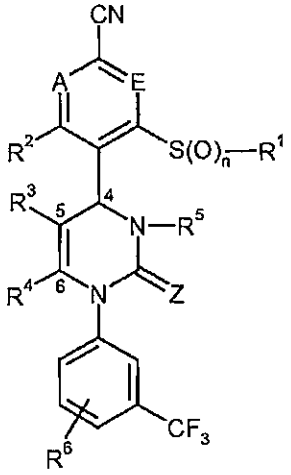
Claims

1. A compound of the formula (I)



(I),

in which

A and E both represent C-$R^7$ or one of the two ring members A and E represents N and the other represents C-$R^7$, in which

$R^7$ represents in each case hydrogen, fluorine or chlorine,

Z represents O or S,

n represents the number 0, 1 or 2,

$R^1$ represents ($C_1$-$C_6$)-alkyl which may be substituted by hydroxyl, ($C_1$-$C_4$)-alkoxy, amino, mono- or di-($C_1$-$C_4$)-alkylamino, hydroxycarbonyl, aminocarbonyl, ($C_3$-$C_6$)-cycloalkyl, phenyl or 5- or 6-membered heteroaryl or up to five times by fluorine, or represents ($C_2$-$C_6$)-alkenyl, ($C_3$-$C_6$)-cycloalkyl, phenyl or 5- or 6-membered heteroaryl,

where the ($C_3$-$C_6$)-cycloalkyl groups mentioned may be substituted up to two times by identical or different substituents from the group consisting of ($C_1$-$C_4$)-alkyl, hydroxyl and ($C_1$-$C_4$)-alkoxy

and

the phenyl and heteroaryl groups mentioned may be substituted up to two times by

identical or different substituents from the group consisting of fluorine, chlorine, cyano, $(C_1-C_4)$-alkyl, difluoromethyl, trifluoromethyl, $(C_1-C_4)$-alkoxy, difluoromethoxy and trifluoromethoxy,

$R^2$ represents hydrogen, fluorine or chlorine,

$R^3$ represents cyano or a group of the formula $-C(=O)-R^8$, $-C(=O)-O-R^8$, $-C(=O)-NH_2$ or $-C(=O)-NH-R^8$, in which

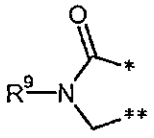
$R^8$ represents $(C_1-C_6)$-alkyl, $(C_3-C_6)$-alkenyl or $(C_3-C_6)$-cycloalkyl,

where $(C_1-C_6)$-alkyl and $(C_3-C_6)$-cycloalkyl for their part may be substituted up to two times by identical or different substituents from the group consisting of hydroxyl, $(C_1-C_4)$-alkoxy, hydroxycarbonyl, $(C_1-C_4)$-alkoxycarbonyl, amino, mono- and di-$(C_1-C_4)$-alkylamino and in $(C_1-C_6)$-alkyl and $(C_3-C_6)$-cycloalkyl in each case one $CH_2$ group may be replaced by an oxygen atom, if this results in a chemically stable compound,

$R^4$ represents methyl or ethyl

or

$R^3$ and $R^4$ are attached to one another and together form a fused group of the formula



in which

* denotes the point of attachment to the 5-position, shown in formula (I), of the dihydropyrimidine ring

and

** denotes the point of attachment to the 6-position, shown in formula (I), of the dihydropyrimidine ring

and

$R^9$ represents hydrogen, $(C_1-C_6)$-alkyl or $(C_3-C_6)$-cycloalkyl,

where $(C_1-C_6)$-alkyl may be substituted by hydroxyl, $(C_1-C_4)$-alkoxy, aminocarbonyl, aminocarbonylamino, $(C_1-C_4)$-acylamino or $(C_3-C_6)$-cycloalkyl,

$R^5$ represents hydrogen or $(C_1-C_6)$-alkyl which may be substituted by cyano, hydroxyl, $(C_1-C_4)$-alkoxy, amino, mono- or di-$(C_1-C_4)$-alkylamino or $(C_3-C_6)$-cycloalkyl or up to three times by fluorine, or represents phenyl, pyridyl or pyrimidinyl,

where phenyl, pyridyl and pyrimidinyl for their part may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, $(C_1-C_4)$-alkyl, trifluoromethyl, $(C_1-C_4)$-alkoxy and trifluoromethoxy,

or

$R^5$ represents a group of the formula $-C(=O)-O-R^{10}$, $-L^1-C(=O)-O-R^{11}$, $-L^2-C(=O)-NR^{12}R^{13}$, $-L^2-SO_2-NR^{12}R^{13}$, $-L^2-C(=O)-NR^{14}-NR^{12}R^{13}$ or $-L^2-SO_2-R^{15}$, in which

$L^1$ represents $(C_1-C_6)$-alkanediyl,

$L^2$ represents a bond or $(C_1-C_6)$-alkanediyl,

$R^{10}$ represents $(C_1-C_6)$-alkyl which may be substituted by $(C_3-C_6)$-cycloalkyl or phenyl,

$R^{11}$ represents hydrogen or $(C_1-C_6)$-alkyl which may be substituted by $(C_3-C_6)$-cycloalkyl or phenyl,

$R^{12}$ and $R^{13}$ are identical or different and independently of one another represent hydrogen, $(C_1-C_6)$-alkyl, $(C_3-C_6)$-cycloalkyl or 4- to 6-membered heterocyclyl,

where $(C_1-C_6)$-alkyl, $(C_3-C_6)$-cycloalkyl and 4- to 6-membered heterocyclyl for their part may be substituted up to two times by identical or different substituents from the group consisting of fluorine, hydroxyl, $(C_1-C_4)$-alkoxy, oxo, amino, mono- or di-$(C_1-C_4)$-alkylamino, hydroxycarbonyl, $(C_1-C_4)$-alkoxycarbonyl and aminocarbonyl

and

in ($C_1$-$C_6$)-alkyl a $CH_2$ group may be replaced by an oxygen atom, if this results in a chemically stable compound,

and

($C_3$-$C_6$)-cycloalkyl and 4- to 6-membered heterocyclyl may additionally be substituted up to two times by identical or different ($C_1$-$C_4$)-alkyl radicals, which for their part may be substituted by hydroxyl, ($C_1$-$C_4$)-alkoxy or hydroxycarbonyl,

or

$R^{12}$ and $R^{13}$ together with the nitrogen atom to which they are attached form a 4- to 6-membered heterocycle which may contain a further ring heteroatom from the group consisting of N, O, S, SO and $SO_2$ and which may be substituted up to two times by identical or different substituents from the group consisting of ($C_1$-$C_4$)-alkyl, hydroxyl, ($C_1$-$C_4$)-alkoxy, oxo, amino, mono- or di-($C_1$-$C_4$)-alkylamino, hydroxycarbonyl, aminocarbonyl, ($C_3$-$C_6$)-cycloalkyl, 4- to 6-membered heterocyclyl and 5- or 6-membered heteroaryl,

where ($C_1$-$C_4$)-alkyl for its part may be substituted by hydroxyl, ($C_1$-$C_4$)-alkoxy or hydroxycarbonyl,

$R^{14}$ represents hydrogen or ($C_1$-$C_4$)-alkyl

and

$R^{15}$ represents ($C_1$-$C_6$)-alkyl, ($C_3$-$C_6$)-cycloalkyl, phenyl or 5- or 6-membered heteroaryl,

where ($C_1$-$C_6$)-alkyl may be substituted by chlorine, hydroxyl, ($C_1$-$C_4$)-alkoxy, mono- or di-($C_1$-$C_4$)-alkylamino or ($C_3$-$C_6$)-cycloalkyl or up to three times by fluorine

and

phenyl and 5-or 6-membered heteroaryl for their part may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, ($C_1$-$C_4$)-alkyl, difluoromethyl, trifluoromethyl, ($C_1$-$C_4$)-alkoxy and trifluoromethoxy,

and

$R^6$ represents hydrogen, fluorine or chlorine,

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

2. The compound of the formula (I) as claimed in claim 1, in which

A and E both represent C-$R^7$ or one of the two ring members A and E represents N and the other represents C-$R^7$, in which

$R^7$ represents in each case hydrogen, fluorine or chlorine,

Z represents O or S,

n represents the number 0, 1 or 2,

$R^1$ represents ($C_1$-$C_6$)-alkyl which may be substituted by hydroxyl, ($C_1$-$C_4$)-alkoxy, amino, mono- or di-($C_1$-$C_4$)-alkylamino, hydroxycarbonyl, aminocarbonyl, ($C_3$-$C_6$)-cycloalkyl or phenyl, or represents ($C_2$-$C_6$)-alkenyl, ($C_3$-$C_6$)-cycloalkyl or phenyl,

where the ($C_3$-$C_6$)-cycloalkyl groups mentioned may be substituted up to two times by identical or different substituents from the group consisting of ($C_1$-$C_4$)-alkyl, hydroxyl and ($C_1$-$C_4$)-alkoxy

and

the phenyl groups mentioned may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, ($C_1$-$C_4$)-alkyl, difluoromethyl, trifluoromethyl, ($C_1$-$C_4$)-alkoxy, difluoromethoxy and trifluoromethoxy,

$R^2$ represents hydrogen, fluorine or chlorine,

$R^3$ represents cyano or a group of the formula -C(=O)-$R^8$, -C(=O)-O-$R^8$, -C(=O)-$NH_2$ or -C(=O)-NH-$R^8$, in which

