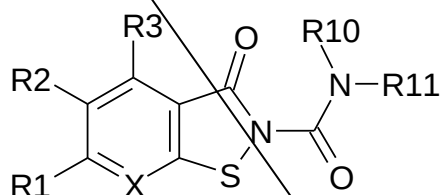


Claims

1. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof,



I

wherein

X is selected from the series consisting of =N- and =N(O)-;

R1, R2 and R3 are independently of one another selected from the series consisting of hydrogen, halogen, (C₁-C₄)-alkyl, (C₁-C₄)-alkyl-O-, nitro, cyano, (C₁-C₄)-alkyl-O-C(O)-, R₄-N(R₅)-C(O)- and R₆-N(R₇)-S(O)₂-;

R₄ is selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl, (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-, phenyl, phenyl-(C₁-C₄)-alkyl-, Het1 and Het1-(C₁-C₄)-alkyl-, wherein Het1 is optionally substituted by one or more identical or different substituents R₈;

R₅, R₆ and R₇ are independently of one another selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl and (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-;

R₈ is selected from the series consisting of halogen, (C₁-C₄)-alkyl, hydroxy, oxo, (C₁-C₄)-alkyl-O- and cyano;

R10 is selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl, (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl- and (C₁-C₄)-alkyl-O-(C₁-C₄)-alkyl-, with the proviso that R10 can only be hydrogen if X is =N(O)-;

5 R11 is selected from the series consisting of (C₁-C₄)-alkyl which is optionally substituted by one or more identical or different substituents R12, (C₃-C₇)-cycloalkyl which is optionally substituted by one or more identical or different substituents R13, and Het2 which is optionally substituted by one or more identical or different substituents R14 and wherein Het2 is bonded via a ring carbon atom;

10 or the groups R10 and R11, together with the nitrogen atom carrying them, form a 4-membered to 12-membered, monocyclic or bicyclic, saturated or partially unsaturated heterocycle which, in addition to the nitrogen atom carrying R10 and R11, comprises 0, 1 or 2 further ring heteroatoms selected from the series consisting of nitrogen,
 15 oxygen and sulfur, which is optionally substituted on ring carbon atoms by one or more identical or different substituents R30, and which is optionally substituted on further ring nitrogen atoms by one or more identical or different substituents R40;

R12 is selected from the series consisting of (C₃-C₇)-cycloalkyl, phenyl, Het3,
 20 hydroxy, (C₁-C₄)-alkyl-O-, (C₁-C₄)-alkyl-C(O)-O-, R15-N(R16)- and R17-C(O)-N(R18)-, wherein phenyl and Het3 independently of one another are optionally substituted by one or more identical or different substituents R19;

R13 is selected from the series consisting of hydroxy, (C₁-C₄)-alkyl-O-, (C₁-C₄)-alkyl-
 25 C(O)-O- and cyano;

R14 is selected from the series consisting of fluorine, (C₁-C₄)-alkyl, hydroxy, (C₁-C₄)-alkyl-O-, (C₁-C₄)-alkyl-C(O)-O-, HO-(C₁-C₄)-alkyl-, (C₁-C₄)-alkyl-O-(C₁-C₄)-alkyl-, (C₁-C₄)-alkyl-C(O)-O-(C₁-C₄)-alkyl- and (C₁-C₄)-alkyl-C(O)-;

30

R15, R16 and R18 are independently of one another selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl and (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-;

5 R17 is selected from the series consisting of (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl, (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-, phenyl and phenyl-(C₁-C₄)-alkyl-;

R19 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, hydroxy, (C₁-C₄)-alkyl-O-, (C₁-C₄)-alkyl-C(O)-O-, cyano, R20-O-C(O)- and R21-N(R22)-C(O)-;

10

R20, R21 and R22 are independently of one another selected from the series consisting of hydrogen and (C₁-C₄)-alkyl;

15 R30 is selected from the series consisting of fluorine, (C₁-C₄)-alkyl, Het2, hydroxy, oxo, (C₁-C₄)-alkyl-O-, R31-N(R32)-, (C₁-C₄)-alkyl-C(O)-, R33-O-C(O)- and R34-N(R35)-C(O)-, wherein Het2 is optionally substituted by one or more identical or different substituents R36;

20 R31, R32, R33, R34 and R35 are independently of one another selected from the series consisting of hydrogen and (C₁-C₄)-alkyl;

R36 is selected from the series consisting of fluorine, (C₁-C₄)-alkyl, hydroxy and oxo;

25 R40 is selected from the series consisting of (C₁-C₄)-alkyl which is optionally substituted by one or more identical or different substituents R41, (C₃-C₇)-cycloalkyl which is optionally substituted by one or more identical or different substituents R42, phenyl which is optionally substituted by one or more identical or different substituents R43, Het1 which is optionally substituted by one or more identical or different substituents R44, (C₁-C₄)-alkyl-C(O)- which is optionally substituted by one or more identical or different substituents R45, (C₃-C₇)-cycloalkyl-C(O)- which is optionally substituted by one or more identical or different substituents R46, phenyl-

30

C(O)- which is optionally substituted by one or more identical or different substituents R47, Het3-C(O)- which is optionally substituted by one or more identical or different substituents R48 and wherein Het3 is bonded via a ring carbon atom, R49-N(R50)-C(O)-, (C₁-C₄)-alkyl-S(O)₂- and R51-N(R52)-S(O)₂-;

