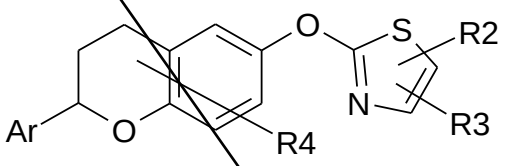
Claims

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

Ar is selected from the series consisting of phenyl and a 5-membered or 6-membered monocyclic aromatic heterocycle, which are all unsubstituted or substituted by one or more identical or different substituents R1, wherein the heterocycle comprises 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur and is bonded via a ring carbon atom;

R1 is selected from the series consisting of halogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-, phenyl, Het1, HO-, $(C_1$-$C_6)$-alkyl-O-, $(C_3$-$C_7)$-cycloalkyl-O-, $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-O-, phenyl-O-, Het1-O- and $(C_1$-$C_6)$-alkyl-$S(O)_n$-, and two groups R1 bonded to adjacent ring carbon atoms in Ar, together with the carbon atoms carrying them, can form a 5-membered to 7-membered mono-unsaturated ring which comprises 0, 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one or more identical or different substituents selected from the series consisting of fluorine and $(C_1$-$C_4)$-alkyl;

R2 is selected from the series consisting of R5-N(R6)-C(O)-, R5-N(R6)-CH_2-, R7-C(O)-NH-CH_2- and R7-$S(O)_2$-NH-CH_2-;

R3 is selected from the series consisting of hydrogen, halogen, (C_1-C_4)-alkyl and (C_1-C_4)-alkyl-O-;

R4 is hydrogen or one or more identical or different substituents selected from the series consisting of halogen, (C_1-C_4)-alkyl and (C_1-C_4)-alkyl-O-;

R5 and R6 are independently of one another selected from the series consisting of hydrogen, (C_1-C_6)-alkyl, (C_3-C_7)-cycloalkyl, (C_6-C_{10})-bicycloalkyl, phenyl, Het1 and Het2, wherein (C_1-C_6)-alkyl is unsubstituted or substituted by one or more identical or different substituents R10, and (C_3-C_7)-cycloalkyl, (C_6-C_{10})-bicycloalkyl and Het2 all are unsubstituted or substituted by one or more identical or different substituents R11,

or the groups R5 and R6, 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 R5 and R6, comprises 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one ore more identical or different substituents R12;

R7 is selected from the series consisting of (C_1-C_6)-alkyl, (C_3-C_7)-cycloalkyl, phenyl, Het2 and Het3, wherein (C_1-C_6)-alkyl, (C_3-C_7)-cycloalkyl and Het2 all are unsubstituted or substituted by one or more identical or different substituents R10, and phenyl and Het3 all are unsubstituted or substituted by one or more identical or different substituents R13;

R10 is selected from the series consisting of R14, fluorine, HO-, oxo, (C_1-C_6)-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-S(O)$_2$-O-, (HO)$_2$P(O)-O-, (HO)$_2$P(O)-O-CH$_2$-O-C(O)-O-, (C_1-C_6)-alkyl-S(O)$_n$-, R16-N(R17)-, R18-C(O)-N(R17)-, R16-N(R17)-C(O)-, R19-O-C(O)- and R16-N(R17)-S(O)$_2$-;

R11 and R12 are independently of one another selected from the series consisting of (C_1-C_4)-alkyl, HO-(C_1-C_4)-alkyl-, R16-N(R17)-(C_1-C_4)-alkyl-, R19-O-C(O)-(C_1-C_4)-

alkyl-, R14, fluorine, HO-, oxo, $(C_1$-$C_6)$-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-$S(O)_2$-O-, $(HO)_2P(O)$-O-, $(HO)_2P(O)$-O-CH_2-O-C(O)-O-, $(C_1$-$C_6)$-alkyl-$S(O)_n$-, R16-N(R17)-, R18-C(O)-N(R17)-, R16-N(R17)-C(O)-, R19-O-C(O)- and R16-N(R17)-$S(O)_2$-;

R13 is selected from the series consisting of halogen, $(C_1$-$C_4)$-alkyl, HO-, $(C_1$-$C_4)$-alkyl-O- and R16-N(R17)-, and two substituents R13 bonded to adjacent ring carbon atoms in R7, together with the carbon atoms carrying them, can form a 5-membered to 7-membered mono-unsaturated ring which comprises 0, 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one or more identical or different substituents selected from the series consisting of fluorine and $(C_1$-$C_4)$-alkyl;

R14 is a 3-membered to 10-membered, monocyclic or bicyclic ring which is saturated, partially unsaturated or aromatic and comprises 0, 1, 2, 3 or 4 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one or more identical or different substituents R20;

R15 and R18 are independently of one another selected from the series consisting of $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-, phenyl-$(C_1$-$C_4)$-alkyl- and Het1-$(C_1$-$C_4)$-alkyl-;

R16 and R17 are independently of one another selected from the series consisting of hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-, phenyl-$(C_1$-$C_4)$-alkyl- and Het1-$(C_1$-$C_4)$-alkyl-,

or the groups R16 and R17, together with the nitrogen atom carrying them, form a 4-membered to 7-membered, monocyclic saturated heterocycle which, in addition to the nitrogen atom carrying R16 and R17, comprises 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur, and which is

unsubstituted or substituted by one ore more identical or different substituents selected from the series consisting of fluorine and $(C_1$-$C_4)$-alkyl;

R19 is selected from the series consisting of hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-, phenyl-$(C_1$-$C_4)$-alkyl- and Het1-$(C_1$-$C_4)$-alkyl-;

R20 is selected from the series consisting of halogen, $(C_1$-$C_4)$-alkyl, HO-$(C_1$-$C_4)$-alkyl-, $(C_3$-$C_7)$-cycloalkyl, HO-, oxo, $(C_1$-$C_6)$-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-$S(O)_2$-O-, $(HO)_2P(O)$-O-, $(HO)_2P(O)$-O-CH_2-O-C(O)-O-, $(C_1$-$C_6)$-alkyl-$S(O)_n$-, R16-N(R17)-, R18-C(O)-N(R17)-, R18-O-C(O)-N(R17)-, NC-, R18-C(O)-, R16-N(R17)-C(O)-, R19-O-C(O)- and R16-N(R17)-$S(O)_2$-;

Het1 is a 5-membered or 6-membered monocyclic aromatic heterocycle comprising 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur, which is unsubstituted or substituted by one or more identical or different substituents selected from the series consisting of halogen, $(C_1$-$C_4)$-alkyl and $(C_1$-$C_4)$-alkyl-O-;

Het2 is a 4-membered to 10-membered monocyclic or bicyclic, saturated or partially unsaturated heterocycle comprising 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

Het3 is a 5-membered to 10-membered monocyclic or bicyclic aromatic heterocycle comprising 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

n is selected from the series consisting of 0, 1 and 2, wherein all numbers n are independent of one another;

wherein all phenyl groups, unless specified otherwise, are unsubstituted or substituted by one or more identical or different substituents selected from the series consisting of halogen, $(C_1\text{-}C_4)$-alkyl and -O-$(C_1\text{-}C_4)$-alkyl;

wherein all cycloalkyl and bicycloalkyl groups, independently of any other substituents which can be present on a cycloalkyl or bicycloalkyl group, can be substituted by one or more identical substituents selected from the series consisting of fluorine and $(C_1\text{-}C_4)$-alkyl;

wherein all alkyl groups, independently of any other substituents which can be present on an alkyl group, can be substituted by one ore more fluorine substituents.

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

Ar is selected from the series consisting of phenyl, thiophenyl, pyridinyl and pyrazinyl, which are all unsubstituted or substituted by one or more identical or different substituents R1;

R1 is selected from the series consisting of halogen, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_7)$-cycloalkyl, $(C_3\text{-}C_7)$-cycloalkyl-$(C_1\text{-}C_4)$-alkyl-, HO-, $(C_1\text{-}C_6)$-alkyl-O-, $(C_3\text{-}C_7)$-cycloalkyl-O-, $(C_3\text{-}C_7)$-cycloalkyl-$(C_1\text{-}C_4)$-alkyl-O- and $(C_1\text{-}C_6)$-alkyl-$S(O)_n$-;

R2 is selected from the series consisting of R5-N(R6)-C(O)-, R5-N(R6)-CH_2-, R7-C(O)-NH-CH_2- and R7-$S(O)_2$-NH-CH_2-;

R3 is selected from the series consisting of hydrogen, halogen and $(C_1\text{-}C_4)$-alkyl;

R4 is hydrogen or one or more identical or different substituents selected from the series consisting of halogen and $(C_1\text{-}C_4)$-alkyl;

R5 and R6 are independently of one another selected from the series consisting of hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, $(C_6$-$C_{10})$-bicycloalkyl and Het2, wherein $(C_1$-$C_6)$-alkyl is unsubstituted or substituted by one or more identical or different substituents R10, and $(C_3$-$C_7)$-cycloalkyl, $(C_6$-$C_{10})$-bicycloalkyl and Het2 all are unsubstituted or substituted by one or more identical or different substituents R11,

or the groups R5 and R6, together with the nitrogen atom carrying them, form a 4-membered to 10-membered, monocyclic or bicyclic, saturated heterocycle which, in addition to the nitrogen atom carrying R5 and R6, comprises 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one ore more identical or different substituents R12;

R7 is selected from the series consisting of $(C_1$-$C_6)$-alkyl, Het2 and Het3, wherein $(C_1$-$C_6)$-alkyl and Het2 all are unsubstituted or substituted by one or more identical or different substituents R10, and Het3 is unsubstituted or substituted by one or more identical or different substituents R13;

R10 is selected from the series consisting of R14, fluorine, HO-, oxo, $(C_1$-$C_6)$-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-S$(O)_2$-O-, $(HO)_2$P(O)-O-, $(HO)_2$P(O)-O-CH_2-O-C(O)-O-, R16-N(R17)-, R18-C(O)-N(R17)-, R16-N(R17)-C(O)- and R19-O-C(O)-;

