI-MS $[M+H]^+$= 466.09
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.94 (d, 1H), 8.51(d, 1H), 8.23 (s,1H), 8.05 (s,1H), 7.83 (s, 1H), 7.70 (d, 1H), 7.48 (d, 1H), 7.41 (dd, 1H), 7.28 (dd, 1H), 7.13-7.24 (m, 7H), 5.50-5.55 (m, 1H), 3.16 (dd, 1H), 2,90(t, 2H), 2.80 (dd, 1H), 2.73-2.79 (m, 2H).

Example 64:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[3-(4-piperidin-1-ylphenyl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 523.18.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.91 (d, 1H), 8.53 (d, 1H), 8.42 (s, 1H), 8.08 (s, 1H), 7.85 (s, 1H), 7.70 (d, 1H), 7.60 (m, 2H), 7.43 (m, 1H), 7.20 (m, 5H), 6.91 (m, 3H), 5.58 (m, 1H), 3.23 (m, 4H), 3.15 (m overlapped, 1H), 1.66-1.60 (m, 6H).

Example 65:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-(3-pyridin-4-yl-1H-pyrazol-1-yl)nicotinamide
ESI-MS $[M+H]^+$= 441.16.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.98 (m, 1H), 8.62-8.53 (m, 4H), 8.09 (s, 1H), 7.87 (m, 1H), 7.75 (m, 1H), 7.67 (m, 2H), 7.54 (m, 1H), 7.18 (m, 6H), 5.56 (m, 1H), 3.15 and

2.78 (each m, 1H).

Example 66:
N-[3-Amino-1-(cyclohexylmethyl)-2,3-dioxopropyl]-2-(3-phenyl-1H-pyrazol-1-yl)nicotinamide
ESI-MS $[M+H]^+$= 446.15.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.77 (d, 1H), 8.59 (m, 1H), 8.51 (d, 1H), 7.96 (s, 1H), 7.87 (m, 3H), 7.76 (s, 1H), 7.51 (dd, 1H), 7.43 (m, 2H), 7.37 (m, 1H), 7.05 (m, 1H), 5.22 (m, 1H), 1.65 (m, 1H), 1.54-1.24 (m, 7H), 1.01 (m, 2H), 0.89-0.68 (m, 3H).

Example 67:
N-[3-Amino-1-(4-chlorobenzyl)-2,3-dioxopropyl]-2-[3-(4-fluorophenyl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 492.09.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.91 (d, 1H), 8.57 (d, 1H), 8.48 (s, 1H), 8.09 (s, 1H), 7.88 (s, 1H), 7.74 (m, 3H), 7.50 (m, 1H), 7.19 (m, 6H), 6.98 (m, 1H), 5.48 (m, 1H), 3.12 (m, 1H), 2.75 (m, 1H).

Example 68:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-{3-[4-(4-methylpiperazin-1-yl)phenyl]-1H-pyrazol-1-yl}nicotinamide
ESI-MS $[M+H]^+$= 538.24.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.91 (d, 1H), 8.54 (m, 1H), 8.42 (m, 1H), 8.08 (s, 1H), 7.86 (s, 1H), 7.69 (dd, 1H), 7.61 (m, 2H), 7.44 (m, 1H), 7.20 (m, 5H), 6.92 (m, 3H), 5.58 (m, 1H), 3.20 (m, 5H), 2.81 (m, 1H), 2.49 (m overlapped by DMSO), 2.26 (s, 3H).

Example 69:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[3-(4-pyrrolidin-1-ylphenyl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 509.25.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.91 (d, 1H), 8.51 (m, 1H), 8.40 (d, 1H), 8.07 (s, 1H), 7.84 8s, 1H), 7.69 (m, 1H), 7.58 (m, 2H), 7.41 (m, 1H), 7.22 (m, 5H), 6.83 (m, 1H), 6.54 (m, 2H), 5.59 (m, 1H), 3.29 (m overlapped by H_2O), 3.10 and 2.83 (each dd, 1H), 2.01 (m, 4H).

Example 70:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[3-(3-chlorophenyl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 474.05.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.91 (d, 1H), 8.58 (d, 1H), 8.50 (d, 1H), 8.01 (s, 1H), 7.84 (s, 1H), 7.81 (s, 1H), 7.73 (m, 2H), 7.49 (dd, 1H), 7.41 (m, 2H), 7.16 (m, 5H), 7.09 (m, 1H), 5.51 (m, 1H), 3.15 and 2.80 (each dd, 1H).

Example 71:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[3-(2-chloro-4-fluorophenyl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 492.05
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.93 (d, 1H), 8.58 (d, 1H), 8.52 (d, 1H), 8.06 (s, 1H), 7.84 (s, 1H), 7.74 (d, 1H), 7.67 (dd, 1H), 7.51 (m, 2H), 7.19 (dd, 1H), 7.15 (m, 5H), 7.01 (d, 1H), 5.51 (m, 1H), 3.12 (dd, 1H), 2.78 (dd, 1H).

Example 72:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-{3-[2-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl}nicotinamide
ESI-MS $[M+H]^+$= 508.06.
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.94 (d, 1H), 8.57 (d, 1H), 8.50 (d,1H), 7.98 (s, 1H), 7.75-7.83 (m, 3H), 7.46-7.74 (m, 4H), 7.09 (s, 5H), 6.67 (s, 1H), 5.40-5.45 (m, 1H), 3.08 (dd, 1H), 2.74-2.80 (dd, 1H).

Example 73:
N-[1-Benzyl-3-(ethylamino)-2,3-dioxopropyl]-2-(3-phenyl-1H-pyrazol-1-yl)nicotinamide
ESI-MS $[M+H]^+$= 468.10
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.92 (d, 1H), 8.70 (t, 1H), 8.54 (dd,1H), 8.47 (d, 1H), 7.75 (d, 2H), 7.71 (d, 1H), 7.76 (dd, 1H), 7.31-7.39 (m, 3H), 7.13-7.21 (m, 5H), 6.99(d, 1H), 5.56-5.61 (m, 1H), 3.10-3.20 (m, 3H), 2.76-2.81 (dd, 1H), 1.05 (t, 3H).

Example 74:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[3-(3-pyrrolidin-1-ylphenyl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 509.15.

Example 75:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[3-(2,3-dihydrobenzo[b]furan-5-yl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 482.1.
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.87 (d, 1H), 8.52 (d, 1H), 8.44 (d,1H), 8.01 (s, 1H), 7.81 (s, 1H), 7.65 (s, 1H), 7.51 (d, 1H), 7.41 (dd, 1H), 7.15-7.21 (m, 6H), 6.88 (d, 1H), 6.75 (d, 1H), 5.56-5.62 (m, 1H), 4.55 (t, 2H), 3.11-3.20 (m, 3H), 2.81 (dd, 1H).

Example 76:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[3-(2-fluorophenyl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 458.07.
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.91 (d, 1H), 8.57 (d,1H), 8.50 (d, 1H), 8.04 (s,

1H), 7.82 (s, 1H), 7.78 (d, 1H), 7.74 (d,1H), 7.49 (dd, 1H), 7.39 (dd, 1H), 7.39 (dd, 1H), 7.19 (dd, 1H), 7.15 (s, 5H), 6.85 (dd, 1H), 5.50-5.56 (m, 1H), 3.12 (dd, 1H), 2.76 (dd, 1H)

Example 77:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-(1H-indazol-1-yl)nicotinamide

77.1 Ethyl 2-(1H-indazol-1-yl)pyridine-3-carboxylate and ethyl 2-(2H-indazol-2-yl)pyridine-3-carboxylate

Reaction of 4.7 g of ethyl 2-chloronicotinate (25.39 mmol) with 2.5 g of indazole (21.16 mmol) afforded a mixture of the isomers which were separated by chromatography on silica gel (eluent: cyclohexane/ethyl acetate 5-40%).
Fraction 1: ethyl 2-(1H-indazol-1-yl)pyridine-3-carboxylate about 80%, contaminated with fraction 2.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.74 (d, 1H), 8.41 (s, 1H), 8.36 (d, 1H), 8.23 (d, 1H), 8.18 (d, 1H), 7.61 (m, 2H), 7.36 (m, 1H), 4.23 (q, 2H), 1.12 (t, 3H).

Fraction 2: ethyl 2-(2H-indazol-2-yl)pyridine-3-carboxylate
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.11 (s, 1H), 8.75 (d, 1h9, 8.24 (d, 1H), 7.83 (d, 1H), 7.67 (m, 2H), 7.36 (m, 1h), 7.15 (m, 1H), 4.26 (q, 2H), 1.05 (t, 3H).

N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-(1H-indazol-1-yl)nicotinamide:
ESI-MS $[M+H]^+$= 414.05.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.93 (d, 1H), 8.64 (dd, 1H), 8.30 (dd, 1H), 8.13 (s, 1H), 8.05 (s, 1H), 7.86 (m, 1H), 7.80 (m, 2H), 7.53 (m, 1H), 7.48 (m, 1H), 7.34 (m, 1H), 7.26 (m, 5H), 5.36 (m, 1H), 3.15 and 2.19 (each dd, 1H).

Example 78:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-(2H-indazol-2-yl)nicotinamide
ESI-MS [M + H+]= 414.05.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.07 (d, 1H), 8.98 (s, 1H), 8.67 (m, 1H), 8.05 (s, 1H), 7.86-7.79 (m, 3H), 7.62 (m, 1H), 7.52 (d, 1H), 7.32-7.19 (m, 6H), 7.12 (m, 1H), 5.41 (m 1H), 3.18 and 2.92 (each dd, 1H).

Example 79:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-[3-(2,4-dichlorophenyl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 508.03
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.93 (d, 1H), 8.57 (d, 1H), 8.51 (d, 1H), 8.06 (s, 1H), 7.84 (s, 1H), 7.74 (d, 1H), 7.68 (s, 1H), 7.65 (d, 1H), 7.49 (dd, 1H), 7.36 (d, 1H), 7.13 (s, 5H), 7.03 (s, 1H), 5.46-5.51 (m, 1H), 3.09 (dd, 1H), 2.75 (dd, 1H).

Example 80:
N-[3-Amino-1-(4-methoxybenzyl)-2,3-dioxopropyl]-2-(3-phenyl-1H-pyrazol-1-yl)nicotinamide
ESI-MS $[M+H]^+$= 470.25.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.89 (m, 1H), 8.50 (m, 2H), 8.49 (s, 1H), 8.04 (s, 1H), 7.80-7.58 (m, 4H), 7.49 (m, 1H), 7.40-7.37 (m, 3H), 7.09 (m, 2H), 7.01 (m, 1H), 6.75 (m, 1H), 5.52 (m, 1H), 3.69 (s, 3H), 3.06 and 2.76 (each dd, 1H).

Example 81:
N-[3-Amino-1-(4-methoxybenzyl)-2,3-dioxopropyl]-2-[3-(4-fluorophenyl)-1H-pyrazol-1-yl]nicotinamide
ESI-MS $[M+H]^+$= 488.25.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.89 (dd, 1H), 8.56 (dd, 1H), 8.47 (s, 1H), 8.07 (s, 1H), 7.86 (s, 1H), 7.76 (m, 3H), 7.48 (dd, 1H), 7.21 (m, 2H), 7.10 (m, 2H), 7.0 (m, 1H), 6.75 (m, 2H), 5.51 (m, 1H), 3.70 (s, 3H), 3.07 and 2.73 (each dd, 1H).