$R^8$ represents ($C_1$-$C_6$)-alkyl, ($C_3$-$C_6$)-alkenyl or ($C_3$-$C_6$)-cycloalkyl,

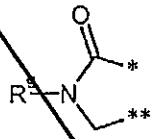
where ($C_1$-$C_6$)-alkyl and ($C_3$-$C_6$)-cycloalkyl for their part may be substituted up to two times by identical or different substituents from the group consisting of hydroxyl, ($C_1$-$C_4$)-alkoxy, hydroxycarbonyl, ($C_1$-$C_4$)-alkoxy-

carbonyl, amino, mono- and di-($C_1$-$C_4$)-alkylamino and in ($C_1$-$C_6$)-alkyl and ($C_3$-$C_6$)-cycloalkyl in each case one $CH_2$ group may be replaced by an oxygen atom, if this results in a chemically stable compound,

$R^4$ represents methyl or ethyl

or

$R^3$ and $R^4$ are attached to one another and together form a fused group of the formula



in which

* denotes the point of attachment to the 5-position, shown in formula (I), of the dihydropyrimidine ring

and

** denotes the point of attachment to the 6-position, shown in formula (I), of the dihydropyrimidine ring

and

$R^9$ represents hydrogen, ($C_1$-$C_6$)-alkyl or ($C_3$-$C_6$)-cycloalkyl,

where ($C_1$-$C_6$)-alkyl may be substituted by hydroxyl, ($C_1$-$C_4$)-alkoxy, aminocarbonyl, ($C_1$-$C_4$)-acylamino or ($C_3$-$C_6$)-cycloalkyl,

$R^5$ represents hydrogen or ($C_1$-$C_6$)-alkyl which may be substituted up to three times by fluorine, or represents phenyl, pyridyl or pyrimidinyl,

where phenyl, pyridyl and pyrimidinyl for their part may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, ($C_1$-$C_4$)-alkyl, trifluoromethyl, ($C_1$-$C_4$)-alkoxy and trifluoromethoxy,

or

$R^5$ represents a group of the formula $-C(=O)-O-R^{10}$, $-L^1-C(=O)-O-R^{11}$, $-L^2-C(=O)-$

$NR^{12}R^{13}$, $-L^2-SO_2-NR^{12}R^{13}$, $-L^2-C(=O)-NR^{14}-NR^{12}R^{13}$ or $-L^2-SO_2-R^{15}$, in which

$L^1$ represents $(C_1-C_6)$-alkanediyl,

$L^2$ represents a bond or $(C_1-C_6)$-alkanediyl,

$R^{10}$ represents $(C_1-C_6)$-alkyl,

$R^{11}$ represents hydrogen or $(C_1-C_6)$-alkyl,

$R^{12}$ and $R^{13}$ are identical or different and independently of one another represent hydrogen, $(C_1-C_6)$-alkyl, $(C_3-C_6)$-cycloalkyl or 4- to 6-membered heterocyclyl,

where $(C_1-C_6)$-alkyl, $(C_3-C_6)$-cycloalkyl and 4- to 6-membered heterocyclyl for their part may be substituted up to two times by identical or different substituents from the group consisting of fluorine, hydroxyl, $(C_1-C_4)$-alkoxy, oxo, amino, mono- or di-$(C_1-C_4)$-alkylamino, hydroxycarbonyl, $(C_1-C_4)$-alkoxycarbonyl and aminocarbonyl and in $(C_1-C_6)$-alkyl a $CH_2$ group may be replaced by an oxygen atom, if this results in a chemically stable compound,

or

$R^{12}$ and $R^{13}$ together with the nitrogen atom to which they are attached form a 4- to 6-membered heterocycle which may contain a further ring heteroatom from the group consisting of N, O, S, SO and $SO_2$ and may be substituted up to two times by identical or different substituents from the group consisting of $(C_1-C_4)$-alkyl, hydroxyl, $(C_1-C_4)$-alkoxy, oxo, amino, mono- and di-$(C_1-C_4)$-alkylamino,

where $(C_1-C_4)$-alkyl for its part may be substituted by hydroxyl or $(C_1-C_4)$-alkoxy,

$R^{14}$ represents hydrogen or $(C_1-C_4)$-alkyl

and

$R^{15}$ represents $(C_1-C_6)$-alkyl, $(C_3-C_6)$-cycloalkyl, phenyl or 5- or 6-membered heteroaryl,

where ($C_1$-$C_6$)-alkyl may be substituted by fluorine, chlorine, hydroxyl, ($C_1$-$C_4$)-alkoxy, mono- or di-($C_1$-$C_4$)-alkylamino

and

phenyl and 5- or 6-membered heteroaryl for their part may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, ($C_1$-$C_4$)-alkyl, trifluoromethyl, ($C_1$-$C_4$)-alkoxy and trifluoromethoxy,

and

$R^6$ represents hydrogen, fluorine or chlorine,

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

3. The compound of the formula (I) as claimed in claim 1 or 2, in which

A and E both represent CH,

Z represents O,

n represents the number 0 or 2,

$R^1$ represents ($C_1$-$C_4$)-alkyl which may be substituted by hydroxyl, ($C_1$-$C_4$)-alkoxy, hydroxycarbonyl, aminocarbonyl, ($C_3$-$C_6$)-cycloalkyl, phenyl or 5-membered heteroaryl or up to three times by fluorine, or represents ($C_3$-$C_6$)-cycloalkyl, phenyl or 5-membered heteroaryl,

where the phenyl and heteroaryl groups mentioned may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, methyl, trifluoromethyl, methoxy and trifluoromethoxy,

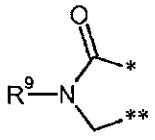
$R^2$ represents hydrogen,

$R^3$ represents cyano, acetyl or (2-hydroxyethoxy)carbonyl,

$R^4$ represents methyl

or

$R^3$ and $R^4$ are attached to one another and together form a fused group of the formula



in which

* denotes the point of attachment to the 5-position, shown in formula (I), of the dihydropyrimidine ring

and

** denotes the point of attachment to the 6-position, shown in formula (I), of the dihydropyrimidine ring

and

$R^9$ represents hydrogen, $(C_1-C_4)$-alkyl or $(C_3-C_6)$-cycloalkyl,

where $(C_1-C_4)$-alkyl may be substituted by hydroxyl or $(C_1-C_4)$-alkoxy,

$R^5$ represents hydrogen or $(C_1-C_4)$-alkyl which may be substituted by cyano or di-$(C_1-C_4)$-alkylamino, or represents a group of the formula $-L^2-C(=O)-NR^{12}R^{13}$, $-L^2-C(=O)-NH-NR^{12}R^{13}$ or $-L^2-SO_2-R^{15}$, in which

$L^2$ represents a bond, $-CH_2-$, $-CH_2CH_2-$ or $-CH(CH_3)-$,

$R^{12}$ represents hydrogen or $(C_1-C_4)$-alkyl which may be substituted by hydroxyl or $(C_1-C_4)$-alkoxy,

$R^{13}$ represents hydrogen, $(C_1-C_6)$-alkyl or $(C_3-C_6)$-cycloalkyl,

where $(C_1-C_6)$-alkyl may be substituted up to two times by identical or different substituents from the group consisting of hydroxyl, $(C_1-C_4)$-alkoxy, hydroxycarbonyl, $(C_1-C_4)$-alkoxycarbonyl and aminocarbonyl and in $(C_1-C_6)$-alkyl a $CH_2$ group may be replaced by an oxygen atom, if this results in a chemically stable compound,

or

$R^{12}$ and $R^{13}$ together with the nitrogen atom to which they are attached form a 5- or 6-membered heterocycle which may contain a further ring heteroatom from

the group consisting of N, O and S and may be substituted by ($C_1$-$C_4$)-alkyl, hydroxyl, ($C_1$-$C_4$)-alkoxy, oxo, hydroxycarbonyl, aminocarbonyl, 4- to 6-membered heterocyclyl or 5- or 6-membered heteroaryl,

where ($C_1$-$C_4$)-alkyl for its part may be substituted by hydroxyl, ($C_1$-$C_4$)-alkoxy or hydroxycarbonyl,

and

$R^{15}$ represents ($C_1$-$C_4$)-alkyl, ($C_3$-$C_6$)-cycloalkyl or phenyl,

where ($C_1$-$C_4$)-alkyl may be substituted by ($C_3$-$C_6$)-cycloalkyl

and

phenyl may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, methyl, trifluoromethyl, methoxy and trifluoromethoxy,

and

$R^6$ represents hydrogen or fluorine,

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

4. The compound of the formula (I) as claimed in one or more of claims 1 to 3, in which

A and E both represent CH,

Z represents O,

n represents the number 0 or 2,

$R^1$ represents ($C_1$-$C_4$)-alkyl which may be substituted by hydroxyl, ($C_1$-$C_4$)-alkoxy, hydroxycarbonyl, aminocarbonyl, ($C_3$-$C_6$)-cycloalkyl or phenyl, or represents ($C_3$-$C_6$)-cycloalkyl or phenyl,

where the phenyl groups mentioned may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, methyl, trifluoromethyl, methoxy and trifluoromethoxy,