R11 and R12 are independently of one another selected from the series consisting of $(C_1$-$C_4)$-alkyl, HO-$(C_1$-$C_4)$-alkyl-, R16-N(R17)-$(C_1$-$C_4)$-alkyl-, R19-O-C(O)-$(C_1$-$C_4)$-alkyl-, fluorine, HO-, oxo, $(C_1$-$C_6)$-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-S$(O)_2$-O-, $(HO)_2$P(O)-O-, $(HO)_2$P(O)-O-CH_2-O-C(O)-O-, R16-N(R17)-, R18-C(O)-N(R17)-, R16-N(R17)-C(O)- and R19-O-C(O)-;

R13 is selected from the series consisting of halogen, $(C_1$-$C_4)$-alkyl, $(C_1$-$C_4)$-alkyl-O- and R16-N(R17)-;

R14 is a 3-membered to 10-membered, monocyclic or bicyclic ring which is saturated, partially unsaturated or aromatic and comprises 0, 1, 2 or 3 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one or more identical or different substituents R20;

R15 and R18 are independently of one another selected from the series consisting of $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-;

R16 and R17 are independently of one another selected from the series consisting of hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-,

or the groups R16 and R17, together with the nitrogen atom carrying them, form a 5-membered to 6-membered, monocyclic saturated heterocycle which, in addition to the nitrogen atom carrying R16 and R17, comprises 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one ore more identical or different substituents selected from the series consisting of fluorine and $(C_1$-$C_4)$-alkyl;

R19 is selected from the series consisting of hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-;

R20 is selected from the series consisting of halogen, $(C_1$-$C_4)$-alkyl, HO-$(C_1$-$C_4)$-alkyl-, $(C_3$-$C_7)$-cycloalkyl, HO-, oxo, $(C_1$-$C_6)$-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-$S(O)_2$-O-, $(HO)_2P(O)$-O-, R16-N(R17)- and NC-;

Het2 is a 4-membered to 10-membered monocyclic or bicyclic, saturated or partially unsaturated heterocycle comprising 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

Het3 is a 5-membered to 10-membered monocyclic or bicyclic aromatic heterocycle comprising 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

n is selected from the series consisting of 0, 1 and 2, wherein all numbers n are independent of one another;

wherein all cycloalkyl and bicycloalkyl groups, independently of any other substituents which can be present on a cycloalkyl or bicycloalkyl group, can be substituted by one or more identical substituents selected from the series consisting of fluorine and (C_1-C_4)-alkyl;

wherein all alkyl groups, independently of any other substituents which can be present on an alkyl group, can be substituted by one ore more fluorine substituents.

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

Ar is selected from the series consisting of phenyl, thiophenyl, pyridinyl and pyrazinyl, which are all unsubstituted or substituted by one or more identical or different substituents R1;

R1 is selected from the series consisting of halogen, (C_1-C_6)-alkyl, HO- and (C_1-C_6)-alkyl-O-;

R2 is selected from the series consisting of R5-N(R6)-C(O)-, R5-N(R6)-CH_2-, R7-C(O)-NH-CH_2- and R7-$S(O)_2$-NH-CH_2-;

R3 is selected from the series consisting of hydrogen, halogen and (C_1-C_4)-alkyl;

R4 is hydrogen or one or more identical or different substituents selected from the series consisting of halogen and (C_1-C_4)-alkyl;

R5 and R6 are independently of one another selected from the series consisting of hydrogen, (C_1-C_6)-alkyl and (C_3-C_7)-cycloalkyl, wherein (C_1-C_6)-alkyl is unsubstituted or substituted by one or more identical or different substituents R10, and (C_3-C_7)-cycloalkyl is unsubstituted or substituted by one or more identical or different substituents R11,

or the groups R5 and R6, together with the nitrogen atom carrying them, form a 4-membered to 10-membered, monocyclic or bicyclic, saturated heterocycle which, in addition to the nitrogen atom carrying R5 and R6, comprises 0 or 1 further ring heteroatom selected from the series consisting of nitrogen and oxygen, and which is unsubstituted or substituted by one ore more identical or different substituents R12;

R7 is selected from the series consisting of (C_1-C_6)-alkyl and Het3, wherein (C_1-C_6)-alkyl is unsubstituted or substituted by one or more identical or different substituents R10, and Het3 is unsubstituted or substituted by one or more identical or different substituents R13;

R10 is selected from the series consisting of R14, fluorine, HO-, oxo, (C_1-C_6)-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-S(O)$_2$-O-, (HO)$_2$P(O)-O-, (HO)$_2$P(O)-O-CH_2-O-C(O)-O-, R16-N(R17)-, R18-C(O)-N(R17)-, R16-N(R17)-C(O)- and R19-O-C(O)-;

R11 and R12 are independently of one another selected from the series consisting of (C_1-C_4)-alkyl, HO-(C_1-C_4)-alkyl-, R16-N(R17)-(C_1-C_4)-alkyl-, fluorine, HO-, oxo, (C_1-C_6)-alkyl-O-, HO-S(O)$_2$-O-, (HO)$_2$P(O)-O-, R16-N(R17)- and R18-C(O)-N(R17)-;

R13 is selected from the series consisting of halogen, (C_1-C_4)-alkyl, (C_1-C_4)-alkyl-O- and R16-N(R17)-;

R14 is a 3-membered to 10-membered, monocyclic or bicyclic ring which is saturated, partially unsaturated or aromatic and comprises 0, 1, 2 or 3 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one or more identical or different substituents R20;

R15 and R18 are independently of one another selected from the series consisting of $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-;

R16 and R17 are independently of one another selected from the series consisting of hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-,

or the groups R16 and R17, together with the nitrogen atom carrying them, form a 5-membered to 6-membered, monocyclic saturated heterocycle which, in addition to the nitrogen atom carrying R16 and R17, comprises 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one ore more identical or different substituents selected from the series consisting of fluorine and $(C_1$-$C_4)$-alkyl;

R19 is selected from the series consisting of hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-;

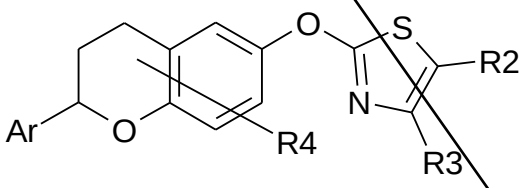
R20 is selected from the series consisting of halogen, $(C_1$-$C_4)$-alkyl, HO-$(C_1$-$C_4)$-alkyl-, $(C_3$-$C_7)$-cycloalkyl, HO-, oxo, $(C_1$-$C_6)$-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-$S(O)_2$-O-, $(HO)_2P(O)$-O-, R16-N(R17)- and NC-;

Het3 is a 5-membered to 10-membered monocyclic or bicyclic aromatic heterocycle comprising 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

wherein all cycloalkyl groups, independently of any other substituents which can be present on a cycloalkyl group, can be substituted by one or more identical substituents selected from the series consisting of fluorine and (C_1-C_4)-alkyl;

wherein all alkyl groups, independently of any other substituents which can be present on an alkyl group, can be substituted by one ore more fluorine substituents.

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, which is a compound of the formula Ie.

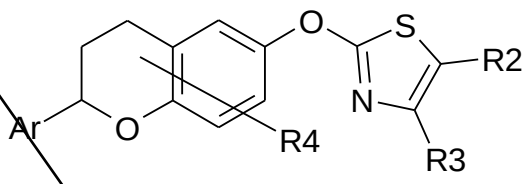


Ie

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 R2 is selected from the series consisting of R5-N(R6)-C(O)- and R5-N(R6)-CH_2-.

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 4, wherein R2 is selected from the series consisting of R7-C(O)-NH-CH_2- and R7-$S(O)_2$-NH-CH_2-.

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 any of claims 1 to 5, which is a compound of the formula Ie,



Ie

wherein

Ar is phenyl which is unsubstituted or substituted by one or more identical or different substituents R1;

R1 is selected from the series consisting of halogen, (C_1-C_6)-alkyl, HO- and (C_1-C_6)-alkyl-O-;

R2 is selected from the series consisting of R5-N(R6)-C(O)- and R5-N(R6)-CH_2-;

R3 is selected from the series consisting of hydrogen, halogen and (C_1-C_4)-alkyl;

R4 is hydrogen or one or more identical or different substituents selected from the series consisting of halogen and (C_1-C_4)-alkyl;

one of the groups R5 and R6 is hydrogen and the other of the groups R5 and R6 is selected from the series consisting of (C_1-C_6)-alkyl and (C_3-C_7)-cycloalkyl, wherein (C_1-C_6)-alkyl is unsubstituted or substituted by one or more identical or different substituents R10, and (C_3-C_7)-cycloalkyl is unsubstituted or substituted by one or more identical or different substituents R11;

R10 is selected from the series consisting of R14, fluorine, HO-, (C_1-C_6)-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-S(O)$_2$-O-, (HO)$_2$P(O)-O-, (HO)$_2$P(O)-O-CH_2-O-C(O)-O-, R16-N(R17)- and R18-C(O)-N(R17)-;

R11 is selected from the series consisting of $(C_1$-$C_4)$-alkyl, HO-$(C_1$-$C_4)$-alkyl-, R16-N(R17)-$(C_1$-$C_4)$-alkyl-, fluorine, HO-, $(C_1$-$C_6)$-alkyl-O-, HO-$S(O)_2$-O-, $(HO)_2P(O)$-O-, R16-N(R17)- and R18-C(O)-N(R17)-;

R14 is a 3-membered to 10-membered, monocyclic or bicyclic ring which is saturated, partially unsaturated or aromatic and comprises 0, 1, 2 or 3 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one or more identical or different substituents R20;

R15 and R18 are independently of one another selected from the series consisting of $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-;

R16 and R17 are independently of one another selected from the series consisting of hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-,

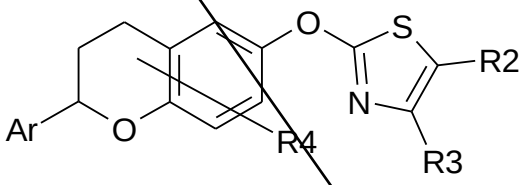
or the groups R16 and R17, together with the nitrogen atom carrying them, form a 5-membered to 6-membered, monocyclic saturated heterocycle which, in addition to the nitrogen atom carrying R16 and R17, comprises 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one ore more identical or different substituents selected from the series consisting of fluorine and $(C_1$-$C_4)$-alkyl;

R20 is selected from the series consisting of halogen, $(C_1$-$C_4)$-alkyl, HO-$(C_1$-$C_4)$-alkyl-, $(C_3$-$C_7)$-cycloalkyl, HO-, oxo, $(C_1$-$C_6)$-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-$S(O)_2$-O-, $(HO)_2P(O)$-O-, R16-N(R17)- and NC-;

wherein all cycloalkyl groups, independently of any other substituents which can be present on a cycloalkyl group, can be substituted by one or more identical substituents selected from the series consisting of fluorine and $(C_1$-$C_4)$-alkyl;

wherein all alkyl groups, independently of any other substituents which can be present on an alkyl group, can be substituted by one ore more fluorine substituents.