Example 82:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-5-cyano-2-(3-phenyl-1H-pyrazol-1-yl)nicotinamide
ESI-MS $[M+H]^+$= 465.3.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.03 (s, 1H), 8.99 (d, 1H), 8.63 (s, 1H), 8.09 (s, 1H), 8.05 (s, 1H), 7.89 (s, 1H), 7.87 (m, 2H), 7.34 (m, 3H), 7.18 (m, 5H), 6.91 (m, 1H), 5.67 (m, 1H), 3.20 (dd, 1H), 2.86 (dd, 1H).

Example 83:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-{3-[3-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl}nicotinamide
ESI-MS $[M+H]^+$= 508.05.
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.91 (d, 1H), 8.57 (d, 1H), 8.51 (d, 1H), 8.49 (s, 1H), 8.03 (s, 1H), 8.00 (d, 1H), 7.80 (s, 1H), 7.76 (d, 1H), 7.68 (d, 1H), 7.61 (dd, 1H), 7.50 (dd, 1H), 7.16 (dd, 1H), 7.09 (s, 5H), 5.42-5.47 (m, 1H), 3.11 (dd, 1H), 2.75 (dd, 1H).

Example 84:
N-(3-Amino-1-benzyl-2,3-dioxopropyl)-2-(4-methyl-3-phenyl-1H-pyrazol-1-yl)nicotinamide
ESI-MS $[M+H]^+$= 454.08.
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.88 (d, 1H), 8.52 (d, 1H), 8.32 (s, 1H), 8.01 (s, 1H), 7.80 (s, 1H), 7.69 (d, 1H), 7.64 (d, 2H), 7.33-7.43 (m, 4H), 7.15 (s, 5H), 5.50-5.55 (m, 1H), 3.12 (dd, 1H), 2.79 (dd, 1H), 2.29 (s, 3H).

Example 85:

N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(2,6-difluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 476.05.
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.81 (d, 1H), 8.58 (d, 1H), 8.49 (d, 1H), 7.91 (s, 1H), 7.78 (d, 1H), 7.73 (s, 1H), 7.51 (dd, 1H), 7.41-7.47 (m, 1H), 7.15 (d, 2H), 7.11 (s, 5H), 6.77 (s, 1H), 5.36-5.41 (m, 1H), 3.09 (dd, 1H), 2.78 (dd, 1H).

Example 86:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(4-methyl-3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 454.07.
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.91 (d, 1H), 8.58 (s,1H), 8.52 (d, 1H), 8.02 (s, 1H), 7.79 (s, 1H), 7.70 (d, 1H), 7.54 (d, 2H), 7.40-7.45 (m, 3H), 7.23-7.32 (m, 5H), 7.19 (dd, 1H), 5.39-5.44 (m, 1H), 3.17 (dd, 1H), 2.90 (dd, 1H), 2.23 (s, 3H).

Example 87:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{3-[4-(1-methylethyl)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 482.09
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.92 (m, 1H), 8.56 (m, 1H), 8.46 (m, 1H), 8.05 (s, 1H), 7.83 (s, 1H), 7.73 (m, 1H), 7.68 (m, 2H), 7.46 (m, 1H), 7.25 (m, 2H), 7.18 (m, 5H), 6.95 (m, 1H), 5.56 (m, 1H), 3.15 (dd, 1H), 2.94 (m, 1H), 2.82 (dd, 1H), 1.26 (d, 6H).

Example 88:
N-[3-Amino-2,3-dioxo-1-(pyridin-3-ylmethyl)propyl]-2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide hydrochloride
ESI-MS $[M+H]^+$= 441.15.
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.16 (d, 1H), 8.69 (s, 1H), 8.58 (m, 2H), 8.46 (d, 1H), 8.31 (d, 1H), 8.16 (s, 1H), 7.95 (s, 1H), 7.85 (dd, 1H), 7.69 (dd, 1H), 7.62 (m, 2H), 7.49 (dd, 1H), 7.35 (m, 3H), 6.98 (d, 1H), 5.39 (m, 1H), 3.36 and 3.03 (each dd, 1H).

Example 89:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(3,5-dichlorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS [M + H+]= 581.09.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.90 (d, 1H), 8.59 (m, 1H), 8.51 (m, 1H), 7.94 (s, 1H), 7.76 (m, 4H), 7.55 (s, 1H), 7.52 (m, 1H), 7.17-7.05 (m, 6H), 7.49 (m, 1H), 3.15 and 2.79 (each dd, 1H).

Example 90:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{3-[2-(methyloxy)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide

ESI-MS $[M+H]^+$= 470.13.
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.90 (d, 1H), 8.54 (d,1H), 8.44 (s, 1H), 8.02 (s, 1H), 7.80 (s, 1H), 7.73 (dd, 2H), 7.44 (t, 1H), 7.32 (t, 1H), 7.15 (m, 5H), 7.10 (d, 1H), 6.96 (d, 1H), 6.92 (t, 1H), 5.52-5.57 (m, 1H), 3.89 (s, 3H), 3.12 (dd, 1H), 2.79 (dd, 1H).

Example 91:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(3,5-difluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 476.16.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.91 (d, 1H), 8.58 (m, 1H), 8.51 (d, 1H), 7.95 (s, 1H), 7.80 (s, 1H), 7.76 (dd, 1H), 7.51 (dd, 1H), 7.45 (m, 2H), 7.14 (m, 7H), 5.47 (m, 1H), 3.14 and 2.77 (each dd, 1H).

Example 92:
N-(3-Amino-1-{[4-(methyloxy)phenyl]methyl}-2,3-dioxopropyl)-2-[3-(2-fluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 488.15.
^{1}H-NMR (500 MHz DMSO) δ ppm: 3.86 (d, 1H), 3.58 (m, 1H), 8.51 (m, 1H), 8.02 (s, 1H), 7.78 (m, 3H), 7.51 (m 1H), 7.41 (m, 1H), 7.29 (m, 1H), 7.20 (m, 1H), 7.05 (m, 2H), 6.86 (s, 1H), 6.71 (m, 2H), 5.47 (m, 1H), 3.68 (s, 3H), 3.04 and 2.72 (each dd, 1H).

Example 93:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(2-methylphenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 454.10.
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.87 (d, 1H), 8.56 (d,1H), 8.49 (d, 1H), 7.97 (s, 1H), 7.77 (m, 2H), 7.54 (d,1H), 7.47 (t, 1H), 7.22 (m, 3H), 7.11 (m, 5H), 6.81 (m, 1H), 5.48-5.42 (m, 1H), 3.09 (dd, 1H), 2.77 (dd, 1H), 2.36 (s, 3H).

Example 94:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(2,4-difluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 476.05.
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.89 (d, 1H), 8.56 (d, 1H), 8.49 (d,1H), 8.06 (s, 1H), 7.84 (s, 1H), 7.76 (dd, 1H), 7.73 (dd, 1H), 7.49 (dd, 1H), 7.33 (dd, 1H), 7.15 (s, 5H), 7.06(dd, 1H), 6.81(dd, 1H), 5.48-5.53 (m, 1H), 3.11 (dd, 1H), 2.73 (dd, 1H).

Example 95:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(2,6-dichlorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 508.05.
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.92 (d, 1H), 8.57 (d, 1H), 8.51 (d, 1H), 8.50 (s, 1H),

7.85 (s, 1H), 7.78 (d, 1H), 7.67 (s, 1H), 7.47-7.53 (m, 3H), 7.40 (dd, 1H), 7.50 (dd, 1H), 7.08 (s, 5H), 6.60 (s, 1H), 5.22-5.27 (m, 1H), 3.09 (dd, 1H), 2.85 (dd, 1H).

Example 96:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(3-{3-[(phenylmethyl)oxy]phenyl}-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 546.17.
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.88 (d, 1H), 8.54-8.56 (m, 1H), 8.45 (d, 1H), 7.97 (s, 1H), 7.73-7.78(m, 2H), 7.45-7.50 (m, 4H), 7.27-7.41 (m, 5H), 7.10-7.20 (m, 6H), 6.97-7.01 (d, 1H), 5.49-5.54 (m, 1H), 5.15 (s, 2H), 3.12 (dd, 1H), 2.80 (dd, 1H).

Example 97:
N-(3-Amino-1-{[4-(methyloxy)phenyl]methyl}-2,3-dioxopropyl)-2-[3-(2,4-difluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M + H]^+$= 506.15.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.85 (d, 1H), 8.58 (dd, 1H), 8.51 (m, 1H), 8.05 (s, 1H), 7.84 (s, 1H), 7.77 (m, 2H), 7.51 (dd, 1H), 7.33 (m, 1H), 7.06 (m, 3H), 6.83 (m, 1H), 6.72 (s, 1H), 6.70 (s, 1H), 5.46 (m, 1H), 3.69 (s, 3H), 3.04 and 2.70 (each dd, 1H).

Example 98:
N-(3-Amino-1-{[4-(methyloxy)phenyl]methyl}-2,3-dioxopropyl)-2-[3-(2,4-dichlorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 538.05.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.87 (d, 1H), 8.60 (m, 1H), 8.53 (d, 1H), 8.04 (s, 1H), 7.83 (s, 1H), 7.80 (dd, 1H), 7.69 (m, 1H), 7.62 (d, 1H), 7.53 (dd, 1H), 7.36 (dd, 1H), 7.04 (m, 3H), 6.69 (s, 1H), 6.67 (s, 1H), 5.44 (m, 1H), 3.68 (s, 3H), 3.03 and 2.70 (each dd, 1H).

Example 99:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(2-chloro-4-morpholin-4-ylphenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 559.15.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.90 (d, 1H), 8.56 (m, 1H), 8.48 (m, 1H), 8.05 (s, 1H), 7.83 (s, 1H), 7.72 (m, 1H), 7.56 (m, 1H), 7.47 (dd, 1H), 7.17 (m, 5H), 7.04 (d, 1H), 6.95 (d, 1H), 6.87 (dd, 1H), 5.56 (m, 1H), 3.77 (m, 4H), 3.20 (m, 4H), 3.15 and 2.81 (each dd, 1H).

Example 100:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-chromeno[4,3-c]pyrazol-2(4H)-ylpyridine-3-carboxamide
ESI-MS $[M+H]^+$= 468.1.
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.97 (d, 1H), 8.54 (d, 1H), 8.27 (s, 1H), 8.05 (s, 1H),

7.83 (s, 1H), 7.74 (d, 1H), 7.46 (dd, 1H), 7.40 (d, 1H), 7.24 (s, 5H), 7.18 (dd, 1H), 6.97 dd, 2H), 5.43-5.54 (m, 1H), 5.31 (s, 2H), 3.16 (dd, 1H), 2.82 (dd, 1H).

Example 101:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{3-[4-(1H-imidazol-1-yl)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 506.1.
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.94 (d, 1H), 8.55 (d, 1H), 8.48 (d, 1H), 8.33 (s, 1H), 8.08 (s, 1H), 7.88 (s, 2H), 7.86 (s, 1H), 7.80 (s, 1H), 7.65-7.71 (m, 3H), 7.47 (dd, 1H), 7.13-7.19 (m, 6H), 7.06 (d, 1H), 5.56-5.60 (m, 1H), 3.14 (dd, 1H), 2.77 (dd, 1H).

Example 102:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(2-fluoro-4-morpholin-4-ylphenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 543.2.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.99 (d, 1H), 8.55 (m, 1H), 8.48 (m, 1H), 8.17 (s, 1H), 7.93 (s, 1H), 7.71 (m, 1H), 7.62 (m, 1H), 7.48 (m, 1H), 7.20 (m, 5H), 6.84-6.75 (m, 3H), 5.59 (m, 1H), 3.77 (m, 4H), 3.22-3.15 (m, 5H), 2.78 (dd, 1H).