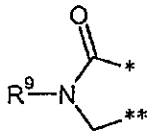
$R^2$ represents hydrogen,

$R^3$ represents cyano or acetyl,

$R^4$ represents methyl

or

$R^3$ and $R^4$ are attached to one another and together form a fused group of the formula



in which

* denotes the point of attachment to the 5-position, shown in formula (I), of the dihydropyrimidine ring

and

** denotes the point of attachment to the 6-position, shown in the formula (I), of the dihydropyrimidine ring

and

$R^9$ represents hydrogen, $(C_1-C_4)$-alkyl or $(C_3-C_6)$-cycloalkyl,

where $(C_1-C_4)$-alkyl may be substituted by hydroxyl or $(C_1-C_4)$-alkoxy,

$R^5$ represents hydrogen, $(C_1-C_4)$-alkyl or a group of the formula $-L^2-C(=O)-NR^{12}R^{13}$, $-L^2-C(=O)-NH-NR^{12}R^{13}$ or $-L^2-SO_2-R^{15}$, in which

$L^2$ represents a bond, $-CH_2-$, $-CH_2CH_2-$ or $-CH(CH_3)-$,

$R^{12}$ represents hydrogen or $(C_1-C_4)$-alkyl which may be substituted by hydroxyl or $(C_1-C_4)$-alkoxy,

$R^{13}$ represents hydrogen, $(C_1-C_6)$-alkyl or $(C_3-C_6)$-cycloalkyl,

where $(C_1-C_6)$-alkyl may be substituted up to two times by identical or different substituents from the group consisting of hydroxyl, $(C_1-C_4)$-alkoxy, hydroxycarbonyl, $(C_1-C_4)$-alkoxycarbonyl and aminocarbonyl and in $(C_1-C_6)$-alkyl a $CH_2$ group may be replaced by an oxygen atom, if this results in

a chemically stable compound,

or

$R^{12}$ and $R^{13}$ together with the nitrogen atom to which they are attached form a 5- or 6-membered heterocycle which may contain a further ring heteroatom from the group consisting of N, O and S and may be substituted by $(C_1-C_4)$-alkyl, hydroxyl, $(C_1-C_4)$-alkoxy or oxo,

where $(C_1-C_4)$-alkyl for its part may be substituted by hydroxyl or $(C_1-C_4)$-alkoxy,

and

$R^{15}$ represents $(C_1-C_4)$-alkyl, $(C_3-C_6)$-cycloalkyl or phenyl,

where phenyl may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, methyl, trifluoromethyl, methoxy and trifluoromethoxy,

and

$R^6$ represents hydrogen or fluorine,

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

5. The compound of the formula (I) as claimed in one or more of claims 1 to 4, in which

A and E both represent CH,

Z represents O,

n represents the number 2,

$R^1$ represents $(C_1-C_4)$-alkyl which may be substituted by hydroxyl, $(C_1-C_4)$-alkoxy, cyclopropyl, cyclobutyl or phenyl or up to three times by fluorine,

$R^2$ represents hydrogen,

$R^3$ represents cyano or (2-hydroxyethoxy)carbonyl,

$R^4$ represents methyl,

$R^5$ represents hydrogen, $(C_1-C_4)$-alkyl or a group of the formula $-L^2-C(=O)-NH-R^{13}$ or $-SO_2-R^{15}$, in which

$L^2$ represents a bond or $-CH_2-$,

$R^{13}$ represents hydrogen or $(C_1-C_4)$-alkyl which may be substituted by hydroxyl or $(C_1-C_4)$-alkoxy, or $(C_3-C_6)$-cycloalkyl

and

$R^{15}$ represents $(C_1-C_4)$-alkyl or $(C_3-C_6)$-cycloalkyl,

and

$R^6$ represents hydrogen,

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

6. The compound of the formula (I) as claimed in one or more of claims 1 to 5, in which

A and E both represent CH,

Z represents O,

n represents the number 2,

$R^1$ represents $(C_1-C_4)$-alkyl which may be substituted by hydroxyl or $(C_1-C_4)$-alkoxy,

$R^2$ represents hydrogen,

$R^3$ represents cyano,

$R^4$ represents methyl,

$R^5$ represents hydrogen, $(C_1-C_4)$-alkyl or a group of the formula $-CH_2-C(=O)-NH-R^{13}$ or $-SO_2-R^{15}$, in which

$R^{13}$ represents hydrogen or $(C_1-C_4)$-alkyl which may be substituted by hydroxyl or $(C_1-C_4)$-alkoxy

and

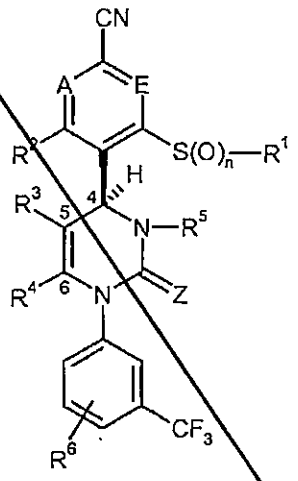
$R^{15}$ represents $(C_1-C_4)$-alkyl or $(C_3-C_6)$-cycloalkyl,

and

$R^6$ represents hydrogen,

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

7. The compound of the formula (I) having the configuration shown in formula (I-*ent*) at the 4-position of the dihydropyrimidine ring as claimed in one or more of claims 1 to 6,



(I-*ent*)

in which

A and E both represent CH,

Z represents O,

n represents the number 2,

$R^1$ represents ($C_1$-$C_4$)-alkyl which may be substituted by hydroxyl or ($C_1$-$C_4$)-alkoxy,

$R^2$ represents hydrogen,

$R^3$ represents cyano,

$R^4$ represents methyl,

$R^5$ represents hydrogen, ($C_1$-$C_4$)-alkyl or a group of the formula $-CH_2-C(=O)-NH-R^{13}$ or $-SO_2-R^{15}$, in which

$R^{13}$ represents hydrogen or ($C_1$-$C_4$)-alkyl which may be substituted by hydroxyl

or ($C_1$-$C_4$)-alkoxy

and

$R^{15}$ represents ($C_1$-$C_4$)-alkyl or ($C_3$-$C_6$)-cycloalkyl,

and

$R^6$ represents hydrogen,

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

8. The compound of the formula (I) as claimed in one or more of claims 1 to 7, selected from the group consisting of:

4-{(4*S*)-5-Acetyl-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-4-yl}-3-(methylsulfonyl)benzonitrile

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(6*S*)-5-Cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-*N*-(2-hydroxyethyl)-4-methyl-2-oxo-3-[3-(trifluoromethyl)phenyl]-3,6-dihydropyrimidine-1(2*H*)-carboxamide

(6*S*)-5-Cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-*N*',*N*'-bis(2-hydroxyethyl)-4-methyl-2-oxo-3-[3-(trifluoromethyl)phenyl]-3,6-dihydropyrimidine-1(2*H*)-carbohydrazide

(6*S*)-5-Cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-*N*-[2-(2-hydroxyethoxy)ethyl]-4-methyl-2-oxo-3-[3-(trifluoromethyl)phenyl]-3,6-dihydropyrimidine-1(2*H*)-carboxamide

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-3-{[(3*S*)-3-hydroxypyrrolidin-1-yl]carbonyl}-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-3-{[4-(2-hydroxyethyl)piperazin-1-yl]carbonyl}-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

2-[(6*S*)-5-Cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-4-methyl-2-oxo-3-[3-(trifluoromethyl)phenyl]-3,6-dihydropyrimidin-1(2*H*)-yl]acetamide

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-(methylsulfonyl)-2-oxo-1-[3-

(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-(cyclopropylsulfonyl)-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-3,6-dimethyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

4-{(4*S*)-6-Methyl-3-(methylsulfonyl)-2,5-dioxo-1-[3-(trifluoromethyl)phenyl]-2,3,4,5,6,7-hexahydro-1*H*-pyrrolo[3,4-d]pyrimidin-4-yl}-3-(methylsulfonyl)benzonitrile

(4*S*)-4-[4-Cyano-2-(methylsulfanyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4*S*)-4-{4-Cyano-2-[(*S*)-methylsulfinyl]phenyl}-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(*rac*)-1-(2-{4-[4-Cyano-2-(methylsulfonyl)phenyl]-2,5-dioxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4,5,7-hexahydro-6*H*-pyrrolo[3,4-d]pyrimidin-6-yl}ethyl)urea

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-3-[(3-hydroxyazetidin-1-yl)carbonyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4*S*)-3-[(3*R*)-3-Aminopiperidin-1-yl]carbonyl-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-3-{[4-(pyridin-2-yl)piperazin-1-yl]carbonyl}-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(6S)-5-cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-N,N-bis(2-hydroxypropyl)-4-methyl-2-oxo-3-[3-(trifluoromethyl)phenyl]-3,6-dihydropyrimidine-1(2H)-carboxamide

(6S)-5-cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-N-(1-hydroxy-2-methylpropan-2-yl)-4-methyl-2-oxo-3-[3-(trifluoromethyl)phenyl]-3,6-dihydropyrimidine-1(2H)-carboxamide

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-3-{[1-(difluoromethyl)-5-methyl-1H-pyrazol-4-yl]sulfonyl}-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-3-[(2-cyanophenyl)sulfonyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4S)-3-(Cyanomethyl)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)-phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

Benzyl 5-cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-4-methyl-2-oxo-3-[3-(trifluoromethyl)-phenyl]-3,6-dihydropyrimidine-1(2*H*)-carboxylate

(4*S*)-4-[4-Cyano-2-(ethylsulfonyl)phenyl]-3,6-dimethyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(*rac*)-4-[4-Cyano-2-((2-hydroxyethyl)sulfonyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)-phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4*S*)-4-{4-Cyano-2-[phenylsulfonyl]phenyl}-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

2-Hydroxyethyl (4*S*)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-(methylsulfonyl)-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carboxylate