8. 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 and 7, which is a compound of the formula Ie,



Ie

wherein

Ar is phenyl which is unsubstituted or substituted by one or more identical or different substituents R1;

R1 is selected from the series consisting of halogen, (C_1-C_6)-alkyl, HO- and (C_1-C_6)-alkyl-O-;

R2 is selected from the series consisting of R5-N(R6)-C(O)- and R5-N(R6)-CH_2-;

R3 is selected from the series consisting of hydrogen, halogen and (C_1-C_4)-alkyl;

R4 is hydrogen or one or more identical or different substituents selected from the series consisting of halogen and (C_1-C_4)-alkyl;

one of the groups R5 and R6 is hydrogen and the other of the groups R5 and R6 is selected from the series consisting of (C_1-C_6)-alkyl and (C_3-C_7)-cycloalkyl, wherein (C_1-C_6)-alkyl is unsubstituted or substituted by one or more identical or different substituents R10, and (C_3-C_7)-cycloalkyl is unsubstituted or substituted by one or more identical or different substituents R11;

R10 is selected from the series consisting of fluorine, HO-, $(C_1$-$C_6)$-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-$S(O)_2$-O-, $(HO)_2P(O)$-O-, $(HO)_2P(O)$-O-CH_2-O-C(O)-O-, R16-N(R17)- and R18-C(O)-N(R17)-;

R11 is selected from the series consisting of $(C_1$-$C_4)$-alkyl, HO-$(C_1$-$C_4)$-alkyl-, R16-N(R17)-$(C_1$-$C_4)$-alkyl-, fluorine, HO-, $(C_1$-$C_6)$-alkyl-O-, HO-$S(O)_2$-O-, $(HO)_2P(O)$-O-, R16-N(R17)- and R18-C(O)-N(R17)-;

R15 and R18 are independently of one another selected from the series consisting of $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-;

R16 and R17 are independently of one another selected from the series consisting of hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-,

or the groups R16 and R17, together with the nitrogen atom carrying them, form a 5-membered to 6-membered, monocyclic saturated heterocycle which, in addition to the nitrogen atom carrying R16 and R17, comprises 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one ore more identical or different substituents selected from the series consisting of fluorine and $(C_1$-$C_4)$-alkyl;

wherein all cycloalkyl groups, independently of any other substituents which can be present on a cycloalkyl group, can be substituted by one or more identical substituents selected from the series consisting of fluorine and $(C_1$-$C_4)$-alkyl;

wherein all alkyl groups, independently of any other substituents which can be present on an alkyl group, can be substituted by one ore more fluorine substituents.

9. A compound of the formula I according to any of claims 1 to 8, which is selected from the series consisting of:

2-(2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid [2-(2-oxo-imidazolidin-1-yl)-ethyl]-amide,
2-(2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid cyclopropylamide,
2-((S)-2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide,
2-(2-Oxo-pyrrolidin-1-yl)-N-[2-(2-o-tolyl-chroman-6-yloxy)-thiazol-5-ylmethyl]-acetamide,
Isoxazole-5-carboxylic acid [2-(2-o-tolyl-chroman-6-yloxy)-thiazol-5-ylmethyl]-amide,
2-(2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid propylamide,
4-Methyl-2-(2-o-tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (isoxazol-5-ylmethyl)-amide,
2-[2-(5-Fluoro-2-methyl-phenyl)-chroman-6-yloxy]-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide,
2-[2-(5-Fluoro-2-methyl-phenyl)-chroman-6-yloxy]-thiazole-5-carboxylic acid propylamide,
Phosphoric acid mono-(2-{[2-((S)-2-o-tolyl-chroman-6-yloxy)-thiazole-5-carbonyl]-amino}-ethyl) ester,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (6,7-dihydro-5H-pyrrolo[2,1-c][1,2,4]triazol-3-ylmethyl)-amide,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid propylamide,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-chloro-pyridin-4-ylmethyl)-amide,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (1,5-dimethyl-1H-pyrazol-4-ylmethyl)-amide,
1,3,5-Trimethyl-1H-pyrazole-4-sulfonic acid [2-(2-phenyl-chroman-6-yloxy)-thiazol-5-ylmethyl]-amide,
2-((R)-2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide, and
[2-(2-Phenyl-chroman-6-yloxy)-thiazol-5-ylmethyl]-pyridin-4-ylmethyl-amine,
or a pharmaceutically acceptable salt thereof.

10. A compound of the formula I according to any of claims 1 to 9, which is selected from the series consisting of:
2-(2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid [2-(2-oxo-imidazolidin-1-yl)-ethyl]-amide,
2-(2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid cyclopropylamide,
2-((S)-2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide,
2-(2-Oxo-pyrrolidin-1-yl)-N-[2-(2-o-tolyl-chroman-6-yloxy)-thiazol-5-ylmethyl]-acetamide,
Isoxazole-5-carboxylic acid [2-(2-o-tolyl-chroman-6-yloxy)-thiazol-5-ylmethyl]-amide,
2-(2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid propylamide,
4-Methyl-2-(2-o-tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (isoxazol-5-ylmethyl)-amide,
2-[2-(5-Fluoro-2-methyl-phenyl)-chroman-6-yloxy]-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide,
2-[2-(5-Fluoro-2-methyl-phenyl)-chroman-6-yloxy]-thiazole-5-carboxylic acid propylamide,
Phosphoric acid mono-(2-{[2-((S)-2-o-tolyl-chroman-6-yloxy)-thiazole-5-carbonyl]-amino}-ethyl) ester,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (6,7-dihydro-5H-pyrrolo[2,1-c][1,2,4]triazol-3-ylmethyl)-amide,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid propylamide,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-chloro-pyridin-4-ylmethyl)-amide,
2-((R)-2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide, and
[2-(2-Phenyl-chroman-6-yloxy)-thiazol-5-ylmethyl]-pyridin-4-ylmethyl-amine,
or a pharmaceutically acceptable salt thereof.

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 10, with the proviso that the compound of the formula

I is not a compound in which simultaneously the group Ar is unsubstituted phenyl or 3-fluorophenyl, the groups R3 and R4 are hydrogen, one of the groups R5 and R6 is hydrogen, the other of the groups R5 and R6 is R40-(C_1-C_4)-alkyl-, and R7 is R40 or R40-(C_1-C_4)-alkyl-, wherein R40 is pyrazolyl which is unsubstituted or substituted by one or more identical or different (C_1-C_4)-alkyl substituents, and the excluded compounds are excluded as the free compounds and in the form of their 2,2,2-trifluoroacetates.

12. 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 10, with the proviso that the compound of the formula I is not one of the following compounds:
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[1-(1,5-dimethyl-1H-pyrazol-4-yl)ethyl]-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[(1,3-dimethyl-1H-pyrazol-4-yl)methyl]-,
1H-Pyrazole-4-sulfonamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1,3,5-trimethyl-,
1H-Pyrazole-4-carboxamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1,5-dimethyl-,
1H-Pyrazole-4-carboxamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1,3,5-trimethyl-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[2-(3,5-dimethyl-1H-pyrazol-1-yl)ethyl]-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[(1-ethyl-3-methyl-1H-pyrazol-4-yl)methyl]-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[(1-methyl-1H-pyrazol-5-yl)methyl]-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[(1,5-dimethyl-1H-pyrazol-3-yl)methyl]-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[(1,3-dimethyl-1H-pyrazol-5-yl)methyl]-,

1H-Pyrazole-4-sulfonamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1,5-dimethyl-,
1H-Pyrazole-4-sulfonamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1-methyl-,
1H-Pyrazole-3-carboxamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1-ethyl-,
1H-Pyrazole-1-acetamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-,
1H-Pyrazole-1-acetamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-3-methyl-,
1H-Pyrazole-5-carboxamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1-ethyl-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[3-(1H-pyrazol-1-yl)propyl]-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[2-(3-methyl-1H-pyrazol-1-yl)ethyl]-,
1H-Pyrazole-4-carboxamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1-ethyl-,
5-Thiazolecarboxamide, N-[(1,5-dimethyl-1H-pyrazol-4-yl)methyl]-2-[[2-(3-fluorophenyl)-3,4-dihydro-2H-1-benzopyran-6-yl]oxy]-,
5-Thiazolecarboxamide, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[(1-ethyl-1H-pyrazol-4-yl)methyl]-,
1H-Pyrazole-1-propanamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-,
1H-Pyrazole-4-sulfonamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-5-methyl-1-(1-methylethyl)-,
5-Thiazolecarboxamide, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[(1,5-dimethyl-1H-pyrazol-4-yl)methyl]-,
5-Thiazolecarboxamide, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[1-(1,5-dimethyl-1H-pyrazol-4-yl)ethyl]-,
5-Thiazolecarboxamide, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[1-(1,3-dimethyl-1H-pyrazol-4-yl)ethyl]-,

5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[(1,5-dimethyl-1H-pyrazol-4-yl)methyl]-,
1H-Pyrazole-4-sulfonamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1-ethyl-,
1H-Pyrazole-5-carboxamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1,3-dimethyl-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[2-(1H-pyrazol-1-yl)ethyl]-,
1H-Pyrazole-5-sulfonamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1-methyl-,
1H-Pyrazole-5-carboxamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1-methyl-,
5-Thiazolecarboxamide, N-[(1,5-dimethyl-1H-pyrazol-4-yl)methyl]-2-[[(2R)-2-(3-fluorophenyl)-3,4-dihydro-2H-1-benzopyran-6-yl]oxy]-,
5-Thiazolecarboxamide, N-[(1,5-dimethyl-1H-pyrazol-4-yl)methyl]-2-[[(2S)-2-(3-fluorophenyl)-3,4-dihydro-2H-1-benzopyran-6-yl]oxy]-,
5-Thiazolecarboxamide, 2-[[(2R)-3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl]oxy]-N-[(1,5-dimethyl-1H-pyrazol-4-yl)methyl]-, and
5-Thiazolecarboxamide, 2-[[(2S)-3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl]oxy]-N-[(1,5-dimethyl-1H-pyrazol-4-yl)methyl]-,
wherein in the excluded compounds the carbon atom in position 2 of the chroman ring, which carries a phenyl group or 3-fluorophenyl group, is present in racemic form, unless specified otherwise, and the excluded compounds are excluded as the free compounds and in the form of their 2,2,2-trifluoroacetates.