5

R41 is selected from the series consisting of (C₃-C₇)-cycloalkyl, hydroxy, (C₁-C₄)-alkyl-O-, R60-N(R61)-, R62-O-C(O)- and R63-N(R64)-C(O)-;

R42 is selected from the series consisting of hydroxy and R65-N(R66)-;

10

R43 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, hydroxy, (C₁-C₄)-alkyl-O-, cyano, R67-O-C(O)- and R68-N(R69)-C(O)-;

R44 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, hydroxy, oxo, (C₁-C₄)-alkyl-O-, R70-N(R71)-, (C₁-C₄)-alkyl-C(O)-N(R72)-, (C₁-C₄)-alkyl-S(O)₂-N(R73)- and Het4, wherein Het4 is optionally substituted by one or more identical or different substituents R74;

15

R45 is selected from the series consisting of (C₃-C₇)-cycloalkyl, cyano, hydroxy, (C₁-C₄)-alkyl-O-, phenyl-O-, phenyl-(C₁-C₄)-alkyl-O-, oxo, R75-N(R76)- and R77-C(O)-N(R78)-;

20

R46 is selected from the series consisting of hydroxy and R79-N(R80)-;

R47 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, (C₁-C₄)-alkyl-O- and R81-N(R82)-C(O)-;

25

R48 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, hydroxy, oxo and (C₁-C₄)-alkyl-O-;

30

R49 and R51 are independently of one another selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl, (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-, phenyl and phenyl-(C₁-C₄)-alkyl-;

- 5 R50 and R52 are independently of one another selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl and (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-;

- 10 R60, R61, R62, R63, R64, R65, R66, R67, R68, R69, R70, R71, R72, R73, R76, R78, R79, R80, R81, R82, R83 and R84 are independently of one another selected from the series consisting of hydrogen and (C₁-C₄)-alkyl;

R74 is selected from the series consisting of fluorine and (C₁-C₄)-alkyl;

- 15 R75 is selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl, (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-, phenyl and phenyl-(C₁-C₄)-alkyl-;

R77 is selected from the series consisting of (C₁-C₄)-alkyl and R83-N(R84)-(C₁-C₄)-alkyl-;

- 20 Het1 is a monocyclic, 4-membered to 7-membered, saturated, partially unsaturated or aromatic heterocycle which comprises 1, 2 or 3 identical or different ring heteroatoms selected from the series consisting of nitrogen oxygen and sulfur, and which is bonded via a ring carbon atom;

- 25 Het2 is a monocyclic, 4-membered to 7-membered, saturated heterocycle which comprises 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

- 30 Het3 is a monocyclic or bicyclic, 4-membered to 12-membered, saturated, partially unsaturated or aromatic heterocycle which comprises 1, 2 or 3 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

Het4 is a monocyclic, 4-membered to 7-membered, saturated heterocycle which comprises a ring nitrogen atom via which Het4 is bonded, and 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur;

5

wherein all phenyl groups are optionally substituted by one or more identical or different substituents selected from the series consisting of halogen, (C₁-C₄)-alkyl, cyano, hydroxy and (C₁-C₄)-alkyl-O-, unless specified otherwise;

10 wherein all cycloalkyl groups, independently of any other substituents which can be present on a cycloalkyl group, are optionally substituted by one or more identical or different substituents selected from the series consisting of fluorine and (C₁-C₄)-alkyl;

wherein all alkyl groups and alkyl groups which are part of another group,
15 independently of any other substituents which can be present on an alkyl group, are optionally substituted by one or more fluorine substituents;

with the proviso that the compound of the formula I is not 3-oxo-3H-isothiazolo[5,4-b]pyridine-2-carboxylic acid diethylamide.

20

2. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof, according to claim 1, wherein X is =N(O)-.

25 3. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof, according to any of claims 1 and 2, wherein R₁, R₂ and R₃ are independently of one another selected from the series consisting of hydrogen, halogen, (C₁-C₄)-alkyl, nitro, cyano, (C₁-C₄)-alkyl-O-C(O)- and R₄-N(R₅)-C(O)-.

30

4. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof, according to any of claims 1 to 3, wherein R1, R2 and R3 are independently of one another selected from the series consisting of hydrogen, halogen, (C₁-C₄)-alkyl and cyano.

5. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof, according to any of claims 1 to 4, wherein R10 is selected from the series consisting of (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl, (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl- and (C₁-C₄)-alkyl-O-(C₁-C₄)-alkyl-.

6. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof, according to any of claims 1 to 5, wherein

X is =N(O)-;

R1, R2 and R3 are independently of one another selected from the series consisting of hydrogen, halogen, (C₁-C₄)-alkyl and cyano;

R10 is selected from the series consisting of (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl, (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl- and (C₁-C₄)-alkyl-O-(C₁-C₄)-alkyl-.

7. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof, according to claim 1, wherein

X is selected from the series consisting of =N- and =N(O)-;

R1, R2 and R3 are independently of one another selected from the series consisting of hydrogen, halogen, (C₁-C₄)-alkyl, cyano, (C₁-C₄)-alkyl-O-C(O)- and R4-N(R5)-C(O)-;

- 5 R4 is selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl and (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-;

R5 is selected from the series consisting of hydrogen and (C₁-C₄)-alkyl;

- 10 R10 is selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl, (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl- and (C₁-C₄)-alkyl-O-(C₁-C₄)-alkyl-, with the proviso that R10 can only be hydrogen if X is =N(O)-;

- 15 R11 is selected from the series consisting of (C₁-C₄)-alkyl which is optionally substituted by one or more identical or different substituents R12, (C₃-C₇)-cycloalkyl which is optionally substituted by one or more identical or different substituents R13, and Het2 which is optionally substituted by one or more identical or different substituents R14 and wherein Het2 is bonded via a ring carbon atom;

- 20 or the groups R10 and R11, together with the nitrogen atom carrying them, form a 4-membered to 10-membered, monocyclic or bicyclic, saturated or partially unsaturated heterocycle which, in addition to the nitrogen atom carrying R10 and R11, comprises 0 or 1 further ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur, which is optionally substituted on ring carbon atoms by one or
25 more identical or different substituents R30, and which is optionally substituted on further ring nitrogen atoms by one or more identical or different substituents R40;

- 30 R12 is selected from the series consisting of phenyl, Het3, hydroxy, (C₁-C₄)-alkyl-O-, R15-N(R16)- and R17-C(O)-N(R18)-, wherein phenyl and Het3 independently of one another are optionally substituted by one or more identical or different substituents R19;

R13 is selected from the series consisting of hydroxy, (C₁-C₄)-alkyl-O- and cyano;

R14 is selected from the series consisting of (C₁-C₄)-alkyl, hydroxy, (C₁-C₄)-alkyl-C(O)-O-, HO-(C₁-C₄)-alkyl-, (C₁-C₄)-alkyl-C(O)-O-(C₁-C₄)-alkyl- and (C₁-C₄)-alkyl-C(O)-;

R15, R16 and R18 are independently of one another selected from the series consisting of hydrogen and (C₁-C₄)-alkyl;

R17 is selected from the series consisting of (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl and (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-;

R19 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, hydroxy, (C₁-C₄)-alkyl-O-, (C₁-C₄)-alkyl-C(O)-O-;

R30 is selected from the series consisting of fluorine, (C₁-C₄)-alkyl, Het2, hydroxy, oxo, (C₁-C₄)-alkyl-O-, R31-N(R32)-, (C₁-C₄)-alkyl-C(O)-, R33-O-C(O)- and R34-N(R35)-C(O)-, wherein Het2 is optionally substituted by one or more identical or different substituents R36;

R31, R32, R33, R34 and R35 are independently of one another selected from the series consisting of hydrogen and (C₁-C₄)-alkyl;

R36 is selected from the series consisting of fluorine, (C₁-C₄)-alkyl, hydroxy and oxo;

R40 is selected from the series consisting of (C₁-C₄)-alkyl which is optionally substituted by one or more identical or different substituents R41, (C₃-C₇)-cycloalkyl which is optionally substituted by one or more identical or different substituents R42, phenyl which is optionally substituted by one or more identical or different substituents R43, Het1 which is optionally substituted by one or more identical or

different substituents R44, (C₁-C₄)-alkyl-C(O)- which is optionally substituted by one or more identical or different substituents R45, (C₃-C₇)-cycloalkyl-C(O)- which is optionally substituted by one or more identical or different substituents R46, phenyl-C(O)- which is optionally substituted by one or more identical or different substituents
 5 R47, Het3-C(O)- which is optionally substituted by one or more identical or different substituents R48 and wherein Het3 is bonded via a ring carbon atom, R49-N(R50)-C(O)-, (C₁-C₄)-alkyl-S(O)₂- and R51-N(R52)-S(O)₂;

R41 is selected from the series consisting of (C₁-C₄)-alkyl-O-, R60-N(R61)-, R62-O-C(O)- and R63-N(R64)-C(O)-;
 10

R42 is selected from the series consisting of R65-N(R66)-;

R43 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, (C₁-C₄)-alkyl-O-, cyano, R67-O-C(O)- and R68-N(R69)-C(O)-;
 15

R44 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, hydroxy, oxo, (C₁-C₄)-alkyl-S(O)₂-N(R73)- and Het4, wherein Het4 is optionally substituted by one or more identical or different substituents R74;
 20

R45 is selected from the series consisting of cyano, (C₁-C₄)-alkyl-O-, phenyl-O-, phenyl-(C₁-C₄)-alkyl-O-, oxo, R75-N(R76)- and R77-C(O)-N(R78)-;
 25

R46 is selected from the series consisting of R79-N(R80)-;

R47 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, (C₁-C₄)-alkyl-O- and R81-N(R82)-C(O)-;
 30

R48 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, hydroxy and oxo;

R49 and R51 are independently of one another selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl and (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-;

R50 and R52 are independently of one another selected from the series consisting of hydrogen and (C₁-C₄)-alkyl;

R60, R61, R62, R63, R64, R65, R66, R67, R68, R69, R73, R76, R78, R79, R80, R81, R82, R83 and R84 are independently of one another selected from the series consisting of hydrogen and (C₁-C₄)-alkyl;

R74 is selected from the series consisting of fluorine and (C₁-C₄)-alkyl;