Example 103:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(5-chloro-2-thienyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 480.5.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.91 (d, 1H), 8.55 (d, 1H), 8.45 (d, 1H), 8.01 (s, 1H), 7.80 (m, 1H), 7.77 (s, 1H), 7.49 (dd, 1H), 7.35 (m, 1H), 7.34 (m, 5H), 7.21 (d, 1H), 6.91 (d, 1H), 5.51 (m, 1H), 3.17 and 2.86 (each dd, 1H).

Example 104:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[4-(2-fluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
4-(2-Fluorophenyl)-1H-pyrazole
11.08 ml of N,N-dimethylformamide was slowly added dropwise to 11.03 ml of $POCl_3$ were at 0-5°C while stirring and, after about 5 minutes a solution of 2-fluorophenylacetic acid (6 g, 38.9 mmol) in 20 ml of N,N-dimethylformamide was added dropwise. The mixture was then heated at 70°C for about 17 hours. The mixture was subsequently quenched with ice-water and the mixture was made alkaline by adding NaOH. The resulting solid was filtered off, the solution was extracted with dichloromethane, and the organic phase was dried and concentrated. The oil obtained in this way was directly dissolved in 50 ml of ethanol. 7.3 ml of hydrazine hydrate were added, and the reaction mixture was heated at 55°C for 3 hours. After the reaction was complete, the solvent was evaporated and the remaining solid was stirred with water and then dried. 2.65 g of 4-(2-fluorophenyl)-1H-pyrazole were obtained.

ESI-MS $[M+H]^+$= 163.1.
^{1}H-NMR (500 MHz DMSO) δ ppm: 13.07 (s, 1H), 8.10 (s broad, 2H), 7.73 (m, 1H), 7.24 (m, 3H).

The 4-(2-fluorophenyl)-1H-pyrazole obtained in this way was then reacted in a manner analogous to the above examples to give N-[3-amino-2,3-dioxo-1-(phenylmethyl)-propyl]-2-[4-(2-fluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide.
ESI-MS $[M+H]^+$= 458.2.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.91 (d, 1H), 8.79 (s broad, 1H), 8.59 (d, 1H), 8.05 (m, 2H), 7.88 (m, 1H), 7.81 (s, 1H), 7.76 (d, 1H), 7.51 (m, 1H), 7.35-7.20 (m, 7H), 7.18 (m, 1H), 5.34 (m, 1H), 3.18 and 2.90 (each dd, 1H).

Example 105:
N-[(1S)-1-Formyl-2-phenylethyl]-2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide

N-[(1S)-2-Hydroxy-1-(phenylmethyl)ethyl]-2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide

Coupling of 1.0 g of 2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxylic acid (3.77 mmol) with 0.63 g of L-phenylalaninol afforded 1.14 g of N-[(1S)-2-hydroxy-1-(phenylmethyl)-ethyl]-2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide as a white solid.
ESI-MS $[M+H]^+$= 399.2.
^{1}H-NMR (500 MHz DMSO) δ ppm: 8.54 (dd, 1H), 8.45 (d, 1H), 8.30 (d, 1H), 7.91 (s, 1H), 7.89 (s, 1H), 7.69 (d, 1H), 7.42 (m, 3H), 7.35 (m, 1H), 7.28 (m, 2H), 7.20 (m, 3H), 7.01 (1H), 4.70 (t, 1H), 4.09 (m, 1H), 3.49 (m, 1H), 3.35 (m, overlapped by H_2O), 2.91 and 2.71 (each dd, 1H).

Oxidation of N-[(1S)-2-hydroxy-1-(phenylmethyl)ethyl]-2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide in a manner analogous to the above examples and subsequent treatment of the resulting crude product with HCl in dioxane and stirring the resulting residue with ether afforded 71 mg of the title compound as a white solid.
ESI-MS [M+H]+
^{1}H-NMR (500 MHz DMSO) δ ppm: 9.58 (s, 1H), 8.99 (d, 1H), 8.58 (dd, 1H), 8.51 (d, 1H), 7.83 (m, 2H), 7.80 (m, 1H), 7.48 (dd, 1H), 7.43 (m, 2H), 7.37 (m, 1H), 7.27-7.19 (m, 5H), 7.05 (d, 1H), 4.48 (m, 1H), 3.13 and 2.87 (each dd, 1H).

Example 106:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(3-phenyl-1H-pyrazol-1-yl)benzamide
ESI-MS $[M+H]^+$= 439.
^{1}H-NMR (400 MHz DMSO) δ ppm: 9.01 (d, 1H), 8.07 (s,1H), 7.8 (s, 1H), 7.82 (d, 1H), 7.73 (d, 2H), 7.70 (d, 1H), 7.59 (dd, 1H), 7.39-7.47 (m, 3H), 7.34 (dd, 2H), 7.23-7.28 (m, 5H), 6.81 (d, 1H), 5.35-5.41 (m, 1H), 3.18 (dd, 1H), 2.78 (dd, 1H).

The compounds of Examples 107 and 108 can be prepared in a manner analogous to the Example 5 using (3S)-amino-2-(R/S)-hydroxy-4-phenyl-butyramide (e.g. prepared according to WO 98/29401 or DE 19642591):

Example 107:
N-[(1S)-3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 440.1;
$[\alpha]_D^{20}$: +71° (c: 1% in DMF; freshly prepared solution)

Example 108:
N-[(1S)-3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(4-fluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 458.2;
$[\alpha]_D^{20}$: +62.5° (c: 1% in dimethylformamide (DMF); freshly prepared solution)

The following examples were prepared in a manner analogous to the above examples

Example 109:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(3-chloro-2-thienyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 480.2

Example 110:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(3-naphthalen-1-yl-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 490.0
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.90 (d, 1H), 8.75 (d, 1H), 8.60 (s, 1H), 8.59 (d,1H), 7.75 (dd, 3H), 7.81 (d, 1H), 7.75 (d, 1H), 7.74 (s, 1H), 7.48-7.63 (m, 4H), 6.91-6.96 (m, 2H), 6.82-6.88 (m, 4H), 5.47-5.53 (m, 1H), 3.02 (dd, 1H), 2.70 (dd, 1H).

Example 111:
N-(3-Amino-1-{[4-(methyloxy)phenyl]methyl}-2,3-dioxopropyl)-2-[3-(2-chloro-4-fluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 522.1

Example 112:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(2,5-dichlorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 508.1.
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.88 (d, 1H), 8.59 (d, 1H), 8.52 (d,1H), 7.94 (s,

1H), 7.79 (d, 1H), 7.76 (s, 1H), 7.64 (d, 1H), 7.50-7.56 (m, 2H), 7.42 (dd, 1H), 7.02-7.10 (m, 6H), 5.35-5.41 (m, 1H), 3.13 (dd, 1H), 2.77 (dd, 1H).

Example 113:
N-[3-Amino-2,3-dioxo-1-({4-[(phenylmethyl)oxy]phenyl}methyl)propyl]-2-[3-(2,4-dichlorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 615.2
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.87 (d, 1H), 8.57 (dd, 1H), 8.51 (d, 1H), 8.04 (s, 1H), 7.83 (s, 1H), 7.77 (dd, 1H), 7.65 (d, 1H), 7.59 (d, 1H), 7.50 (dd, 1H), 7.30-7.43 (m, 6H), 7.04 (d, 2H), 7.02 (s, 1H), 6.75 (d, 2H), 5.39-5.45 (m, 1H), 4.97 (s, 2H), 3.01 (dd, 1H), 2.68 (dd, 1H).

Example 114:
N-{-3-Amino-1-[(4-fluorophenyl)methyl]-2,3-dioxopropyl}-2-[3-(2,4-dichlorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 526.1
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.91 (d, 1H), 8.58 (dd, 1H), 8.52 (d, 1H), 8.05 (s, 1H), 7.85 (s, 1H), 7.78 (d, 1H), 7.67 (d, 1H), 7.59 (d, 1H), 7.51 (dd, 1H), 7.35 (dd, 1H), 7.13 (dd, 2H), 7.03 (d, 1H), 6.90 (dd, 2H), 5.38-5.44 (m, 1H), 3.06 (dd, 1H), 2.72 (dd, 1H).

Example 115:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(2,3-dichlorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 508.1
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.92 (d, 1H), 8.58 (dd, 1H), 8.53 (d,1H), 8.01 (s, 1H), 7.79 (s, 1H), 7.76 (dd, 1H), 7.64 (dd, 1H), 7.56 (dd, 1H), 7.50 (dd, 1H), 7.33 (dd, 1H), 7.12 (s, 5H), 7.02 (d, 1H), 5.44-5.50 (m, 1H), 3.09 (dd, 1H), 2.76 (dd, 1H).

Example 116:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(2,4,6-trifluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 494.04

Example 117:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{3-[2,4-bis(methyloxy)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 500.2
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.88 (d, 1H), 8.52 (dd, 1H), 8.41 (d, 1H), 8.04 (s, 1H), 7.82 (s, 1H), 7.67 (t, 2H), 7.41 (dd, 1H), 7.17 (s, 5H), 6.88 (d, 1H), 6.63 (d, 1H), 6.49 (dd, 1H), 5.54-5.59 (m, 1H), 3.87 (s, 3H), 3.80 (s, 3H), 3.16 (dd, 1H), 2.79 (dd, 1H).

Example 118:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(2,2-difluoro-1,3-benzodioxol-5-yl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 520.1

Example 119:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(2,2-difluoro-1,3-benzodioxol-4-yl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 520.1

Example 120:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(2,3-dichloro-6-fluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 526.1
^{1}H-NMR (400 MHz DMSO) δ ppm: 8.96 (d, 1H), 8.58 (d, 1H), 8.54 (d,1H), 7.86 (s, 1H), 7.79 (d, 1H), 7.69 (s, 1H), 7.45-7.58 (m, 3H), 7.03-7.13 (m, 5H), 6.64 (d, 1H), 5.21-5.27 (m, 1H), 3.08 (dd, 1H), 2.84 (dd, 1H).

Example 121:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{3-[3,5-dimethyl-2-(methyloxy)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 498.02

Example 122:
N-{3-Amino-1-[(4-bromophenyl)methyl]-2,3-dioxopropyl}-2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 518.1

Example 123:
N-{3-Amino-1-[(4-fluorophenyl)methyl]-2,3-dioxopropyl}-2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 458.1

Example 124:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(3-{2-[(trifluoromethyl)oxy]phenyl}-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 524.2

Example 125:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{3-[4-fluoro-2-(methyloxy)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide

ESI-MS $[M+H]^+$= 488.1.

Example 126:
N-(3-Amino-1-{[4-(methyloxy)phenyl]methyl}-2,3-dioxopropyl)-2-{3-[3-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 537.5

Example 127:
N-[3-Amino-2,3-dioxo-1-({4-[(phenylmethyl)oxy]phenyl}methyl)propyl]-2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 546.3

Example 128:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-5-phenyl-2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 516.25.

Example 129:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(1,3-benzoxazol-5-yl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H_2O+H]$+= 499.1

Example 130:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{3-[5-fluoro-2-(methyloxy)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 488.1

Example 131:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{3-[5-chloro-2-(methyloxy)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 504.1

Example 132:
N-[3-Amino-2,3-dioxo-1-({4-[(trifluoromethyl)oxy]phenyl}methyl)propyl]-2-[3-(4-fluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 542.1

Example 133:
N-[3-Amino-2,3-dioxo-1-({4-[(trifluoromethyl)oxy]phenyl}methyl)propyl]-2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 524.1

Example 134:
N-[3-Amino-2,3-dioxo-1-({4-[(trifluoromethyl)oxy]phenyl}methyl)propyl]-2-{3-[3-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 592.1.