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

9. The compound of the formula (I) as claimed in one or more of claims 1 to 7, selected from

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carboxamide

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(6*S*)-5-Cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-*N*-(2-hydroxyethyl)-4-methyl-2-oxo-3-[3-(trifluoromethyl)phenyl]-3,6-dihydropyrimidine-1(2*H*)-carboxamide

(6*S*)-5-Cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-*N'*,*N'*-bis(2-hydroxyethyl)-4-methyl-2-oxo-3-[3-(trifluoromethyl)phenyl]-3,6-dihydropyrimidine-1(2*H*)-carbohydrazide

2-[(6*S*)-5-Cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-4-methyl-2-oxo-3-[3-(trifluoromethyl)-phenyl]-3,6-dihydropyrimidin-1(2*H*)-yl]acetamide

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-3-[2-oxo-2-(3-oxopiperazin-1-yl)ethyl]-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-(methylsulfonyl)-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-{[2-(trifluoromethoxy)phenyl]sulfonyl}-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-(ethylsulfonyl)-2-oxo-1-[3-(trifluoromethyl)-phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-(cyclopropylsulfonyl)-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-3,6-dimethyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

4-{(4*S*)-6-Methyl-3-(methylsulfonyl)-2,5-dioxo-1-[3-(trifluoromethyl)phenyl]-2,3,4,5,6,7-hexahydro-1*H*-pyrrolo[3,4-d]pyrimidin-4-yl}-3-(methylsulfonyl)benzonitrile

(*rac*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-*N*-(2-hydroxyethyl)-6-methyl-2,5-dioxo-1-[3-(trifluoromethyl)phenyl]-1,2,4,5,6,7-hexahydro-3*H*-pyrrolo[3,4-d]pyrimidine-3-carboxamide

(4*S*)-4-{4-Cyano-2-[(*S*)-methylsulfinyl]phenyl}-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-3-[(1,2-dimethyl-1H-imidazol-4-yl)sulfonyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4S)-3-(Cyanomethyl)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)-phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4S)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-3-(4-cyanophenyl)-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4S)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-1,3-bis[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

4-(4*S*)-3,6-Dimethyl-2,5-dioxo-1-[3-(trifluoromethyl)phenyl]-2,3,4,5,6,7-hexahydro-1*H*-pyrrolo-[3,4-d]pyrimidin-4-yl-3-(methylsulfonyl)benzonitrile

(4*S*)-4-[4-Cyano-2-(ethylsulfonyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4*S*)-4-[4-Cyano-2-(ethylsulfonyl)phenyl]-3,6-dimethyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

(4*S*)-4-[4-Cyano-2-(ethylsulfonyl)phenyl]-6-methyl-3-(methylsulfonyl)-2-oxo-1-[3-(trifluoromethyl)-phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

2-Hydroxyethyl (4*S*)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-(methylsulfonyl)-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carboxylate

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

10. The compound of the formula (I) as claimed in one or more of claims 1 to 7, with the structure

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-3,6-dimethyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

11. The compound of the formula (I) as claimed in one or more of claims 1 to 7, with the structure

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-(methylsulfonyl)-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

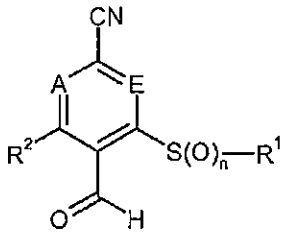
or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

12. The compound of the formula (I) as claimed in one or more of claims 1 to 7, with the structure

(4*S*)-4-[4-Cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

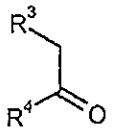
13. A process for preparing a compound of the formula (I) as defined in one or more of claims 1 to 12, characterized in that a compound of the formula (II)



(II),

in which A, E, n, $R^1$ and $R^2$ have the meanings given in claims 1 to 12,

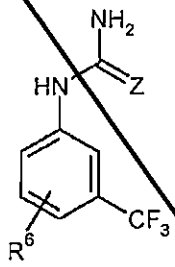
is reacted in the presence of an acid or an acid anhydride in a 3-component one-pot reaction or sequentially with a compound of the formula (III)



(III),

in which $R^3$ and $R^4$ have the meanings given in claims 1 to 12

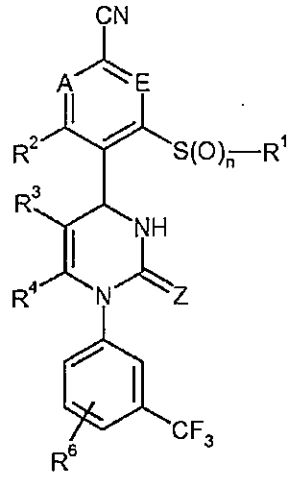
and a compound of the formula (IV)



(IV),

in which Z and $R^6$ have the meanings given in claims 1 to 12,

to give a compound of the formula (I-A)



(I-A),

in which A, B, Z, n, $R^1$, $R^2$, $R^3$, $R^4$ and $R^6$ each have the meanings given above,

and this compound is, in the case that $R^5$ in formula (I) does not represent hydrogen, reacted in the presence of a base with a compound of the formula (V)

$$R^{5A}\text{–}X \quad (V),$$

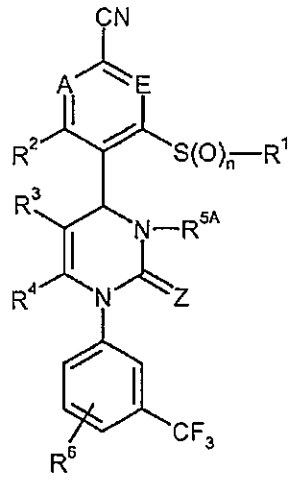
in which

$R^{5A}$ has the meaning of $R^5$ given in claims 1 to 12, but does not represent hydrogen,

and

X represents a leaving group, such as, for example, halogen, mesylate, tosylate or triflate,

to give a compound of the formula (I-B)



(I-B),

in which A, E, Z, n, $R^1$, $R^2$, $R^3$, $R^4$, $R^{5A}$ and $R^6$ each have the meanings given above,

and the compound of the formula (I-A) or (I-B) obtained in this manner is, if appropriate, separated by methods known to the person skilled in the art into its enantiomers and/or diastereomers and/or converted with the appropriate (i) solvents and/or (ii) bases or acids into its solvates, salts and/or solvates of the salts.

14. The compound as defined in one or more of of claims 1 to 12 for the treatment and/or prevention of diseases.

15. The compound as defined in one or more of claims 1 to 12 for use in a method for the treatment and/or prevention of pulmonary arterial hypertension (PAH) and other forms of pulmonary hypertension (PH), of chronic-obstructive pulmonary diseases (COPD), of acute lung injury (ALI), of acute respiratory distress syndrome (ARDS), of pulmonary emphysema, of alpha-1 antitrypsin deficiency (AATD) and of cystic fibrosis (CF).

16. The compound as defined in one or more of of claims 1 to 12 for the treatment and/or prevention of bronchiectasy.

17. The use of a compound as defined in one or more of claims 1 to 12 for preparing a medicament for the treatment and/or prevention of pulmonary arterial hypertension (PAH) and other forms of pulmonary hypertension (PH), or chronic-obstructive pulmonary diseases (COPD), of acute lung injury (ALI), of acute respiratory distress syndrome (ARDS), of pulmonary emphysema, of alpha-1 antitrypsin deficiency (AATD) and of cystic fibrosis (CF).

18. A medicament comprising a compound as defined in one or more of claims 1 to 12 in combination with one or more inert non-toxic pharmaceutically acceptable auxiliaries.

19. A medicament comprising a compound as defined in one or more of claims 1 to 12 in combination with one or more further active compounds selected from the group of the kinase inhibitors, the matrix metalloprotease inhibitors, stimulators and activators of soluble guanylate cyclase, prostacyclin analogs, endothelin receptor antagonists, phosphodiesterase inhibitors, beta-adrenergic receptor agonists, anticholinergics and glucocorticoids.

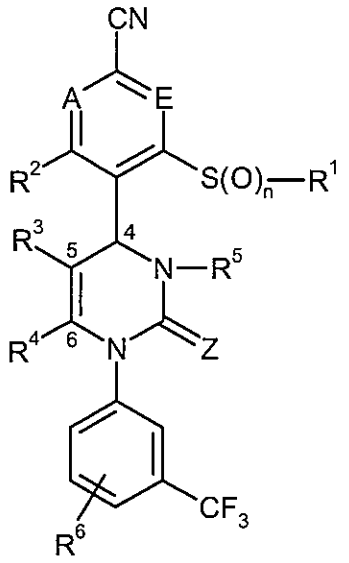
20. The medicament as claimed in claim 18 or 19 for the treatment and/or prevention of pulmonary arterial hypertension (PAH) and other forms of pulmonary hypertension (PH), or chronic-obstructive pulmonary diseases (COPD), of acute lung injury (ALI), of acute respiratory distress syndrome (ARDS), of pulmonary emphysema, of alpha-1 antitrypsin deficiency (AATD) and of cystic fibrosis (CF).

21. The medicament as claimed in claim 18 or 19 for the treatment and/or prevention of bronchiectasy.

22. Use of at least one medicament as defined in one or more of claims 18 to 20 for the production of a medicament for the treatment and/or prevention of pulmonary arterial hypertension (PAH) and other forms of pulmonary hypertension (PH), or chronic-obstructive pulmonary diseases (COPD), of acute lung injury (ALI), of acute respiratory distress syndrome (ARDS), of pulmonary emphysema, of alpha-1 antitrypsin deficiency (AATD) and of cystic fibrosis (CF) in humans and animals.

