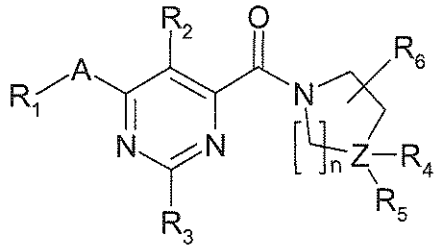
Summary

In a first aspect, there is provided compounds according to formula (I),



(I)

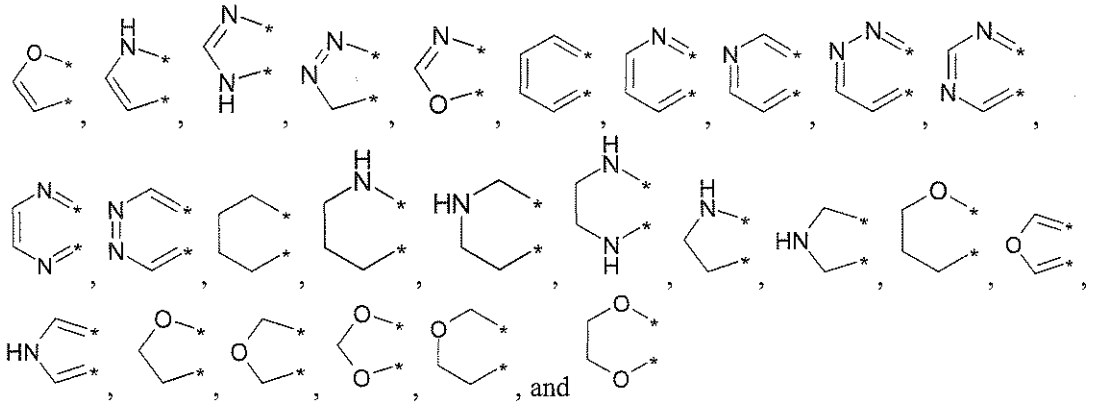
wherein

R_1 is $-L_1-R_7$, and wherein L_1 is a bond or a group selected from among methylene, ethylene, and ethenylene, and wherein R_7 is a ring selected from among cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, pyrrolidinyl, piperidinyl, azepanyl, tetrahydrofuranyl, tetrahydropyranyl, oxepanyl, phenyl, pyridyl, and furanyl,

wherein L_1 if different from a bond is optionally substituted with one or more groups selected from among methyl, and ethyl,

wherein the ring R_7 is optionally substituted with one or more groups selected from among -F, -Cl, -methyl, -ethyl, -propyl, -i-propyl, -cyclopropyl, -t-butyl, $-CF_3$, $-O-CF_3$, -CN, -O-methyl, furanyl and phenyl, wherein said furanyl and said phenyl are optionally independently substituted by one or more groups selected from among $-C_1-C_3$-alkyl, halogen, $-OCH_3$, $-CF_3$, and $-OCF_3$,

or wherein the ring R_7 is bi-valently substituted by one or more groups selected from among



on two neighbouring ring atoms, such that an annellated ring is formed.

wherein R_2 is selected from among -H, -halogen, -CN, -O-C_1-C_4-alkyl, -C_1-C_4-alkyl, -CH=CH_2, -C≡CH, -CF_3, -OCF_3, -OCF_2H, and -$OCFH_2$;

wherein R_3 is selected from among -H, -methyl, -ethyl, -propyl, -i-propyl, -cyclopropyl, -OCH_3, and –CN;

wherein R_4 and R_5 are independently selected from among an electron pair, -H, and a group selected from among -C_1-C_6-alkyl, -NH_2, -C_3-C_8-cycloalkyl, -C_3-C_8-heterocyclyl, -C_5-C_{10}-aryl, -C_5-C_{10}-heteroaryl, and -C(O)-N(R_8,$R_{8'}$), with R_8 and $R_{8'}$ independently being selected from among -H, and -C_1-C_6-alkyl,

and wherein R_4 and R_5 if different from an electron pair or -H are optionally independently substituted with one or more groups selected from among -halogen, -OH, -CF_3, -CN, -C_1-C_6-alkyl, -O-C_1-C_6-alkyl, -O-C_3-C_8-cycloalkyl, -O-C_3-C_8-heterocyclyl, -O-C_5-C_{10}-aryl, -O-C_5-C_{10}-heteroaryl, -C_0-C_6-alkylene-CN, -C_0-C_4-alkylene-O-C_1-C_4-alkyl, -C_0-C_4-alkylene-O-C_3-C_8-cycloalkyl, -C_0-C_4-alkylene-O-C_3-C_8-heterocyclyl, -C_0-C_4-alkylene-O-C_5-C_{10}-aryl, -C_0-C_4-alkylene-O-C_5-C_{10}-heteroaryl, -C_0-C_4-alkylene-Q-C_0-C_4-alkyl-N(R_9,$R_{9'}$), -C_0-C_4-alkylene-N(R_{10})-Q-C_1-C_4-alkyl, -C_0-C_4-alkylene-N(R_{10})-Q-C_3-C_8-cycloalkyl, -C_0-C_4-alkylene-N(R_{10})-Q-C_3-C_8-heterocyclyl, -C_0-C_4-alkylene-N(R_{10})-Q-C_5-C_{10}-aryl, -C_0-C_4-alkylene-N(R_{10})-Q-C_5-C_{10}-heteroaryl, -C_0-C_4-alkylene-Q-N(R_{11},$R_{11'}$), -C_0-C_4-alkylen-N(R_{12})-Q-N(R_{13},$R_{13'}$), -C_0-C_4-alkylen-R_{14}, -C_0-C_4-alkylene-Q-C_1-C_6-alkyl, -C_0-C_4-alkylene-Q-C_3-C_8-cycloalkyl, -C_0-C_4-alkylene-Q-C_3-C_8-heterocyclyl, -C_0-C_4-alkylene-Q-C_5-C_{10}-aryl, -C_0-C_4-alkylene-Q-C_5-C_{10}-heteroaryl, -C_0-C_4-alkylene-O-Q-N(R_{15},$R_{15'}$), and -C_0-C_4-alkylene-N(R_{16})-Q-O-(R_{17}),