13. A compound of the formula I according to any of claims 1 to 12, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, which is 2-(2-o-tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide.

14. A compound of the formula I according to any of claims 1 to 12, which is 2-((S)-2-o-tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide.

15. A compound of the formula I according to any of claims 1 to 12, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, which is isoxazole-5-carboxylic acid [2-(2-o-tolyl-chroman-6-yloxy)-thiazol-5-ylmethyl]-amide.

16. A compound of the formula I according to any of claims 1 to 12, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, which is 2-(2-o-tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid propylamide.

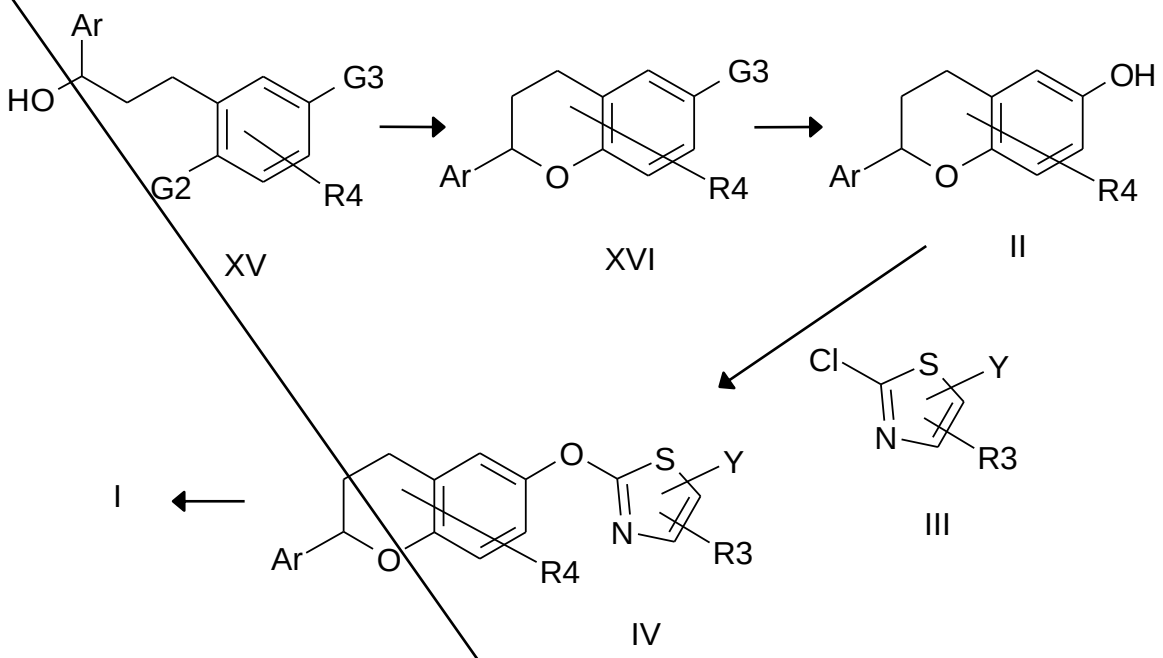
17. A compound of the formula I according to any of claims 1 to 12, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, which is 2-[2-(5-fluoro-2-methyl-phenyl)-chroman-6-yloxy]-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide.

18. A compound of the formula I according to any of claims 1 to 12, which is phosphoric acid mono-(2-{[2-((S)-2-o-tolyl-chroman-6-yloxy)-thiazole-5-carbonyl]-amino}-ethyl) ester, or a pharmaceutically acceptable salt thereof.

19. A compound of the formula I according to any of claims 1 to 12, which is 2-((R)-2-o-tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide.

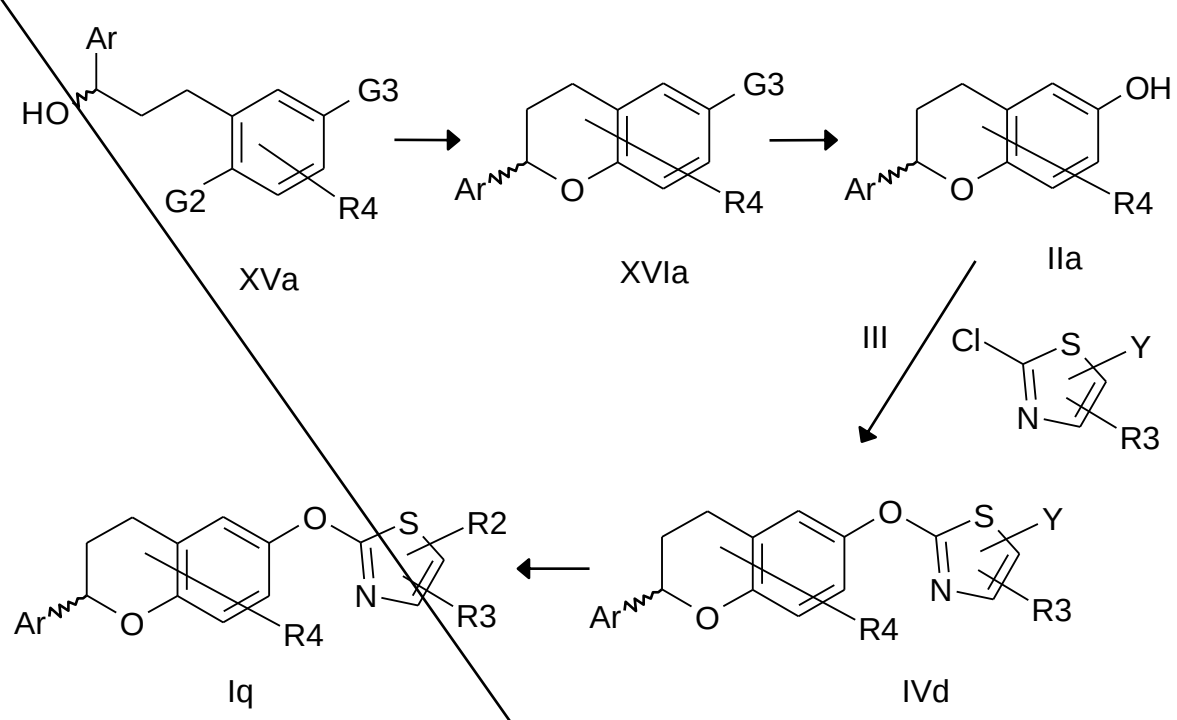
20. A compound of the formula I according to any of claims 1 to 12, which is phosphoric acid mono-(2-{[2-((S)-2-o-tolyl-chroman-6-yloxy)-thiazole-5-carbonyl]-amino}-ethyl) ester disodium salt.

21. A process for the preparation of a compound of the formula I as claimed in any of claims 1 to *20*,



which comprises cyclizing a compound of the formula XV to a compound of the formula XVI, converting the compound of the formula XVI into a compound of the formula II, reacting the compound of the formula II with a compound of the formula III to give a compound of the formula IV, and converting the compound of the formula IV into a compound of the formula I, wherein the groups Ar, R3 and R4 in the compounds of the formulae II, III, IV, XV and XVI are defined as in the compounds of the formula I, the group G2 in the compounds of the formula XV is a hydroxy group or a nucleophilically substitutable leaving group, the group G3 in the compounds of the formulae XV and XVI is bromine or (C_1-C_4)-alkyl-O-, and the group Y in the compounds of the formulae III and IV is R50-O-C(O)-, H-C(O)- or NC-, wherein R50 is (C_1-C_4)-alkyl.

22. The process according to claim 21, wherein a compound of the formula Iq is prepared in which the chiral carbon atom carrying the group Ar is present in uniform configuration,



which comprises cyclizing a compound of the formula XVa, in which the chiral carbon atom carrying the group Ar is present in uniform configuration, to a compound of the formula XVIa, converting the compound of the formula XVIa into a compound of the formula IIa, reacting the compound of the formula IIa with a compound of the formula III to give a compound of the formula IVd, and converting the compound of the formula IVd into a compound of the formula Iq, wherein the groups Ar, R2, R3 and R4 in the compounds of the formulae Iq, IIa, III, IVd, XVa and XVIa are defined as in the compounds of the formula I, the group G2 in the compounds of the formula XVa, the group G3 in the compounds of the formulae XVa and XVIa and the group Y in the compounds of the formulae III and IVd are defined as in compounds of the formulae XV, XVI, III and IV in claim 21.

23. 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 20, for use as a pharmaceutical.

24. 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

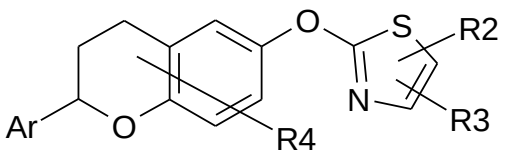
pharmaceutically acceptable salt thereof, according to any of claims 1 to 20, and a pharmaceutically acceptable carrier.

25. 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 20, for use as an inhibitor of the sodium-calcium-exchanger (NCX) or in the treatment of heart failure, cardiac arrhythmias, stroke, dementia, hypertension, cardiac ischemia, renal failure, shock or age-related disorders.

26. Use of 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 20, for the manufacture of a medicament for the inhibition of the sodium-calcium-exchanger (NCX) or for the treatment of heart failure, cardiac arrhythmias, stroke, dementia, hypertension, cardiac ischemia, renal failure, shock or age-related disorders.