R75 is selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl and (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-;

R77 is selected from the series consisting of (C₁-C₄)-alkyl and R83-N(R84)-(C₁-C₄)-alkyl-;

Het1 is a monocyclic, 4-membered to 7-membered, saturated, partially unsaturated or aromatic heterocycle which comprises 1, 2 or 3 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur, and which is bonded via a ring carbon atom;

Het2 is a monocyclic, 4-membered to 7-membered, saturated heterocycle which comprises 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

Het3 is a monocyclic or bicyclic, 4-membered to 12-membered, saturated, partially unsaturated or aromatic heterocycle which comprises 1, 2 or 3 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

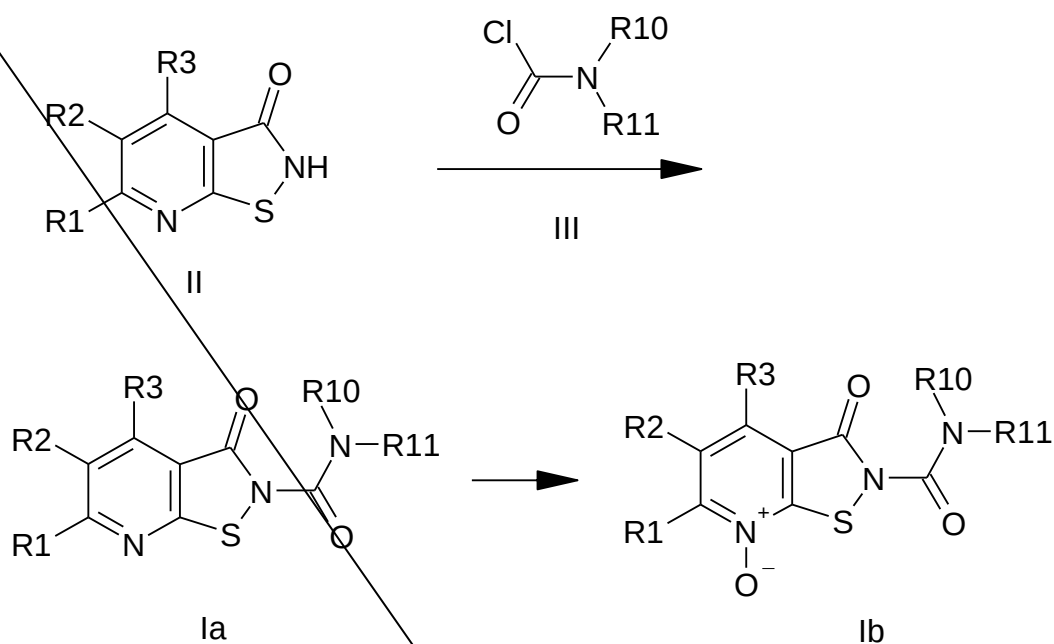
Het4 is a monocyclic, 4-membered to 7-membered, saturated heterocycle which comprises a ring nitrogen atom via which Het4 is bonded, and 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur;

- 5 wherein all phenyl groups are optionally substituted by one or more identical or different substituents selected from the series consisting of halogen, (C₁-C₄)-alkyl, cyano, hydroxy and (C₁-C₄)-alkyl-O-, unless specified otherwise;

- 10 wherein all cycloalkyl groups, independently of any other substituents which can be present on a cycloalkyl group, are optionally substituted by one or more identical or different substituents selected from the series consisting of fluorine and (C₁-C₄)-alkyl;

- 15 wherein all alkyl groups and alkyl groups which are part of another group, independently of any other substituents which can be present on an alkyl group, are optionally substituted by one or more fluorine substituents.

8. A process for the preparation of a compound of the formula I as claimed in any of claims 1 to 7, which comprises reacting a compound of the formula II with a compound of the formula III to give a compound of the formula I in which X is =N- (formula Ia) and, for the preparation of a compound of the formula I in which X is =N(O)- (formula Ib), oxidizing this compound, wherein the groups R₁, R₂, R₃, R₁₀ and R₁₁ in the compounds of the formulae II and III are defined as in the compounds of the formula I.
- 20



9. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof,
5 according to any of claims 1 to 7, for use as a pharmaceutical.

10. A pharmaceutical composition, comprising a compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof, according to any of claims 1 to 7, and a
10 pharmaceutically acceptable carrier.

11. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof, according to any of claims 1 to 7, for use as an inhibitor of transglutaminases or in
15 the treatment of degenerative joint diseases, degenerative intervertebral disk diseases, osteoarthritis, neurodegenerative diseases, cancer, celiac disease, fibrosis or liver cirrhosis.

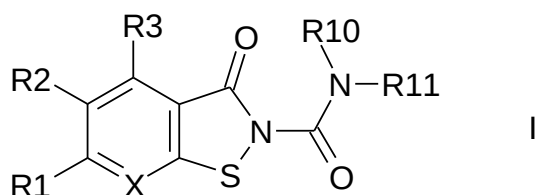
12. Use of a compound of the formula I, in any of its stereoisomeric forms or a
20 mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt

thereof, according to any of claims 1 to 7, for the manufacture of a medicament for the inhibition of transglutaminases or for the treatment of degenerative joint diseases, degenerative intervertebral disk diseases, osteoarthritis, neurodegenerative diseases, cancer, celiac disease, fibrosis or liver cirrhosis.