wherein Q is selected from among -C(O)-, and -SO_2-,

wherein R_{12}, R_{16}, are independently selected from among -H, -C_1-C_6-alkyl, and -C_3-C_6-cycloalkyl,

wherein R_9, $R_{9'}$, R_{10}, R_{11}, $R_{11'}$, R_{13}, $R_{13'}$, R_{15}, $R_{15'}$, are independently selected from among -H, -C_1-C_6-alkyl, and -C_3-C_6-cycloalkyl,

or wherein R_9 and $R_{9'}$, R_{11} and $R_{11'}$, R_{13} and $R_{13'}$, R_{15} and $R_{15'}$ together form a –C_2-C_6-alkylene group,

wherein R_{14} and R_{17} are independently selected from among -H, -C_1-C_6-alkyl, -C_5-C_{10}-aryl, -C_5-C_{10}-heteroaryl, -C_3-C_8-cycloalkyl, and -C_3-C_8-heterocyclyl, wherein said -C_3-C_8-heterocyclyl optionally comprises nitrogen and/or -SO_2- in the ring,

and wherein R_{14} and R_{17} are optionally substituted with one or more groups selected from among -OH, -OCH_3, -CF_3, -OCF_3, -CN, -halogen, -C_1-C_4-alkyl, =O, and -SO_2-C_1-C_4-alkyl,

or wherein R_4 and / or R_5 are independently a group of the structure -L_2-R_{18},

wherein L_2 is selected from among -NH- and -N(C_1-C_4-alkyl)-,

wherein R_{18} is selected from among -C_5-C_{10}-aryl, -C_5-C_{10}-heteroaryl, -C_3-C_8-cycloalkyl, and -C_3-C_8-heterocyclyl,

wherein R_{18} is optionally substituted by one or more groups selected from among halogen, -CF_3, -OCF_3, -CN, -OH, -O-C_1-C_4-alkyl, -C_1-C_6-alkyl, -NH-C(O)-C_1-C_6-alkyl, -N(C_1-C_4-alkyl)-C(O)-C_1-C_6-alkyl, -C(O)-C_1-C_6-alkyl, -S(O)$_2$-C_1-C_6-alkyl, -NH-S(O)$_2$-C_1-C_6-alkyl, -N(C_1-C_4-alkyl)-S(O)$_2$-C_1-C_6-alkyl, and -C(O)-O-C_1-C_6-alkyl,

and wherein R_4, R_5 and R_{18} are optionally further substituted by spiro-C_3-C_8-cycloalkyl or spiro-C_3-C_8-heterocyclyl such that together with R_4, R_5 and/or R_{18} a spirocycle is formed, wherein said spiro-C_3-C_8-heterocyclyl optionally comprises one or more groups selected from among nitrogen, -C(O)-, -SO_2-, and -N(SO_2-C_1-C_4-alkyl)- in the ring,

or wherein R_4, R_5 and R_{18} are optionally further bi-valently substituted by one or more spirocyclic or annellated ring forming groups selected from among -C_1-C_6-alkylene, -C_2-C_6-alkenylene, and -C_4-C_6-alkynylene, in which one or two carbon centers may optionally be replaced by one or two hetero atoms selected from among N, O and S and which may optionally be substituted by one or more groups on one ring atom or on two neighbouring ring atoms selected from among -OH, -NH_2, -C_1-C_3-alkyl, O-C_1-C_6-alkyl, -CN, -CF_3, -OCF_3, and halogen;

wherein R_6 is selected from among -H, -C_1-C_4-alkyl, -OH, -O-C_1-C_4-alkyl, -halogen, -CN, -CF_3, and -OCF_3;

wherein A is selected from among a single bond, -CH_2-, -O-, -S-, and -NH-;

wherein n is 1, 2 or 3;

wherein Z is C or N,

as well as in form of their acid addition salts with pharmacologically acceptable acids.

In a second aspect, there is provided a compound as defined herein for use as a medicament.

In a third aspect, there is provided the compound as defined herein for use in the treatment of osteoarthritis, diabetic nephropathy, low back pain, neuropathic pain or a pain disease.

In a fourth aspect, there is provided the use of the compound as defined herein in the manufacture of a medicament for the treatment of osteoarthritis, diabetic nephropathy, low back pain, neuropathic pain or a pain disease.