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

Ar is selected from the series consisting of phenyl and a 5-membered or 6-membered monocyclic aromatic heterocycle, which are all unsubstituted or substituted by one or more identical or different substituents R1, wherein the heterocycle comprises 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur and is bonded via a ring carbon atom;

R1 is selected from the series consisting of halogen, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_7)$-cycloalkyl, $(C_3\text{-}C_7)$-cycloalkyl-$(C_1\text{-}C_4)$-alkyl-, phenyl, Het1, HO-, $(C_1\text{-}C_6)$-alkyl-O-, $(C_3\text{-}C_7)$-cycloalkyl-O-, $(C_3\text{-}C_7)$-cycloalkyl-$(C_1\text{-}C_4)$-alkyl-O-, phenyl-O-, Het1-O- and $(C_1\text{-}C_6)$-alkyl-$S(O)_n$-, and two groups R1 bonded to adjacent ring carbon atoms in Ar, together with the carbon atoms carrying them, can form a 5-membered to 7-membered mono-unsaturated ring which comprises 0, 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one or more identical or different substituents selected from the series consisting of fluorine and $(C_1\text{-}C_4)$-alkyl;

R2 is selected from the series consisting of R5-N(R6)-C(O)-, R5-N(R6)-CH_2-, R7-C(O)-NH-CH_2- and R7-$S(O)_2$-NH-CH_2-;

R3 is selected from the series consisting of hydrogen, halogen, (C_1-C_4)-alkyl and (C_1-C_4)-alkyl-O-;

R4 is hydrogen or one or more identical or different substituents selected from the series consisting of halogen, (C_1-C_4)-alkyl and (C_1-C_4)-alkyl-O-;

R5 and R6 are independently of one another selected from the series consisting of hydrogen, (C_1-C_6)-alkyl, (C_3-C_7)-cycloalkyl, (C_6-C_{10})-bicycloalkyl, phenyl, Het1 and Het2, wherein (C_1-C_6)-alkyl is unsubstituted or substituted by one or more identical or different substituents R10, and (C_3-C_7)-cycloalkyl, (C_6-C_{10})-bicycloalkyl and Het2 all are unsubstituted or substituted by one or more identical or different substituents R11,

or the groups R5 and R6, 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 R5 and R6, comprises 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one ore more identical or different substituents R12;

R7 is selected from the series consisting of (C_1-C_6)-alkyl, (C_3-C_7)-cycloalkyl, phenyl, Het2 and Het3, wherein (C_1-C_6)-alkyl, (C_3-C_7)-cycloalkyl and Het2 all are unsubstituted or substituted by one or more identical or different substituents R10, and phenyl and Het3 all are unsubstituted or substituted by one or more identical or different substituents R13;

R10 is selected from the series consisting of R14, fluorine, HO-, oxo, (C_1-C_6)-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-$S(O)_2$-O-, $(HO)_2P(O)$-O-, $(HO)_2P(O)$-O-CH_2-O-C(O)-O-, (C_1-C_6)-alkyl-$S(O)_n$-, R16-N(R17)-, R18-C(O)-N(R17)-, R16-N(R17)-C(O)-, R19-O-C(O)- and R16-N(R17)-$S(O)_2$-;

R11 and R12 are independently of one another selected from the series consisting of (C_1-C_4)-alkyl, HO-(C_1-C_4)-alkyl-, R16-N(R17)-(C_1-C_4)-alkyl-, R19-O-C(O)-(C_1-C_4)-

alkyl-, R14, fluorine, HO-, oxo, $(C_1$-$C_6)$-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-$S(O)_2$-O-, $(HO)_2P(O)$-O-, $(HO)_2P(O)$-O-CH_2-O-C(O)-O-, $(C_1$-$C_6)$-alkyl-$S(O)_n$-, R16-N(R17)-, R18-C(O)-N(R17)-, R16-N(R17)-C(O)-, R19-O-C(O)- and R16-N(R17)-$S(O)_2$-;

R13 is selected from the series consisting of halogen, $(C_1$-$C_4)$-alkyl, HO-, $(C_1$-$C_4)$-alkyl-O- and R16-N(R17)-, and two substituents R13 bonded to adjacent ring carbon atoms in R7, together with the carbon atoms carrying them, can form a 5-membered to 7-membered mono-unsaturated ring which comprises 0, 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one or more identical or different substituents selected from the series consisting of fluorine and $(C_1$-$C_4)$-alkyl;

R14 is a 3-membered to 10-membered, monocyclic or bicyclic ring which is saturated, partially unsaturated or aromatic and comprises 0, 1, 2, 3 or 4 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one or more identical or different substituents R20;

R15 and R18 are independently of one another selected from the series consisting of $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-, phenyl-$(C_1$-$C_4)$-alkyl- and Het1-$(C_1$-$C_4)$-alkyl-;

R16 and R17 are independently of one another selected from the series consisting of hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-, phenyl-$(C_1$-$C_4)$-alkyl- and Het1-$(C_1$-$C_4)$-alkyl-,

or the groups R16 and R17, together with the nitrogen atom carrying them, form a 4-membered to 7-membered, monocyclic saturated heterocycle which, in addition to the nitrogen atom carrying R16 and R17, comprises 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur, and which is

unsubstituted or substituted by one ore more identical or different substituents selected from the series consisting of fluorine and $(C_1$-$C_4)$-alkyl;

R19 is selected from the series consisting of hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-, phenyl-$(C_1$-$C_4)$-alkyl- and Het1-$(C_1$-$C_4)$-alkyl-;

R20 is selected from the series consisting of halogen, $(C_1$-$C_4)$-alkyl, HO-$(C_1$-$C_4)$-alkyl-, $(C_3$-$C_7)$-cycloalkyl, HO-, oxo, $(C_1$-$C_6)$-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-$S(O)_2$-O-, $(HO)_2P(O)$-O-, $(HO)_2P(O)$-O-CH_2-O-C(O)-O-, $(C_1$-$C_6)$-alkyl-$S(O)_n$-, R16-N(R17)-, R18-C(O)-N(R17)-, R18-O-C(O)-N(R17)-, NC-, R18-C(O)-, R16-N(R17)-C(O)-, R19-O-C(O)- and R16-N(R17)-$S(O)_2$-;

Het1 is a 5-membered or 6-membered monocyclic aromatic heterocycle comprising 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur, which is unsubstituted or substituted by one or more identical or different substituents selected from the series consisting of halogen, $(C_1$-$C_4)$-alkyl and $(C_1$-$C_4)$-alkyl-O-;

Het2 is a 4-membered to 10-membered monocyclic or bicyclic, saturated or partially unsaturated heterocycle comprising 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

Het3 is a 5-membered to 10-membered monocyclic or bicyclic aromatic heterocycle comprising 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

n is selected from the series consisting of 0, 1 and 2, wherein all numbers n are independent of one another;

wherein all phenyl groups, unless specified otherwise, are unsubstituted or substituted by one or more identical or different substituents selected from the series consisting of halogen, $(C_1$-$C_4)$-alkyl and -O-$(C_1$-$C_4)$-alkyl;

wherein all cycloalkyl and bicycloalkyl groups, independently of any other substituents which can be present on a cycloalkyl or bicycloalkyl group, can be substituted by one or more identical substituents selected from the series consisting of fluorine and $(C_1$-$C_4)$-alkyl;

wherein all alkyl groups, independently of any other substituents which can be present on an alkyl group, can be substituted by one ore more fluorine substituents.

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

Ar is selected from the series consisting of phenyl, thiophenyl, pyridinyl and pyrazinyl, which are all unsubstituted or substituted by one or more identical or different substituents R1;

R1 is selected from the series consisting of halogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-, HO-, $(C_1$-$C_6)$-alkyl-O-, $(C_3$-$C_7)$-cycloalkyl-O-, $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-O- and $(C_1$-$C_6)$-alkyl-$S(O)_n$-;

R2 is selected from the series consisting of R5-N(R6)-C(O)-, R5-N(R6)-CH_2-, R7-C(O)-NH-CH_2- and R7-$S(O)_2$-NH-CH_2-;

R3 is selected from the series consisting of hydrogen, halogen and $(C_1$-$C_4)$-alkyl;

R4 is hydrogen or one or more identical or different substituents selected from the series consisting of halogen and $(C_1$-$C_4)$-alkyl;

R5 and R6 are independently of one another selected from the series consisting of hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, $(C_6$-$C_{10})$-bicycloalkyl and Het2, wherein $(C_1$-$C_6)$-alkyl is unsubstituted or substituted by one or more identical or different substituents R10, and $(C_3$-$C_7)$-cycloalkyl, $(C_6$-$C_{10})$-bicycloalkyl and Het2 all are unsubstituted or substituted by one or more identical or different substituents R11,

or the groups R5 and R6, together with the nitrogen atom carrying them, form a 4-membered to 10-membered, monocyclic or bicyclic, saturated heterocycle which, in addition to the nitrogen atom carrying R5 and R6, comprises 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one ore more identical or different substituents R12;

R7 is selected from the series consisting of $(C_1$-$C_6)$-alkyl, Het2 and Het3, wherein $(C_1$-$C_6)$-alkyl and Het2 all are unsubstituted or substituted by one or more identical or different substituents R10, and Het3 is unsubstituted or substituted by one or more identical or different substituents R13;

R10 is selected from the series consisting of R14, fluorine, HO-, oxo, $(C_1$-$C_6)$-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-S$(O)_2$-O-, $(HO)_2$P(O)-O-, $(HO)_2$P(O)-O-CH_2-O-C(O)-O-, R16-N(R17)-, R18-C(O)-N(R17)-, R16-N(R17)-C(O)- and R19-O-C(O)-;

R11 and R12 are independently of one another selected from the series consisting of $(C_1$-$C_4)$-alkyl, HO-$(C_1$-$C_4)$-alkyl-, R16-N(R17)-$(C_1$-$C_4)$-alkyl-, R19-O-C(O)-$(C_1$-$C_4)$-alkyl-, fluorine, HO-, oxo, $(C_1$-$C_6)$-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-S$(O)_2$-O-, $(HO)_2$P(O)-O-, $(HO)_2$P(O)-O-CH_2-O-C(O)-O-, R16-N(R17)-, R18-C(O)-N(R17)-, R16-N(R17)-C(O)- and R19-O-C(O)-;