Example 135:
N-(3-Amino-1-{[4-(methyloxy)phenyl]methyl}-2,3-dioxopropyl)-2-(3-naphthalen-1-yl-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 520.2

Example 136:
N-(3-Amino-1-{[4-(methyloxy)phenyl]methyl}-2,3-dioxopropyl)-2-{3-[4-fluoro-2-(methyloxy)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 518.2

Example 137:
N-(3-Amino-1-{[4-(methyloxy)phenyl]methyl}-2,3-dioxopropyl)-2-[3-(2,2-difluoro-1,3-benzodioxol-5-yl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 550.1

Example 138:
N-[3-Amino-2,3-dioxo-1-({4-[(trifluoromethyl)oxy]phenyl}methyl)propyl]-2-(3-naphthalen-1-yl-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 573.5

Example 139:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{3-[4-chloro-2-(methyloxy)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 504.1

Example 140:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(8-chlorochromeno[4,3-c]pyrazol-2(4H)-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 502.2

Example 141:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(4,5-dihydro-2H-[1]benzoxepino[5,4-c]pyrazol-2-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 482.1

Example 142:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[7-(methyloxy)chromeno[4,3-c]pyrazol-

2(4H)-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 498.1

Example 143:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(8-chloro-9-methylchromeno[4,3-c]pyrazol-2(4H)-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 516.2

Example 144:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[8-(1-methylethyl)chromeno[4,3-c]pyrazol-2(4H)-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 510.2

Example 145:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(2-chloro-3-fluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 492.1

Example 146:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(4-fluoronaphthalen-1-yl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 508.1

Example 147:
N-{3-Amino-1-[(4-fluorophenyl)methyl]-2,3-dioxopropyl}-2-{3-[3-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 526.2

Example 148:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{4-[(diethylamino)methyl]-3-(4-fluorophenyl)-1H-pyrazol-1-yl}pyridine-3-carboxamide methanesulfonate
ESI-MS $[M+H]^+$= 543.20 (free base)

Example 149:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(4-fluorophenyl)-4-(morpholin-4-ylmethyl)-1H-pyrazol-1-yl]pyridine-3-carboxamidee Methanesulfonat
ESI-MS $[M+H]^+$= 557.2 (free base)

Example 150:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{3-[4-fluoro-2-(morpholin-4-ylmethyl)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide methanesulfonate
ESI-MS $[M+H]^+$= 557.2 (free base)

Example 151:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{3-[2,5-bis(methyloxy)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 500.1

Example 152:
N-{3-Amino-1-[(4-fluorophenyl)methyl]-2,3-dioxopropyl}-2-(3-{2-[(trifluoromethyl)oxy]phenyl}-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 542.1

Example 153:
N-(3-Aamino-1-{[4-(methyloxy)phenyl]methyl}-2,3-dioxopropyl)-2-[3-(2,3-dichlorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 538.2

Example 154:
N-{3-Amino-1-[(4-fluorophenyl)methyl]-2,3-dioxopropyl}-2-[3-(2-chloro-3-fluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 511.1

Example 155:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{3-[2-chloro-3-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 542.2

Example 156:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(3-isoquinolin-5-yl-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 491.1

Example 157:
N-(3-Amino-1-{[4-(methyloxy)phenyl]methyl}-2,3-dioxopropyl)-2-[3-(2-chloro-3-fluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 522.2

Example 158:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-5-[(methylsulfonyl)amino]-2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 533.2

Example 159:

N-{3-Amino-1-[(4-fluorophenyl)methyl]-2,3-dioxopropyl}-2-[3-(2,3-dichlorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 526.2

Example 160:
N-[3-amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(3-quinolin-8-yl-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 491.1

Example 161
N-{3-Amino-1-[(4-fluorophenyl)methyl]-2,3-dioxopropyl}-2-[3-(2,3-dichlorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 607.2

Example 162:
N-{3-Amino-1-[(3-fluorophenyl)methyl]-2,3-dioxopropyl}-2-(3-{2-[(trifluoromethyl)oxy]phenyl}-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 542.2

Example 163:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{3-[2-(morpholin-4-ylmethyl)-5-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 607.25

Example 164:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(2,3-dihydro-1-benzofuran-7-yl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 482.1

Example 165:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(4-fluorophenyl)-4-(2-morpholin-4-ylethyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 571.2

Example 166:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(3-{2-[(difluoromethyl)oxy]phenyl}-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 506.1

Example 167:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(3-{2-[(diethylamino)methyl]-4-fluorophenyl}-1H-pyrazol-1-yl)pyridine-3-carboxamide

ESI-MS $[M+H]^+$= 543.25

Example 168:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(3-{3-[(trifluoromethyl)oxy]phenyl}-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 524.15

Example 169:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(4-fluorophenyl)-4-(pyrrolidin-1-ylmethyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 541.25

Example 170:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{3-(4-fluorophenyl)-4-[(methyloxy)methyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 502.2

Example 171:
N-{3-Amino-1-[(4-bromophenyl)methyl]-2,3-dioxopropyl}-2-[3-(4-fluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 536.1

Example 172:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-5-(dimethylamino)-2-(3-phenyl-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 483.25

Example 173:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-thiochromeno[4,3-c]pyrazol-2(4H)-ylpyridine-3-carboxamide
ESI-MS $[M+H]^+$= 484.2

Example 174:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(5,5-dioxidothiochromeno[4,3-c]pyrazol-2(4H)-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 516.2

Example 175:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(6-chlorochromeno[4,3-c]pyrazol-2(4H)-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 502.3

Example 176:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{4-[(dimethylamino)methyl]-3-[3-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 565.2

Example 177:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{4-(morpholin-4-ylmethyl)-3-[3-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 607.25

Example 178:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{4-(pyrrolidin-1-ylmethyl)-3-[3-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 591.25

Example 179:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-{3-(4-fluorophenyl)-4-[(phenyloxy)methyl]-1H-pyrazol-1-yl}pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 564.15

Example 180:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(3-{2-[(diethylamino)methyl]-3-(trifluoromethyl)phenyl}-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 593.15

Example 181:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(8-fluorochromeno[4,3-c]pyrazol-2(4H)-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 486.2

Example 182:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[6-(ethyloxy)chromeno[4,3-c]pyrazol-2(4H)-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 512.3

Example 183:
N-[3-Aamino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[8-(methyloxy)chromeno[4,3-c]pyrazol-2(4H)-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 498.2

Example 184:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[4-chloro-3-(4-fluorophenyl)-1H-

pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 492.1

Example 185:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[4-(dimethylamino)-3-(4-fluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 483.55

Example 186:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(8-methylchromeno[4,3-c]pyrazol-2(4H)-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 482.1

Example 187:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(4-fluorophenyl)-4-{[(methylsulfonyl)amino]methyl}-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 565.15.

Example 188:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-5-cyano-2-[3-(2-fluorophenyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 483.15

Example 189:
Ethyl-3-[({2-[3-(4-fluorophenyl)-1H-pyrazol-1-yl]pyridin-3-yl}carbonyl)amino]-2-oxo-4-phenylbutanoate

Ethyl-3-amino-2-hydroxy-4-phenylbutanoate was prepared according to WO 2005/124673. The title compound was prepared in a manner analogous to the above Examples.
ESI-MS $[M+H]^+$= 487.14

Example 190:
2-[3-(4-Fluorophenyl)-1H-pyrazol-1-yl]-N-[3-(methylamino)-2,3-dioxo-1-(phenylmethyl)propyl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 472.15

Example 191:
2-[3-(5-Fluoropyridin-2-yl)-1H-pyrazol-1-yl]-N-[3-(methylamino)-2,3-dioxo-1-(phenylmethyl)propyl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 459.1

The 3-alkyl- and 3-cycloalkyl-1H-pyrazole used in the following examples were prepared in a manner analogous to the methode described above for 3-isopropyl-1H-pyrazol (Trofimenko et al.; Inorganic Chemistry 1989, 28(6), 1091-1101).

Example 192:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(3-cyclohexyl-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 446.2

Example 193:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-(3-tricyclo[3.3.1.1^{3,7}]dec-1-yl-1H-pyrazol-1-yl)pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 498.2

Example 194:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(2,2-dimethylpropyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 434.2

Example 195:
N-[3-Amino-2,3-dioxo-1-(phenylmethyl)propyl]-2-[3-(1,1-dimethylethyl)-1H-pyrazol-1-yl]pyridine-3-carboxamide
ESI-MS $[M+H]^+$= 420.2

Biological investigation of inhibition of calpain and cathepsins

The following solutions and buffers were employed:

- HBS (for 40 ml): 800 µl 1M HEPES; 2.16 ml 100 mM KCl; 4.8 ml 1M NaCl; 3.59 ml 5% glucose; 60 µl 1M $MgSO_4$; 400 µl 100 mM Na pyruvate, 28.19 ml water; pH 7.2-7.5.
- lysis buffer (for 20 ml): 400 µl 1M Tris pH 8.2; 2.74 ml 1M NaCl; 520 µl 0.5M EDTA; 2 ml 10% triton X-100; 0.8 ml (= 1:25) CompletePlus (1 tablet/2 ml H_2O); 200 µl 100 mM Pefabloc; 13.34 ml water, pH 8.2.
- TBST (10x) (for 1l): 100 mM Tris (12.1 g); 1.5M NaCl (87 g); 1% Tween 20 (10 g), adjusted to pH 8.

I Enzyme inhibition in vitro:

Testing for blockade of the corresponding enzymic activities was carried out by means of kinetic fluorescence assays (excitation 390 nm, emission 460 nm).

Apparent Ki values were calculated from the experimentally determined IC_{50}

values by the Cheng-Prussoff relation assuming a reversible competitive enzyme inhibition. The Km values of the substrates used under the assay conditions indicated above were: 90 µM (Z-Phe-Arg-AMC, cathepsin B), 10 µM (Z-Gly-Pro-Arg-AMC, cathepsin K), 2 µM (Z-Phe-Arg-AMC, cathepsin L), and 30 µM (Z-Val-Val-Arg-AMC, cathepsin S).
The indicated Ki values are averages of the inhibition constants calculated on the basis of 2 to 4 independent dose-effect plots.

The following assays were used:

1. Calpain I:
   20 nM calpain-I – isolated from human erythrocytes (Calbiochem #208713), 100 µM Suc-Leu-Tyr-AMC (Bachem #I-1355) as substrate in buffer with 62 mM imidazole, 0.3 mM $CaCl_2$, 0.10% CHAPS, 0.05% BSA, 1 mM DTT at pH 7.3 and room temperature.
2. Cathepsin B:
   0.25 nM cathepsin B – isolated from human liver (Calbiochem #219362), 100 µM Z-Phe-Arg-AMC (Bachem #I-1160) as substrate 50 mM MES, 2 mM EDTA, 0.05% Brij 35, 2.5 mM L-cysteine, pH 6.0, room temperature.
3. Cathepsin K:
   3 nM cathepsin K – activated from recombinant human procathepsin K from E. coli (Calbiochem #342001), 10 µM Z-Gly-Pro-Arg-AMC (Biomol #P-142) as substrate in 50 mM MES, 2 mM EDTA, 0.05% Brij 35, 2.5 mM L-cysteine, pH 6.0, room temperature.
4. Cathepsin L:
   1 nM cathepsin L – isolated from human liver (Calbiochem #219402), 2 µM Z-Phe-Arg-AMC (Bachem #I-1160) as substrate in 50 mM MES, 2 mM EDTA, 0.05% Brij 35, 2.5 mM L-cysteine, pH 6.0, room temperature.
5. Cathepsin S:
   0.5 nM recombinant human cathepsin S from E. coli (Calbiochem #219343), 20 µM Z-Val-Val-Arg-AMC (Bachem #I-1540) as substrate in 50 mM MES, 2 mM EDTA, 0.05% Brij 35, 2.5 mM L-cysteine, pH 6.0, room temperature.