Claims

1. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof,

5



wherein

10 X is selected from the series consisting of =N- and =N(O)-;

R1, R2 and R3 are independently of one another selected from the series consisting of hydrogen, halogen, (C₁-C₄)-alkyl, (C₁-C₄)-alkyl-O-, nitro, cyano, (C₁-C₄)-alkyl-O-C(O)-, R4-N(R5)-C(O)- and R6-N(R7)-S(O)₂-;

15

R4 is selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl, (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-, phenyl, phenyl-(C₁-C₄)-alkyl-, Het1 and Het1-(C₁-C₄)-alkyl-, wherein Het1 is optionally substituted by one or more identical or different substituents R8;

20

R5, R6 and R7 are independently of one another selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl and (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-;

R8 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, hydroxy, oxo, (C₁-C₄)-alkyl-O- and cyano;

25

R10 is selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl, (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl- and (C₁-C₄)-alkyl-O-(C₁-C₄)-alkyl-, with the proviso that R10 can only be hydrogen if X is =N(O)-;

- 5 R11 is selected from the series consisting of (C₁-C₄)-alkyl which is optionally substituted by one or more identical or different substituents R12, (C₃-C₇)-cycloalkyl which is optionally substituted by one or more identical or different substituents R13, and Het2 which is optionally substituted by one or more identical or different substituents R14 and wherein Het2 is bonded via a ring carbon atom;

10 or the groups R10 and R11, together with the nitrogen atom carrying them, form a 4-membered to 12-membered, monocyclic or bicyclic, saturated or partially unsaturated heterocycle which, in addition to the nitrogen atom carrying R10 and R11, comprises 0, 1 or 2 further ring heteroatoms selected from the series consisting of nitrogen,
 15 oxygen and sulfur, which is optionally substituted on ring carbon atoms by one or more identical or different substituents R30, and which is optionally substituted on further ring nitrogen atoms by one or more identical or different substituents R40;

R12 is selected from the series consisting of (C₃-C₇)-cycloalkyl, phenyl, Het3,
 20 hydroxy, (C₁-C₄)-alkyl-O-, (C₁-C₄)-alkyl-C(O)-O-, R15-N(R16)- and R17-C(O)-N(R18)-, wherein phenyl and Het3 independently of one another are optionally substituted by one or more identical or different substituents R19;

R13 is selected from the series consisting of hydroxy, (C₁-C₄)-alkyl-O-, (C₁-C₄)-alkyl-
 25 C(O)-O- and cyano;

R14 is selected from the series consisting of fluorine, (C₁-C₄)-alkyl, hydroxy, (C₁-C₄)-alkyl-O-, (C₁-C₄)-alkyl-C(O)-O-, HO-(C₁-C₄)-alkyl-, (C₁-C₄)-alkyl-O-(C₁-C₄)-alkyl-, (C₁-C₄)-alkyl-C(O)-O-(C₁-C₄)-alkyl- and (C₁-C₄)-alkyl-C(O)-;

30

R15, R16 and R18 are independently of one another selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl and (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-;

- 5 R17 is selected from the series consisting of (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl, (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-, phenyl and phenyl-(C₁-C₄)-alkyl-;

R19 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, hydroxy, (C₁-C₄)-alkyl-O-, (C₁-C₄)-alkyl-C(O)-O-, cyano, R20-O-C(O)- and R21-N(R22)-C(O)-;

10

R20, R21 and R22 are independently of one another selected from the series consisting of hydrogen and (C₁-C₄)-alkyl;

- 15 R30 is selected from the series consisting of fluorine, (C₁-C₄)-alkyl, Het2, hydroxy, oxo, (C₁-C₄)-alkyl-O-, R31-N(R32)-, (C₁-C₄)-alkyl-C(O)-, R33-O-C(O)- and R34-N(R35)-C(O)-, wherein Het2 is optionally substituted by one or more identical or different substituents R36;

- 20 R31, R32, R33, R34 and R35 are independently of one another selected from the series consisting of hydrogen and (C₁-C₄)-alkyl;

R36 is selected from the series consisting of fluorine, (C₁-C₄)-alkyl, hydroxy and oxo;

- 25 R40 is selected from the series consisting of (C₁-C₄)-alkyl which is optionally substituted by one or more identical or different substituents R41, (C₃-C₇)-cycloalkyl which is optionally substituted by one or more identical or different substituents R42, phenyl which is optionally substituted by one or more identical or different substituents R43, Het1 which is optionally substituted by one or more identical or different substituents R44, (C₁-C₄)-alkyl-C(O)- which is optionally substituted by one or more identical or different substituents R45, (C₃-C₇)-cycloalkyl-C(O)- which is optionally substituted by one or more identical or different substituents R46, phenyl-
- 30

C(O)- which is optionally substituted by one or more identical or different substituents R47, Het3-C(O)- which is optionally substituted by one or more identical or different substituents R48 and wherein Het3 is bonded via a ring carbon atom, R49-N(R50)-C(O)-, (C₁-C₄)-alkyl-S(O)₂- and R51-N(R52)-S(O)₂-;