R13 is selected from the series consisting of halogen, $(C_1$-$C_4)$-alkyl, $(C_1$-$C_4)$-alkyl-O- and R16-N(R17)-;

R14 is a 3-membered to 10-membered, monocyclic or bicyclic ring which is saturated, partially unsaturated or aromatic and comprises 0, 1, 2 or 3 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one or more identical or different substituents R20;

R15 and R18 are independently of one another selected from the series consisting of $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-;

R16 and R17 are independently of one another selected from the series consisting of hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-,

or the groups R16 and R17, together with the nitrogen atom carrying them, form a 5-membered to 6-membered, monocyclic saturated heterocycle which, in addition to the nitrogen atom carrying R16 and R17, comprises 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one ore more identical or different substituents selected from the series consisting of fluorine and $(C_1$-$C_4)$-alkyl;

R19 is selected from the series consisting of hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-;

R20 is selected from the series consisting of halogen, $(C_1$-$C_4)$-alkyl, HO-$(C_1$-$C_4)$-alkyl-, $(C_3$-$C_7)$-cycloalkyl, HO-, oxo, $(C_1$-$C_6)$-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-$S(O)_2$-O-, $(HO)_2P(O)$-O-, R16-N(R17)- and NC-;

Het2 is a 4-membered to 10-membered monocyclic or bicyclic, saturated or partially unsaturated heterocycle comprising 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

Het3 is a 5-membered to 10-membered monocyclic or bicyclic aromatic heterocycle comprising 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

n is selected from the series consisting of 0, 1 and 2, wherein all numbers n are independent of one another;

wherein all cycloalkyl and bicycloalkyl groups, independently of any other substituents which can be present on a cycloalkyl or bicycloalkyl group, can be substituted by one or more identical substituents selected from the series consisting of fluorine and (C_1-C_4)-alkyl;

wherein all alkyl groups, independently of any other substituents which can be present on an alkyl group, can be substituted by one ore more fluorine substituents.

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

Ar is selected from the series consisting of phenyl, thiophenyl, pyridinyl and pyrazinyl, which are all unsubstituted or substituted by one or more identical or different substituents R1;

R1 is selected from the series consisting of halogen, (C_1-C_6)-alkyl, HO- and (C_1-C_6)-alkyl-O-;

R2 is selected from the series consisting of R5-N(R6)-C(O)-, R5-N(R6)-CH_2-, R7-C(O)-NH-CH_2- and R7-$S(O)_2$-NH-CH_2-;

R3 is selected from the series consisting of hydrogen, halogen and (C_1-C_4)-alkyl;

R4 is hydrogen or one or more identical or different substituents selected from the series consisting of halogen and (C_1-C_4)-alkyl;

R5 and R6 are independently of one another selected from the series consisting of hydrogen, (C_1-C_6)-alkyl and (C_3-C_7)-cycloalkyl, wherein (C_1-C_6)-alkyl is unsubstituted or substituted by one or more identical or different substituents R10, and (C_3-C_7)-cycloalkyl is unsubstituted or substituted by one or more identical or different substituents R11,

or the groups R5 and R6, together with the nitrogen atom carrying them, form a 4-membered to 10-membered, monocyclic or bicyclic, saturated heterocycle which, in addition to the nitrogen atom carrying R5 and R6, comprises 0 or 1 further ring heteroatom selected from the series consisting of nitrogen and oxygen, and which is unsubstituted or substituted by one ore more identical or different substituents R12;

R7 is selected from the series consisting of (C_1-C_6)-alkyl and Het3, wherein (C_1-C_6)-alkyl is unsubstituted or substituted by one or more identical or different substituents R10, and Het3 is unsubstituted or substituted by one or more identical or different substituents R13;

R10 is selected from the series consisting of R14, fluorine, HO-, oxo, (C_1-C_6)-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-S(O)$_2$-O-, (HO)$_2$P(O)-O-, (HO)$_2$P(O)-O-CH_2-O-C(O)-O-, R16-N(R17)-, R18-C(O)-N(R17)-, R16-N(R17)-C(O)- and R19-O-C(O)-;

R11 and R12 are independently of one another selected from the series consisting of (C_1-C_4)-alkyl, HO-(C_1-C_4)-alkyl-, R16-N(R17)-(C_1-C_4)-alkyl-, fluorine, HO-, oxo, (C_1-C_6)-alkyl-O-, HO-S(O)$_2$-O-, (HO)$_2$P(O)-O-, R16-N(R17)- and R18-C(O)-N(R17)-;

R13 is selected from the series consisting of halogen, (C_1-C_4)-alkyl, (C_1-C_4)-alkyl-O- and R16-N(R17)-;

R14 is a 3-membered to 10-membered, monocyclic or bicyclic ring which is saturated, partially unsaturated or aromatic and comprises 0, 1, 2 or 3 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one or more identical or different substituents R20;

R15 and R18 are independently of one another selected from the series consisting of $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_7)$-cycloalkyl and $(C_3\text{-}C_7)$-cycloalkyl-$(C_1\text{-}C_4)$-alkyl-;

R16 and R17 are independently of one another selected from the series consisting of hydrogen, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_7)$-cycloalkyl and $(C_3\text{-}C_7)$-cycloalkyl-$(C_1\text{-}C_4)$-alkyl-,

or the groups R16 and R17, together with the nitrogen atom carrying them, form a 5-membered to 6-membered, monocyclic saturated heterocycle which, in addition to the nitrogen atom carrying R16 and R17, comprises 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one ore more identical or different substituents selected from the series consisting of fluorine and $(C_1\text{-}C_4)$-alkyl;

R19 is selected from the series consisting of hydrogen, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_7)$-cycloalkyl and $(C_3\text{-}C_7)$-cycloalkyl-$(C_1\text{-}C_4)$-alkyl-;

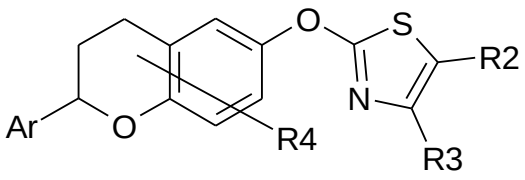
R20 is selected from the series consisting of halogen, $(C_1\text{-}C_4)$-alkyl, HO-$(C_1\text{-}C_4)$-alkyl-, $(C_3\text{-}C_7)$-cycloalkyl, HO-, oxo, $(C_1\text{-}C_6)$-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-$S(O)_2$-O-, $(HO)_2P(O)$-O-, R16-N(R17)- and NC-;

Het3 is a 5-membered to 10-membered monocyclic or bicyclic aromatic heterocycle comprising 1 or 2 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur;

wherein all cycloalkyl groups, independently of any other substituents which can be present on a cycloalkyl group, can be substituted by one or more identical substituents selected from the series consisting of fluorine and (C_1-C_4)-alkyl;

wherein all alkyl groups, independently of any other substituents which can be present on an alkyl group, can be substituted by one ore more fluorine substituents.

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, which is a compound of the formula Ie.

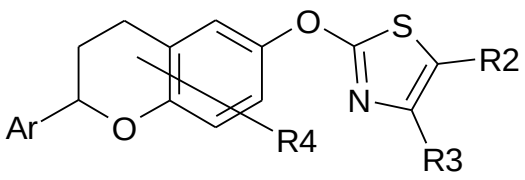


Ie

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 R2 is selected from the series consisting of R5-N(R6)-C(O)- and R5-N(R6)-CH_2-.

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 4, wherein R2 is selected from the series consisting of R7-C(O)-NH-CH_2- and R7-$S(O)_2$-NH-CH_2-.

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 any of claims 1 to 5, which is a compound of the formula Ie,



Ie

wherein

Ar is phenyl which is unsubstituted or substituted by one or more identical or different substituents R1;

R1 is selected from the series consisting of halogen, (C_1-C_6)-alkyl, HO- and (C_1-C_6)-alkyl-O-;

R2 is selected from the series consisting of R5-N(R6)-C(O)- and R5-N(R6)-CH_2-;

R3 is selected from the series consisting of hydrogen, halogen and (C_1-C_4)-alkyl;

R4 is hydrogen or one or more identical or different substituents selected from the series consisting of halogen and (C_1-C_4)-alkyl;

one of the groups R5 and R6 is hydrogen and the other of the groups R5 and R6 is selected from the series consisting of (C_1-C_6)-alkyl and (C_3-C_7)-cycloalkyl, wherein (C_1-C_6)-alkyl is unsubstituted or substituted by one or more identical or different substituents R10, and (C_3-C_7)-cycloalkyl is unsubstituted or substituted by one or more identical or different substituents R11;

R10 is selected from the series consisting of R14, fluorine, HO-, (C_1-C_6)-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-S(O)$_2$-O-, (HO)$_2$P(O)-O-, (HO)$_2$P(O)-O-CH_2-O-C(O)-O-, R16-N(R17)- and R18-C(O)-N(R17)-;

R11 is selected from the series consisting of $(C_1$-$C_4)$-alkyl, HO-$(C_1$-$C_4)$-alkyl-, R16-N(R17)-$(C_1$-$C_4)$-alkyl-, fluorine, HO-, $(C_1$-$C_6)$-alkyl-O-, HO-$S(O)_2$-O-, $(HO)_2P(O)$-O-, R16-N(R17)- and R18-C(O)-N(R17)-;

R14 is a 3-membered to 10-membered, monocyclic or bicyclic ring which is saturated, partially unsaturated or aromatic and comprises 0, 1, 2 or 3 identical or different ring heteroatoms selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one or more identical or different substituents R20;

R15 and R18 are independently of one another selected from the series consisting of $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-;

R16 and R17 are independently of one another selected from the series consisting of hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-,

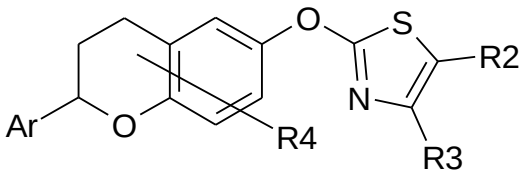
or the groups R16 and R17, together with the nitrogen atom carrying them, form a 5-membered to 6-membered, monocyclic saturated heterocycle which, in addition to the nitrogen atom carrying R16 and R17, comprises 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one ore more identical or different substituents selected from the series consisting of fluorine and $(C_1$-$C_4)$-alkyl;

R20 is selected from the series consisting of halogen, $(C_1$-$C_4)$-alkyl, HO-$(C_1$-$C_4)$-alkyl-, $(C_3$-$C_7)$-cycloalkyl, HO-, oxo, $(C_1$-$C_6)$-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-$S(O)_2$-O-, $(HO)_2P(O)$-O-, R16-N(R17)- and NC-;

wherein all cycloalkyl groups, independently of any other substituents which can be present on a cycloalkyl group, can be substituted by one or more identical substituents selected from the series consisting of fluorine and $(C_1$-$C_4)$-alkyl;

wherein all alkyl groups, independently of any other substituents which can be present on an alkyl group, can be substituted by one ore more fluorine substituents.