The results of the in vitro determination are indicated in Table 1. The following abbreviations are used in Table 1:

The the "Calpain activity" column, ++ stands for a calpain Ki (Ki(calpain)) of $\leq$ 40 nM and + means: 40 nM < Ki(Calpain) $\leq$ 100 nM.

The "Sel. cat. B" column indicates the Ki(cathepsin B)/Ki(calpain) ratio. In this connection, ++ means a Ki(cathepsin B)/Ki(calpain) ratio of $\geq$ 30 and + means 10 $\leq$ Ki(cathepsin B)/Ki(calpain) < 30.

The "Sel. cat. K" column indicates the Ki(cathepsin K)/Ki(calpain) ratio. In this connection, ++ means a Ki(cathepsin K)/Ki(calpain) ratio of $\geq$ 30 and + means 10 $\leq$ Ki(cathepsin K)/Ki(calpain) < 30.

The "Sel. cat. L" column indicates the Ki(cathepsin L)/Ki(calpain) ratio. In this connection, ++ means a Ki(cathepsin L)/Ki(calpain) ratio of $\geq$ 50 and + means 30 $\leq$ Ki(cathepsin L)/Ki(calpain) < 50.

The "Sel. cat. S" column indicates the Ki(cathepsin S)/Ki(calpain) ratio. In this connection, ++ means a Ki(cathepsin S)/Ki(calpain) ratio of $\geq$ 100 and + means 50 $\leq$ Ki(cathepsin S)/Ki(calpain) < 100.

Table 1:

Example	Calpain activity	Sel cat. B	Sel cat. K	Sel cat. L	Sel cat. S
2	++			++	
4	++				
5	++	+	+	++	++
6	++				+
9	++			+	++
10	++				
12	++				
13	+			++	+
14	+				++
15	++			++	+
16	+			+	+
17	++			++	+
18	++			+	++
19	++				
20	++				
21	++				
22	++			+	++
23	++			+	
24	++			+	
25	++				
26	++				++
27	++	++	+	+	
28	++	+			

Example	Calpain activity	Sel cat. B	Sel cat. K	Sel cat. L	Sel cat. S
29	++		+	++	++
31	++	++	+	+	
32	++	+			
33	++	+			+
35	+	+	+	++	++
38	+	+	+	++	++
39	+			++	++
40	++	+		++	++
42	++				++
43	+				++
44	++				+
45	++				+
46	+				++
47	++				++
48	+	+	+	++	++
49	+			+	++
50	+	+	+	+	+
52	+				++
54	+	++	++	++	++
55	++	+	+	++	++
57	+			++	++
58	++	+	+	++	++
59	++			++	+
60	+	+	+	++	+
61		+			++
62	+			++	++
63	++	+	+	++	++
64	++	+			++
65					++
66	++		+	+	++
67	+	+	+	++	++
68	+		+		++
69	+	+	+	++	++
70	++	+	+	++	++
71	+	++	++	++	++
72	+	+	+	+	++
74	++	++	++		++
75	+		+	++	++

Example	Calpain activity	Sel cat. B	Sel cat. K	Sel cat. L	Sel cat. S
76	++	++	+	++	++
77	++				
78	+			++	+
79	+	++	++	++	++
80	+	++	+	++	++
81	++	+	+	++	++
82	+	++	++	++	
83	++	+	++	++	++
84	++	+		++	++
85	++	+	++	++	++
86	++			++	
87	++	++	++	++	++
88	+	+	++	++	++
89	+	+	+	++	++
90	++	++	+	++	++
91	++	++	+	++	++
92	+	++	+	++	++
93	++	++	+	++	++
94	+	++	+	++	++
95	++	++	++	++	++
96	++	++	++	++	++
97	++	++	+	++	++
98	++	++	++	++	++
99	++	++	++	++	++
100	++	+	++	++	++
101	++				++
102	++	+	++	++	++
103	++	+	+	++	++
104	++				+
105	++	++		++	++
106	++			+	++
107	++	+	+	++	++
109	++	++	++	++	++
110	++	++	++	++	++
111	++	++	++	++	++
112	++	++	++	++	++
114	+	++	++	++	++
115	++	++	++	++	++

Example	Calpain activity	Sel cat. B	Sel cat. K	Sel cat. L	Sel cat. S
116	++	++	+	++	++
117	++	++	++	++	++
118	++	++	+	++	++
119	++	++	++	++	++
120	++	++	++	+	++
121	++	++	++	++	++
122	++	++		++	++
123	++	++	++	++	++
124	++	++	++	++	++
125	++	++	++	++	++
126	++	++	++	++	++
127	++	++	++	++	++
129	+				++
130	++	++	++	++	++
131	++	++	++	++	++
132	+	+	++	++	++
133	+	++	++	++	++
134		++	++	+	+
135	++	++	++	++	++
136	++	++	++	++	++
137	+	+	+	++	++
138		++	++	++	++
139	+	+	++	++	++
140	++	+	++	++	++
141	+			++	++
142	++	+	+	++	++
143	+	++	++	++	++
144	++	+		++	++
151	+	++	++	++	
152	++	++	++	++	++
153	++	++	++	++	++
154		++	++	++	++
155	+	++	++	++	++
156		+		+	++
157	++	++	++	++	++
158	+	++	++	++	++
160	+	++	++	++	++
161		+		+	++

Example	Calpain activity	Sel cat. B	Sel cat. K	Sel cat. L	Sel cat. S
162	+	++	++	++	++
163	+	+	+	+	++
164	++	+	++	++	++
165	+				++
166	++	+	++	++	++
168	++	+	+	++	++
170	+			+	
173	++	+	+	++	++
174	++	+	+	++	++
175	++	++	++	++	++
176					++
177	+				++
178	+				++
179				+	++
183	++	+	+	++	++
184	+	+	+	++	++
187	+			+	++
188	+		++	++	
192	+		+	++	++
193	++	++	++	++	++

II Spectrin molt-4 asssay to determine cellular calpain inhibition:

The assay design and procedure were as disclosed by Chatterjee; BMC 1998, 6, pp. 509-522; the EC_{50} values are calculated from the percentage degradation of spectrin as a function of the dose.

Cell culture conditions: the molt-4 cells are maintained in RPMI 1640 + Glutamax™ I medium (Gibco) with 10% FCS and 50 µg/ml gentamicin at 37°C, 5% CO_2 and split 1:15 twice a week.

Preparation of the molt-4 cells: the cells are washed, counted and taken up in a concentration of 2×10^7 cells/ml in HBS buffer.

Dilution of the inhibitor substances: all the inhibitors are dissolved in a concentration of 10^{-2} M in DMSO. The stock solution is then diluted 1:15 in DMSO (= 6.67×10^{-4} M). Thereafter the stock solution diluted 1:15 is diluted 1:4 in DMSO in two steps (= 1.67×10^{-4} M and 4.17×10^{-5} M). Thereafter, these three solutions are further diluted 1:50 in HBS buffer to give solutions having a

concentration of 1.33×10^{-5} M, 3.36×10^{-6} M and 8.34×10^{-7} M.

Test mixture: for each mixture, 10^6 cells (see above) are introduced into a 1.5 ml Eppendorf tube. To these are added in each case 150 µl of the diluted substances (final conc. 10-5 M; 2.5×10^{-6} M and 6.25×10^{-7} M) and thoroughly mixed. A negative control and a positive control are used as controls. In this case, initially only 150 µl of HBS buffer is pipetted onto the cells. All the mixtures are incubated at 37°C, 5% CO_2 in an incubator for 10 min. Thereafter, except for the negative control, in each case $CaCl_2$ (final conc. 5 mM) and ionomycin (final conc. 5 µM) are added, thoroughly mixed and incubated at 37°C, 5% CO_2 in an incubator for 30 min. Then centrifuge at 700 g for 5 min. The supernatants are discarded and the pellets are taken up in 20 µl of lysis buffer. The mixtures are subsequently placed on ice for 30-60 min and then centrifuged at 15000g for 15 min. The supernatants are removed and put into new Eppendorf tubes. The protein determination is then carried out thereon, e.g. with a MicroBCA assay (Pierce).

SDS-PAGE electrophoresis: 10 µg of total protein from each mixture are put into a new Eppendorf tube and, after pipetting in the same volume of 2× Tris-glycine SDS sample buffer (Invitrogen) and 1/10 volume of 1M DTT, thoroughly mixed and heated at 95°C for 15 min. The solutions are briefly centrifuged and loaded onto a 6% SDS gel (Invitrogen). The gel is run at 100V with 1× Tris-glycine laemmli buffer (Biomol) until the lower band of the marker has reached the base of the gel.

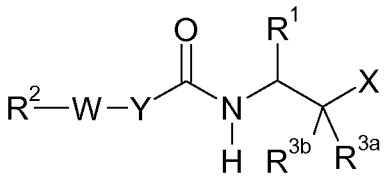
Western blotting: the gel is removed from the apparatus and blotted onto nitrocellulose in 1× Tris-glycine transfer buffer (Invitrogen) + 20% methanol with 1.5 A/cm^2 in a FastBlot chamber (Biometra) for 30 min. The nitrocellulose filter is removed, briefly washed in TBST buffer and blocked in TBST/5% milk powder for 1 h at RT (room temperature). The blocked nitrocellulose is then incubated with an anti-spectrin Ab (Chemicon) (1:10000 in TBST/5% milk powder) at RT for 3 h or at 4°C overnight. The nitrocellulose is washed 3× in TBST buffer. It is then incubated with anti-mouse IgG (POD) antibody (Sigma) (1:10000 in TBST/5% milk powder) at room temperature for 1 h.

The nitrocellulose is then washed 5× in TBST buffer. In the next step, 5 ml of prepared solution of the SuperSignal® West Pico chemiluminescence substrate (Pierce) are put on the filter and incubated for 5 min. The nitrocellulose is then taken out of the solution, gently dabbed dry and inserted into a development folder film (Tropix). A digital image analysis system (VersaDoc, Biorad) is used to record and quantify the ECL (QuantityOne), and the percentage degradation of

spectrin is calculated from the data. Graph-pad prism is used to fit the percentage spectrum degradation as a function of the dose to a sigmoidal dose-effect plot (top fixed at 100% and bottom at 0%), and the EC 50% is calculated.