**Claims**

1. A compound of the formula (I)



(I),

in which

A and E both represent C-$R^7$, in which

$R^7$ represents in each case hydrogen, fluorine or chlorine,

Z represents O,

n represents the number 0, 1 or 2,

$R^1$ represents ($C_1$-$C_6$)-alkyl which may be substituted by hydroxyl, ($C_1$-$C_4$)-alkoxy, amino, mono- or di-($C_1$-$C_4$)-alkylamino, hydroxycarbonyl, aminocarbonyl, ($C_3$-$C_6$)-cycloalkyl, phenyl or 5- or 6-membered heteroaryl or up to five times by fluorine, or represents ($C_2$-$C_6$)-alkenyl, ($C_3$-$C_6$)-cycloalkyl, phenyl or 5- or 6-membered heteroaryl,

where the ($C_3$-$C_6$)-cycloalkyl groups mentioned may be substituted up to two times by identical or different substituents from the group consisting of ($C_1$-$C_4$)-alkyl, hydroxyl and ($C_1$-$C_4$)-alkoxy

and

the phenyl and heteroaryl groups mentioned may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, ($C_1$-$C_4$)-alkyl, difluoromethyl, trifluoromethyl, ($C_1$-$C_4$)-alkoxy, difluoromethoxy and trifluoromethoxy,

$R^2$ represents hydrogen, fluorine or chlorine,

$R^3$ represents cyano or a group of the formula -C(=O)-$R^8$, -C(=O)-O-$R^8$, -C(=O)-$NH_2$ or -C(=O)-NH-$R^8$, in which

$R^8$ represents ($C_1$-$C_6$)-alkyl, ($C_3$-$C_6$)-alkenyl or ($C_3$-$C_6$)-cycloalkyl,

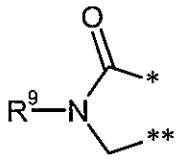
where ($C_1$-$C_6$)-alkyl and ($C_3$-$C_6$)-cycloalkyl for their part may be substituted up to two times by identical or different substituents from the group consisting of hydroxyl, ($C_1$-$C_4$)-alkoxy, hydroxycarbonyl, ($C_1$-$C_4$)-alkoxycarbonyl, amino, mono- and di-($C_1$-$C_4$)-alkylamino and in

($C_1$-$C_6$)-alkyl and ($C_3$-$C_6$)-cycloalkyl in each case one $CH_2$ group may be replaced by an oxygen atom, if this results in a chemically stable compound,

$R^4$ represents methyl or ethyl

or

$R^3$ and $R^4$ are attached to one another and together form a fused group of the formula



in which

* denotes the point of attachment to the 5-position, shown in formula (I), of the dihydropyrimidine ring

and

** denotes the point of attachment to the 6-position, shown in formula (I), of the dihydropyrimidine ring

and

$R^9$ represents hydrogen, ($C_1$-$C_6$)-alkyl or ($C_3$-$C_6$)-cycloalkyl,

where ($C_1$-$C_6$)-alkyl may be substituted by hydroxyl, ($C_1$-$C_4$)-alkoxy, aminocarbonyl, aminocarbonylamino, ($C_1$-$C_4$)-acylamino or ($C_3$-$C_6$)-cycloalkyl,

$R^5$ represents hydrogen or ($C_1$-$C_6$)-alkyl which may be substituted by cyano, hydroxyl, ($C_1$-$C_4$)-alkoxy, amino, mono- or di-($C_1$-$C_4$)-alkylamino or ($C_3$-$C_6$)-cycloalkyl or up to three times by fluorine, or represents phenyl, pyridyl or pyrimidinyl,

where phenyl, pyridyl and pyrimidinyl for their part may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, ($C_1$-$C_4$)-alkyl, trifluoromethyl, ($C_1$-$C_4$)-alkoxy and trifluoromethoxy,

or

$R^5$ represents a group of the formula $-C(=O)-O-R^{10}$, $-L^1-C(=O)-O-R^{11}$, $-L^2-C(=O)-NR^{12}R^{13}$, $-L^2-SO_2-NR^{12}R^{13}$, $-L^2-C(=O)-NR^{14}-NR^{12}R^{13}$ or $-L^2-SO_2-R^{15}$, in which

$L^1$ represents ($C_1$-$C_6$)-alkanediyl,

$L^2$ represents a bond or ($C_1$-$C_6$)-alkanediyl,

$R^{10}$ represents ($C_1$-$C_6$)-alkyl which may be substituted by ($C_3$-$C_6$)-cycloalkyl or phenyl,

$R^{11}$ represents hydrogen or ($C_1$-$C_6$)-alkyl which may be substituted by ($C_3$-$C_6$)-cycloalkyl or phenyl,

$R^{12}$ and $R^{13}$ are identical or different and independently of one another represent hydrogen, ($C_1$-$C_6$)-alkyl, ($C_3$-$C_6$)-cycloalkyl or 4- to 6-membered heterocyclyl,

where ($C_1$-$C_6$)-alkyl, ($C_3$-$C_6$)-cycloalkyl and 4- to 6-membered heterocyclyl for their part may be substituted up to two times by identical or different substituents from the

group consisting of fluorine, hydroxyl, ($C_1$-$C_4$)-alkoxy, oxo, amino, mono- or di-($C_1$-$C_4$)-alkylamino, hydroxycarbonyl, ($C_1$-$C_4$)-alkoxycarbonyl and aminocarbonyl

and

in ($C_1$-$C_6$)-alkyl a $CH_2$ group may be replaced by an oxygen atom, if this results in a chemically stable compound,

and

($C_3$-$C_6$)-cycloalkyl and 4- to 6-membered heterocyclyl may additionally be substituted up to two times by identical or different ($C_1$-$C_4$)-alkyl radicals, which for their part may be substituted by hydroxyl, ($C_1$-$C_4$)-alkoxy or hydroxycarbonyl,

or

$R^{12}$ and $R^{13}$ together with the nitrogen atom to which they are attached form a 4- to 6-membered heterocycle which may contain a further ring heteroatom from the group consisting of N, O, S, SO and $SO_2$ and which may be substituted up to two times by identical or different substituents from the group consisting of ($C_1$-$C_4$)-alkyl, hydroxyl, ($C_1$-$C_4$)-alkoxy, oxo, amino, mono- or di-($C_1$-$C_4$)-alkylamino, hydroxycarbonyl, aminocarbonyl, ($C_3$-$C_6$)-cycloalkyl, 4- to 6-membered heterocyclyl and 5- or 6-membered heteroaryl,

where ($C_1$-$C_4$)-alkyl for its part may be substituted by hydroxyl, ($C_1$-$C_4$)-alkoxy or hydroxycarbonyl,

$R^{14}$ represents hydrogen or ($C_1$-$C_4$)-alkyl

and

$R^{15}$ represents ($C_1$-$C_6$)-alkyl, ($C_3$-$C_6$)-cycloalkyl, phenyl or 5- or 6-membered heteroaryl,

where ($C_1$-$C_6$)-alkyl may be substituted by chlorine, hydroxyl, ($C_1$-$C_4$)-alkoxy, mono- or di-($C_1$-$C_4$)-alkylamino or ($C_3$-$C_6$)-cycloalkyl or up to three times by fluorine

and

phenyl and 5-or 6-membered heteroaryl for their part may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, ($C_1$-$C_4$)-alkyl, difluoromethyl, trifluoromethyl, ($C_1$-$C_4$)-alkoxy and trifluoromethoxy,

and

$R^6$ represents hydrogen, fluorine or chlorine,

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

2. The compound of the formula (I) as claimed in claim 1, in which

A and E both represent C-$R^7$, in which

$R^7$ represents in each case hydrogen, fluorine or chlorine,

Z represents O,

n represents the number 0, 1 or 2,

$R^1$ represents $(C_1-C_6)$-alkyl which may be substituted by hydroxyl, $(C_1-C_4)$-alkoxy, amino, mono- or di-$(C_1-C_4)$-alkylamino, hydroxycarbonyl, aminocarbonyl, $(C_3-C_6)$-cycloalkyl or phenyl, or represents $(C_2-C_6)$-alkenyl, $(C_3-C_6)$-cycloalkyl or phenyl,

where the $(C_3-C_6)$-cycloalkyl groups mentioned may be substituted up to two times by identical or different substituents from the group consisting of $(C_1-C_4)$-alkyl, hydroxyl and $(C_1-C_4)$-alkoxy

and

the phenyl groups mentioned may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, $(C_1-C_4)$-alkyl, difluoromethyl, trifluoromethyl, $(C_1-C_4)$-alkoxy, difluoromethoxy and trifluoromethoxy,

$R^2$ represents hydrogen, fluorine or chlorine,

$R^3$ represents cyano or a group of the formula $-C(=O)-R^8$, $-C(=O)-O-R^8$, $-C(=O)-NH_2$ or $-C(=O)-NH-R^8$, in which

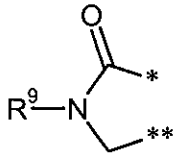
$R^8$ represents $(C_1-C_6)$-alkyl, $(C_3-C_6)$-alkenyl or $(C_3-C_6)$-cycloalkyl,

where $(C_1-C_6)$-alkyl and $(C_3-C_6)$-cycloalkyl for their part may be substituted up to two times by identical or different substituents from the group consisting of hydroxyl, $(C_1-C_4)$-alkoxy, hydroxycarbonyl, $(C_1-C_4)$-alkoxycarbonyl, amino, mono- and di-$(C_1-C_4)$-alkylamino and in $(C_1-C_6)$-alkyl and $(C_3-C_6)$-cycloalkyl in each case one $CH_2$ group may be replaced by an oxygen atom, if this results in a chemically stable compound,