5

R41 is selected from the series consisting of (C₃-C₇)-cycloalkyl, hydroxy, (C₁-C₄)-alkyl-O-, R60-N(R61)-, R62-O-C(O)- and R63-N(R64)-C(O)-;

R42 is selected from the series consisting of hydroxy and R65-N(R66)-;

10

R43 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, hydroxy, (C₁-C₄)-alkyl-O-, cyano, R67-O-C(O)- and R68-N(R69)-C(O)-;

R44 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, hydroxy, oxo,

15

(C₁-C₄)-alkyl-O-, R70-N(R71)-, (C₁-C₄)-alkyl-C(O)-N(R72)-, (C₁-C₄)-alkyl-S(O)₂-N(R73)- and Het4, wherein Het4 is optionally substituted by one or more identical or different substituents R74;

R45 is selected from the series consisting of (C₃-C₇)-cycloalkyl, cyano, hydroxy, (C₁-C₄)-alkyl-O-, phenyl-O-, phenyl-(C₁-C₄)-alkyl-O-, oxo, R75-N(R76)- and R77-C(O)-N(R78)-;

20

R46 is selected from the series consisting of hydroxy and R79-N(R80)-;

25

R47 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, (C₁-C₄)-alkyl-O- and R81-N(R82)-C(O)-;

R48 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, hydroxy, oxo and (C₁-C₄)-alkyl-O-;

30

R49 and R51 are independently of one another selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl, (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-, phenyl and phenyl-(C₁-C₄)-alkyl-;

- 5 R50 and R52 are independently of one another selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl and (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-;

- R60, R61, R62, R63, R64, R65, R66, R67, R68, R69, R70, R71, R72, R73, R76, R78, R79, R80, R81, R82, R83 and R84 are independently of one another selected from
10 the series consisting of hydrogen and (C₁-C₄)-alkyl;

R74 is selected from the series consisting of fluorine and (C₁-C₄)-alkyl;

- R75 is selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl, (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-, phenyl and phenyl-(C₁-C₄)-alkyl-;
15

R77 is selected from the series consisting of (C₁-C₄)-alkyl and R83-N(R84)-(C₁-C₄)-alkyl-;

- 20 Het1 is a monocyclic, 4-membered to 7-membered, saturated, partially unsaturated or aromatic heterocycle which comprises 1, 2 or 3 identical or different ring heteroatoms selected from the series consisting of nitrogen oxygen and sulfur, and which is bonded via a ring carbon atom;

- 25 Het2 is a monocyclic, 4-membered to 7-membered, saturated heterocycle which comprises 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

- Het3 is a monocyclic or bicyclic, 4-membered to 12-membered, saturated, partially
30 unsaturated or aromatic heterocycle which comprises 1, 2 or 3 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

Het4 is a monocyclic, 4-membered to 7-membered, saturated heterocycle which comprises a ring nitrogen atom via which Het4 is bonded, and 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur;

5

wherein all phenyl groups are optionally substituted by one or more identical or different substituents selected from the series consisting of halogen, (C₁-C₄)-alkyl, cyano, hydroxy and (C₁-C₄)-alkyl-O-, unless specified otherwise;

10 wherein all cycloalkyl groups, independently of any other substituents which can be present on a cycloalkyl group, are optionally substituted by one or more identical or different substituents selected from the series consisting of fluorine and (C₁-C₄)-alkyl;

wherein all alkyl groups and alkyl groups which are part of another group,
15 independently of any other substituents which can be present on an alkyl group, are optionally substituted by one or more fluorine substituents;

with the proviso that the compound of the formula I is not 3-oxo-3H-isothiazolo[5,4-b]pyridine-2-carboxylic acid diethylamide.

20

2. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof, according to claim 1, wherein X is =N(O)-.

25 3. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof, according to any of claims 1 and 2, wherein R₁, R₂ and R₃ are independently of one another selected from the series consisting of hydrogen, halogen, (C₁-C₄)-alkyl, nitro, cyano, (C₁-C₄)-alkyl-O-C(O)- and R₄-N(R₅)-C(O)-.

30

4. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof, according to any of claims 1 to 3, wherein R1, R2 and R3 are independently of one another selected from the series consisting of hydrogen, halogen, (C₁-C₄)-alkyl and cyano.

5. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof, according to any of claims 1 to 4, wherein R10 is selected from the series consisting of (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl, (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl- and (C₁-C₄)-alkyl-O-(C₁-C₄)-alkyl-.

6. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof, according to any of claims 1 to 5, wherein

X is =N(O)-;

R1, R2 and R3 are independently of one another selected from the series consisting of hydrogen, halogen, (C₁-C₄)-alkyl and cyano;

R10 is selected from the series consisting of (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl, (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl- and (C₁-C₄)-alkyl-O-(C₁-C₄)-alkyl-.

7. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof, according to claim 1, wherein

X is selected from the series consisting of =N- and =N(O)-;

R1, R2 and R3 are independently of one another selected from the series consisting of hydrogen, halogen, (C₁-C₄)-alkyl, cyano, (C₁-C₄)-alkyl-O-C(O)- and R4-N(R5)-C(O)-;

- 5 R4 is selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl and (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-;

R5 is selected from the series consisting of hydrogen and (C₁-C₄)-alkyl;

- 10 R10 is selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl, (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl- and (C₁-C₄)-alkyl-O-(C₁-C₄)-alkyl-, with the proviso that R10 can only be hydrogen if X is =N(O)-;

- 15 R11 is selected from the series consisting of (C₁-C₄)-alkyl which is optionally substituted by one or more identical or different substituents R12, (C₃-C₇)-cycloalkyl which is optionally substituted by one or more identical or different substituents R13, and Het2 which is optionally substituted by one or more identical or different substituents R14 and wherein Het2 is bonded via a ring carbon atom;

- 20 or the groups R10 and R11, together with the nitrogen atom carrying them, form a 4-membered to 10-membered, monocyclic or bicyclic, saturated or partially unsaturated heterocycle which, in addition to the nitrogen atom carrying R10 and R11, comprises 0 or 1 further ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur, which is optionally substituted on ring carbon atoms by one or
25 more identical or different substituents R30, and which is optionally substituted on further ring nitrogen atoms by one or more identical or different substituents R40;

- 30 R12 is selected from the series consisting of phenyl, Het3, hydroxy, (C₁-C₄)-alkyl-O-, R15-N(R16)- and R17-C(O)-N(R18)-, wherein phenyl and Het3 independently of one another are optionally substituted by one or more identical or different substituents R19;

R13 is selected from the series consisting of hydroxy, (C₁-C₄)-alkyl-O- and cyano;

5 R14 is selected from the series consisting of (C₁-C₄)-alkyl, hydroxy, (C₁-C₄)-alkyl-C(O)-O-, HO-(C₁-C₄)-alkyl-, (C₁-C₄)-alkyl-C(O)-O-(C₁-C₄)-alkyl- and (C₁-C₄)-alkyl-C(O)-;

10 R15, R16 and R18 are independently of one another selected from the series consisting of hydrogen and (C₁-C₄)-alkyl;

R17 is selected from the series consisting of (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl and (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-;

15 R19 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, hydroxy, (C₁-C₄)-alkyl-O-, (C₁-C₄)-alkyl-C(O)-O-;

20 R30 is selected from the series consisting of fluorine, (C₁-C₄)-alkyl, Het2, hydroxy, oxo, (C₁-C₄)-alkyl-O-, R31-N(R32)-, (C₁-C₄)-alkyl-C(O)-, R33-O-C(O)- and R34-N(R35)-C(O)-, wherein Het2 is optionally substituted by one or more identical or different substituents R36;

R31, R32, R33, R34 and R35 are independently of one another selected from the series consisting of hydrogen and (C₁-C₄)-alkyl;

25 R36 is selected from the series consisting of fluorine, (C₁-C₄)-alkyl, hydroxy and oxo;

30 R40 is selected from the series consisting of (C₁-C₄)-alkyl which is optionally substituted by one or more identical or different substituents R41, (C₃-C₇)-cycloalkyl which is optionally substituted by one or more identical or different substituents R42, phenyl which is optionally substituted by one or more identical or different substituents R43, Het1 which is optionally substituted by one or more identical or

different substituents R44, (C₁-C₄)-alkyl-C(O)- which is optionally substituted by one or more identical or different substituents R45, (C₃-C₇)-cycloalkyl-C(O)- which is optionally substituted by one or more identical or different substituents R46, phenyl-C(O)- which is optionally substituted by one or more identical or different substituents
 5 R47, Het3-C(O)- which is optionally substituted by one or more identical or different substituents R48 and wherein Het3 is bonded via a ring carbon atom, R49-N(R50)-C(O)-, (C₁-C₄)-alkyl-S(O)₂- and R51-N(R52)-S(O)₂;

R41 is selected from the series consisting of (C₁-C₄)-alkyl-O-, R60-N(R61)-, R62-O-
 10 C(O)- and R63-N(R64)-C(O)-;

R42 is selected from the series consisting of R65-N(R66)-;

R43 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, (C₁-C₄)-alkyl-O-,
 15 cyano, R67-O-C(O)- and R68-N(R69)-C(O)-;

R44 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, hydroxy, oxo, (C₁-C₄)-alkyl-S(O)₂-N(R73)- and Het4, wherein Het4 is optionally substituted by one or more identical or different substituents R74;
 20

R45 is selected from the series consisting of cyano, (C₁-C₄)-alkyl-O-, phenyl-O-, phenyl-(C₁-C₄)-alkyl-O-, oxo, R75-N(R76)- and R77-C(O)-N(R78)-;

R46 is selected from the series consisting of R79-N(R80)-;
 25

R47 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, (C₁-C₄)-alkyl-O- and R81-N(R82)-C(O)-;

R48 is selected from the series consisting of halogen, (C₁-C₄)-alkyl, hydroxy and oxo;
 30

R49 and R51 are independently of one another selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl and (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-;

5 R50 and R52 are independently of one another selected from the series consisting of hydrogen and (C₁-C₄)-alkyl;

10 R60, R61, R62, R63, R64, R65, R66, R67, R68, R69, R73, R76, R78, R79, R80, R81, R82, R83 and R84 are independently of one another selected from the series consisting of hydrogen and (C₁-C₄)-alkyl;

R74 is selected from the series consisting of fluorine and (C₁-C₄)-alkyl;