Claims:

1. A carboxamide compound of the formula I



I

in which

R^1 is hydrogen, C_1-C_{10}-alkyl, C_2-C_{10}-alkenyl, C_2-C_{10}-alkynyl, where the last 3 radicals mentioned may be partly or completely halogenated and/or have 1, 2 or 3 substituents R^{1a},
C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, where a CH_2 group in the cycloalkyl moiety of the last two radicals mentioned may be replaced by O, NH, or S, or two adjacent C atoms may form a double bond, where the cycloalkyl moiety may further have 1, 2, 3 or 4 radicals R^{1b},
aryl, hetaryl, aryl-C_1-C_6-alkyl, aryl-C_2-C_6-alkenyl, hetaryl-C_1-C_4-alkyl or hetaryl-C_2-C_6-alkenyl, where aryl and hetaryl in the last 6 radicals mentioned may be unsubstituted or carry 1, 2, 3 or 4 identical or different radicals R^{1c}; where

R^{1a} is selected independently of one another from OH, SH, COOH, CN, OCH_2COOH, C_1-C_6-alkoxy, C_1-C_6-halolkoxy, C_3-C_7-cycloalkyloxy, C_1-C_6-alkylthio, C_1-C_6-haloalkylthio, $COOR^{a1}$, $CONR^{a2}R^{a3}$, $SO_2NR^{a2}R^{a3}$, $-NR^{a2}$-SO_2-R^{a4}, NR^{a2}-CO-R^{a5}, SO_2-R^{a4}, $NR^{a6}R^{a7}$,

R^{1b} is selected independently of one another from OH, SH, COOH, CN, OCH_2COOH, halogen, phenyl which optionally has 1, 2 or 3 substituents R^{1d}, or C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-alkylthio, where the alkyl moieties in the last 3 substituents mentioned may be partly or completely halogenated and/or have 1, 2 or 3 substituents R^{1a}, $COOR^{b1}$, $CONR^{b2}R^{b3}$, $SO_2NR^{b2}R^{b3}$, NR^{b2}-SO_2-R^{b4}, NR^{b2}-CO-R^{b5}, SO_2-R^{b4}, $NR^{b6}R^{b7}$, where
in addition two R^{1b} radicals may together form a C_1-C_4-alkylene group, or 2 R^{1b} radicals bonded to adjacent C atoms of cycloalkyl may form together with the carbon atoms to which they are bonded also a benzene ring,

R^{1c} is selected independently of one another from OH, SH, halogen, NO_2, NH_2, CN, CF_3, CHF_2, CH_2F, O-CF_3, O-CHF_2, O-CH_2F, COOH, OCH_2COOH, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-alkoxy-C_1-C_4-alkyl, C_1-C_6-alkylthio, where the alkyl moieties in the last 4 substituents

mentioned may be partly or completely halogenated and/or have 1, 2 or 3 substituents R^{1a},
C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-cycloalkyloxy, where the cycloalkyl moiety of the last three radicals mentioned may have 1, 2, 3 or 4 R^{1b} radicals,
aryl, hetaryl, O-aryl, O-CH_2-aryl, where the last three radicals mentioned are unsubstituted in the aryl moiety or may carry 1, 2, 3 or 4 R^{1d} radicals,
$COOR^{c1}$, $CONR^{c2}R^{c3}$, $SO_2NR^{c2}R^{c3}$, NR^{c2}-SO_2-R^{c4}, NR^{c2}-CO-R^{c5},
SO_2-R^{c4},
-$(CH_2)_p$-$NR^{c6}R^{c7}$ with p = 0, 1, 2, 3, 4, 5 or 6 and
O-$(CH_2)_q$-$NR^{c6}R^{c7}$ with q = 2, 3, 4, 5 or 6; where

R^{a1}, R^{b1} and R^{c1} are independently of one another H, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{1a}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, aryl, aryl-C_1-C_4-alkyl, hetaryl or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{1d},
R^{a2}, R^{b2} and R^{c2} are independently of one another H, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{1a}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, aryl, aryl-C_1-C_4-alkyl, hetaryl or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{1d}, and
R^{a3}, R^{b3} and R^{c3} are independently of one another H, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{1a}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, aryl, aryl-C_1-C_4-alkyl, hetaryl or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{1d}, or
the two radicals R^{a2} and R^{a3}, or R^{b2} and R^{b3} or R^{c2} and R^{c3} form together with the N atom a 3 to 7-membered, optionally substituted nitrogen heterocycle which may optionally have 1, 2 or 3 further different or identical heteroatoms from the group of O, N, S as ring members,
R^{a4}, R^{b4} and R^{c4} are independently of one another C_1-C_6-alkyl, C_1-C_6-

haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{1a}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, aryl, aryl-C_1-C_4-alkyl, hetaryl or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{1d}, and

R^{a5}, R^{b5} and R^{c5} have independently of one another one of the meanings mentioned for R^{a1}, R^{b1} and R^{c1};

R^{a6}, R^{b6} and R^{c6} are independently of one another H, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{1a}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, CO-C_1-C_6-alkyl, CO-O-C_1-C_6-alkyl, SO_2-C_1-C_6-alkyl, aryl, hetaryl, O-aryl, OCH_2-aryl, aryl-C_1-C_4-alkyl, hetaryl-C_1-C_4-alkyl, CO-aryl, CO-hetaryl, CO-(aryl-C_1-C_4-alkyl), CO-(hetaryl-C_1-C_4-alkyl), CO-O-aryl, CO-O-hetaryl, CO-O-(aryl-C_1-C_4-alkyl), CO-O-(hetaryl-C_1-C_4-alkyl), SO_2-aryl, SO_2-hetaryl, SO_2-(aryl-C_1-C_4-alkyl) or SO_2-(hetaryl-C_1-C_4-alkyl), where aryl and hetaryl in the last 18 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{1d}, and

R^{a7}, R^{b7} and R^{c7} are independently of one another H, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{1a}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, aryl, aryl-C_1-C_4-alkyl, hetaryl or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{1d}, or

the two radicals R^{a6} and R^{a7}, or R^{b6} and R^{b7} or R^{c6} and R^{c7} form together with the N atom a 3 to 7-membered, optionally substituted nitrogen heterocycle which may optionally have 1, 2 or 3 further different or identical heteroatoms from the group of O, N and S as ring members,

or two radicals R^{1b} and R^{1c} bonded to adjacent C atoms form together with the C atoms to which they are bonded a 4, 5, 6 or 7-membered, optionally substituted carbocycle or an optionally substituted heterocycle which has 1, 2 or 3 different or identical heteroatoms from the group of O, N and S as ring members;

R^{1d} is selected from halogen, OH, SH, NO_2, COOH, $C(O)NH_2$, CHO, CN, NH_2, OCH_2COOH, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_1-C_6-alkylthio, C_1-C_6-haloalkylthio, CO-C_1-C_6-alkyl, CO-O-C_1-C_6-alkyl, NH-C_1-C_6-alkyl, NHCHO, NH-C(O)C_1-C_6-alkyl, and

SO_2-C_1-C_6-alkyl;

R^2 is hydrogen, C_1-C_{10}-alkyl, C_1-C_{10}-alkoxy, C_2-C_{10}-alkenyl, C_2-C_{10}-alkynyl, where the last 4 radicals mentioned may be partly or completely halogenated and/or have 1, 2 or 3 substituents R^{2a},

C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, where a CH_2 group in the cycloalkyl moiety of the last two radicals mentioned may be replaced by O, NH, or S, or two adjacent C atoms may form a double bond, where the cycloalkyl moiety may additionally have 1, 2, 3 or 4 R^{2b} radicals;
aryl, O-aryl, O-CH_2-aryl, hetaryl, aryl-C_1-C_6-alkyl, aryl-C_2-C_6-alkenyl, hetaryl-C_1-C_4-alkyl or hetaryl-C_2-C_6-alkenyl, where aryl and hetaryl in the last 8 radicals mentioned may be unsubstituted or carry 1, 2, 3 or 4 identical or different R^{2c} radicals; where

R^{2a} has one of the meanings indicated for R^{1a},
R^{2b} has one of the meanings indicated for R^{1b}, and
R^{2c} has one of the meanings indicated for R^{1c};

R^{3a} and R^{3b} are independently of one another hydroxy or C_1-C_4-alkoxy, or together with the carbon atom to which they are bonded are C=O;

X is hydrogen or a radical of the formulae C(=O)-O-R^{x1}, C(=O)-N$R^{x2}R^{x3}$, C(=O)-N(R^{x4})-(C_1-C_6-alkylene)-N$R^{x2}R^{x3}$ or C(=O)-N(R^{x4})N$R^{x2}R^{x3}$, in which

R^{x1} is hydrogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{xa}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, where alkyl, alkenyl, alkoxy, alkynyl, cycloalkyl, heterocycloalkyl in the last 6 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xa}, or aryl, aryl-C_1-C_4-alkyl, hetaryl or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xd},

R^{x2} is H, OH, CN, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{xa}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, CO-C_1-C_6-alkyl, CO-O-C_1-C_6-alkyl, SO_2-C_1-C_6-alkyl, O-C_1-C_6-alkyl, where alkyl, alkoxy, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl in the last 10 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xa},

aryl, O-aryl, O-CH_2-aryl, hetaryl, O-CH_2-hetaryl, aryl-C_1-C_4-alkyl, hetaryl-C_1-C_4-alkyl, CO-aryl, CO-hetaryl, CO-(aryl-C_1-C_4-alkyl), CO-(hetaryl-C_1-C_4-alkyl), CO-O-aryl, CO-O-hetaryl, CO-O-(aryl-C_1-C_4-alkyl), CO-O-(hetaryl-C_1-C_4-alkyl), SO_2-aryl, SO_2-hetaryl, SO_2-(aryl-C_1-C_4-alkyl) or SO_2-(hetaryl-C_1-C_4-alkyl), where aryl and hetaryl in the last 19 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xd}, and

R^{x3} is H, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{xa}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, where alkyl, alkenyl, alkoxy, alkynyl, cycloalkyl, heterocycloalkyl in the last 6 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xa},
aryl, aryl-C_1-C_4-alkyl, hetaryl or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xd}, or
the two radicals R^{x2} and R^{x3} form together with the N atom a 3 to 7-membered nitrogen heterocycle which may optionally have 1, 2 or 3 further different or identical heteroatoms from the group of O, N, S as ring members, and which may have 1, 2 or 3 substituents R^{xb},

R^{x4} is H, OH, CN, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{xa}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, CO-C_1-C_6-alkyl, CO-O-C_1-C_6-alkyl, SO_2-C_1-C_6-alkyl, where alkyl, alkenyl, alkoxy, alkynyl, cycloalkyl, heterocycloalkyl in the last 9 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xa},
aryl, O-aryl, O-CH_2-aryl, hetaryl, aryl-C_1-C_4-alkyl, hetaryl-C_1-C_4-alkyl, CO-aryl, CO-hetaryl, CO-(aryl-C_1-C_4-alkyl), CO-(hetaryl-C_1-C_4-alkyl), CO-O-aryl, CO-O-hetaryl, CO-O-(aryl-C_1-C_4-alkyl), CO-O-(hetaryl-C_1-C_4-alkyl), SO_2-aryl, SO_2-hetaryl, SO_2-(aryl-C_1-C_4-alkyl) or SO_2-(hetaryl-C_1-C_4-alkyl), where aryl and hetaryl in the last 18 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xd}, and

where R^{xa} has one of the meanings indicated for R^{1a}, R^{xb} has one of the meanings indicated for R^{1b}, and R^{xd} has one of the meanings indicated for R^{1d};

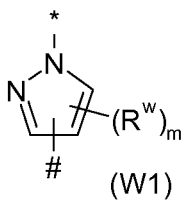
Y is a divalent, aromatic or 6-membered heteroaromatic radical which has 1 or 2 nitrogen atoms as ring members and which optionally has 1 or 2 identical or different substituents R^y:

R^y is selected independently of one another from OH, SH, halogen, NO_2, NH_2, CN, CF_3, CHF_2, CH_2F, O-CF_3, O-CHF_2, O-CH_2F, COOH, OCH_2COOH, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-alkoxy-C_1-C_4-alkyl, C_1-C_6-alkylthio, where the last 4 radicals mentioned may be partly or completely halogenated and/or have 1, 2 or 3 substituents R^{ya},
C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-cycloalkyl-O, where the cycloalkyl moiety in the last three radicals mentioned may have 1, 2, 3 or 4 R^{yb} radicals,
aryl, O-aryl, CH_2-aryl, O-CH_2-aryl, where the last 4 radicals mentioned are unsubstituted in the aryl moiety or may carry 1, 2, 3 or 4 radicals R^{yd},
$COOR^{y1}$, $CONR^{y2}R^{y3}$, $SO_2NR^{y2}R^{y3}$, -NH-SO_2-R^{y4},
NH-CO-R^{y5}, SO_2-R^{y4},
-$(CH_2)_p$-$NR^{y6}R^{y7}$ with p = 0, 1, 2, 3, 4, 5 or 6 and
O-$(CH_2)_q$-$NR^{y6}R^{y7}$ with q = 2, 3, 4, 5 or 6;