$R^4$ represents methyl or ethyl

or

$R^3$ and $R^4$ are attached to one another and together form a fused group of the formula



in which

* denotes the point of attachment to the 5-position, shown in formula (I), of the dihydropyrimidine ring

and

** denotes the point of attachment to the 6-position, shown in formula (I), of the dihydropyrimidine ring

and

$R^9$ represents hydrogen, $(C_1-C_6)$-alkyl or $(C_3-C_6)$-cycloalkyl,

where (C1-C6)-alkyl may be substituted by hydroxyl, (C1-C4)-alkoxy, aminocarbonyl, (C1-C4)-acylamino or (C3-C6)-cycloalkyl,

$R^5$ represents hydrogen or $(C_1-C_6)$-alkyl which may be substituted up to three times by fluorine, or represents phenyl, pyridyl or pyrimidinyl,

where phenyl, pyridyl and pyrimidinyl for their part may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, ($C_1$-$C_4$)-alkyl, trifluoromethyl, ($C_1$-$C_4$)-alkoxy and trifluoromethoxy,

or

$R^5$ represents a group of the formula -C(=O)-O-$R^{10}$, -$L^1$-C(=O)-O-$R^{11}$, -$L^2$-C(=O)-$NR^{12}R^{13}$, -$L^2$-$SO_2$-$NR^{12}R^{13}$, -$L^2$-C(=O)-$NR^{14}$-$NR^{12}R^{13}$ or -$L^2$-$SO_2$-$R^{15}$, in which

$L^1$ represents ($C_1$-$C_6$)-alkanediyl,

$L^2$ represents a bond or ($C_1$-$C_6$)-alkanediyl,

$R^{10}$ represents ($C_1$-$C_6$)-alkyl,

$R^{11}$ represents hydrogen or ($C_1$-$C_6$)-alkyl,

$R^{12}$ and $R^{13}$ are identical or different and independently of one another represent hydrogen, ($C_1$-$C_6$)-alkyl, ($C_3$-$C_6$)-cycloalkyl or 4- to 6-membered heterocyclyl,

where ($C_1$-$C_6$)-alkyl, ($C_3$-$C_6$)-cycloalkyl and 4- to 6-membered heterocyclyl for their part may be substituted up to two times by identical or different substituents from the group consisting of fluorine, hydroxyl, ($C_1$-$C_4$)-alkoxy, oxo, amino, mono- or di-($C_1$-$C_4$)-alkylamino, hydroxycarbonyl, ($C_1$-$C_4$)-alkoxycarbonyl and aminocarbonyl and in ($C_1$-$C_6$)-alkyl a $CH_2$ group may be replaced by an oxygen atom, if this results in a chemically stable compound,

or

$R^{12}$ and $R^{13}$ together with the nitrogen atom to which they are attached form a 4- to 6-membered heterocycle which may contain a further ring heteroatom from the group consisting of N, O, S, SO and $SO_2$ and may be substituted up to two times by identical or different substituents from the group consisting of ($C_1$-$C_4$)-alkyl, hydroxyl, ($C_1$-$C_4$)-alkoxy, oxo, amino, mono- and di-($C_1$-$C_4$)-alkylamino,

where ($C_1$-$C_4$)-alkyl for its part may be substituted by hydroxyl or ($C_1$-$C_4$)-alkoxy,

$R^{14}$ represents hydrogen or ($C_1$-$C_4$)-alkyl

and

$R^{15}$ represents ($C_1$-$C_6$)-alkyl, ($C_3$-$C_6$)-cycloalkyl, phenyl or 5- or 6-membered heteroaryl,

where ($C_1$-$C_6$)-alkyl may be substituted by fluorine, chlorine, hydroxyl, ($C_1$-$C_4$)-alkoxy, mono- or di-($C_1$-$C_4$)-alkylamino

and

phenyl and 5- or 6-membered heteroaryl for their part may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, (C1-C4)-alkyl, trifluoromethyl, (C1-C4)-alkoxy and trifluoromethoxy,

and

$R^6$ represents hydrogen, fluorine or chlorine,

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

3. The compound of the formula (I) as claimed in claim 1 or 2, in which

A and E both represent CH,

Z represents O,

n represents the number 0 or 2,

$R^1$ represents $(C_1-C_4)$-alkyl which may be substituted by hydroxyl, $(C_1-C_4)$-alkoxy, hydroxycarbonyl, aminocarbonyl, $(C_3-C_6)$-cycloalkyl, phenyl or 5-membered heteroaryl or up to three times by fluorine, or represents $(C_3-C_6)$-cycloalkyl, phenyl or 5-membered heteroaryl,
where the phenyl and heteroaryl groups mentioned may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, methyl, trifluoromethyl, methoxy and trifluoromethoxy,

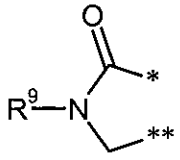
$R^2$ represents hydrogen,

$R^3$ represents cyano, acetyl or (2-hydroxyethoxy)carbonyl,

$R^4$ represents methyl

or

$R^3$ and $R^4$ are attached to one another and together form a fused group of the formula



in which

* denotes the point of attachment to the 5-position, shown in formula (I), of the dihydropyrimidine ring

and

** denotes the point of attachment to the 6-position, shown in formula (I), of the dihydropyrimidine ring

and

$R^9$ represents hydrogen, $(C_1-C_4)$-alkyl or $(C_3-C_6)$-cycloalkyl,
where $(C_1-C_4)$-alkyl may be substituted by hydroxyl or $(C_1-C_4)$-alkoxy,

$R^5$ represents hydrogen or $(C_1-C_4)$-alkyl which may be substituted by cyano or di-$(C_1-C_4)$-alkylamino, or represents a group of the formula $-L^2-C(=O)-NR^{12}R^{13}$, $-L^2-C(=O)-NH-NR^{12}R^{13}$ or $-L^2-SO_2-R^{15}$, in which

$L^2$ represents a bond, $-CH_2-$, $-CH_2CH_2-$ or $-CH(CH_3)-$,

$R^{12}$ represents hydrogen or $(C_1-C_4)$-alkyl which may be substituted by hydroxyl or $(C_1-C_4)$-alkoxy,

$R^{13}$ represents hydrogen, $(C_1-C_6)$-alkyl or $(C_3-C_6)$-cycloalkyl,
where $(C_1-C_6)$-alkyl may be substituted up to two times by identical or different substituents from the group consisting of hydroxyl, $(C_1-C_4)$-alkoxy, hydroxycarbonyl,

($C_1$-$C_4$)-alkoxycarbonyl and aminocarbonyl and in ($C_1$-$C_6$)-alkyl a $CH_2$ group may be replaced by an oxygen atom, if this results in a chemically stable compound,

or

$R^{12}$ and $R^{13}$ together with the nitrogen atom to which they are attached form a 5- or 6-membered heterocycle which may contain a further ring heteroatom from the group consisting of N, O and S and may be substituted by ($C_1$-$C_4$)-alkyl, hydroxyl, ($C_1$-$C_4$)-alkoxy, oxo, hydroxycarbonyl, aminocarbonyl, 4- to 6-membered heterocyclyl or 5- or 6-membered heteroaryl,

where ($C_1$-$C_4$)-alkyl for its part may be substituted by hydroxyl, ($C_1$-$C_4$)-alkoxy or hydroxycarbonyl,

and

$R^{15}$ represents ($C_1$-$C_4$)-alkyl, ($C_3$-$C_6$)-cycloalkyl or phenyl,

where ($C_1$-$C_4$)-alkyl may be substituted by ($C_3$-$C_6$)-cycloalkyl

and

phenyl may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, methyl, trifluoromethyl, methoxy and trifluoromethoxy,

and

$R^6$ represents hydrogen or fluorine,

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

4. The compound of the formula (I) as claimed in claim 1, or 2 or 3, in which

A and E both represent CH,

Z represents O,

n represents the number 0 or 2,

$R^1$ represents ($C_1$-$C_4$)-alkyl which may be substituted by hydroxyl, ($C_1$-$C_4$)-alkoxy, hydroxycarbonyl, aminocarbonyl, ($C_3$-$C_6$)-cycloalkyl or phenyl, or represents ($C_3$-$C_6$)-cycloalkyl or phenyl,

where the phenyl groups mentioned may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, methyl, trifluoromethyl, methoxy and trifluoromethoxy,

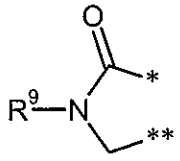
$R^2$ represents hydrogen,

$R^3$ represents cyano or acetyl,

$R^4$ represents methyl

or

$R^3$ and $R^4$ are attached to one another and together form a fused group of the formula



in which

* denotes the point of attachment to the 5-position, shown in formula (I), of the dihydropyrimidine ring

and

** denotes the point of attachment to the 6-position, shown in the formula (I), of the dihydropyrimidine ring

and

$R^9$ represents hydrogen, $(C_1-C_4)$-alkyl or $(C_3-C_6)$-cycloalkyl,

where $(C_1-C_4)$-alkyl may be substituted by hydroxyl or $(C_1-C_4)$-alkoxy,

$R^5$ represents hydrogen, $(C_1-C_4)$-alkyl or a group of the formula $-L^2-C(=O)-NR^{12}R^{13}$, $-L^2-C(=O)-NH-NR^{12}R^{13}$ or $-L^2-SO_2-R^{15}$, in which