15 R75 is selected from the series consisting of hydrogen, (C₁-C₄)-alkyl, (C₃-C₇)-cycloalkyl and (C₃-C₇)-cycloalkyl-(C₁-C₄)-alkyl-;

R77 is selected from the series consisting of (C₁-C₄)-alkyl and R83-N(R84)-(C₁-C₄)-alkyl-;

20 Het1 is a monocyclic, 4-membered to 7-membered, saturated, partially unsaturated or aromatic heterocycle which comprises 1, 2 or 3 identical or different ring heteroatoms selected from the series consisting of nitrogen oxygen and sulfur, and which is bonded via a ring carbon atom;

25 Het2 is a monocyclic, 4-membered to 7-membered, saturated heterocycle which comprises 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

30 Het3 is a monocyclic or bicyclic, 4-membered to 12-membered, saturated, partially unsaturated or aromatic heterocycle which comprises 1, 2 or 3 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

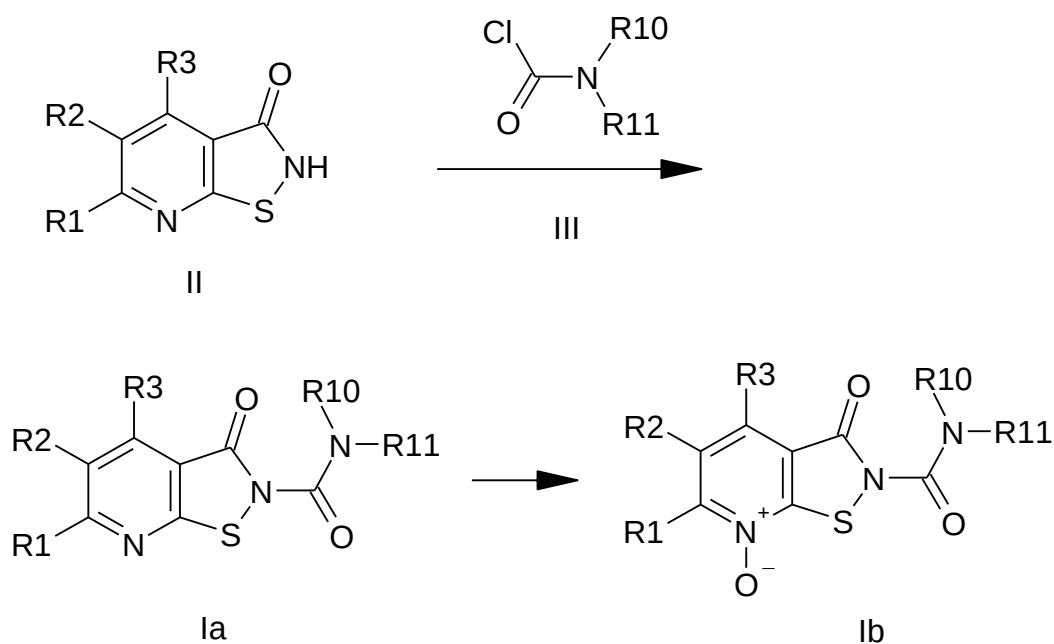
Het4 is a monocyclic, 4-membered to 7-membered, saturated heterocycle which comprises a ring nitrogen atom via which Het4 is bonded, and 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur;

- 5 wherein all phenyl groups are optionally substituted by one or more identical or different substituents selected from the series consisting of halogen, (C₁-C₄)-alkyl, cyano, hydroxy and (C₁-C₄)-alkyl-O-, unless specified otherwise;

- 10 wherein all cycloalkyl groups, independently of any other substituents which can be present on a cycloalkyl group, are optionally substituted by one or more identical or different substituents selected from the series consisting of fluorine and (C₁-C₄)-alkyl;

- 15 wherein all alkyl groups and alkyl groups which are part of another group, independently of any other substituents which can be present on an alkyl group, are optionally substituted by one or more fluorine substituents.

8. A process for the preparation of a compound of the formula I as claimed in any of claims 1 to 7, which comprises reacting a compound of the formula II with a compound of the formula III to give a compound of the formula I in which X is =N- (formula Ia) and, for the preparation of a compound of the formula I in which X is =N(O)- (formula Ib), oxidizing this compound, wherein the groups R₁, R₂, R₃, R₁₀ and R₁₁ in the compounds of the formulae II and III are defined as in the compounds of the formula I.
- 20



9. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof,
5 according to any of claims 1 to 7, for use as a pharmaceutical.

10. A pharmaceutical composition, comprising a compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof, according to any of claims 1 to 7, and a
10 pharmaceutically acceptable carrier.

11. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt thereof, according to any of claims 1 to 7, for use as an inhibitor of transglutaminases or in
15 the treatment of degenerative joint diseases, degenerative intervertebral disk diseases, osteoarthritis, neurodegenerative diseases, cancer, celiac disease, fibrosis or liver cirrhosis.

12. Use of a compound of the formula I, in any of its stereoisomeric forms or a
20 mixture of stereoisomeric forms in any ratio, or a pharmaceutically acceptable salt

thereof, according to any of claims 1 to 7, for the manufacture of a medicament for the treatment of degenerative joint diseases, degenerative intervertebral disk diseases, osteoarthritis, neurodegenerative diseases, cancer, celiac disease, fibrosis or liver cirrhosis.