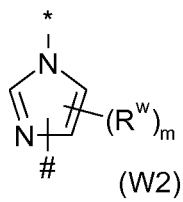
or two R^y radicals bonded to adjacent C atoms form together with the C atoms to which they are bonded a 4, 5, 6 or 7-membered, optionally substituted carbocycle or an optionally substituted heterocycle which has 1, 2 or 3 different or identical heteroatoms from the group of O, N, S as ring members, where

R^{ya} has one of the meanings indicated for R^{1a},
R^{yb} has one of the meanings indicated for R^{1b},
R^{yd} has one of the meanings indicated for R^{1d},
R^{y1} has one of the meanings indicated for R^{c1},
R^{y2} has one of the meanings indicated for R^{c2},
R^{y3} has one of the meanings indicated for R^{c3},
R^{y4} has one of the meanings indicated for R^{c4},
R^{y5} has one of the meanings indicated for R^{c5},
R^{y6} has one of the meanings indicated for R^{c6}, and
R^{y7} has one of the meanings indicated for R^{c7};

W is a radical of the formulae W1 or W2 which is linked via nitrogen:



(W1)



(W2)

in which

* means the linkage to Y, and # means the linkage to R^2,

m is 0, 1 or 2, and

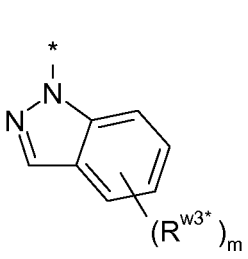
R^w is selected from OH, SH, halogen, NO_2, NH_2, CN, CF_3, CHF_2, CH_2F, O-CF_3, O-CHF_2, O-CH_2F, COOH, OCH_2COOH, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-alkoxy-C_1-C_4-alkyl, C_1-C_6-alkylthio, where the last 4 radicals mentioned may be partly or completely halogenated and/or have 1, 2 or 3 substituents R^{wa},
C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-cycloalkyloxy, where the cycloalkyl moiety of the last three radicals mentioned may have 1, 2, 3 or 4 radicals R^{wb},
aryl, O-aryl, O-CH_2-aryl, hetaryl, where the last four radicals mentioned are unsubstituted in the aryl moiety or may carry 1, 2, 3 or 4 radicals R^{wd},
$COOR^{w1}$, $CONR^{w2}R^{w3}$, $SO_2NR^{w2}R^{w3}$, NR^{w2}-SO_2-R^{w4},
NR^{w2}-CO-R^{w5}, SO_2-R^{w4},
-$(CH_2)_p$-$NR^{w6}R^{w7}$ with p = 0, 1, 2, 3, 4, 5 or 6 and
O-$(CH_2)_q$-$NR^{w6}R^{w7}$ with q = 2, 3, 4, 5 or 6;

or two R^w radicals bonded to adjacent C atoms form together with the C atoms to which they are bonded a 4, 5, 6 or 7-membered, optionally substituted carbocycle or an optionally substituted heterocycle which has 1, 2 or 3 different or identical heteroatoms from the group of O, N, S as ring members, where

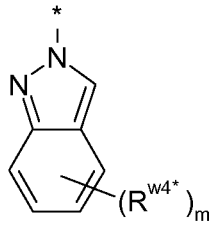
R^{wa} has one of the meanings indicated for R^{1a},
R^{wb} has one of the meanings indicated for R^{1b},
R^{wd} has one of the meanings indicated for R^{1d},
R^{w1} has one of the meanings indicated for R^{c1},
R^{w2} has one of the meanings indicated for R^{c2},
R^{w3} has one of the meanings indicated for R^{c3},
R^{w4} has one of the meanings indicated for R^{c4},
R^{w5} has one of the meanings indicated for R^{c5},
R^{w6} has one of the meanings indicated for R^{c6},
R^{w7} has one of the meanings indicated for R^{c7},

or

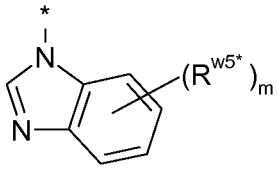
W forms together with R^2 a bi- or tricyclic radical of the formulae W3, W4, W5, W6, W7 or W8 which is linked via nitrogen:



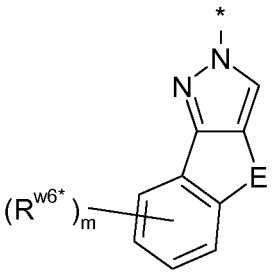
(W3)



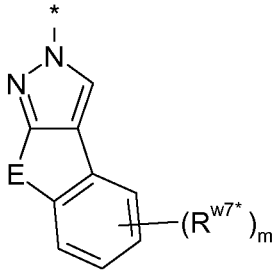
(W4)



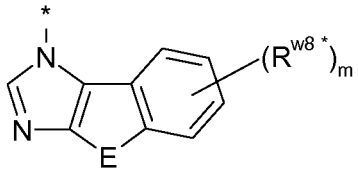
(W5)



(W6)



(W7)



(W8)

in which

* means the linkage to Y,

m is 0, 1 or 2, and

R^{w3*}, R^{w4*}, R^{w5*}, R^{w6*}, R^{w7*} and R^{w8*} have independently of one another one of the meanings indicated for R^w,

E has one of the following meanings: $-CR_E^2R_E^3-$, $-CHR_E^2-CHR_E^3$, $CH_2-CH_2-CH_2-$, $-CO-$, $-CO-NR_E^1-$, $-NR_E^1-CO-$, $-O-$, $-CH_2-O-$, $-O-CH_2-$, $-S-$, $-S-CH_2-$, $-CH_2-S-$, $-SO-$, CH_2-SO-, $-SO-CH_2-$, $-SO_2-$, $-CH_2-SO_2-$, $-SO_2-CH_2-$, $-NR_E^1-$, $-NR_E^1-CH_2-$, $-CH_2-NR_E^1$, $-SO_2-NR_E^1-$, $-NR_E^1-SO_2-$, $-CO-O-$, $-O-CO-$, $-C(=CR_E^2R_E^3)-$, $-CR_E^2=CR_E^3-$, where

R_E^1 is H, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R_E^{1a}, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, CO-C_1-C_6-alkyl, CO-O-C_1-C_6-alkyl, SO_2-C_1-C_6-alkyl, aryl, hetaryl, aryl-C_1-C_4-alkyl, hetaryl-C_1-C_4-alkyl, CO-aryl, CO-hetaryl, CO-(aryl-C_1-C_4-alkyl), CO-(hetaryl-C_1-C_4-alkyl), CO-O-aryl, CO-O-hetaryl, CO-O-(aryl-C_1-C_4-alkyl), CO-O-(hetaryl-C_1-C_4-alkyl), SO_2-aryl, SO_2-hetaryl, SO_2-(aryl-C_1-C_4-alkyl) or SO_2-(hetaryl-C_1-C_4-alkyl), where aryl and hetaryl in the last 16 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R_E^{1d}, and

R_E^2, R_E^3 are independently of one another selected from hydrogen, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_2-C_6-alkenyl, C_2-C_6-alkynyl, where the last 4 radicals mentioned may be partly or completely halogenated and/or have 1, 2 or 3 substituents R_E^{1a}, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-cycloalkyl-O, where a CH_2 group in the cycloalkyl moiety of the last three radicals

mentioned may be replaced by O, NH, or S, or two adjacent C atoms may form a double bond, where the cycloalkyl moiety may further have 1, 2, 3 or 4 R_E^{1b} radicals,
aryl, hetaryl, aryl-C_1-C_6-alkyl, or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 4 radicals mentioned may be unsubstituted or carry 1, 2, 3 or 4 identical or different radicals R_E^{1d}; and where

R_E^{1a} has one of the meanings indicated for R^{1a}, R_E^{1b} has one of the meanings indicated for R^{1b}, and R_E^{1d} has one of the meanings indicated for R^{1d};

and the tautomers thereof, the prodrugs thereof and the pharmaceutically suitable salts thereof.

2. The carboxamide compound as claimed in claim 1, in which W is a radical of the formulae W1 or W2, or the group W-R^2 is W6.

3. The carboxamide compound as claimed in claim 2, in which m is 0 or 1 and, when m = 1, R^w is selected from OH, F, Cl, CN, CF_3, C_1-C_6-alkyl which is unsubstituted or may have 1, 2 or 3 substituents R^{wa}, or C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy and C_3-C_7-cycloalkyl.

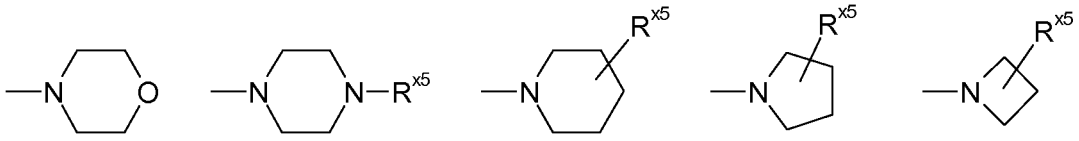
4. The carboxamide compound as claimed in any of the preceding claims, in which X in the formula I is a C(=O)-$NR^{x2}R^{x3}$ radical in which R^{x2} and R^{x3} have one of the aforementioned meanings.

5. The carboxamide compound as claimed in claim 4, in which

R^{x2} is H, OH, CN, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{xa}, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_4-alkyl, C_3-C_7-heterocycloalkyl-C_1-C_4-alkyl, C_1-C_6-alkoxy-C_1-C_4-alkyl, aryl, hetaryl, aryl-C_1-C_4-alkyl or hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 4 radicals mentioned are unsubstituted or have 1, 2 or 3 substituents R^{xd}, and

R^{x3} is H, C_1-C_6-alkyl, C_1-C_6-haloalkyl or C_1-C_6-alkyl which has 1, 2 or 3 substituents R^{xa}, or

$NR^{x2}R^{x3}$ is a nitrogen heterocycle of the following formulae:



in which R^{x5} is hydrogen or has the meaning indicated in claim 1 for R^{xb}.

6. The carboxamide compound as claimed in claim 5, in which X is $C(O)-NH_2$.

7. The carboxamide compound as claimed in any of the preceding claims, in which R^1 is selected from
C_1-C_{10}-alkyl which may be partly or completely halogenated and/or have 1, 2 or 3 substituents R^{1a},
C_3-C_7-cycloalkyl-C_1-C_4-alkyl, where the cycloalkyl moiety may have 1, 2, 3 or 4 radicals R^{1b},
phenyl-C_1-C_4-alkyl and hetaryl-C_1-C_4-alkyl, where phenyl and hetaryl in the last 2 radicals mentioned may be unsubstituted or carry 1, 2, 3 or 4 identical or different radicals R^{1c}.

8. The carboxamide compound as claimed in any of the preceding claims, in which R^2 is different from hydrogen.

9. The carboxamide compound as claimed in claim 8, in which R^2 is selected from:
C_1-C_{10}-alkyl which may be partly or completely halogenated and/or have 1, 2 or 3 substituents R^{2a},
aryl, hetaryl, aryl-C_1-C_6-alkyl, aryl-C_2-C_6-alkenyl and hetaryl-C_1-C_4-alkyl, where aryl and hetaryl in the last 5 radicals mentioned may be unsubstituted or carry 1, 2, 3 or 4 identical or different radicals R^{2c}.

10. The carboxamide compound as claimed in claim 9, in which R^2 is selected from aryl and hetaryl, where aryl and hetaryl may be unsubstituted or carry 1, 2, 3 or 4 identical or different radicals R^{2c}.