$L^2$ represents a bond, $-CH_2-$, $-CH_2CH_2-$ or $-CH(CH_3)-$,

$R^{12}$ represents hydrogen or $(C_1-C_4)$-alkyl which may be substituted by hydroxyl or $(C_1-C_4)$-alkoxy,

$R^{13}$ represents hydrogen, $(C_1-C_6)$-alkyl or $(C_3-C_6)$-cycloalkyl,

where $(C_1-C_6)$-alkyl may be substituted up to two times by identical or different substituents from the group consisting of hydroxyl, $(C_1-C_4)$-alkoxy, hydroxycarbonyl, $(C_1-C_4)$-alkoxycarbonyl and aminocarbonyl and in $(C_1-C_6)$-alkyl a $CH_2$ group may be replaced by an oxygen atom, if this results in a chemically stable compound,

or

$R^{12}$ and $R^{13}$ together with the nitrogen atom to which they are attached form a 5- or 6-membered heterocycle which may contain a further ring heteroatom from the group consisting of N, O and S and may be substituted by $(C_1-C_4)$-alkyl, hydroxyl, $(C_1-C_4)$-alkoxy or oxo,

where $(C_1-C_4)$-alkyl for its part may be substituted by hydroxyl or $(C_1-C_4)$-alkoxy,

and

$R^{15}$ represents $(C_1-C_4)$-alkyl, $(C_3-C_6)$-cycloalkyl or phenyl,

where phenyl may be substituted up to two times by identical or different substituents from the group consisting of fluorine, chlorine, cyano, methyl, trifluoromethyl, methoxy and trifluoromethoxy,

and

$R^6$ represents hydrogen or fluorine,

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

5. The compound of the formula (I) as claimed in any of claims 1 to 4, in which

A and E both represent CH,

Z represents O,

n represents the number 2,

$R^1$ represents ($C_1$-$C_4$)-alkyl which may be substituted by hydroxyl, ($C_1$-$C_4$)-alkoxy, cyclopropyl, cyclobutyl or phenyl or up to three times by fluorine,

$R^2$ represents hydrogen,

$R^3$ represents cyano or (2-hydroxyethoxy)carbonyl,

$R^4$ represents methyl,

$R^5$ represents hydrogen, ($C_1$-$C_4$)-alkyl or a group of the formula $-L^2-C(=O)-NH-R^{13}$ or $-SO_2-R^{15}$, in which

$L^2$ represents a bond or $-CH_2-$,

$R^{13}$ represents hydrogen or ($C_1$-$C_4$)-alkyl which may be substituted by hydroxyl or ($C_1$-$C_4$)-alkoxy, or ($C_3$-$C_6$)-cycloalkyl

and

$R^{15}$ represents ($C_1$-$C_4$)-alkyl or ($C_3$-$C_6$)-cycloalkyl,

and

$R^6$ represents hydrogen,

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

6. The compound of the formula (I) as claimed in any of claims 1 to 5, in which

A and E both represent CH,

Z represents O,

n represents the number 2,

$R^1$ represents ($C_1$-$C_4$)-alkyl which may be substituted by hydroxyl or ($C_1$-$C_4$)-alkoxy,

$R^2$ represents hydrogen,

$R^3$ represents cyano,

$R^4$ represents methyl,

$R^5$ represents hydrogen, ($C_1$-$C_4$)-alkyl or a group of the formula $-CH_2-C(=O)-NH-R^{13}$ or $-SO_2-R^{15}$, in which

$R^{13}$ represents hydrogen or ($C_1$-$C_4$)-alkyl which may be substituted by hydroxyl or ($C_1$-$C_4$)-alkoxy

and

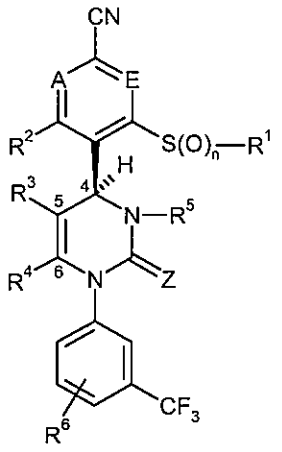
$R^{15}$ represents ($C_1$-$C_4$)-alkyl or ($C_3$-$C_6$)-cycloalkyl,

and

$R^6$ represents hydrogen,

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

7. The compound of the formula (I) having the configuration shown in formula (I-*ent*) at the 4-position of the dihydropyrimidine ring as claimed in one or more of claims 1 to 6,



(I-*ent*)

in which

A and E both represent CH,

Z represents O,

n represents the number 2,

$R^1$ represents ($C_1$-$C_4$)-alkyl which may be substituted by hydroxyl or ($C_1$-$C_4$)-alkoxy,

$R^2$ represents hydrogen,

$R^3$ represents cyano,

$R^4$ represents methyl,

$R^5$ represents hydrogen, ($C_1$-$C_4$)-alkyl or a group of the formula -$CH_2$-C(=O)-NH-$R^{13}$ or -$SO_2$-$R^{15}$, wherein

$R^{13}$ represents hydrogen or ($C_1$-$C_4$)-alkyl which may be substituted by hydroxyl or ($C_1$-$C_4$)-alkoxy and

$R^{15}$ represents ($C_1$-$C_4$)-alkyl or ($C_3$-$C_6$)-cycloalkyl, and

$R^6$ represents hydrogen,

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

8. The compound of the formula (I) as claimed in one or more of claims 1 to 7, selected from the group consisting of:

4-{(4S)-5-acetyl-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-4-yl}-3-(methylsulfonyl)benzonitrile

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(6S)-5-cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-N-(2-hydroxyethyl)-4-methyl-2-oxo-3-[3-(trifluoromethyl)phenyl]-3,6-dihydropyrimidin-1(2H)-carboxamide

(6S)-5-cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-N',N'-bis(2-hydroxyethyl)-4-methyl-2-oxo-3-[3-(trifluoromethyl)phenyl]-3,6-dihydropyrimidin-1(2H)-carbohydrazide

(6S)-5-cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-N-[2-(2-hydroxyethoxy)ethyl]-4-methyl-2-oxo-3-[3-(trifluoromethyl)phenyl]-3,6-dihydropyrimidin-1(2H)-carboxamide

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-3-{[(3S)-3-hydroxypyrrolidin-1-yl]carbonyl}-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-3-{[4-(2-hydroxyethyl)piperazin-1-yl]-carbonyl}-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

2-[(6S)-5-cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-4-methyl-2-oxo-3-[3-(trifluoromethyl)-phenyl]-3,6-dihydropyrimidin-1(2H)-yl]acetamide

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-(methylsulfonyl)-2-oxo-1-[3-(trifluoro-methyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-(cyclopropylsulfonyl)-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-3,6-dimethyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

4-{(4S)-6-methyl-3-(methylsulfonyl)-2,5-dioxo-1-[3-(trifluoromethyl)phenyl]-2,3,4,5,6,7-hexahydro-1H-pyrrolo[3,4-d]pyrimidin-4-yl}-3-(methylsulfonyl)benzonitrile

(4S)-4-[4-cyano-2-(methylsulfanyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4S)-4-{4-cyano-2-[(S)-methylsulfinyl]phenyl}-6-methyl-2-oxo-1-[3-(trifluoromethyl)-phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(*rac*)-1-(2-{4-[4-cyano-2-(methylsulfonyl)phenyl]-2,5-dioxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4,5,7-hexahydro-6H-pyrrolo[3,4-d]pyrimidin-6-yl}ethyl)urea

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-3-[(3-hydroxyazetidin-1-yl)carbonyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4S)-3-[(3R)-3-aminopiperidin-1-yl]carbonyl-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-3-{[4-(pyridin-2-yl)piperazin-1-yl]-carbonyl}-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(6S)-5-cyano-6-[4-cyan-2-(methylsulfonyl)phenyl]-N,N-bis(2-hydroxypropyl)-4-methyl-2-oxo-3-[3-(trifluoromethyl)phenyl]-3,6-dihydropyrimidin-1(2H)-carboxamide

(6S)-5-cyano-6-[4-cyan-2-(methylsulfonyl)phenyl]-N-(1-hydroxy-2-methylpropan-2-yl)-4-methyl-2-oxo-3-[3-(trifluoromethyl)phenyl]-3,6-dihydropyrimidin-1(2H)-carboxamide

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-3-{[1-(difluoromethyl)-5-methyl-1H-pyrazol-4-yl]-sulfonyl}-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-3-[(2-cyanphenyl)sulfonyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4S)-3-(cyanomethyl)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

benzyl 5-cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-4-methyl-2-oxo-3-[3-(trifluoromethyl)phenyl]-3,6-dihydropyrimidin-1(2H)-carboxylate

(4S)-4-[4-cyano-2-(ethylsulfonyl)phenyl]-3,6-dimethyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(*rac*)-4-[4-cyano-2-((2-hydroxyethyl)sulfonyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4S)-4-{4-cyano-2-[phenylsulfonyl]phenyl}-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

2-hydroxyethyl (4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-(methylsulfonyl)-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carboxylate