8. 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 and 7, which is a compound of the formula Ie,



Ie

wherein

Ar is phenyl which is unsubstituted or substituted by one or more identical or different substituents R1;

R1 is selected from the series consisting of halogen, (C_1-C_6)-alkyl, HO- and (C_1-C_6)-alkyl-O-;

R2 is selected from the series consisting of R5-N(R6)-C(O)- and R5-N(R6)-CH_2-;

R3 is selected from the series consisting of hydrogen, halogen and (C_1-C_4)-alkyl;

R4 is hydrogen or one or more identical or different substituents selected from the series consisting of halogen and (C_1-C_4)-alkyl;

one of the groups R5 and R6 is hydrogen and the other of the groups R5 and R6 is selected from the series consisting of (C_1-C_6)-alkyl and (C_3-C_7)-cycloalkyl, wherein (C_1-C_6)-alkyl is unsubstituted or substituted by one or more identical or different substituents R10, and (C_3-C_7)-cycloalkyl is unsubstituted or substituted by one or more identical or different substituents R11;

R10 is selected from the series consisting of fluorine, HO-, $(C_1$-$C_6)$-alkyl-O-, R15-C(O)-O-, R15-NH-C(O)-O-, HO-$S(O)_2$-O-, $(HO)_2P(O)$-O-, $(HO)_2P(O)$-O-CH_2-O-C(O)-O-, R16-N(R17)- and R18-C(O)-N(R17)-;

R11 is selected from the series consisting of $(C_1$-$C_4)$-alkyl, HO-$(C_1$-$C_4)$-alkyl-, R16-N(R17)-$(C_1$-$C_4)$-alkyl-, fluorine, HO-, $(C_1$-$C_6)$-alkyl-O-, HO-$S(O)_2$-O-, $(HO)_2P(O)$-O-, R16-N(R17)- and R18-C(O)-N(R17)-;

R15 and R18 are independently of one another selected from the series consisting of $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-;

R16 and R17 are independently of one another selected from the series consisting of hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and $(C_3$-$C_7)$-cycloalkyl-$(C_1$-$C_4)$-alkyl-,

or the groups R16 and R17, together with the nitrogen atom carrying them, form a 5-membered to 6-membered, monocyclic saturated heterocycle which, in addition to the nitrogen atom carrying R16 and R17, comprises 0 or 1 further ring heteroatom selected from the series consisting of nitrogen, oxygen and sulfur, and which is unsubstituted or substituted by one ore more identical or different substituents selected from the series consisting of fluorine and $(C_1$-$C_4)$-alkyl;

wherein all cycloalkyl groups, independently of any other substituents which can be present on a cycloalkyl group, can be substituted by one or more identical substituents selected from the series consisting of fluorine and $(C_1$-$C_4)$-alkyl;

wherein all alkyl groups, independently of any other substituents which can be present on an alkyl group, can be substituted by one ore more fluorine substituents.

9. A compound of the formula I according to any of claims 1 to 8, which is selected from the series consisting of:

2-(2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid [2-(2-oxo-imidazolidin-1-yl)-ethyl]-amide,
2-(2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid cyclopropylamide,
2-((S)-2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide,
2-(2-Oxo-pyrrolidin-1-yl)-N-[2-(2-o-tolyl-chroman-6-yloxy)-thiazol-5-ylmethyl]-acetamide,
Isoxazole-5-carboxylic acid [2-(2-o-tolyl-chroman-6-yloxy)-thiazol-5-ylmethyl]-amide,
2-(2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid propylamide,
4-Methyl-2-(2-o-tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (isoxazol-5-ylmethyl)-amide,
2-[2-(5-Fluoro-2-methyl-phenyl)-chroman-6-yloxy]-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide,
2-[2-(5-Fluoro-2-methyl-phenyl)-chroman-6-yloxy]-thiazole-5-carboxylic acid propylamide,
Phosphoric acid mono-(2-{[2-((S)-2-o-tolyl-chroman-6-yloxy)-thiazole-5-carbonyl]-amino}-ethyl) ester,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (6,7-dihydro-5H-pyrrolo[2,1-c][1,2,4]triazol-3-ylmethyl)-amide,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid propylamide,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-chloro-pyridin-4-ylmethyl)-amide,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (1,5-dimethyl-1H-pyrazol-4-ylmethyl)-amide,
1,3,5-Trimethyl-1H-pyrazole-4-sulfonic acid [2-(2-phenyl-chroman-6-yloxy)-thiazol-5-ylmethyl]-amide,
2-((R)-2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide, and
[2-(2-Phenyl-chroman-6-yloxy)-thiazol-5-ylmethyl]-pyridin-4-ylmethyl-amine,
or a pharmaceutically acceptable salt thereof.

10. A compound of the formula I according to any of claims 1 to 9, which is selected from the series consisting of:
2-(2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid [2-(2-oxo-imidazolidin-1-yl)-ethyl]-amide,
2-(2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid cyclopropylamide,
2-((S)-2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide,
2-(2-Oxo-pyrrolidin-1-yl)-N-[2-(2-o-tolyl-chroman-6-yloxy)-thiazol-5-ylmethyl]-acetamide,
Isoxazole-5-carboxylic acid [2-(2-o-tolyl-chroman-6-yloxy)-thiazol-5-ylmethyl]-amide,
2-(2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid propylamide,
4-Methyl-2-(2-o-tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (isoxazol-5-ylmethyl)-amide,
2-[2-(5-Fluoro-2-methyl-phenyl)-chroman-6-yloxy]-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide,
2-[2-(5-Fluoro-2-methyl-phenyl)-chroman-6-yloxy]-thiazole-5-carboxylic acid propylamide,
Phosphoric acid mono-(2-{[2-((S)-2-o-tolyl-chroman-6-yloxy)-thiazole-5-carbonyl]-amino}-ethyl) ester,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (6,7-dihydro-5H-pyrrolo[2,1-c][1,2,4]triazol-3-ylmethyl)-amide,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid propylamide,
2-(2-Phenyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-chloro-pyridin-4-ylmethyl)-amide,
2-((R)-2-o-Tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide, and
[2-(2-Phenyl-chroman-6-yloxy)-thiazol-5-ylmethyl]-pyridin-4-ylmethyl-amine,
or a pharmaceutically acceptable salt thereof.

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 10, with the proviso that the compound of the formula

I is not a compound in which simultaneously the group Ar is unsubstituted phenyl or 3-fluorophenyl, the groups R3 and R4 are hydrogen, one of the groups R5 and R6 is hydrogen, the other of the groups R5 and R6 is R40-(C_1-C_4)-alkyl-, and R7 is R40 or R40-(C_1-C_4)-alkyl-, wherein R40 is pyrazolyl which is unsubstituted or substituted by one or more identical or different (C_1-C_4)-alkyl substituents, and the excluded compounds are excluded as the free compounds and in the form of their 2,2,2-trifluoroacetates.

12. 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 10, with the proviso that the compound of the formula I is not one of the following compounds:
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[1-(1,5-dimethyl-1H-pyrazol-4-yl)ethyl]-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[(1,3-dimethyl-1H-pyrazol-4-yl)methyl]-,
1H-Pyrazole-4-sulfonamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1,3,5-trimethyl-,
1H-Pyrazole-4-carboxamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1,5-dimethyl-,
1H-Pyrazole-4-carboxamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1,3,5-trimethyl-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[2-(3,5-dimethyl-1H-pyrazol-1-yl)ethyl]-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[(1-ethyl-3-methyl-1H-pyrazol-4-yl)methyl]-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[(1-methyl-1H-pyrazol-5-yl)methyl]-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[(1,5-dimethyl-1H-pyrazol-3-yl)methyl]-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[(1,3-dimethyl-1H-pyrazol-5-yl)methyl]-,

1H-Pyrazole-4-sulfonamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1,5-dimethyl-,
1H-Pyrazole-4-sulfonamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1-methyl-,
1H-Pyrazole-3-carboxamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1-ethyl-,
1H-Pyrazole-1-acetamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-,
1H-Pyrazole-1-acetamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-3-methyl-,
1H-Pyrazole-5-carboxamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1-ethyl-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[3-(1H-pyrazol-1-yl)propyl]-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[2-(3-methyl-1H-pyrazol-1-yl)ethyl]-,
1H-Pyrazole-4-carboxamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1-ethyl-,
5-Thiazolecarboxamide, N-[(1,5-dimethyl-1H-pyrazol-4-yl)methyl]-2-[[2-(3-fluorophenyl)-3,4-dihydro-2H-1-benzopyran-6-yl]oxy]-,
5-Thiazolecarboxamide, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[(1-ethyl-1H-pyrazol-4-yl)methyl]-,
1H-Pyrazole-1-propanamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-,
1H-Pyrazole-4-sulfonamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-5-methyl-1-(1-methylethyl)-,
5-Thiazolecarboxamide, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[(1,5-dimethyl-1H-pyrazol-4-yl)methyl]-,
5-Thiazolecarboxamide, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[1-(1,5-dimethyl-1H-pyrazol-4-yl)ethyl]-,
5-Thiazolecarboxamide, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[1-(1,3-dimethyl-1H-pyrazol-4-yl)ethyl]-,

5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[(1,5-dimethyl-1H-pyrazol-4-yl)methyl]-,
1H-Pyrazole-4-sulfonamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1-ethyl-,
1H-Pyrazole-5-carboxamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1,3-dimethyl-,
5-Thiazolemethanamine, 2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-N-[2-(1H-pyrazol-1-yl)ethyl]-,
1H-Pyrazole-5-sulfonamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1-methyl-,
1H-Pyrazole-5-carboxamide, N-[[2-[(3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl)oxy]-5-thiazolyl]methyl]-1-methyl-,
5-Thiazolecarboxamide, N-[(1,5-dimethyl-1H-pyrazol-4-yl)methyl]-2-[[(2R)-2-(3-fluorophenyl)-3,4-dihydro-2H-1-benzopyran-6-yl]oxy]-,
5-Thiazolecarboxamide, N-[(1,5-dimethyl-1H-pyrazol-4-yl)methyl]-2-[[(2S)-2-(3-fluorophenyl)-3,4-dihydro-2H-1-benzopyran-6-yl]oxy]-,
5-Thiazolecarboxamide, 2-[[(2R)-3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl]oxy]-N-[(1,5-dimethyl-1H-pyrazol-4-yl)methyl]-, and
5-Thiazolecarboxamide, 2-[[(2S)-3,4-dihydro-2-phenyl-2H-1-benzopyran-6-yl]oxy]-N-[(1,5-dimethyl-1H-pyrazol-4-yl)methyl]-,
wherein in the excluded compounds the carbon atom in position 2 of the chroman ring, which carries a phenyl group or 3-fluorophenyl group, is present in racemic form, unless specified otherwise, and the excluded compounds are excluded as the free compounds and in the form of their 2,2,2-trifluoroacetates.