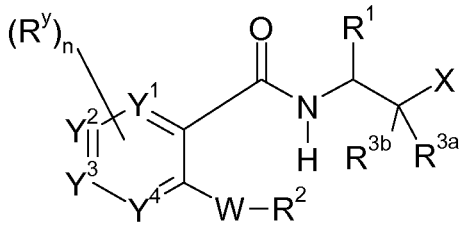
11. The carboxamide compound as claimed in any of the preceding claims, in which Y in the formula I is a divalent heteroaromatic radical which is selected from pyridindiyl and pyrimidindiyl and optionally has 1 or 2 identical or different substituents R^y.

12. The carboxamide compound as claimed in any of the preceding claims, in which R^y is selected from OH, F, Cl, NH_2, CN, CF_3, $-CHF_2$, $O-CF_3$, $O-CHF_2$, $O-CH_2F$, C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_1-C_6-alkylamino, C_1-C_6-dialkylamino, pyrrolidinyl, piperidinyl, morpholinyl, imidazolyl, C_1-C_4-alkoxy, C_1-C_4-alkoxy-C_1-C_4-alkyl, $CONR^{y2}R^{y3}$, $SO_2NR^{y2}R^{y3}$, $-NH-SO_2-R^{y4}$, $-(CH_2)_p-NR^{y6}R^{y7}$, $NH-CO-R^{y5}$, in which p is 1, 2, 3, 4, or 5, and R^{y2}, R^{y3}, R^{y4}, R^{y5}, R^{y6}, R^{y7} are H or C_1-C_6-alkyl,
phenyl, benzyl and O-benzyl, where the phenyl ring in the last 3 groups mentioned may have 1, 2 or 3 substituents selected from halogen, OH, SH, NO_2, COOH, $C(O)NH_2$, CHO, CN, NH_2, OCH_2COOH, C_1-C_6-alkyl, C_1-C_6-haloalkyl,

C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_1-C_6-alkylthio, C_1-C_6-haloalkylthio, CO-C_1-C_6-alkyl, CO-O-C_1-C_6-alkyl, NH-C_1-C_6-Alkyl, NHCHO, NH-C(O)C_1-C_6-alkyl, and SO_2-C_1-C_6-alkyl.

13. The carboxamide compound as claimed in any of the preceding claims, in which W is bonded to a C atom of Y which is located in the position ortho to the C atom of Y which is connected to the carbonyl group.

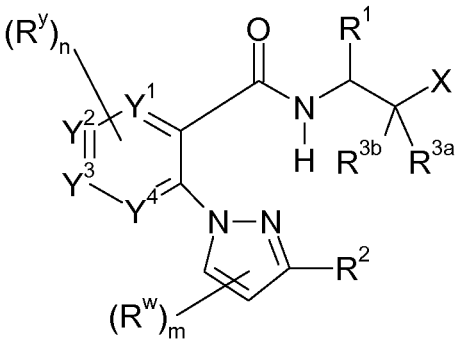
14. The carboxamide compound as claimed in any of the preceding claims, which corresponds to the formula I-A



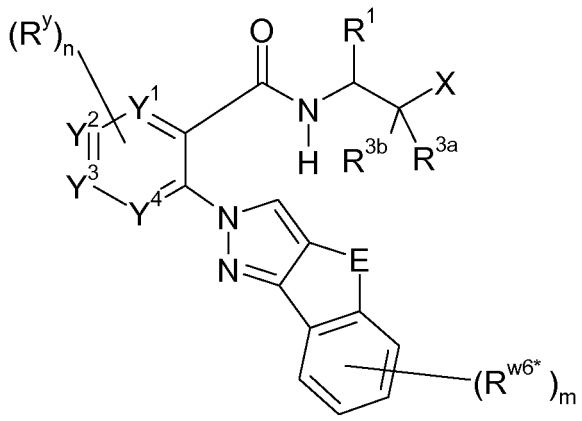
(I-A)

in which X, W, R^1, R^2, R^{3a}, R^{3b}, R^y have the aforementioned meanings, n is 0, 1 or 2, one of the variables Y^1, Y^2, Y^3 and Y^4 is a nitrogen atom, and the remaining variables Y^1, Y^2, Y^3 or Y^4 are CH, the tautomers thereof, the prodrugs thereof and the pharmaceutically suitable salts thereof.

15. The carboxamide compound as claimed in any of the preceding claims, which corresponds to the formulae I-A' or I-A",



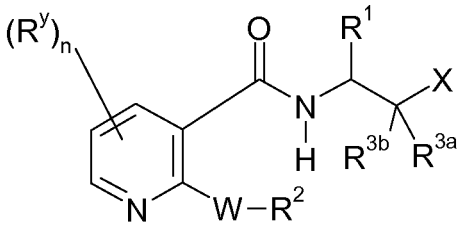
(I-A')



I-A"

in which m, E, X, R^1, R^2, R^{3a}, R^{3b}, R^y, R^w and R^{w6*} have the aforementioned meanings, n is 0, 1 or 2, one of the variables Y^1, Y^2, Y^3 and Y^4 is a nitrogen atom, and the remaining variables Y^1, Y^2, Y^3 and Y^4 are CH, the tautomers thereof, the prodrugs thereof and the pharmaceutically suitable salts thereof.

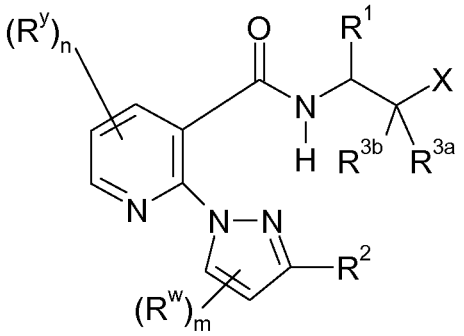
16. The carboxamide compound as claimed in any of the preceding claims, which corresponds to the formula I-A.a,



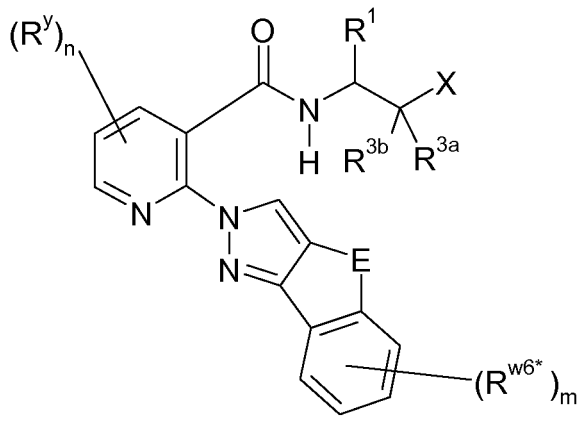
(I-A.a)

in which X, W, R^1, R^2, R^{3a}, R^{3b}, R^y have the aforementioned meanings, and n is 0, 1 or 2, the tautomers thereof, the prodrugs thereof and the pharmaceutically suitable salts thereof.

17. The carboxamide compound as claimed in claim 16, which corresponds to the formulae I-A.a' or I-A.a"



(I-A.a')



I-A.a"

in which m, E, R^1, R^{3a}, R^{3b}, R^2, R^y, R^w and R^{w6*} have the aforementioned meanings, n is 0, 1 or 2, the tautomers thereof, the prodrugs thereof and the pharmaceutically suitable salts thereof.

18. The carboxamide compound as claimed in any of the preceding claims, which has the S configuration at the carbon atom carrying the group R^1.

19. The carboxamide compound as claimed in any of the preceding claims, which has a Ki of $\leq$ 100 nM in vitro for the inhibition of calpain.

20. The carboxamide compound as claimed in any of the preceding claims, which has a selectivity in vitro in relation to the inhibition of cathepsin B (ratio of Ki for cathepsin B to Ki for calpain) of > 10.

21. The carboxamide compound as claimed in any of the preceding claims, which has a selectivity in vitro in relation to the inhibition of cathepsin K (ratio of Ki for cathepsin K to Ki for calpain) of > 10.

22. The carboxamide compound as claimed in any of the preceding claims, which has a selectivity in vitro in relation to the inhibition of cathepsin L (ratio of Ki for cathepsin L to Ki for calpain) of > 30.

23. The carboxamide compound as claimed in any of the preceding claims, which has a selectivity in vitro in relation to the inhibition of cathepsin S (ratio of Ki for cathepsin S to Ki for calpain) of > 50.

24. The use of carboxamide compounds as claimed in any of the preceding claims, the tautomers thereof, the prodrugs thereof and the pharmaceutically suitable salts thereof for the manufacture of a medicament.

25. A medicament comprising at least one carboxamide compound as claimed in any

of claims 1 to 23, a tautomer, a prodrug or a pharmaceutically suitable salt thereof.

26. The use of carboxamide compounds as claimed in any of claims 1 to 23, the tautomers thereof, the prodrugs thereof and the pharmaceutically suitable salts thereof for the treatment of a disorder, an impairment or a condition which is associated with an elevated calpain activity.

27. The use of carboxamide compounds as claimed in any of claims 1 to 23, the tautomers thereof, the prodrugs thereof and the pharmaceutically suitable salts thereof for the treatment of neurodegenerative disorders or impairments.

28. The use as claimed in claim 27, where a neurodegenerative disorder occurring as a result of a chronic brain supply deficit, an ischemia or a trauma is involved.

29. The use as claimed in claim 27 for the treatment of Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis or Huntington's disease.

30. The use as claimed in claim 27 for the treatment of multiple sclerosis and concomitant damage to the nervous system.

31. The use of carboxamide compounds as claimed in any of claims 1 to 23, the tautomers thereof, the prodrugs thereof and the pharmaceutically suitable salts thereof for the treatment of epilepsy.

32. The use of carboxamide compounds as claimed in any of claims 1 to 23, the tautomers thereof, the prodrugs thereof and the pharmaceutically suitable salts thereof for the treatment of pain.

33. The use of carboxamide compounds as claimed in any of claims 1 to 23, the tautomers thereof, the prodrugs thereof and the pharmaceutically suitable salts thereof for the treatment of damage to the heart following cardiac ischemias, damage to the kidneys following renal ischemias, skeletal muscle damage, muscular dystrophies, damage resulting from proliferation of smooth muscle cells, coronary vasospasms, cerebral vasospasms, macular degeneration, cataracts of the eyes, or restenosis of the blood vessels following angioplasty.

34. The use of carboxamide compounds as claimed in any of claims 1 to 23, the tautomers thereof, the prodrugs thereof and the pharmaceutically suitable salts thereof for the chemotherapy of tumors and metastasis thereof.

35. The use of carboxamide compounds as claimed in any of claims 1 to 23, the

tautomers thereof, the prodrugs thereof and the pharmaceutically suitable salts thereof for the treatment of HIV patients.

36. The use of carboxamide compounds as claimed in any of claims 1 to 23, the tautomers thereof, the prodrugs thereof and the pharmaceutically suitable salts thereof for the treatment of a disorder or an impairment associated with an elevated interleukin-I, TNF or Aß level.

37. A method for the therapeutic and/or prophylactic treatment of a mammal requiring a treatment, by administering an effective amount of at least one compound as claimed in any of claims 1 to 23 for the treatment of a disease, of a condition or of an impairment as set forth in any of claims 26 to 36.

38. The carboxamide compound as claimed in any of claims 1 to 23 for use in therapy.

39. The carboxamide compound as claimed in any of claims 1 to 23 for use in therapy of a disorder, an impairment or a condition which is associated with an elevated calpain activity.

40. The carboxamide compound as claimed in any of claims 1 to 23 for use in therapy of a disorder, an impairment or a condition as set forth in any of claims 26 to 36.