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

9. The compound of the formula (I) as claimed in one or more of claims 1 to 7, selected from the group consisting of:

(4*S*)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carboxamide

(4*S*)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(6*S*)-5-cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-N-(2-hydroxyethyl)-4-methyl-2-oxo-3-[3-(trifluoromethyl)Phenyl]-3,6-dihydropyrimidin-1(2*H*)-carboxamide

(6*S*)-5-cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-*N*',*N*'-bis(2-hydroxyethyl)-4-methyl-2-oxo-3-[3-(trifluoromethyl)phenyl]-3,6-dihydropyrimidin-1(2*H*)-carbohydrazide

2-[(6*S*)-5-cyano-6-[4-cyano-2-(methylsulfonyl)phenyl]-4-methyl-2-oxo-3-[3-(trifluoromethyl)phenyl]-3,6-dihydropyrimidin-1(2*H*)-yl]acetamide

(4*S*)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-3-[2-oxo-2-(3-oxopiperazin-1-yl)ethyl]-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4*S*)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-(methylsulfonyl)-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4*S*)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-{[2-(trifluoromethoxy)phenyl]sulfonyl}-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4*S*)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-(ethylsulfonyl)-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4*S*)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-(cyclopropylsulfonyl)-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4*S*)-4-[4-cyano-2-(methylsulfonyl)phenyl]-3,6-dimethyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

4-{(4*S*)-6-methyl-3-(methylsulfonyl)-2,5-dioxo-1-[3-(trifluoromethyl)phenyl]-2,3,4,5,6,7-hexahydro-1*H*-pyrrolo[3,4-d]pyrimidin-4-yl}-3-(methylsulfonyl)benzonitrile

(*rac*)-4-[4-cyano-2-(methylsulfonyl)phenyl]-*N*-(2-hydroxyethyl)-6-methyl-2,5-dioxo-1-[3-(trifluoromethyl)phenyl]-1,2,4,5,6,7-hexahydro-3*H*-pyrrolo[3,4-d]pyrimidin-3-carboxamide

(4*S*)-4-{4-cyano-2-[(*S*)-methylsulfinyl]phenyl}-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4S-4-[4-cyano-2-(methylsulfonyl)phenyl]-3-[(1,2-dimethyl-1H-imidazol-4-yl)sulfonyl]-6- methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4*S*)-3-(cyanomethyl)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4*S*)-4-[4-cyano-2-(methylsulfonyl)phenyl]-3-(4-cyanophenyl)-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4*S*)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-1,3-bis[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

4-(4*S*)-3,6-dimethyl-2,5-dioxo-1-[3-(trifluoromethyl)phenyl]-2,3,4,5,6,7-hexahydro-*1H*-pyrrolo[3,4-d]pyrimidin-4-yl-3-(methylsulfonyl)benzonitrile

(4*S*)-4-[4-cyano-2-(ethylsulfonyl)phenyl]-6-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4*S*)-4-[4-cyano-2-(ethylsulfonyl)phenyl]-3,6-dimethyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

(4*S*)-4-[4-cyano-2-(ethylsulfonyl)phenyl]-6-methyl-3-(methylsulfonyl)-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

2-hydroxyethyl (4*S*)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-(methylsulfonyl)-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidin-5-carboxylate

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

10. The compound of the formula (I) as claimed in one or more of claims 1 to 7, with the structure

(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-3,6-dimethyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

11. The compound of the formula (I) as claimed in one or more of claims 1 to 7, with the structure

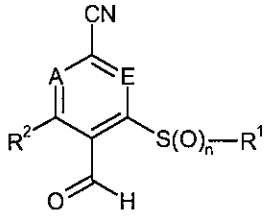
(4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-3-(methylsulfonyl)-2-oxo-l-[3-(trifluoro-methyl)phenyl] -1,2,3,4-tetrahydropyrimidine-5-carbonitrile

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

12. The compound of the formula (I) as claimed in one or more of claims 1 to 7, with the structure ((4S)-4-[4-cyano-2-(methylsulfonyl)phenyl]-6-methyl-2-oxo-l-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetrahydropyrimidine-5-carbonitrile

or a pharmaceutical acceptable salt, a solvate or a solvate of a salt thereof.

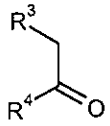
13. A process for preparing a compound of the formula (I) as defined in claims 1 to 12, characterized in that a compound of the formula (II)




(II),

in which A, E, n, $R^1$ and $R^2$ have the meanings given in claims 1 to 12,

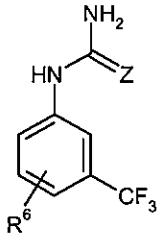
is reacted in the presence of an acid or an acid anhydride in a 3-component one-pot reaction or sequentially with a compound of the formula (III)




(III),

in which $R^3$ and $R^4$ have the meanings given in claims 1 to 12

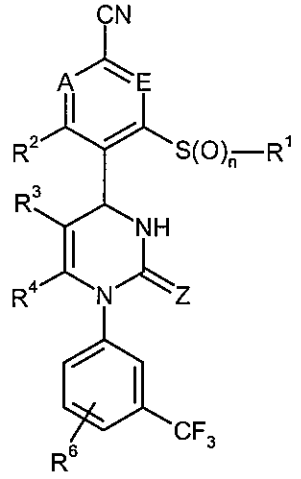
and a compound of the formula (IV)




(IV),

in which Z and $R^6$ have the meanings given in claims 1 to 12,

to give a compound of the formula (I-A)



(I-A),

in which A, E, Z, n, $R^1$, $R^2$, $R^3$, $R^4$ and $R^6$ each have the meanings given above,

and this compound is, in the case that $R^5$ in formula (I) does not represent hydrogen, reacted in the presence of a base with a compound of the formula (V)

$R^{5A}$–X (V),

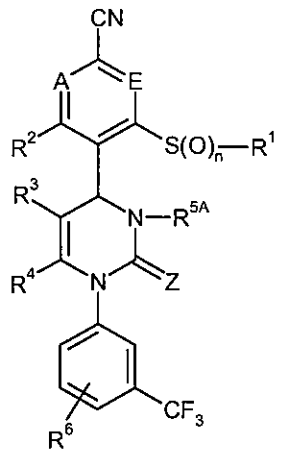
in which

$R^{5A}$ has the meaning of $R^5$ given in claims 1 to 12, but does not represent hydrogen,

and

X represents a leaving group, such as, for example, halogen, mesylate, tosylate or triflate,

to give a compound of the formula (I-B)



(I-B),

in which A, E, Z, n, $R^1$, $R^2$, $R^3$, $R^4$, $R^{5A}$ and $R^6$ each have the meanings given above,

and the compound of the formula (I-A) or (I-B) obtained in this manner is, if appropriate, separated by methods known to the person skilled in the art into its enantiomers and/or diastereomers and/or converted with the appropriate (i) solvents and/or (ii) bases or acids into its solvates, salts and/or solvates of the salts.

14. The compound as defined in one or more of claims 1 to 12 for use in a method for the treatment and/or prevention of pulmonary arterial hypertension (PAH) and other forms of pulmonary hypertension (PH), or chronic-obstructive pulmonary diseases (COPD), of acute lung injury (ALI), of

acute respiratory distress syndrome (ARDS), of pulmonary emphysema, of alpha-1 antitrypsin deficiency (AATD) and of cystic fibrosis (CF).

15. The compound as defined in one or more of claims 1 to 12 for the treatment and/or prevention of bronchiectasy.

16. The compound as defined in one or more of claims 1 to 12 for the treatment and/or prevention of chronic wounds.

17. The use of a compound as defined in one or more of claims 1 to 12 for preparing a medicament for the treatment and/or prevention of pulmonary arterial hypertension (PAH) and other forms of pulmonary hypertension (PH), or chronic-obstructive pulmonary diseases (COPD), of acute lung injury (ALI), of acute respiratory distress syndrome (ARDS), of pulmonary emphysema, of alpha-1 antitrypsin deficiency (AATD) and of cystic fibrosis (CF).

18. A medicament comprising a compound as defined in one or more of claims 1 to 12 in combination with one or more inert non-toxic pharmaceutically acceptable auxiliaries.

19. A medicament comprising a compound as defined in one or more of claims 1 to 12 in combination with one or more further active compounds selected from the group of the kinase inhibitors, the matrix metalloprotease inhibitors, stimulators and activators of soluble guanylate cyclase, prostacyclin analogs, endothelin receptor antagonists, phosphodiesterase inhibitors, beta-adrenergic receptor agonists, anticholinergics and glucocorticoids.

20. The medicament as claimed in claim 18 or 19 for the treatment and/or prevention of pulmonary arterial hypertension (PAH) and other forms of pulmonary hypertension (PH), or chronic-obstructive pulmonary diseases (COPD), of acute lung injury (ALI), of acute respiratory distress syndrome (ARDS), of pulmonary emphysema, of alpha-1 antitrypsin deficiency (AATD) and of cystic fibrosis (CF).

21. The medicament as claimed in claim 18 or 19 for the treatment and/or prevention of bronchiectasy.

22. The medicament as claimed in claim 18 or 19 for the treatment and/or prevention of chronic wounds.

23. Use of at least one medicament as defined in one or more of claims 18 to 20 for the production of a medicament for the treatment and/or prevention of pulmonary arterial hypertension (PAH) and other forms of pulmonary hypertension (PH), or chronic-obstructive pulmonary diseases (COPD), of acute lung injury (ALI), of acute respiratory distress syndrome (ARDS), of pulmonary emphysema, of alpha-1 antitrypsin deficiency (AATD) and of cystic fibrosis (CF) in humans and animals.