13. A compound of the formula I according to any of claims 1 to 12, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, which is 2-(2-o-tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide.

14. A compound of the formula I according to any of claims 1 to 12, which is 2-((S)-2-o-tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide.

15. A compound of the formula I according to any of claims 1 to 12, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, which is isoxazole-5-carboxylic acid [2-(2-o-tolyl-chroman-6-yloxy)-thiazol-5-ylmethyl]-amide.

16. A compound of the formula I according to any of claims 1 to 12, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, which is 2-(2-o-tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid propylamide.

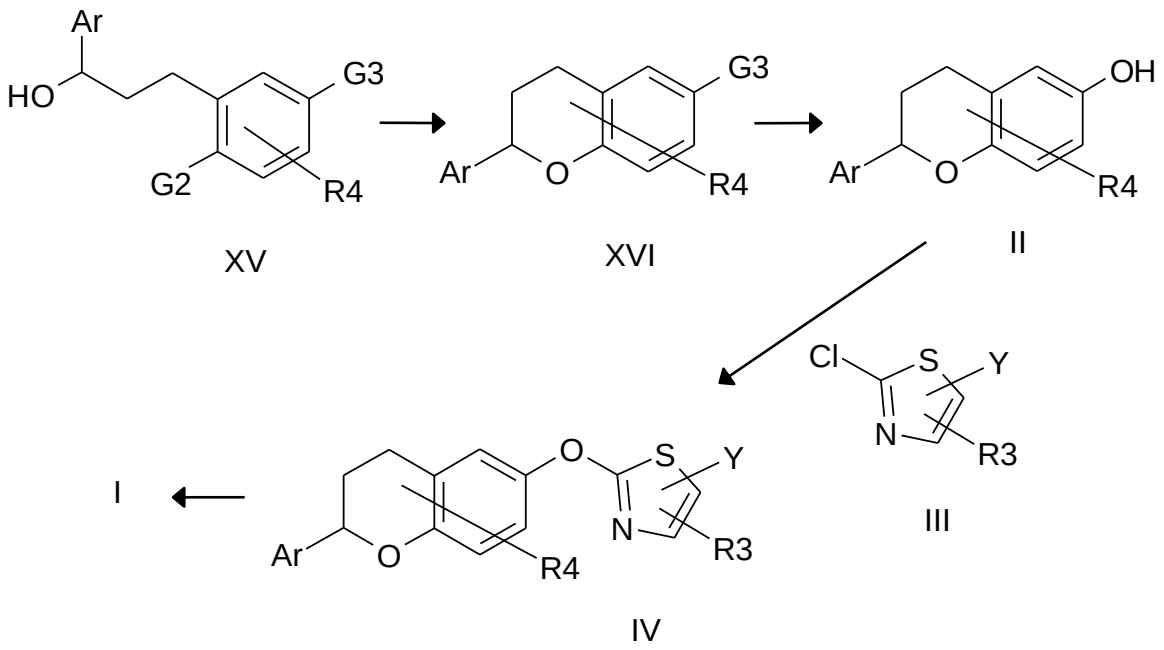
17. A compound of the formula I according to any of claims 1 to 12, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, which is 2-[2-(5-fluoro-2-methyl-phenyl)-chroman-6-yloxy]-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide.

18. A compound of the formula I according to any of claims 1 to 12, which is phosphoric acid mono-(2-{[2-((S)-2-o-tolyl-chroman-6-yloxy)-thiazole-5-carbonyl]-amino}-ethyl) ester, or a pharmaceutically acceptable salt thereof.

19. A compound of the formula I according to any of claims 1 to 12, which is 2-((R)-2-o-tolyl-chroman-6-yloxy)-thiazole-5-carboxylic acid (2-hydroxy-ethyl)-amide.

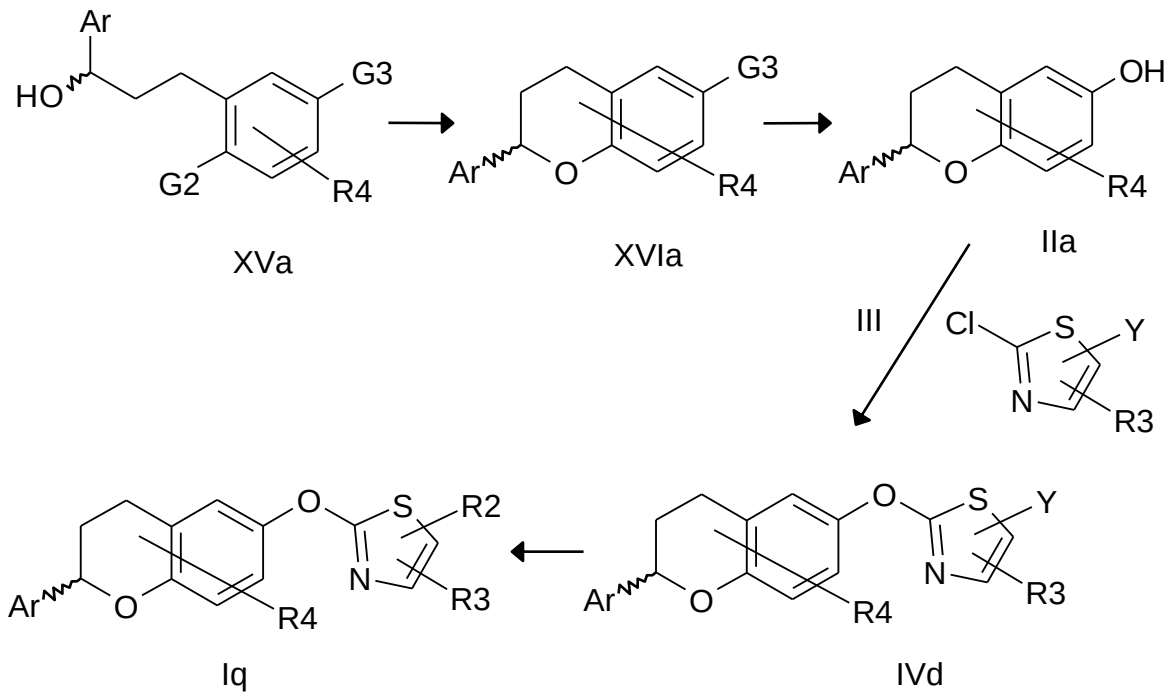
20. A compound of the formula I according to any of claims 1 to 12, which is phosphoric acid mono-(2-{[2-((S)-2-o-tolyl-chroman-6-yloxy)-thiazole-5-carbonyl]-amino}-ethyl) ester disodium salt.

21. A process for the preparation of a compound of the formula I as claimed in any of claims 1 to *20*,



which comprises cyclizing a compound of the formula XV to a compound of the formula XVI, converting the compound of the formula XVI into a compound of the formula II, reacting the compound of the formula II with a compound of the formula III to give a compound of the formula IV, and converting the compound of the formula IV into a compound of the formula I, wherein the groups Ar, R3 and R4 in the compounds of the formulae II, III, IV, XV and XVI are defined as in the compounds of the formula I, the group G2 in the compounds of the formula XV is a hydroxy group or a nucleophilically substitutable leaving group, the group G3 in the compounds of the formulae XV and XVI is bromine or (C_1-C_4)-alkyl-O-, and the group Y in the compounds of the formulae III and IV is R50-O-C(O)-, H-C(O)- or NC-, wherein R50 is (C_1-C_4)-alkyl.

22. The process according to claim 21, wherein a compound of the formula Iq is prepared in which the chiral carbon atom carrying the group Ar is present in uniform configuration,



which comprises cyclizing a compound of the formula XVa, in which the chiral carbon atom carrying the group Ar is present in uniform configuration, to a compound of the formula XVIa, converting the compound of the formula XVIa into a compound of the formula IIa, reacting the compound of the formula IIa with a compound of the formula III to give a compound of the formula IVd, and converting the compound of the formula IVd into a compound of the formula Iq, wherein the groups Ar, R2, R3 and R4 in the compounds of the formulae Iq, IIa, III, IVd, XVa and XVIa are defined as in the compounds of the formula I, the group G2 in the compounds of the formula XVa, the group G3 in the compounds of the formulae XVa and XVIa and the group Y in the compounds of the formulae III and IVd are defined as in compounds of the formulae XV, XVI, III and IV in claim 21.

23. 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 20, for use as a pharmaceutical.

24. 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 20, and a pharmaceutically acceptable carrier.

25. 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 20, for use in the treatment of heart failure, cardiac arrhythmias, stroke, dementia, hypertension, cardiac ischemia, renal failure, shock or age-related disorders.

26. Use of 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 20, for the manufacture of a medicament for the treatment of heart failure, cardiac arrhythmias, stroke, dementia, hypertension, cardiac ischemia, renal failure, shock or age-related disorders.